# ON THE POSTERIOR PARIETAL CORTEX AND SACCADIC EYE MOVEMENTS

by

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## ABSTRACT

In this dissertation, I report the results of a series of studies designed to investigate the role of the posterior parietal cortex of primates in the control of saccadic eye movements. Most of the work involved single neurone recordings from awake, behaving macaques, trained to perform a variety of visual and oculomotor tasks.

In chapter 1 I review the relevant clinical, anatomical and physiological literature. Here I introduce the lateral intraparietal area (LIP), a recently described subdivision of the macaque posterior parietal cortex. It is the focus of most of the work reported in this dissertation.

In chapters 2 and 3, I report the results of a detailed, quantitative study of the properties of visual and saccade-related neurones in areas LIP and 7a. Many neurones are found to have both visual (light-sensitive - LS) and motor (saccade - S) fields. Moreover, many also manifest activity during the delay period of a memory saccade task. This memory (M) activity is shown to be in motor coordinates and to reflect the monkey's intention to make a saccade into the neurone's motor field. Area LIP is found to be physiologically distinguishable from neighbouring area 7a, in particular by its high proportion of pre-saccadic neurones.

In chapter 4, I report that the LS, M and S activity of neurones in areas LIP and 7a is modulated by eye position, and suggest that this modulation may play an important role in the coordinate transformations underlying the programming of saccades, and the representation of visual space.

In chapter 5, I introduce a novel experimental paradigm, the "delayed double saccade". I show that M activity in area LIP generally reflects the monkey's intention to make the next in a sequence of saccades.

In chapter 6, I provide further evidence that M activity in area LIP reflects the monkey's plan to make the next saccade: alterations in the monkey's intentions, even in the absence of overt behaviour, are manifested in alterations in neuronal activity in area LIP.

In chapter 7, memory saccades to auditory targets are used to investigate the generality of the intention activity in area LIP. Some neurones seem to encode the forthcoming saccade, regardless of the cue to move. Other neurones exhibit modality-specific responses.

In chapter 8, a detailed, behavioural study of memory saccades in monkey and man is presented. The most striking finding here is that memory saccades tend to show an "upshift": they consistently end above the target location.

In chapter 9 I present evidence for a neural analogue of this behavioural upshift in area LIP.

These findings are summarised in chapter 10. Related issues are discussed and a series of possible future studies is suggested.

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ὃν οἱ θεοὶ φιλοῦσιν ἀποθνήσκει νέος

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# Chapter 1

## Introduction

# Chapter 1

*"The present wide interest in the parietal lobes...will soon pass, no doubt..."*

So wrote MacDonald Critchley (1953, p. *v*) in the introduction to his masterly monograph "The Parietal Lobes". I should hesitate before disagreeing with Critchley, but I venture that "the present wide interest" in this fascinating area of the brain will continue for a long while, and that many years will pass before the parietal cortex yields all its secrets to the neurologist's acumen and the physiologist's electrode.

I became interested in the posterior parietal cortex by two avenues. First, what is at the heart of the bizarre deficits that follow damage to the posterior parietal lobes? The effects of damage to this region of the association cortex are puzzling. Why, for example, can the patient not reach accurately for the examiner's pen? He is not blind. He can move his arm. He understands the instruction. And yet he cannot perform this seemingly simple task. But, hold, what are we requiring the patient to do? Is the task as easy as we suppose? The patient must localise the pen with respect to his body. Where is it in relation to his hand? How far must he reach? The image of the pen is localised on the retina, but how does the image relate to the location of pen itself? If the eye moves, the image must also move if the pen stays still. But how does the brain "know" whether the pen or the eye has moved? And how does the brain use the visual information to direct actions in quite a different frame of reference, that of the muscles? Clearly some fairly complicated calculations underlie this apparently trivial task. This is my second path: how do we construct stable percepts of our world and use sensory information to control our movements within it?

Of course, this is an impossibly large research agenda. I settled on what I hoped (and still hope!) to be an experimentally tractable subset of issues: the role of the posterior parietal cortex (PPC) in the control of saccadic eye movements.

The virtues of the oculomotor system from the physiologist's point of view have frequently been touted (e.g., Robinson 1981): the eyeball may be treated as a simple ball joint, it moves with few degrees of freedom, it offers a constant load, it is moved by a few, well-studied muscles, its movements may be accurately and conveniently measured... And yet many of the problems that confront the

skeletomuscular system are also faced by the oculomotor system, albeit in a simpler form. For instance, how is the pattern of photoreceptor activity transformed into a motor command, a pattern of motoneurone firing, to foveate the object of interest?

One of the cardinal symptoms of PPC damage is the inability to make visually-guided movements. The results of anatomical, physiological and stimulation studies also suggest that the PPC may play a vital role in the sensorimotor transformations underlying the production of visually-guided movements, of both the limbs and the eyes.

In this chapter, I shall briefly review what is known of the role of the posterior parietal cortex (PPC) of primates in the production of saccadic eye movements. I will discuss the literature on the effects of parietal lesions in man and monkey, then review the relevant anatomy, then consider the results of single unit recording experiments in monkeys trained to perform oculomotor tasks, before closing with a brief review of the relevant electrophysiological and regional cerebral blood studies in man. I hope to show that there is strong evidence that the PPC, and in particular the lateral intraparietal area, LIP (see below), plays an important role in the visuomotor integration for, and the planning of, saccades.

## HUMAN LESIONS

Lesions to the posterior parietal lobes in man have long been known to cause a variety of visual and motor disorders. Interestingly, these deficits are not generally "primary", in that the basic sensory and motor apparatus appears to be intact; rather damage seems to affect higher order sensorimotor integration. For example, a parietal patient may fail to reach an object placed in front of him, despite having normal visual acuity (he is not blind) and being able to make the correct arm movement (he is not paralysed or akinetic). PPC lesions may result in a plethora of effects, including visuo-spatial disorientation, misreaching, neglect, finger agnosia, dyscalculia, reading and writing disorders, constructional apraxia, apraxia for dressing, somatic deficits. Of interest are the marked differences in the effects of right and left PPC lesions in man (especially in the visuo-spatial domain). Unfortunately, I must largely restrict my attention here to deficits in saccadic eye movements, and leave the reader in the more capable hands of Critchley (1953), Hyvarinen (1982a, b), Andersen (1987), Stein (1989) and Husain (1991) for general reviews of this fascinating topic.

### Balint's syndrome

Balint, the Hungarian neurologist, first described (1907, 1909; see also Husain and Stein 1988) an eye movement disorder following biparietal damage in man. There are in fact three signs in the syndrome that has come to bear his name:

1. Psychic paralysis of gaze - an inability to look to a peripheral visual target, but otherwise having normal ocular motility. Here "psychic" is used to stress that automatic movements are normal.

2. Optic ataxia (Allison et al., 1969; Luria et al., 1963; Hauser et al. 1980; Rondot et al. 1977; Rondot, 1988) - inaccurate reaching to visual targets in the absence of any primary sensory or motor disorder.

3. Simultagnosia (Wolpert 1924) - the patient can only attend ("see") one visual object at a time. It is important to note that this deficit is seen regardless of the angular size of the object and in the absence of visual field deficits. (Due to nature's lack of respect for functional boundaries in the brain, lesions that involve PPC may also

compromise the visual field of the patient; however, it is important to stress that the deficits in visual perception that follow PPC lesions are not explicable on the grounds of simple sensory loss.)

**The nature of the saccadic deficit after parietal damage**

The saccadic deficit of Balint's syndrome is typically restricted to looking to visual targets spontaneously or when requested to do so by the examiner (Balint, 1909; Cogan and Adams, 1953; Godwin-Austen, 1965; Allison et al., 1969). They can saccade to an auditory target (Holmes, 1918, case 1; Holmes and Horrax, 1919; Allison et al., 1969), execute a right or left saccade on verbal command (not to a visual target) (Godwin-Austen, 1965; Holmes, 1918, case 5; Waltz, 1961, case 1; Allison et al., 1969; Kase et al., 1977, case 1) and can look to part of the body that has been touched (Holmes, 1918, case 1; Holmes and Horrax, 1919). Hecaen and Ajuriaguerra (1954), Allison et al. (1969) and Pierrot-Deseilligny et al. (1986) have reported that these patients make few eye movements. Many are initially in the wrong direction and then the eyes wander until they chance to land on the target. Wandering gaze is commonly reported in Balint's syndrome (see Girotti et al. 1982).

Leushina and Kok (1961) and Pierrot-Deseilligny et al. (1991b) have reported difficulties in the execution of memory saccades following PPC lesions (accuracy was poorer and latencies increased).

Cogan (1965) distinguished between oculomotor apraxia, which generally follows biparietal lesions, and a paralysis of gaze, typically the result of bifrontal lesions. In the former, there is a difficulty in initiating eye movements, with no limit to the excursion of the eyes; in the latter, excursions of the eyes are very limited. Ocular motor apraxia may also be due to biparietofrontal lesions (Pierrot-Deseilligny et al. 1988; Leigh and Zee 1991).

Recently, Pierrot-Deseilligny et al. (1986) reported a patient who suffered a right followed, six weeks later, by a left side infarct of the PPC. Clinically, visually-guided saccades appeared normal after the first insult, but were bilaterally disturbed following the second infarct. That saccadic deficits are pronounced following bilateral and not unilateral lesions is a common finding (see Andersen and Gnadt (1989) for review). Pierrot-Deseilligny and colleagues suggest that the superoanterior extremity of the angular gyrus and the adjacent

intraparietal sulcus (which were damaged bilaterally) are mainly involved in the control of these movements. As we shall see below, this conclusion is in accord with much recent work with monkeys.

Pierrot-Deseilligny et al. (1987) reported that saccadic latencies are bilaterally increased following unilateral PPC infarcts, whereas lesions of the (presumed) FEF typically result in shortened latency saccades.

**Possible explanations**

Although there is clear evidence that PPC lesions cause saccadic deficits, an important question is whether these are the result of some "deeper" sensory or attentional problem. It is well documented that PPC lesion cause a wide range of deficits, especially in visuo-spatial and attentional domains. Holmes (1918, 1919) espoused the view that the deficits in visually-guided saccades are merely a result of spatial mislocalization. Other authors have also suggested that the gaze dyspraxias due to PPC lesions may be a consequence of visual disorders, although they have not all followed Holmes in the clarity of their explanations (e.g., Botez 1979 - due to "simultagnosia"; Waltz 1961 - due to "bilateral visual amorphosynthesis"; Girotti et al. 1982 - due to "loss of panoramic vision"). Indeed, Balint's patient suffered from an inability to redirect his attention, once it was "locked" on a visual object. He did not notice other objects in his visual field. One might argue that his difficulty in making voluntary saccades to visual targets might have been secondary to his attentional disorder.

I do not think that all the saccadic problems may be ascribed to some underlying attentional or visuo-spatial deficit, for the following reasons:

First, although saccadic deficits are most often observed when the patient is required to make visually-guided voluntary saccades, there are cases of oculomotor apraxia in which saccades on command are absent or deficient (e.g., Pierrot-Deseilligny et al., 1988; Waltz, 1961, case 2 - although this patient had mainly left frontal damage; the two patients of Cogan and Adams 1953 - one with frontal and one with frontal and parietal damage). Indeed, two of Holmes' (1918) patients were unable to saccade to a point touched on their bodies.

Second, the three cardinal symptoms of Balint's syndrome do not necessarily co-occur; apraxia of gaze may occur in the absence of other spatial deficits (de Renzi 1982). One might have predicted impaired

saccades in all cases of visual disorientation.

Third, although visual neglect due to PPC lesions is commonly associated with increased saccadic latencies, this is not invariably the case (Pierrot-Deseilligny et al. 1987).

Fourth, unilateral PPC lesions lead to contralateral neglect, but *bilateral* saccadic deficits (Pierrot-Deseilligny et al., 1991a).

Fifth, cases of optic ataxia offer important clues: that different combinations of arm and field effects are seen in both monkeys and man (reviewed in Husain 1991) suggests that visual mislocalisation can only account for some cases of misreaching. If the deficit were solely due to visual mislocalisation, one would expect field effects (in which movements of either arm in the affected visual field are impaired), but not arm effects (in which movements of, say, the right arm are impaired regardless of the visual field). A double dissociation between hemispatial neglect and optic ataxia (Perenin and Vighetto, 1988) shows that visually-guided hand movements can be impaired in the absence of visuospatial perceptual problems. See also the discussion of Haaxman and Kuypers (1974) in the section below on monkey lesions.

Some authors have been tempted to turn this question on its head, and ask instead whether spatial disorientation itself is a consequence of improper control and integration of the "optic reflexes" (see, e.g., Pieron, 1923). That patients with severely disordered eye movements as a result of brainstem lesions can easily reach to visual targets (e.g., Holmes, 1918; Allison et al., 1969) argues against this view, however.

In all, the evidence suggests that the saccadic deficit seen in some PPC lesioned patients may indeed be, in some cases, "primary", and not simply a consequence of attentional or other visuospatial problems. However, it is clear that these various functions are intimately linked, and that we might be dichotomising too readily. We should perhaps bear in mind Poincare's (1905) assertion that, "when it is said that we "localise" such an object in such a point in space...it simply means that we represent to ourselves the movements that must take place to reach that object".

**Other oculomotor deficits that may also occur after PPC damage**

1. Poor or absent smooth pursuit (e.g., Hecaen and Ajuriaguerra, 1954; Godwin-Austen, 1965).

2. Poor accommodation and vergence (Holmes, 1918; Holmes and Horrax, 1919; Cogan and Adams, 1963; Godwin-Austen,1965).
3. Absence of a blink reflex to an approaching target (Holmes, 1918; Holmes and Horrax, 1919), although, as Holmes speculated, this may be due to a lack of depth perception.
4. Occasional problems in the maintenance of fixation (Godwin-Austen, 1965; Paterson and Zangwill, 1944; Leushina and Kok, 1961).
5. Optokinetic nystagmus is occasionally disturbed (Carmichael et al.,1954; Cogan and Loeb, 1949; Critchley, 1953; Smith, 1963; Smith and Cogan, 1959)

## MONKEY LESION STUDIES

Since the observation of Munk (1881) that ablation of the posterior parietal-anterior occipital cortex abolishes the blink reflex to contralateral stimuli and causes difficulties in eye movements, most lesion studies in monkeys have concentrated on deficits in reaching rather than oculomotor control (for a review, see Hyvarinen, 1982a ). However, Stein (1978) showed that cooling area 7 slows eye movements to the contralateral side. Similarly, Quintana et al. (1989) found slow inaccurate eye movements after cooling areas 5 and 7 bilaterally. Latto (1978) demonstrated that visual search is impaired after PPC lesions.

Lynch and McLaren (1983) show that (uni- and bilateral) inferior parietal (IPL) lesions cause mild deficits in OKN. However, these authors went on to demonstrate (Lynch and McLaren, 1989) that IPL or IPL-plus-adjacent-prestriate lesioned monkeys have increased saccadic latencies (4/5 animals) and decreased accuracy (2/5 animals). After unilateral lesions, these deficits were usually seen only in the contralateral hemifield. These modest deficits are similar to those reported following lesions of the frontal eye fields (FEF) (Deng et al., 1986; Lynch and Allison 1985; Schiller et al. 1980). It is tempting to speculate that the mild deficits observed after either an IPL or FEF lesion are due to the ability of the other area to perform similar functions to the damaged area. This proposal is supported by the findings of Lynch et al. (1986) that combined FEF and IPL-prestriate lesions cause severe deficits in visual pursuit and saccadic control.

Tusa et al. (1986) have reported deficits in the initiation of voluntary and reflexive saccades contralateral to the lesion in a hemidecorticated monkey. In addition, such monkeys show deficits in all saccades made in the craniotopic space contralateral to the lesion. Clearly, the lesions in this experiment are too large to allow one to draw conclusions as to where the damage critical for causing these saccadic deficits is; however, they do not contradict the findings of the studies of Lynch and others discussed above.

Since the most florid symptoms of PPC damage in man (at least) are those of spatial vision and attention, it might be tempting to ascribe the more motoric deficits to these more sensory problems. However, the results of Haaxman and Kuypers (1974) suggest that this is only a partial

answer. They severed the occipito-frontal connexions in monkeys and observed contralateral optic ataxia (which would be predicted by a disconnexion of the sensory from the motor centres). However, no paralysis of fixation (nor visual attention deficits) was observed, suggesting that the eye movement deficits in Balint's and related cases are not due to the frontal "motor" cortices being deprived of accurate visuospatial input from the posterior "sensory" cortices. Indeed, Valenstein et al. (1982) have proposed that the hemi-neglect that frequently follows unilateral PPC damage in monkey and man be considered a deficit in motor intention, rather than sensory neglect. They trained monkeys to respond with the hand contralateral to the sensory cue. Following PPC lesions, monkeys were impaired in reaching with the contralesional arm and not in responding to contralesional cues.

## ANATOMY

### Cytoarchitectonic subdivisions of PPC

The PPC lies in the caudal aspect of the parietal lobe. It is divided into the inferior and superior parietal lobules (IPL and SPL, respectively) by the intraparietal sulcus. Different subdivisions of the PPC can be defined on cytoarchitectonic, connexional and functional grounds. Unfortunately, there is no clear consensus on the subdivision of the PPC into areas (see fig. 1).

In monkey, SPL - area 5 of Brodmann (1905) or area PE of von Bonin and Bailey (1947) - seems to contain exclusively somatosensory association cortex and will therefore not be further discussed here. IPL - Brodmann's area 7 - is largely visual and visuomotor in function. It lies at the pinnacle of the dorsal ("where") stream of cortical visual information processing, critically involved in the spatial aspects of vision (Ungerleider and Mishkin, 1982; Haxby et al. 1991). IPL may be further divided into a caudomedial area called 7a by Vogt and Vogt (1919) or PG by von Bonin and Bailey (1947) and a more laterorostral area, 7b or PF. IPL includes cortex on the gyral surface, in the lateral bank of the intraparietal sulcus (LIP), in the anterior bank of the caudal third of the superior temporal sulcus (STS) and a small amount on the medial wall of the hemisphere.

Although the exact homologies between PPC areas in humans and monkeys are not clear, it seems reasonable to follow von Bonin and Bailey (1947) and Eidelberg and Galaburda (1984) and equate SPL in monkey with SPL in man (i.e., their monkey PF and PG = von Economo's (1929) human PF and PG) and IPL in monkey with IPL in man (i.e., their monkey PE = von Economo's human PE). SPL lesions in monkey and man produce similar somatosensory deficits, and in contrast IPL lesions in both species result in similar visual and oculomotor disorders (see Andersen, 1987, for a more detailed discussion of this topic). However, it is worth noting that PPC has enlarged in area about 20 times from monkey to man, compared with an average cortical enlargement of only 12 times, and that most of that increase has been in the IPL (Hyvarinen, 1982a). This, and the enhanced behavioural abilities of man, suggest that some areas of human IPL may be unique. Indeed, Brodmann (1907) considered the

human IPL to consist of two novel cytoarchitectonic zones: area 39 (the angular gyrus) and area 40 (the supramarginal gyrus). He and others (von Economo 1929, Critchley 1953; Geshwind 1965; Braak 1980; Mesulam 1985) have argued that areas 5 and 7 in man (both in the SPL) are homologous with areas 5 (SPL) and 7 (IPL), respectively, in monkey.

**Connexions of area 7; an overview**

PPC has been further subdivided on anatomical (primarily connexional) and physiological grounds over the last decade. What once seemed a large but manageable number of connexions (e.g., Hyvarinen, 1982b, listed over 70) is now almost overwhelming (see, e.g., Andersen et al. 1990). Indubitably, finer parcellation of PPC will occur over the next few years, and with it yet more connexional detail. I shall attempt to give a general appreciation of the connexions of area 7, and then concentrate on the two subdivisions (areas LIP and 7a) which are the subject of the physiological experiments described elsewhere in this thesis. Further, more detailed accounts may be found in Hyvarinen (1982a, b; Andersen 1987; Andersen et al. 1990; Pandya and Yeterian 1985). Note that many of the studies cited were completed before the recent Balkanisation of area 7.

The IPL is reciprocally connected with many areas: ipsilateral SI and SII (Pandya and Seltzer 1982), area 5 (Caminiti and Sbriccoli 85), area Tpt (Pandya and Kuypers 1969), area 19 (Rockland and Pandya, 79; Maunsell and van Essen 83), area 22 and the planum temporale (Divac et al. 1977), areas 4, 6, 8, 9-12, 45 and 46 in the frontal lobes (Pandya and Kuypers 1969) and the cingulate gyrus (Mesulam et al. 1977; Stanton et al. 1977).

Subcortical afferents include the superior colliculus via the pulvinar (Andersen et al. 1985) and the basal ganglia and cerebellum (via VA in thalamus). It projects to the pulvinar (Andersen et al. 1985a), the superior colliculus (Petras 1971), the basal ganglia (Peele, 1942; Kemp and Powell, 1970; Petras 1971) and the cerebellar hemispheres via the pons (Glickstein et al. 1980).

Thus area 7 appears to be a site of convergence of visual (especially), somatosensory (particularly area 7b), auditory, motor (both limb and eye) and limbic activities. It does indeed seem to be prototypical association cortex, where various modalities are "associated".

However, much recent work has led to revision of our concept of association cortex in general, and PPC in particular. Area 7 has been subdivided into a number of physiologically and connexionally distinct areas. These tend to be specialised to deal primarily with sensory input of but one modality. Thus while it is undeniably true that the PPC, as a whole, is a site of massive convergence of sensory, motor and limbic information, particular subdivisions are dedicated to specific subsets of this incoming flood, and these subdivisions in turn have specific outputs (see, for example, Hyvarinen 1982a, b; Andersen et al. 1990; Pandya and Yeterian 1985).

**Subdivisions of area 7**

Area 7 has been subdivided into a number of subdivisions (see Andersen 1987; Andersen et al. 1990) on anatomical and physiological grounds. Hyvarinen (1981) and Hyvarinen and Sheplin (1979) reported that cells in the medial aspect of the gyrus (area 7a) were mainly visual and visuomotor, whereas those in the more lateral portion (area 7b) were mainly somato-sensory and -motor. Robinson and Burton (1980a, b) confirmed a predominantly somatosensory role for area 7b and reported a crude somatotopic map in this area. Area 7b is primarily somatosensory and is not further considered here. Using more rigourous experimental procedures, Andersen et al. (1990) were able to confirm the general distinction drawn by Hyvarinen between areas 7a and 7b. Area 7a was originally defined on cytoarchitectonic grounds by Vogt and Vogt (1919). It has since been parcelled into at least two areas: area 7a "proper" on the crown of the gyrus and the lateral intraparietal area (LIP) in the caudal half of the lateral bank of the intraparietal sulcus (reviewed in Andersen 1987).

Area 7a has reciprocal connexions with at least 22 other cortical areas, including MST, superior temporal polysensory (STP), fundus superior temporal (FTP), inferotemporal (IT), lateral and medial TF and TEO in the temporal lobes; LIP, the dorsal prelunate (DP), parieto-occipital (PO), medial intraparietal (MIP), posterior intraparietal (PIP), medial dorsal parietal (MDP), medial PG (PGm), and 7b areas in the parieto-occipital cortex; areas 8a, 46, 45, 11, and the supplementary eye fields (SEF) in the frontal lobes; and areas LC and LA in the cingulate (Andersen et al. 1990).

It receives from the medial pulvinar (Asanuma et al. 1985; Yeterian and Pandya 1985), which in turn receives from the dorsal pretectum and the deep (oculomotor) layers of the superior colliculus (Benevento and Fallon 1975, Benevento and Standage 1983; Harting et al. 1980). It is of interest that the medial pulvinar connects with many of the same, "higher", cortical areas as area 7a (such as the STS and the cingulate - reviewed in Andersen 1987). Lesions of the pulvinar in both monkey (e.g., Ungerleider and Christensen 1977) and man (Ogren et al. 1984) suggest that it plays a role in visual attention. Physiological studies also support this contention (Petersen et al. 1985).

Area 7a projects to the ventral, lateral and dorsolateral nuclei of the lateral margin of the pons (May and Andersen 1986).

Area LIP has reciprocal corticocortical connexions with areas PO, DP, 7a, MST, MT (or V5), V4, dorsal and ventral V3 (V3d and V3v), V3A, TEO, TF, 8a and 46 (Andersen et al. 90). In addition, dorsal but not ventral LIP connects with TEa and TEm in the temporal lobe, and with IPa, a multimodal association area in the caudal bank of the superior temporal cortex (Blatt et al. 1990). Baizer et al. (1991) have recently compared the afferents of the lateral intraparietal cortex (areas LIP and VIP - deeper within the bank of the sulcus) and of areas TEO and TE. They confirmed the connexions of LIP found by Andersen et al. (1990), and further noted that it receives primarily from those parts of prestriate areas V2, V3, V4 and V4t that represent the peripheral visual field (in contrast to areas TEO and TE, which receive from the central representations ot V2, V3, V4 and V4t).

It receives from the lateral pulvinar (Asanuma et al. 1985; Yeterian and Pandya 1985), which in turn receives from the dorsal pretectum and the deep (oculomotor) layers of the superior colliculus (Benevento and Fallon 1975, Benevento and Standage 1983; Harting et al. 1980). Neurones in the dorsal lateral pulvinar have large, bilateral visual receptive fields and show some saccade-related activity (Robinson et al. 1985).

Furthermore, it connects with the anterior pretectal nucleus and the intermediate (motor) layers of the superior colliculus (Fries 1984; Lynch et al. 1985; Asanuma et al. 1985).

LIP projects to the dorsal and dorsolateral pons (May and Andersen 86). This projection is very like that of the FEF to the pons (Kunzle and

Akert 1977; Brodal 1978). The DLPN in turn project to regions of the cerebellum concerned with saccadic and smooth pursuit eye movements (reviewed in May and Andersen 1986).

**Comparison of areas LIP and 7a**

On the basis on the laminar arrangement of their interconnexions (Maunsell and van Essen 1983, Felleman and van Essen 1991) , it has been proposed that the LIP to area 7a projection is a "feedforward" one, whereas that from area 7a to LIP is "feedback" (Andersen et al. 1990). Such analyses allow one to construct a putative hierarchy of processing within the occipitoparietal pathway (fig. 2). As we shall see in chapter 2, the latency of visual responses in areas 7a and LIP support this suggestion. In general, area 7a has the most pronounced connexions of all PPC areas with high order regions of the temporal, frontal and cingulate cortices.

LIP has much stronger connexions with the FEF and SC than area 7a (Barbas and Mesulam 1981; Fries 1984; Lynch et al. 1985; Asanuma et al. 1985). Area 7a's strongest frontal connexions are with area 46 of Walker (Andersen et al. 90), whereas LIP projects most strongly to area 8a (which contains much of the FEF).

The patterns of connexions detailed above suggest that LIP may well be the most important PPC area in the programming of saccadic eye movements. As we shall see, this view is supported by the results of physiological studies. Area 7a, on the other hand, occupies a higher position in the hierarchy of visual areas and probably represents the pinnacle of the dorsal ("where") pathway (Ungerleider and Mishkin 1982). Its extensive connexions with other high level cortical areas suggest it plays a more vital role in higher spatial functions, such as visuospatial attention.

## PHYSIOLOGY OF PPC, WITH SPECIAL REFERENCE TO VISUAL AND OCULOMOTOR ACTIVITY

Over the past two decades, the IPL, along with the SPL, has been studied extensively in the awake behaving monkey. Neurones with complicated somatic response properties have been reported in SPL (Duffy and Burchfield, 1971; Sakata et al. 1973; Mountcastle et al. 1975). Mountcastle et al. (1975) also reported "arm projection" and "manipulation" units in both IPL and SPL (see also Hyvarinen and Poranen 1974). SPL seems to be involved in higher order somatosensation and somatomotor integration.

Neurones with somatosensory, somatomotor, visual and oculomotor responses have been found in the IPL. It appears that there is some separation of function: neurones with somatic properties are concentrated laterally (area 7b) and those with visual and oculomotor responses are more medial (area 7a) (Hyvarinen 1981; Hyvarinen and Sheplin 1979; Robinson and Burton 1980a, b; Andersen et al. 1990).

Vestibular responses have been reported in area 2v at the junction of areas 2, 5 and 7b (Schwartz and Fredrickson 1971; Butter and Buettner 1978) and in the parieto-insular cortex (Akbarian et al. 1988; Grusser et al. 1990a, b). Auditory responsive cells are found only in area Tpt at the temporoparietal junction (Hyvarinen 1982a, b; Leinonen et al. 1980).

For reviews of PPC neuronal properties, see Hyvarinen (1982a, b), Andersen (1987), Stein (1989) and Husain (1991). Below I shall concentrate of the visual and oculomotor properties of IPL neurones. In the main, earlier studies of area 7a do not make the distinction between area 7a "proper" on the surface, and area LIP in the lateral bank of the intraparietal sulcus (see above).

### Area 7a: light sensitive units

Most cells in this area have clear visual receptive fields, often very large, covering an entire hemifield and sometimes crossing the midline (e.g., Yin and Mountcastle 1977, Robinson et al. 1978; Hyvarinen, 1981; Motter and Mountcastle, 1981; Andersen et al., 1987). Such cells have been generally found to be homogeneously excitatory throughout their receptive fields (rf's) (although some inhibitory and

off responses are seen). The response is usually strongest at the rf centre, and falls off to one third at an average distance of 30 deg (Andersen et al. 1985b).

Interestingly, the visual activity of most of these cells is gated by eye position, i.e., although their receptive fields remains retinotopic, the amplitude of the responses depend on the position of the eye in the orbit (Andersen and Mountcastle, 1983; Andersen et al., 1985b). Such activity could underlie a representation of visual stimuli in craniotopic space (Zipser and Andersen, 1988). Such eye position effects are discussed at length in chapter 4.

Foveal sparing: although the rf's are large, they often have a "scotoma", typically in the foveal region (Yin and Mountcastle 1977; Motter and Mountcastle, 1981).

Light sensitive neurones are often sensitive to movement of visual stimuli towards or away from the fovea. Motter and Mountcastle (1981) referred to this as radial opponent vector organization. Steinmetz et al. (1987) have shown that a population of such neurones can encode the direction of a stimulus with an accuracy of 9 deg. Such neurones are sensitive to a wide range of stimulus speeds, 10 - 800 deg/s, and may play a role in the detection of optic flow during locomotion.

Sakata et al. (1985) reported area 7a units that were responsive to rotation and size change of visual objects. It seems as though many of these units were actually recorded from the anterior bank of the STS (including area MST).

Units that are classifiable as "light sensitive" may also fall into other classes (such as fixation or saccade, as discussed below).

**Area 7a: fixation units**

A second important class of neurones was described by Mountcastle et al. (1975). These units fired when the monkey was fixating an object of interest. However, the motor act of fixation, rather than passive visual stimulation was what drove these units (Mountcastle et al. 1975). They also paused during saccades (Yin and Mountcastle 1977). Lynch et al. (1977) defined the gaze fields of such neurones as the zone in space in which fixation of a visual target was associated with increased firing of the unit. They described units with gaze fields

limited to one or two quadrants of the visual field; and others with full field gaze fields.

Subsequent investigations (Sakata et al. 1980, Andersen et al. 1985b) have shown that almost all fixation neurones have gaze fields, and moreover that they are typically a monotonic function of eye position. Andersen (1987) has argued that such units are better considered "eye position" units as they signal the orbital eye position rather than the fact that the animal is fixating. Sakata et al. (1980) have demonstrated that fixation units may be active even when the animal is making "spontaneous" eye movements in the dark. This finding bolsters the contention that fixation units be considered eye position cells. Rolls et al. (1979) have shown that such units do not distinguish the affective nature of the stimulus.

Robinson et al. (1978) contended that the apparently fixation-related activity of such neurones was actually due to visual responsiveness. They maintained that "full field" units in fact had tonic responses to foveal stimuli. "Limited gaze field" units were responding when a particular contour in the visual fields excited them.

This report stimulated further, more controlled experiments that have demonstrated that at least some "fixation activity" is indeed related to eye position and cannot be considered an artifact of visual stimulation. Such units show eye position-dependent changes of activity when the monkey fixates remembered locations in the dark (Sakata et al. 1980; Andersen et al. 1985b). Andersen et al. (1985b) used prisms to alter eye position while keeping the retinal stimulation constant. They showed that such cells do carry true eye position signals. They also showed that 80% of such cells were also visually responsive.

Sakata et al. (1980) reported that some cells are selective for fixation in depth.

**Area 7a: smooth pursuit (visual tracking) units**

Mountcastle et al. (1975) were the first to observe such units, which were active when the monkey tracked an object of interest. They did not fire during steady fixation. Since their firing started before pursuit in a given direction was initiated, it was suggested that they served a "command" function.

Robinson et al. (1978) challenged this interpretation, again

suggesting that the apparently pursuit related activity was in fact visual in nature (either due to movement of the background or retinal slip). However, Sakata et al. (1978) showed that such units continued to fire when the target was briefly turned off during pursuit, and Lynch (1980) pointed out that these units fired before pursuit was initiated.

**Area 7a: saccade units**

Hyvarinen and Poranen (1974) reported cells ("looking" units) that responded to eye movements, but their study was rather qualitative and lacked eye movement recordings. Lynch et al. (1977), in a more carefully controlled study with eye movement recordings, reported neurones that fired before and during saccades to visual targets. They reported that such units were direction but not amplitude tuned, and began firing on average 55 ms before the saccade. These authors proposed that such units might issue general commands to make saccades. These units were also reported to be non-light sensitive and to have eye position-dependent activity (Yin and Mountcastle 1978; see chapter 4 for further discussion).

Again, Robinson et al. (1978) challenged these findings. Once more, the crux of their criticism was that the saccade cells were visually sensitive and that the apparently saccade-dependent activity might be an artifact of visual stimulation (either target appearance or sweeping of the background across the rf during the movement). Subsequently, Motter and Mountcastle (1981) showed that many saccade units were also light-sensitive.

Andersen et al. (1987) used a delayed saccade paradigm to show that many area 7a units do in fact carry *both* visual and saccade-related signals. Thus the controversy between the groups of Goldberg and Mountcastle would seem to be resolved. Although saccade-related activity is commonly seen in 7a cells, it tends to follow the onset of the saccade by an average of 55 ms (Andersen et al. 1987; Gnadt and Andersen, 1988) and be less robust than the saccade-related firing in LIP (see chapter 2). It is possible that some of the apparent differences in the reported latencies are a result of differences in the neuronal populations sampled in different studies. As noted above, areas 7a and LIP have only recently been clearly demarcated. It appears that Mountcastle and colleagues recorded from both the crown of the sulcus

(area 7a) and the lateral bank of the IPS (LIP), whereas Robinson and coworkers mainly recorded from area 7a.

These issues are investigated and discussed in detail in chapters 2 and 3.

### Area 7a: attentional effects

Human and monkey lesion studies strongly impute the IPL with an important role in visuospatial attention. Not surprisingly, therefore, Yin and Mountcastle (1977, 1978) and Robinson et al. (1978) reported that the response to a visual stimulus increased if it were the target of a saccade. This enhancement was specific to the unit's rf and therefore could not be ascribed to general arousal. Bushnell et al. (1981) went on to show that this attentional enhancement did not depend on the animal making a subsequent saccade to the target; he merely had to attend to it (e.g., to detect its dimming). Thus this attentional effect differs from saccade-contingent enhancement seen in the FEF and SC (reviewed in Heilman et al. 1987). Mountcastle et al. (1981) showed that the effect depended on the behavioural state of the animal. Mountcastle et al. (1984) demonstrated that there is a general increase in the responsiveness of visual neurones when attention is covertly shifted away from the direction of gaze. This increase is not limited to the peripheral attentional target location.

### Area 7a: summary of visual and eye movement cell types

Researchers from several different laboratories have concurred that there are four basic types of visual and eye movement responses in area 7a: light-sensitive, fixation, smooth pursuit and saccade. It has also become clear that a given unit may fall into more than one category. Thus, for example, a unit may have both visual and saccade-related activity, and be modulated by eye position. Some of the controversies that have arisen have been resolved by the application of new paradigms, such as the delayed saccade. It is important to bear in mind that most of the studies reported above were conducted before the currently accepted division of "old" area 7a into "new" area 7a on the gyral surface and area LIP in the sulcus.

**Lateral intraparietal area (LIP)**

The lateral intraparietal area (LIP) lies in the lateral bank of the intraparietal sulcus, and has been only recently delineated on anatomical and functional grounds (see above). Therefore some earlier studies (e.g., Mountcastle et al., 1975, Robinson et al., 1978) failed to distinguish it from the cortex lying on the surface of the gyrus of the IPL (area 7a). By several criteria LIP has been imputed with a role in saccades: (1) It has powerful (relative to area 7a and indeed other subdivisions of the PPC) connexions with other areas related to saccades, such as the FEF, superior colliculus and the dorsal and dorsolateral pons (Barbas and Mesulam, 1981; Asanuma et al., 1985; Lynch et al., 1985; May and Andersen, 1986). (2) Shibutani et al. (1984) have reported that it has the lowest threshold for eliciting saccades by electrical stimulation of IPL regions. (3) Preliminary studies by Andersen and colleagues suggested that saccade-related neurones were more common in LIP than area 7a (Andersen, Siegel, Essick and Asanuma, 1985) and that many of the saccade-related neurons in LIP fire presaccadically (Gnadt and Andersen 1988). The major goal of this thesis was to study in a detailed, quantitative fashion the roles of areas 7a and especially LIP in saccadic eye movements:

First, areas LIP and 7a may be distinguished on physiological grounds; most importantly in the current context by the finding that area 7a cells are mainly postsaccadic, whereas LIP cells are often presaccadic. This issue is investigated in detail in chapter 2.

Second, many carry both visual and saccade-related signals. In area 7a the latter responses are mostly post-saccadic, whereas they are typically presaccadic in LIP. Chapters 2 and 3 of this thesis contain a detailed, quantitative analysis of these activities.

Third, when tested with delayed saccades, many LIP units show a sustained "memory" response that persists from the offset of the target until the saccade is made. This activity appears to encode the motor error of the forthcoming saccade. Chapters 2 and 3 of this thesis contain a detailed, quantitative analysis of this activity. Chapters 5, 6 and 7 discuss further experiments designed to test the hypothesis that this memory activity reflects the monkey's intention to make a saccade of a certain vector.

Fourth, the activity of most units in both areas is influenced by eye

position. The nature of this modulation is investigated in chapter 4.

Although the activity of LIP units has mainly been tested in saccadic paradigms, and the connexional and physiological data strongly argue for an important role for LIP in the planning of saccadic eye movements, it is likely that LIP plays a role in other visual and visuomotor behaviours. Gnadt and Mays (1989), for example, have suggested that LIP plays a role in the control of vergence eye movements and coding of the three dimensions of visual space.

**Area 7b**

Most cells in this area respond to somatosensory stimuli (Hyvarinen and Sheplin, 1979; Robinson and Burton, 1980a,b; Hyvarinen, 1981; Andersen et al. 1990). Some cells are active when the monkey reaches or manipulates objects with his hand (Mountcastle et al., 1975; Andersen, Siegel, Essick and Asanuma, 1985). Only 10% of neurons in this area have been reported to respond to visual or visual-and-somatosensory stimuli (Robinson and Burton, 1980a,b; Hyvarinen, 1981). In addition the connexions of this area are primarily with other somatosensory regions (Andersen et al., 1990). Thus there is little evidence to suggest a saccade-related role for 7b.

**Medial superior temporal area (MST)**

This area in the anterior bank of the superior temporal sulcus seems to be primarily concerned with the analysis of complex visual motion stimuli, e.g., size change and rotation (Sakata et al., 1985; Saito et al., 1986), and smooth pursuit eye movements (Sakata et al., 1983; Newsome et al., 1985, 1988). Several extrastriate visual areas, e.g., MT, project directly to it; and it, in turn, projects to 7a and LIP (Maunsell and van Essen, 1983; Seltzer and Pandya, 1984; Andersen et al., 1990). Although there is no evidence for a direct role of MST in saccades, it could for example provide important information regarding moving targets to areas such as LIP.

**Other areas**

Other visual areas have been defined on connexional grounds, e.g., the ventral intraparietal (VIP) (Maunsell and van Essen, 1983) and dorsal prelunate (DP) (Andersen et al. 1990) areas. However, they have not been extensively explored physiologically.

## HUMAN STUDIES ON THE VISUAL AND OCULOMOTOR ACTIVITY IN PPC

### Event-related potential studies

Event-related potential (ERP) studies in humans offer some evidence in support of the visual and saccade roles for PPC suggested by the monkey physiology data. A short latency negative potential occurs at 100-200 ms after a visual stimulus; it is usually larger over the contralateral hemisphere and enhanced if the subject attends to it (van Voorhis and Hillyard, 1977; Harter et al.,1982; Hillyard et al. 1985; Neville and Lawson 1987). These results seem consistent with the properties of light sensitive neurones in area 7a. A longer latency positive wave (300-500 ms) follows; it appears to be involved in stimulus selection and decision making (Hillyard and Kutas 1983). Lhermitte et al. (1985) showed that it is reduced in neglecting PPC patients. The possible single unit correlates of this wave have not been identified, but a combined single unit/ERP study of monkey PPC would be quite feasible.

In addition, ERP studies have revealed saccade-related activity over human PPC. The premotor positivity (PMP) which precedes saccades by 100-200 ms is maximal over parietal cortex (Brickett et al. 1984; Kurtzburg and Vaughan 1982; Thickbroom and Mastaglia 1985). The PMP is thought to be related to the formation of the motor plan (Deecke et al. 1976; Husain 1987).

### Human regional cerebral blood flow (rCBF) studies

When subjects are required to direct their attention to a visual object, there is increased rCBF in PPC (Roland 1982; Reivich et al. 1983). These studies also showed preferential activation of the right PPC, consistent with neuropsychological studies showing that the right PPC is more important than the left in visuospatial attention. Melamed and Larsen (1979) and Fox et al. (1985) have reported rCBF increases in PPC related to saccades. Thus there is further evidence from humans consistent with monkey physiology data.

## FIGURE LEGENDS

**Figure 1:**

Parcellation schemes of PPC in monkey and man. (A) and (C) Brodmann's (1905, 1907) subdivisions of monkey (*Ceropithecus*) and human cortex (respectively). (B) von Bonin and Bailey's (1947) subdivision of monkey (*Macaca mulatta*) cortex. (D) von Economo's (1929) subdivisions of human cortex. See text for details.

**Figure 2:**

A recently proposed hierarchy (from Andersen et al. 1990) illustrating the connexions of subdivisions of the IPL with other visual cortical areas. "Higher" areas appear above lower areas (this analysis is based on the laminar distribution of sources and terminations of projections). Dotted lines indicate "mixed" projections between areas surmised to be at equivalent levels in the hierarchy. The boldface square encloses the areas of the PPC and the adjoining dorsal prelunate area.

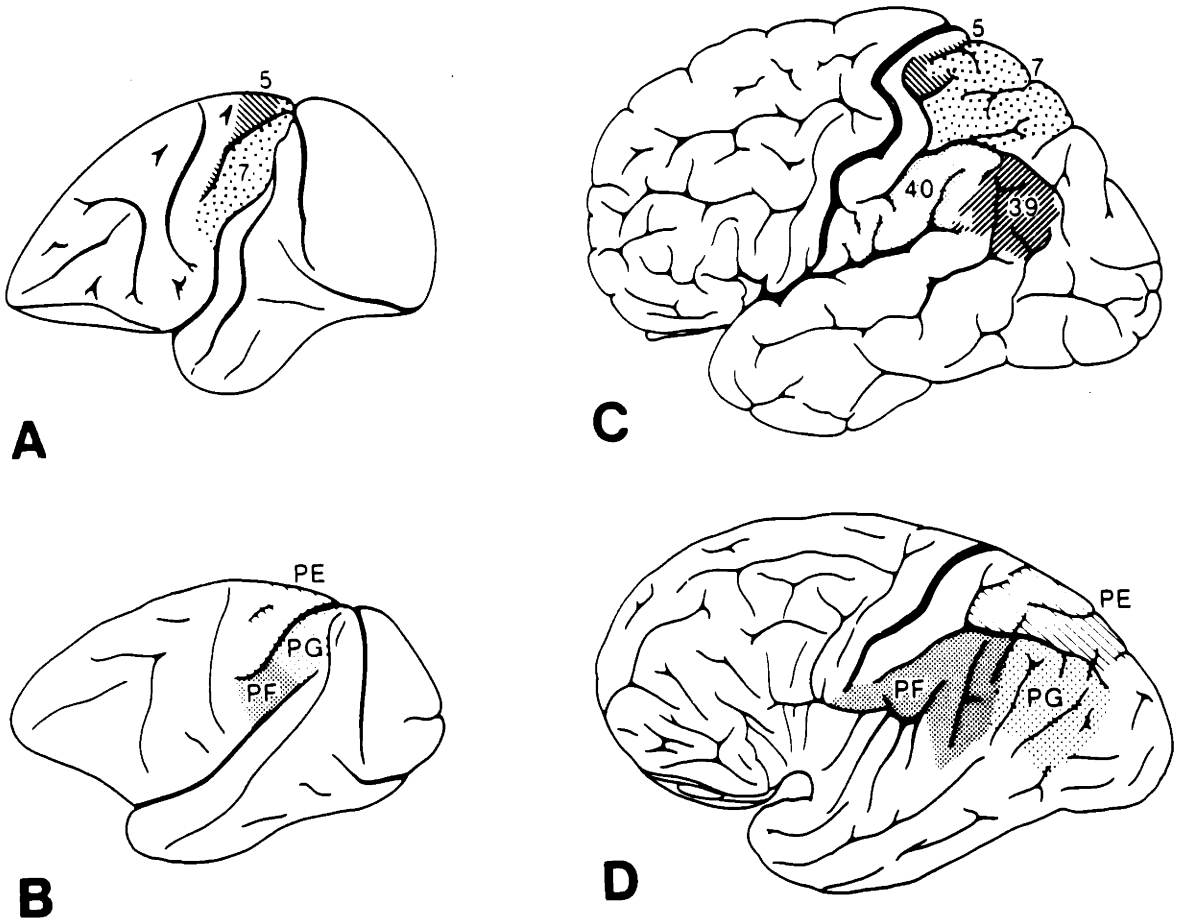



Figure 1

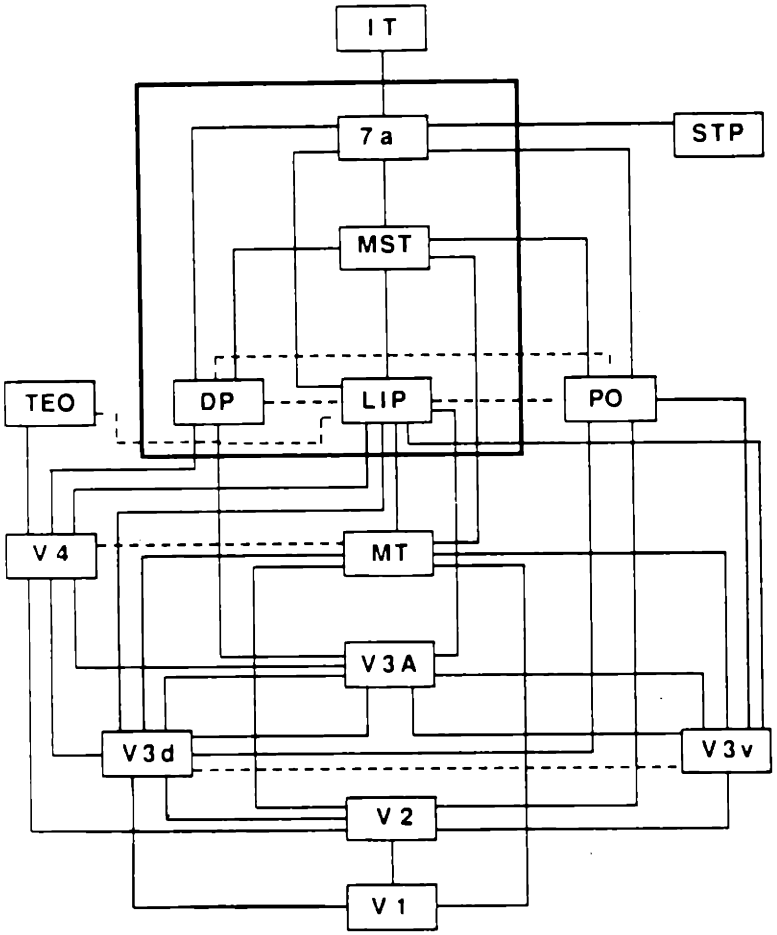



Figure 2

# Chapter 2

## Visual, motor intention and saccade-related activity in area LIP: temporal characteristics and comparison with area 7a

## SUMMARY

1. The cortex of the inferior parietal lobule (IPL) contains neurones whose activity is related to saccadic eye movements. The exact role of the IPL in relation to saccades, however, remains unclear. In this and the following chapter we approach this problem by quantifying many of the spatial and temporal parameters of the saccade-related activity. These parameters have hitherto been largely unstudied.

2. The activity of single neurones was recorded from *Macaca mulatta* monkeys while they were performing a delayed saccade task. The analysis presented here is based on 161 neurones recorded from the lateral intra-parietal area (LIP), a recently defined subdivision of the IPL; and 54 neurones recorded from the neighbouring part of the IPL, area 7a. Overall, 409 IPL neurones were isolated in this study.

3. The typical activity of IPL neurones during the delayed saccade task has three basic phases: light-sensitive (LS), memory (M) and saccade-related (S). These basic phases are common to neurones of both areas LIP and 7a. In each phase (LS, M, S), individual neurones may or may not be active. Most LIP neurones, however, are active in more than one phase.

4. In order to compare the activity levels of different neurones, the actual firing rate was weighted by each neurone's background level, yielding an "activity index" for each neurone, in each phase of the task. We calculated the activity index for the LS and M phases, and for three phases related to the saccade: a presaccadic, a saccade-coincident, and a post-saccadic phase. For area LIP neurones, the median values of the activity index were high for the LS, M, pre-saccadic, and saccade-coincident activities, and slightly lower in the post-saccadic period. In area 7a, the median values were low for the LS phase, and, in particular, for the M and pre-saccadic phases; somewhat higher coincident with the saccade; and high post-saccadically.

5. In area LIP, in each phase, 49%-63% of the neurones had excitatory activity, and 10%-17% had inhibitory responses.

6. In contrast, in area 7a, excitatory responses were most frequent in the post-saccadic phase (56%). Excitation was particularly infrequent during M (28%) and Pre-S (22%). The incidence of inhibitory responses varied too (4%-18%). The time course of inhibition was roughly

opposite that of excitation; the highest frequency of inhibitory responses occurred during the saccade.

7. The latency of the S activity was defined as the time, relative to the beginning of the saccade, when the activity became significantly higher than background. In area LIP, latencies ranged from 200 msec before the saccade to 200 msec after the saccade. The mean latency in area LIP was 10.5 msec before the saccade. In area 7a the latencies ranged from 50 msec before the saccade to 380 msec after the saccade. The mean latency in area 7a was 140 msec after the saccade.

8. A neurone was considered pre-saccadic if its activity varied significantly from the background by the time the saccade started. In other words, the latency of the neurone's S activity had to be less than or equal to 0 msec. In area LIP, 72% (61/85) of the neurones were pre-saccadic. In area 7a, only 18% (6/33) of the units were pre-saccadic.

9. The offset time of the saccadic activity was defined as the time the activity outlasted the saccade. The S activity usually lasted well beyond the saccade. The median offset time for LIP neurones was 120 msec. The median offset time for 7a neurones was 300 msec (but note that the S activity of most area 7a neurones only started post-saccadically).

10. The duration of the S activity was computed from its latency and offset, and from the duration of the saccadic movement (typically 60 msec). For both areas LIP and 7a, the distribution of durations was approximately Gaussian. The parameter values of the distributions were also similar for both areas (median 210 msec in both LIP and 7a). Thus the duration of the S activity is usually considerably longer than the duration of the saccade itself.

11. In area LIP, the onset latencies of the light-sensitive activity ranged from 50 to 270 msec, with median 110 msec. In area 7a, although the range was similar to that of LIP, typically the LS latencies were longer (median 160 msec).

12. In summary, area LIP contains vigorous activity in anticipation of the saccade, during the LS, M, and pre-saccadic periods. Area 7a is active mainly during and after the saccade. These results suggest that area LIP participates in the planning of saccades. Area 7a, however, probably primarily subserves different functions.

## INTRODUCTION

Much evidence suggests that the inferior parietal lobule (IPL) of primates plays a role in visually-guided saccadic eye movements. Lesions to the IPL in humans often produce deficits in these movements. These deficits are neither purely sensory nor purely motor in origin. Balint, the first to describe these deficits, coined the phrase "psychic paralysis of gaze" (Balint 1907, 1909; see Husain and Stein 1988). Similar deficits have also been observed following IPL lesions in monkeys (for reviews of these deficits in humans and monkeys, see chapter 1, Andersen 1987; Hyvarinen 1982a, b; Stein 1989; Husain 1991). These deficits in saccades are similar in strength to those that follow frontal eye field lesions; combined lesions result in much more severe deficits (Lynch et al. 1986; Lynch and McLaren 1989). Saccades can be evoked by low-threshold electrical stimulation of the IPL (Shibutani et al. 1984, Thier, pers. com.). Electrophysiological studies of the IPL have revealed saccade-related single unit activity (Hyvarinen and Poranen 1974; Lynch et al. 1977; reviewed in chapter 1).

In spite of the general acceptance of the involvement of the IPL in saccades, its exact role remains unclear. A major source of ambiguity has been the insufficient determination of the sensory and motor components of the functions of the IPL. For instance, parallel to their effect on saccades, parietal lesions often result in a deficit in visual attention (Critchley 1953). A confounding factor for these distinctions may be the subtle sensorimotor interactions that are at the core of visually-guided saccades. Although visually-guided saccades are movements, and must be planned and executed like any other movement, they are both initiated by and affect visual perception. Also, saccades are intimately tied to visual attention.

The ambiguity of the sensory and motor components has not been entirely resolved by electrophysiological studies. Mountcastle and his colleagues proposed that the IPL contains "a command apparatus for the behavioral acts of manual and visual exploration of the immediately surrounding extrapersonal space" (Mountcastle et al. 1975). An alternative hypothesis, however, was offered by Robinson et al. (1978), stating that the IPL is a sensory association area. Robinson et al. maintained that the movement-related IPL neural activity was not motor but sensory; that is, that presaccadic activity in visually-guided

saccades is a visual response to the target stimulus for the saccade.

In order to distinguish between the sensory and motor components of the responses of IPL fixation and saccade neurons, Andersen et al. (1987) introduced new paradigms to the study of the IPL. This and other studies led Andersen (1987) to propose that a major function of the IPL is sensorimotor integration. One paradigm was the delayed saccade, in which the visual and saccade-related responses are separated in time. Many IPL neurones were found to have both responses. Hence, the IPL carries not only visual, but also oculomotor-related signals. However, only a small minority of the neurones reported by Andersen et al. (1987) had oculomotor activity that preceded the eye movement. Thus most of the saccade-related activity that was reported could not reflect motor planning, because it started after the movement.

Recently, anatomical studies of the IPL have shown that it contains several distinct areas (see chapter 1). Andersen et al. (1985a) defined a new area in the caudal third of the lateral bank of the intraparietal sulcus (lateral intraparietal area - LIP). The remainder of the caudal IPL, area 7a, is restricted to the gyral surface. Area LIP has much stronger connexions than area 7a to established oculomotor-related centres such as the superior colliculus, the frontal eye field, and dorsal and dorsolateral pons (Andersen et al. 1990a; May and Andersen 1986). These connexions suggest that the subdivision of the IPL that is most likely to be involved in saccades is area LIP. The five presaccadic neurones found by Andersen et al. (1987) were, indeed, all located in LIP.

The electrophysiological differences between areas LIP and 7a have not been studied. The anatomical connexions of these areas lead to several important questions: First, is area LIP specifically related to movement planning? A necessary condition for an area to participate in the planning of saccades is to have neurones that are pre-saccadic. Considering this condition, we ask, first, if there is a difference between areas LIP and 7a in terms of the latencies of the saccade-related activity. Second, are the patterns of neural activity, evoked during the delayed saccade task in areas LIP and 7a, similar or different from each other? Third, is there, in either area, sensorimotor integration taking place on the level of the single neurones? Fourth, are there differences between these areas in terms of the visual response - in particular, its

timing? Areas LIP and 7a are known to have different connexions with the extrastriate visual cortical areas (Andersen et al. 1990; reviewed in chapter 1). These and other issues are addressed in this chapter by examining in detail the response of area LIP neurones in a memory saccade task. This task was designed to tease apart activities related to the visual stimulus, the planning of the eye movement during the memory period, and the eye movement itself.

# METHODS

## Animals, surgery, animal care

Two 5 kg male *Macaca mulatta* monkeys were used in this study. Before the beginning of training a head post was mounted in a dental acrylic skull cap and a scleral search coil was implanted (Robinson 1963; Judge et al. 1980). A second surgical procedure took place once the animals became proficient in their task; in this procedure a recording chamber was mounted over the posterior parietal cortex (Brodmann's areas 5 and 7). Four to 8 months later, in a third procedure, a chamber was mounted over the posterior parietal cortex of the second hemisphere. All surgical procedures were carried out under general anesthesia (10 mg/kg Ketamine i.m. followed by 10 mg/kg Nembutal, i.v.), and with sterile conditions. An analgesic was given post-operatively. The post-operative care consisted of close monitoring of the animal until after full recovery from the anaesthesia. After each surgical procedure the monkeys rested for a week, and were treated with systemic antibiotics.

During the training and the recording periods the animals were deprived of water in their home cages. We carefully monitored the amount of apple juice received by the animal as reward; if the full daily ration was not reached, it was supplemented by water after the sessions. Each week the animals had at least two days of rest, with unrestricted water supply.

During the recording period, the recording chamber was flushed daily with sterile saline, and antibiotics were applied to the dura before closing the chamber for the night. Occasionally the animals were lightly anaesthetized with ketamine and their dura was scraped to prevent an accumulation of granulation tissue.

Routine veterinarian care was given to the animals. The general well being of the animals were observed in accordance with NIH guidelines.

## Experimental set-up, data collection

Both training and recording sessions were conducted in a completely darkened room. The animal was monitored continuously

with a remote camera and an infrared light source. The monkey was positioned with its head fixed 57 cm in front of a large, featureless back-projection screen. Stimuli appeared on the screen as 0.5 deg diameter spots, 45 candella/ $m^2$ against a totally dark background. Stimulus timing and location were controlled by fast-response electronic shutters and x,y galvanometer mirror systems under computer control. To correct for the error in eccentricity caused by the use of a tangent screen, the computer adjusted the command to the x,y galvanometers so that stimuli with the correct eccentricities were displayed to the animal.

Eye position was measured using a scleral search coil system (Robinson 1963; Judge et al. 1980). Eye position was typically sampled at 500 Hz; in some cases 100 Hz. Each daily session was started by a calibration run, in which the animal fixated stimuli presented at 9 locations. These locations, in degrees, were (x,y)=(20*i*, 20*j*) where *i*,*j*=-1,0,1, and (0,0) is straight ahead of the animal (such that the eyes are approximately in the primary position). These locations will henceforth be called the "20 deg grid". Linear approximations for the horizontal and vertical eye position signals were calculated from this calibration run. Eye position calibration varied from day to day by, at most, a few per cent.

Action potential recordings were made with platinum-iridium electrodes covered with glass, with 1-5 MΩ impedance at 1 KHz. The electrodes were advanced through the dura into the parietal cortex using a Chubbuck microdrive with 1 mm resolution in depth. Signals were fed into an amplifier and single units were isolated using a variable-delay window discriminator. The time of spike acceptance was determined by the computer with 0.1 ms resolution.

**Training; delayed-saccade task**

One week after the first surgery (for the acrylic skull cap and the eye coil), training was begun. Initially the animals learned to fixate a fixation spot, and then to make visually-guided saccades (in which the onset of a peripheral target coincided with the offset of the fixation spot). Subsequently the animals were trained to withhold their saccade in the delayed saccade paradigm. Finally they were trained in the other paradigms used in this and related studies (see elsewhere in this thesis). Throughout all training and recording sessions, the heads were

fixed. Following a successful trial the monkeys received as reinforcement a drop of apple juice. The monkeys performed 1000-3000 trials daily, usually 4 days a week.

The experiment was controlled by a laboratory computer. Trials of the delayed saccade task were organized in the following way (illustrated in figure 2): the appearance of a fixation spot signalled to the monkey the beginning of a trial. The monkey had to fixate the spot within 1 s. The moment the eye foveated the fixation spot was called "fixation onset". If the monkey failed to fixate the spot within the given 1 s, the trial was aborted, declared a "miss", and an inter-trial interval was begun.

At a specified time, usually 800 ms after fixation was attained, a peripheral target spot appeared on the screen. The target stimulus was presented briefly (typically for 300 msec, occasionally 500 msec), and then disappeared. The fixation spot remained illuminated while the peripheral stimulus was presented, and the monkey was not allowed to break fixation. After the peripheral target spot was extinguished, the fixation spot remained on the screen for some time. The interval from the offset of the target to the offset of the fixation spot is called the "delay" period. Its duration was usually 400 or 2000 ms. During the delay period the monkey was required to continue to fixate the fixation spot.

The offset of the fixation spot served as the "go" signal for the saccade. Within 500 ms the monkey had to move his eyes into a window centred on the location at which the peripheral target had previously appeared. Following this eye movement, the monkey had to keep his eye in the new position for at least 500 ms. If the monkey fulfilled all these conditions, the trial came to a successful end (a "hit") and the animal was rewarded with a drop of apple juice. If a trial had reached the "fixation onset" stage but subsequently the monkey either moved his eyes before the "go" signal, or did not enter the target window soon enough after the "go", or moved out of the target window before 500 ms, the trial was aborted and declared an "error".

The subsequent intertrial interval was a pause (randomly varied from 500 to 2000 ms), during which the collection program accomplished book-keeping and data display tasks.

Data was collected in "runs". A run was a sequence of trials from 9 classes, whose order was pseudorandomly interleaved. Trials of the same class had identical stimulus presentations and behavioral

requirements. In the delayed saccade task, 8 of the 9 classes had the temporal pattern of stimulation and behavior that was described above. The only difference between the classes was the location of the stimulus. The target could be presented in any of the 8 locations on an imaginary 15 deg grid (described in the previous section) - that is, in any of 8 directions separated by 45 degs. The ninth class was a control class, and it is described next.

Since the "go" signal in the protocol described above was the offset of the fixation spot, if a neurone had a foveal off-response, this visual activity would have occurred just before the saccade, and might have thus been mistakenly considered saccade-related. In order to preclude this possibility the following protocol was applied in the ninth class: as in the other classes, trials in this class began with the onset of the fixation spot. The monkey had to fixate the spot within 1 s; otherwise, a "miss" was declared and the trial aborted. After "fixation onset", the fixation spot stayed on for the same duration as the other classes, and the monkey had to continue to fixate it. However, no peripheral target was flashed during this fixation, and after the offset of the fixation spot, the monkey had to keep his eye within the fixation window for another 500 ms. If the monkey broke fixation before this period was over, the trial was declared an "error". One of the following two variations of the described basic paradigm was used. In the first variation (see figure 2b), after the dark fixation, the fixation spot reappeared for another 500 ms. The monkey had to continue fixating the spot as long as it was on. This variation allowed us to examine if the neurone had a foveal on-response. In the other variation, from 800 to 1100 ms after key-down the target projector flashed at location (0,0), overlapping the fixation spot. The monkey had to maintain his fixation for the whole duration of the trial. In this case the total illumination in the control trials was the same as that of the delayed saccades. If a fixation-off response was observed, the neurone was not further analyzed.

Another piece of evidence that the saccade response was not due to the offset of the fixation point was that almost all saccade responses were selective for the directions of the eye movements. If the cells were simply responding to the offset of the fixation light, they would have responded to all subsequent directions of eye movements.

Once a neurone was isolated, it was studied in a run of delayed

saccades, usually with 400 ms delay. The run typically continued until at least 8 to 10 hits were collected in each class. Additional types of runs, including delayed saccades with longer delays, were subsequently recorded (see later chapters).

The spatial windows used for determining adequate eye position were squares with side length ±5 to 10 deg centred on the fixation spot or on the target. The reason for these relatively large windows is that delayed saccades made in complete darkness exhibit systematic spatial errors. In particular, upgoing saccades tend to be hypermetric, while downgoing saccades are almost invariably hypometric. These effects are described in detail in chapter 8. This contrasts with the accuracy of visually-guided saccades, for which virtually flawless performance could be achieved with ±1.5 deg side-length windows.

**Histology; allocation of units to cortical areas**

After recording from both hemispheres, one monkey was sacrificed. In the last few weeks of the experiment involving this monkey, several marking lesions were made in both hemispheres by passing small DC currents through the recording electrode at different depths. At the conclusion of the experiment, the monkey was given an overdose of sodium pentobarbitol and then perfused transcardially with heparinized saline. Guide wires were lowered into the brain at selected recording-chamber coordinates immediately after the animal was sacrificed. The wires were used as landmarks for blocking the posterior parietal cortex and for determining the locations of the recording tracts made early in the experiments. Good agreement was found between the locations of the guide wires and the coordinates of the marking lesions, indicating that the locations of the early recordings (determined from the coordinate system of the microdrive) were reasonably accurate.

Thirty micron thick sections were cut and alternately stained with thionin for cytoarchitecture and by the Gallyas method for myeloarchitecture (Gallyas 1979). Areas within the IPL were identified on architectural and physiological criteria. In particular, we differentiated between areas LIP and 7a primarily on myeloarchitectural grounds. The majority of area LIP is identified by the densely myelinated area on the posterior aspect of the lateral bank of the intraparietal sulcus. This densely myelinated region is

approximately 10 mm long in the anterior-posterior dimension of the sulcus and 3 to 4 mm wide in the dorsal-ventral axis (Ungerleider & Desimone, 1986; Andersen et al., 1990). Ungerleider and Desimone (1986) have referred to this densely myelinated zone as VIP*. Area LIP continues 1 to 2 mm dorsal to the densely myelinated area (Blatt et al., 1990).

One hemisphere was recorded from a second monkey. This animal is currently being used in related experiments. We defined a functional criterion for determining if a given neurone belonged to area LIP or to area 7a. This criterion was based on the analysis of the results from the sacrificed monkey, and on data from previous monkeys not included in the present study.

We recorded many neurones from the gyral cortex, that is, with depth less than 2500 mm from the top of neural activity, at different chamber coordinates. Since the cortex of the superior parietal gyrus (area 5 of Brodmann) is somatosensory, while the cortex of the inferior parietal lobule is visual-oculomotor (Hyvarinen 1982a, b; Mountcastle et al. 1975), we were able to draw with some confidence the line of the sulcus on the chamber map. Neurones that were lateral to this line, and whose depth was at most 2500 mm, were classified to area 7a. Because of the inclination of the recording chamber, penetrations that reached area LIP had either to pass through area 5 or to descend along the sulcus. If the electrode passed through area 5, a subsequent completely "quiet" zone followed (without neural activity), as the electrode traversed the intraparietal sulcus before entering area LIP. Upon entering LIP visual or oculomotor neurones were found. This zone was presumably the sulcus. The subsequent cortex, at least 2500 mm under the top of neural activity, was considered LIP.

Figure 1 shows the sites of penetrations, in which area LIP and area 7a neurones were encountered, made into the two hemispheres of the first monkey. Representative sections illustrate the estimated locations of neurones recorded in these hemispheres.

**Data analysis**

The responses we recorded typically depend on many parameters. Each phase can be excitatory or inhibitory (or neither); each phase can have its own preferred direction, latency, and level of activity. Unbiased analysis of the activity of these neurones was therefore quite complex, particularly when groups of neurones were compared (that is, areas LIP and 7a). Towards this end a relational data base was constructed (4th Dimension, Acius). Several analyses were made on the raw data on the laboratory computer, and the results were extracted and imported into the data base. Because this arrangement is not standard we will briefly describe it.

The data base contained four files important for the present discussion: A 'Penetrations' file contained the date and chamber coordinates of each penetration, depth of the dura and the top of neural activity, electrode impedance, intervals in the track of the electrode suspected as white matter, and several additional parameters. A 'Cells' file, linked to the Penetrations file, included primarily the depth in which each neurone was recorded, its run list, and evaluation of the quality of the recording. A 'Fields' file, linked to the Cells file, had a record for every run that used the delayed saccade task; the record contained 104 parameters imported from the laboratory computer (11 phases times 9 parameters for each phase, plus some additional data). Only the parameters that were found to be interesting are described here. A fourth file, 'Timing', also linked to the Cells file, contained LS and S latencies, duration and offset of the S activity, and additional parameters for each cell. Selections of neurones (such as 'area LIP neurones') were exported to various statistical and graphical Macintosh programs. In particular, we used Data Desk (Odesta) for data exploration. We feel that this arrangement helped us reach reliable quantitative characterization of the activity in areas 7a and LIP.

**Definition of activity index**

In order to compare levels of activity evoked in different neurones, we decided to take into consideration that the compared neurones typically differ not only in their 'responses', but also in their background levels. Hence to compare 'net responses' we first assigned to each neurone a 'net' level of activity (its activity index), based on its response and background levels. For each neurone, in a given phase, we measured the mean response rates for saccades in the eight directions $r_1,...,r_8$, and the corresponding mean background rates, $b_1,...,b_8$. Each $r_i$ and $b_i$ are the means of at least 8 trials in the given direction. We then took as a general mean background the mean of $b_1,...,b_8$. We also determined the maximal rate $r_{max} = \max\{r_1,...,r_8\}$ and the minimal rate $r_{min}$. Neurones satisfying $r_{max} \geq 1.2 \cdot$background) were considered potentially excitatory, and their activity index was defined in the following manner:

activity index =

$(r_{max} - \text{background}) / \text{background}^{1/2}$ if background $\geq 1$ imp/s

$r_{max} - \text{background}$ otherwise.

A good correspondence was found between neurones that were subjectively classified as having a clearly excitatory response, and those having an activity index higher than 2.0.

Otherwise (i.e., if $r_{max} < 1.2 \cdot$background), neurones were considered potentially inhibitory, and their activity index was calculated thus:

activity index =

$(r_{min} - \text{background}) / \text{background}^{1/2}$ if background $\geq 1$ imp/s

$r_{min} - \text{background}$ otherwise.

Neurones were usually considered clearly inhibitory if their activity index was -2.0 or less.

Neurones showing excitation in some directions but inhibition in other directions were considered excitatory. Often such mixed responses were in opposing directions ("push-pull"). Careful distinction between the excitatory and inhibitory components of mixed fields is beyond the scope of the present analysis.

An advantage of the activity index is that it is a continuous function. It can be used to select sub-samples of units with levels of response of various 'quality'. We wondered if our findings would be different if we limited our sample only to the 'best" neurones (that fulfilled some criteria). We examined most of the questions discussed in chapters 2 and 3 with higher activity index thresholds. We did not find any significant effects of these different selections. Hence we feel reassured that our results do not reflect an artifact of our method of response selection.

We have also repeated parts of the analysis described in chapters 2 and 3 employing a statistical acceptance criterion, the t-test. The results were consistent with those based on the activity index, and will therefore not be presented here.

**Definition of phases**

The activity index was utilized to evaluate the level of activity of the population in several phases. A list of the standard phases used in this chapter follows. (In a few neurones the times of the "slices" were slightly changed, to fit their pattern of activity). (1) background, 300-700 ms from "fixation onset"; (2) light-sensitive (LS), 75-275 ms from target onset; (3) memory (M), 200-400 ms from target offset; (4) pre-saccadic activity (Pre-S), 200 to 25 ms *before* the beginning of the saccade; (5) saccade-coincident (S-Co), 25 ms before the saccade to 75 ms after the beginning of the saccade; (6) post-saccadic (Post-S), 200-500 ms after the beginning of the saccade. The last three phases are based on alignments of the trials on the beginning of the saccade, as previously described. (Additional phases were tested during our initial exploration of the data, but are not presented because they did not yield significantly different results from those we do present.)

The phases Pre-S, S-Co, and Post-S, defined above, are fixed with respect to the saccadic movement. Together, these phases cover most of the interval from 200 ms before the saccade, to 500 ms after the saccade. Typically, a saccadic discharge lasts for only part of this 700 ms interval; but the timing of the discharge varies from one neurone to another. We refer to this discharge as "saccadic" (S). We investigate some of its attributes (such as latency). Examining S, based on its timing variability, is complementary to the study of the fixed intervals Pre-S, S-Co, and Post-S.

**Determination of the start and end of the saccadic movement**

Eye position was usually sampled at the rate of 500 Hz. Eye velocity was computed from the eye position signal using a 2-point central difference algorithm modelled as an ideal differentiator in series with a low-pass filter (Bahill et al. 1982; Usui and Amidror 1982). A fluctuation of the tangential eye velocity was recognized as a saccade if it was higher than a threshold, usually 50 deg/s., for at least 25 ms. In this case the beginning of the saccade was defined as the time at which the velocity increased to above 10 deg/s, and the end of the saccade as the time at which the velocity decreased to below 50 deg/s (to screen out post-saccadic drift).

**Determination of the time the LS and S activities begin (or end)**

Onset and offset times were determined for the LS and S activities using the same procedure. To simplify its description, we illustrate the procedure for the case of the latency of the S activity (see figure 8a).

The spike records from a given class (i.e., trials in a single given direction) were aligned on the beginning of the saccade. A "baseline" interval was determined. It was always well before the onset of the activity (for S activity latency, typically from 400 to 100 ms before the saccade). A second, "detect", interval was also defined; it started well before the saccade and continued well after it (for S activity latency, typically from 100 ms before the saccade to 400 after it).

Both intervals were partitioned into bins, usually 20 ms long. The number of spikes in each bin, in each trial, was counted. For the baseline interval, all these counts were grouped together into a sampled baseline distribution. The number of samples in the baseline distribution was thus (duration of baseline interval / bin duration) x (number of trials in class).

In the detect interval each bin was treated separately. A sampled detect distribution thus had the same number of samples as trials in the class.

Each bin in the detect interval was compared separately with the baseline interval. The means of these two distributions (i.e., baseline and detect) were compared using a standard t-test with an alpha level of 0.05. The programs were adapted from Press et al. (1988). We determined, for each bin in the detect interval, whether its activity was significantly different from that of the baseline interval. Significantly different bins were marked (arrows in figure 8a).

If the activity starts abruptly (as in figure 11a), a continuous series of bins was recognized as significantly different from the baseline. In this case the latency of the activity was defined as the midpoint of the first recognized bin (relative to the onset of the saccade). If the rise in activity was less abrupt, or the data more noisy, an isolated bin was occasionally recognized as significantly different from the baseline. Therefore, usually only the first recognized bin that was followed by another recognized bin was defined as the latency of the response.

Note that this definition of latency determines when the activity is

already significantly different from that in the baseline. It is an upper bound for the time of start of the activity: the activity may begin slightly before its specified latency.

# RESULTS

## Database

We isolated 409 single units from two hemispheres of one monkey and one hemisphere of a second monkey. The present analysis is based on 215 units, selected according to the following criteria: first, reliable classification of the unit into either area LIP (161 units) or area 7a (54 units); second, lack of a foveal off-response; third, duration and quality of the recording and the resulting completeness of study.

## Activity of IPL neurones in the delayed-saccade task

Figure 2a shows activity recorded from an LIP neurone while the monkey was performing the delayed saccade task. The response of this neurone shows phases of activity that are typical of IPL neurones in this task. Many neurones, however, show only some of these phases.

A target stimulus in the receptive field of the neurone triggers a strong discharge. Such discharge is often maintained until the stimulus is extinguished (as it is in figure 2a). Since no eye movements are made during this visual stimulation, nor for some time following it, the discharge is light sensitive (LS).

During the delay period, after the target stimulus is turned off, activity often remains elevated above the background level until the saccade is made, although it may be somewhat reduced relative to the LS activity. This phase of activity is called memory (M) because in this part of the task the monkey has to remember the location in which the target had previously appeared, and to which subsequently he must saccade. Note that during the M phase there is neither visual stimulation nor any eye movement.

Around the time of the saccade, another burst is often observed. In figure 2a it begins somewhat before the saccade, and continues after the saccade is completed. Since the saccade is made in the dark, long after the target stimulus was extinguished, this burst is not visual, and it is termed saccade-related (S). Hence, the delayed saccade paradigm allows us to separate temporally the visual and oculomotor responses of these neurones.

Nevertheless, since the "go" signal (the offset of the fixation spot) is

visual, a control has to be made to preclude the possibility that this visual stimulation is the cause of the S discharge. This control is shown in figure 2b; trials of this class were always randomly interleaved with the delayed saccades. Here no target stimulus is presented to the monkey before the fixation spot is turned off. The monkey may not move his eyes even after the fixation spot is extinguished. The background activity in figure 2b remains unchanged when the fixation spot disappears, and then reappears. "Fixation off" responses were observed in a few neurones; these neurones were not further analysed. None of the neurones discussed in this thesis had a fixation off response.

In conclusion, the delayed saccade task temporally separates the sensory (LS) and motor-related (S) responses. In visually-guided saccades, these responses are coincident. In addition, the delayed saccade reveals a new type of activity, sensorimotor memory (M).

**Sensorimotor nature of the M activity**

Figure 3 shows that the memory activity is not simply a long-lasting LS response. Had the memory activity been an LS response, it would not be affected by the length of the delay period. Figures 3a,b depict data from an LIP neurone that was tested with different delay periods (500 ms in Figure 3a, 1300 ms in Figure 3c). The duration of the memory activity in these two cases is clearly different: in the trials of figure 3a the activity is cut off at the end of the saccade, whereas at the same point of time in figure 3c the activity is maintained.

In trials of both delay periods (figures 3a and 3c) the activity begins with the sensory event, and is maintained until the completion of motor act; in both, the saccade is accompanied by activity that subsequently declines to baseline. It follows that the memory activity in this neurone is sensorimotor in nature.

Figures 3b, d display data recorded from a different LIP neurone, showing that the memory response can also be inhibitory. For this neurone, too, the duration of the memory response (in this case, inhibition) is determined by the length of the delay period. Another aspect of the activity of this neurone is a rise in the level of activity that starts at the beginning of the trial and proceeds until the presentation of the target stimulus. Such anticipatory activity was observed in a few

neurones. It is, of course, not spatially selective, since it occurs before the appearance of the peripheral target, and is thus common to all target locations.

**Population profile of the activity**

So far only examples of single neurones have been presented. Next we ask how is the activity distributed over the population of neurones of areas LIP and 7a. Here we face the following problem: we cannot compare directly the rates of firing of different neurones because their background rates may be different. We must weight the response rate of each neurone according to its own background rate. Towards this aim we defined in the methods section a "activity index" that is a function of a neurone's response and background rate, and quantifies the strength of the response.

Figure 4 illustrates the median values of the activity index in the various phases of the task. In area LIP the median activity index is high throughout the trial, peaking for the LS and S-Co phases. Note that this result does not reveal whether the same or different neurones are active in each phase. This question will be discussed below.

In area 7a, the profile of the median activity index values is very different (figure 4). The medians are low for LS, M, and, in particular, for Pre-S. During S-Co the median is somewhat higher; it peaks after the saccade (Post-S). Thus, unlike area LIP which is active before, during and after the saccade, area 7a is relatively inactive prior to the saccade, and activity in it increases during the saccade and peaks after the saccade. This pattern suggests that area LIP may play a role in the planning of saccades, while area 7a does not. In the next sections we shall examine this pattern of activity in more detail.

Figure 4 displays the median of the absolute values of the activity indices - thus reflecting both excitatory and inhibitory responses. Selection of only excitatory responses (positive activity indices) yields similar results. The means of the activity indices also show the same characteristics.

It should not be inferred that area 7a has smaller visual responses, in general, than area LIP. Only in this specific task can we say that the visual responsiveness of area 7a is lower than that of LIP. Note also that the post-saccadic activity in area 7a is high, and thus the low LS and M median activity indices of area 7a do not reflect a general

unresponsiveness of this area.

**Background rates**

The activity index is lower in area 7a than in area LIP before the saccade because activity is lower in area 7a in these phases, not because of the background rates in the two areas. Figure 5 shows that the background rates in area LIP are indeed somewhat higher than those of area 7a. Since the background rate reflects fixation behaviour, figure 5 may indicate that fixation activity is stronger in area LIP - at least in the specific conditions of the present task. A similar result was observed in a different series of experiments by Andersen et al. (1990).

**Distribution of the activity in phases and in combinations of phases**

The following criterion was used to characterise a neurone as "active": an excitatory response is defined by an activity index 2.0 or greater; an inhibitory response, by activity index -2.0 or smaller (see Methods for details).

We repeated the analysis of this section with a second criterion: a neurone was considered to have a response if its firing rate was significantly different from baseline, using a t-test with long bins (at least 200 ms). Since the results were similar, we present only the results obtained by the first criterion.

Figure 6 shows, for both areas LIP and 7a, the fractions of neurones that had excitatory or inhibitory responses. In area LIP, the fraction of excitatory neurones is similar in all phases (49%-63%). During the LS and S-Co phases, excitation is most frequent (both 63%). The fraction of inhibitory neurones in LIP also does not vary much from phase to phase (10%-17%). The total fraction of responding neurones, excitatory or inhibitory, was, in all phases, 62%-77%. The fraction of inhibitory neurones, out of the total number with excitatory or inhibitory responses, also did not vary much - from 14% (15/106) in the LS to 25% (24/95) in the Pre-S phase (N=145 for area LIP).

In contrast, in area 7a the fraction of neurones with excitatory responses varied considerably from phase to phase. Before and during the saccade, these fractions were small relative to LIP: from 44% of neurones with excitatory activity in the LS, down during M to only

22% in Pre-S, and up again - 40% for S-Co. Only during the post-saccadic phase, was the frequency of excitation (56%) as high as that in LIP. The incidence of inhibitory responses varied too (4%-18%). The time course of inhibition was roughly opposite that of excitation; the highest frequency of inhibitory responses (18%) occurred during the saccade. Consequently, the total fraction of responsive neurones (excitatory or inhibitory) varied from 48% in LS, down to 36% in Pre-S, and up to 64% in Post-S (N=50). The fraction of inhibitory responses out of the total responding varied in area 7a from 8% for LS (2/24), to 30% for M (6/20), peaking for Pre-S - 39% (7/18), and dropping to 12% (4/32) post-saccadically.

In individual neurones, each of the phases of the activity may or may not appear; when they appear, they may be excitatory or inhibitory, and of varying intensities. Figure 7 shows that for 145 LIP neurones studied, 124 (86%) had excitatory activity in *at least* one phase. Out of these neurones 83 (67%) had excitatory activity in more than one phase; 48 (39%) were excitatory in LS, M and S-Co phases. If one also counts the inhibitory phases, these fractions become even larger (65/145, 45%, responsive in the three phases). It thus becomes clear that the LS, M and S activities are integrated in LIP at the level of the single neurones.

A similar analysis to the one of figure 7 was not done for area 7a, because most of its neurones have little LS and M activities in this task.

Although it is clear that inhibitory responses occur in the IPL in the delayed-saccade task, we shall not discuss them in detail in the subsequent sections, because their low spike rates make them hard to study quantitatively.

**Latency of the S activity**

We determined the latency of the S activity with respect to the onset of the saccade in 85 area LIP and 33 area 7a neurones. Neurones with clear, robust S activity were selected for this analysis. The procedure is described in the Methods section. Note that negative latency values represent activity starting before the saccade, and positive values represent activity that follows the saccade.

The analysis is illustrated for an area LIP neurone in figure 8a. The latency determined here was 10 ms. Note that the last histogram bin before the saccade shows that the mean rate has already increased; however, this bin is not recognized statistically. This example illustrates that the latency values obtained in this method are higher bounds: they describe when the S activity has sufficiently developed to be significantly different from the baseline; but the saccadic activity could start earlier, and take time to grow.

Figure 8b shows that, in area LIP, the S activity of 61/85 units (72%) has started by the time the saccade begins (these units have latency less than or equal 0 ms). In contrast, in area 7a (figure 8c) only 6/33 units (18%) have S activity starting by that time.

Even though the distribution of latencies in area LIP (figure 8b) is centered on the beginning of the saccade, its range is large: -200 msec to 200 ms. In area 7a the range of the observed latencies is shifted to later values: -50 to 380 ms. (Indeed, even higher latencies might exist in some neurones; they would not show in our data because trials were terminated 500 ms after the completion of the saccade). The distribution of latencies in area 7a is broader; this is reflected in a higher value of its standard deviation (134 ms, cf. 78 ms in LIP).

The mean latency in area LIP is presaccadic (-10.5 ms). The mean latency in area 7a is post-saccadic (140 ms). This difference is statistically significant (2-sample t-test with separate variance estimates, t=6.06, df=40, null hypothesis rejected with alpha=0.01).

**Activity offset and duration of the S activity**

We determined how long after the end of the saccade the S activity lasted. Figure 9a illustrates the procedure. The statistical method used for this comparison is identical to the one used for the measurement of the latencies (see Methods). Here, the trial traces are aligned on the end of the saccade. The 'detect' interval begins at the end of the saccade, and continues close to the end of the trials. The 'baseline' interval in this case is taken from the fixation interval in the beginning of the trial, before the presentation of the target stimulus; the reason is that we test when the activity level returns to background. Note that at the end of the trial the monkey had to keep his eye for 500 ms where the stimulus had been, i.e., to "fixate" a remembered location although

without a visual stimulus. The time of offset of the S activity is defined as the midpoint of the last 20 ms bin marked by the t-test, relative to the end of the saccade.

Figure 9b illustrates the results for area LIP. The S activity clearly outlast the saccade, often by more than 100 ms (the median offset is 120 ms).

The results for area 7a (not shown) are similar, although the graph spreads out to higher values (the median is 300 ms) since many area 7a neurones are post-saccadic.

Now that we have the latency and the offset times of the S activity for each saccade, we can add them to the time of the saccade itself to obtain the duration of the S activity. The distributions of these durations, for area LIP and for area 7a, are shown in figures 10a and 10b, respectively.

For both areas LIP and 7a, the distributions obtained for the S activity durations were approximately Gaussian. The parameters of these distributions were also similar: the median duration was 210 ms in both LIP and 7a; and the mean ± s.d. was 211±104 ms for area LIP, 235±113 ms in area 7a.

The similarity of the distribution of the durations in the two areas indicates that the main difference between the S activity in the two areas is in the time they start, that is, their latency with respect to saccade onset. Note that the duration of the burst is usually considerably longer than the duration of the movement which is normally about 60 ms for the 15-20 deg saccades used in the present study. Since, for more than half the LIP units, the S activity begins before the saccade, we conclude that typically in area LIP the S activity is peri-saccadic. In area 7a, however, it is typically post-saccadic.

**Latency of the LS activity**

The latency of the LS activity was defined as the time, relative to the onset of the target stimulus, when the activity became significantly higher than that of the previous fixation interval (background). This procedure is illustrated in figure 11a for an area LIP neurone. The final part of the initial fixation (at least 300 ms), immediately preceding the presentation of the target, was used as the baseline interval. The detect interval started when the target light was turned on, and continued at

least for the duration of the target stimulus (in some neurones, with late LS activity, it was continued even further). The onset latency for this cell was 90 ms.

Sixty-three neurones from area LIP that had clear LS responses were used for this analysis. Figure 11b shows the distribution of LS latencies obtained from these neurones. The shortest LS latency found is 50 ms; the sample median is 110 ms. 51 LIP neurones (81%) have LS latencies less than 140 ms; the rest of the units had their LS latencies spread in a range of much higher values (max 270 ms), giving the distribution of the LS latencies a skewed shape.

The LS activity recorded from area 7a is, at least in the present behavioural task, considerably weaker than that of area LIP, as was illustrated earlier. Only 13 of the neurones studied in area 7a had a response robust enough for their LS latencies to be reliably evaluated. The distribution of the LS latencies of these neurones is presented in figure 11c. Comparison of figures 11b and 11c shows clearly that the typical LS latency values of area 7a are higher than those of area LIP; the median LS latency of area 7a is 170 ms. The difference in means between the distributions of these two areas is statistically significant (two sample t-test with separate variance estimates, $t=3.405$, $df=16$, $P<0.01$; mean±sd for LIP 116±46 ms; for area 7a 165±48 ms).

The functional significance of this difference in LS latencies is not clear. It may reflect a longer anatomical pathway, since LIP occupies a lower position than 7a in the hierarchy of visual cortical areas. (Area LIP can be reached from striate cortex with only one stop in extrastriate cortex, e.g., in area MT; while reaching area 7a requires at least two stops - see Andersen et al. 1990). It might be argued that the difference in latencies may also be due to the difference in strength of the response between areas LIP and 7a, since weak responses typically have longer latencies. However, the area 7a neurones included in this analysis all had an activity index over 2, the same requirement as for area LIP neurones, and thus this the overall difference in the level of activity does not directly explain the different LS latencies.

## DISCUSSION

### Sensorimotor integration in area LIP

In this chapter we have shown that in area LIP there are both visual and saccade-related activities. Moreover, the integration of these types of activity occurs on the level of single neurones. The sensorimotor nature of the activity in area LIP is exemplified by the existence of memory responses within it. Since these responses are initiated by a visual stimulus and terminated by a motor act, they are sensorimotor in nature.

Area 7a, in contrast, shows weaker activity in the periods up to and including the saccade. The most prominent activity in the population of area 7a units studied was post-saccadic. This suggests that, unlike area LIP, area 7a does not play a major role in the planning of saccades.

In area LIP 63% (91/145) units have clear, excitatory LS responses. The same percentage of neurones have clear, excitatory S-Co responses. If a neurone has excitatory LS activity, there is a 69% (63/91) probability that it will also have S-Co activity (and vice versa). These percentages are even higher if one counts units with either excitatory or inhibitory responses. Clearly, then, some form of visuomotor integration is likely to be occurring at the level of individual LIP neurones.

In the present study we have confirmed and extended the results of Gnadt and Andersen (1988) on memory responses in IPL neurones. Many (57%, 83/145) area LIP neurones show a maintained activity during the delay period of a delayed saccade trial, that is, after offset of the target until the saccade is made. Furthermore, 76% (48/63) of the neurones having both LS and S-Co responses also have M activity. It is important to recall that there is no visual stimulation nor movement during this delay period. Typically the memory activity is excitatory, but in some units the firing is suppressed to below background (see Results; figure 3). The memory activity is spatially tuned, typically closely matching the LS and presaccadic tuning of the unit. We suggest (see chapter 6) that this activity reflects the planning of saccades.

**Functional differences between areas LIP and 7a**

Until recently, area 7 has been treated as a single area in physiological investigations (e.g. Hyvarinen and Poranen 1974; Mountcastle et al. 1975; Robinson et al. 1978). However, in the last few years several anatomical studies have suggested that area 7 may be partitioned into subdivisions, including areas LIP and 7a. (e.g., Seltzer and Pandya 1980; Barbas and Mesulam 1981; Pandya and Seltzer 1982; Lynch et al. 1985; Andersen et al. 1985, 1990; Asanuma et al. 1985; Blatt et al. 1990; reviewed in chapter 1). However, the functional significance of these subdivisions had not been carefully investigated physiologically.

In the present study we have found clear differences in the patterns of activity between areas LIP and 7a, when tested in the same animals, and with the same paradigm (the delayed saccade). First, in terms of the average activity of the population: in area LIP there is a strong response to the visual stimulus, and the activity remains high until the completion of the saccade itself. In contrast, in area 7a the most prominent activity in the population of units studied was post-saccadic (see section "Population profile of the response"). Second, clear presaccadic activity was found in 72 % (61/85) of the neurones tested in area LIP, but only in 18% (6/33) of the units from area 7a. The mean latency of the S activity was -10.5 msec in area LIP, but +140 msec in area 7a (see section "latency of the S activity"). The duration of the S activity was nevertheless similar (median 210 ms in both areas). Third, the visual response was also quicker in area LIP than in 7a; the median latency for the LS response was 110 ms in LIP and 170 ms in area 7a.

These differences between the activity in areas LIP and 7a are consistent with the different connexions of the two areas. Area LIP was originally defined on the basis of its much stronger connexions than area 7a (or, indeed, other IPL subdivisions) with known saccade centres, such as the superior colliculus and the frontal eye fields (Andersen et al. 1985a, 1990; Lynch et al. 1985). This pattern of connections supports the hypothesis that area LIP, specifically, plays a role in the preparation of saccades. Also, area LIP occupies a lower position than area 7a in the hierarchy of visual cortical areas; area LIP can be reached from striate cortex with only one stop in extrastriate cortex (e.g., in area MT), while reaching area 7a requires at least two stops (Andersen et al. 1990). This

is consistent with the shorter LS latencies in LIP, as compared to those of area 7a.

The apparently weak LS responses in area 7a reported in this chapter are probably due to the specific paradigm that we have used. We did not make any attempt to find the "optimal" visual stimuli for the neurones we recorded. We do not wish to suggest that area 7a is not a visual area.

In summary, we have shown that there are clear differences between areas LIP and 7a in the timing and strength of the responses of neurones during delayed saccades. Although typically the ranges of these parameters (e.g., S activity latencies) in LIP and 7a overlap to some degree, the differences in their distributions are significant. We believe that these differences establish the existence of a difference in function between these two areas. More specifically, these findings suggest that a major function of area LIP, but not of area 7a, is in the planning of visually-guided saccadic eye movements.

**Planning of saccades *vs.* dynamic control**

Evidence presented in this and subsequent chapters suggests that the large proportion of pre-saccadic LIP neurones that have tonic, M activity, may be involved in the planning of saccades. The S activity of many LIP neurones starts before and lasts at least for the duration of the saccade. Do LIP neurones with such S activity have a role in the "real time" dynamic control of saccades (in the sense of Robinson's 1975, or related, models of the execution of saccades)? We did not set out to investigate this issue in the present experiment and we cannot rule out the possibility that a minority of LIP neurones do participate in dynamic control of saccades. Nevertheless, we believe that this is not the case for most LIP neurones for the following reasons. First, the S activity of most LIP neurones is much longer (mean 211 ms) than the duration of the saccadic movement itself (about 60 ms). Second, the firing rate usually does not vary much during the saccade. We therefore conclude that LIP is likely to play a role in higher level processes related to the planning of saccades, rather than in the control of the execution of such movements.

**Relation to previous delayed response studies**

Various delayed response tasks have been used to investigate neuronal mechanisms of short-term memory in several other areas of the brain, e.g., the prefrontal cortex (Fuster 1973; Watanabe 1986; Joseph and Barone 1987), the nucleus dorsalis (Fuster and Alexander 1973), the inferotemporal cortex (Fuster and Jervey 1982) and the hippocampus (Watanabe and Niki 1985). Neurones in the premotor cortex (e.g., Wise and Mauritz 1985), area 5 (Crammond and Kalaska 1989) and the putamen (Alexander 1987) have been shown to demonstrate directionally specific delay period activity in tasks requiring the monkey to make arm movements to the remembered locations of visual targets. Sustained activity during the delay period of the delayed saccade task has been recorded in the substantia nigra pars reticularis (Hikosaka and Wurtz 1983c), the caudate nucleus (Hikosaka and Wurtz 1989), and in the prefrontal cortex and the frontal eye fields (Funahashi et al. 1989, 1990). These high-level motor areas, like area LIP, may participate in the planning of movements, and the delay period activity may be a common manifestation of this role.

## LEGENDS

**Figure 1:**

Reconstructions of the locations of neurones recorded in the left (figure 1a) and right (figure 1b) hemispheres of the first monkey. The panels on the top left of figures 1a and 1b show the entry points of electrode penetrations. The other panels show the reconstructed locations of recording sites drawn onto representative coronal sections. The dotted lines indicate the border between area LIP, in the bank of the intraparietal sulcus, and area 7a, on the gyral surface.

**Figure 2:**

(a) Sequence of events in a memory saccade and a typical response of an LIP neurone. (b) Sequence of events and response of the same LIP neurone to a control task, demonstrating that the S activity is not a response to the offset of the fixation spot. Onset and offset times, for both target and fixation spot, are indicated both in the schemes at the lower part of the figures, and by the dotted vertical lines above. Shown, from the top, are the spike rasters, where each horizontal trace represents a trial, and each tick within a line marks the time of occurance of a spike; the resulting histogram (bin width 25 msec); and the horizontal and vertical eye position traces of the various trials, superimposed. Trials are aligned on the sensory events (note variable saccadic latencies). Figure 2a illustrates the three typical phases of activity (LS, M, and S) described in the text. The lack of activity in figure 2b demonstrates that this neurone has neither on nor off visual response to the fixation spot.

**Figure 3:**

Delayed saccade tasks with delay periods of different durations, showing that the memory activity is initiated by the visual stimulation and is terminated by the saccade. Figures 3a, c show the response of an area LIP neurone in memory saccade trials with delays of 500 and 1300 ms. The increased level of activity is maintained throughout the delay period until the saccade is made. Figures 3b, d show the response of

another area LIP neurone, which shows an inhibition of activity during the delay period. The shown memory saccades are with delays of 400 and 2000 ms. Memory inhibition is maintained until the saccade is made. Shown, from the top, are the spike rasters and the histograms; the horizontal and vertical eye position traces of the various trials, are superimposed. Trials are aligned on the sensory events. The vertical dotted lines denote, from the left, the of onset and offset of the target, and the offset of fixation spot.

**Figure 4:**

The median of the absolute value of the activity index is a measure for the overall level of response. It is calculated for each phase of the delayed saccade task, for neurones from areas 7a and LIP. Activity in area LIP remains relatively high throughout the trial. In contrast, activity in area 7a is low until the saccade is made.

**Figure 5:**

The distributions of background spike rates for neurones in areas LIP and 7a. The background rate of a neurone is measured during the initial fixation in delayed saccade trials, before target presentation. LIP background rates, thus defined, tend to be higher than those of area 7a.

**Figure 6:**

The percentage of neurones from areas LIP and 7a showing excitatory or inhibitory responses, during each phase of the delayed saccade task. A neurone was deemed to show an excitatory (or inhibitory) response during a given phase if its activity index during that period was greater than 2.0 (or less than -2.0).

**Figure 7:**

The numbers and percentages of LIP neurones with excitatory responses in each phase LS, M and S-Co and combinations thereof. Of the 145 LIP neurons, 63% show excitatory LS responses, 50% excitatory M responses and 63% excitatory S-Co responses.

**Figure 8:**

Latency of the saccade-related activity. (a) Determination of the latency for an individual LIP neurone. Delayed-saccade trials, in the neuron's preferred direction, were aligned on the beginning of the saccade. Those histogram bins within the "detect" interval that showed significantly higher activity than the "base" period were marked (by small arrows beneath histogram bins). The latency of the S activity was defined as the time from the beginning of the saccades to the midpoint of the first marked bin. (Hence negative latency implies presaccadic start of the S activity). Shown, from the top, are the spike rasters and the histograms; the horizontal and vertical eye position traces of the various trials, superimposed. Vertical dotted line denotes beginning of the saccades. (b) Distribution of latencies of the S activity for neurones in area LIP. (c) Distribution of latencies of the S activity for neurones in area 7a.

**Figure 9:**

Activity offset of saccade-related activity in area LIP neurones. (a) Determination of the S activity offset for an individual LIP neurone. Delayed-saccade trials, in the neuron's preferred direction, were aligned on the end of the saccade. Those histogram bins within the "detect" interval that showed significantly higher activity than the "base" period were marked (by small arrows beneath histogram bins). The offset of the S activity was defined as the time from the end of the saccades to the midpoint of the first marked bin. Shown, from the top, are the spike rasters and the histograms; the horizontal and vertical eye position traces of the various trials, superimposed. Vertical dotted line denotes the end of the saccades. (b) Distribution of the S activity offsets for neurones in area LIP.

**Figure 10:**

Duration of the saccade-related activity. (a) Distribution of durations in area LIP. (b) Distribution of durations in area 7a.

**Figure 11:**

Latency of the LS activity. (a) Determination of the LS latency for an individual LIP neurone. Delayed-saccade trials, in the neurone's preferred direction, were aligned on the time of presentation of the target stimulus. Those histogram bins within the "detect" interval that showed significantly higher activity than the "base" period were marked (by small arrows beneath histogram bins). The latency of the LS activity was defined as the time from the target presentation to the midpoint of the first marked bin. Shown, from the top, are the spike rasters and the histograms; the horizontal and vertical eye position traces of the various trials, superimposed. The vertical dotted lines denote, from the left, the of onset and offset of the target, and the offset of fixation spot. (b) Distribution of latencies of the LS activity for neurones in area LIP. (c) Distribution of latencies of the LS activity for neurones in area 7a.

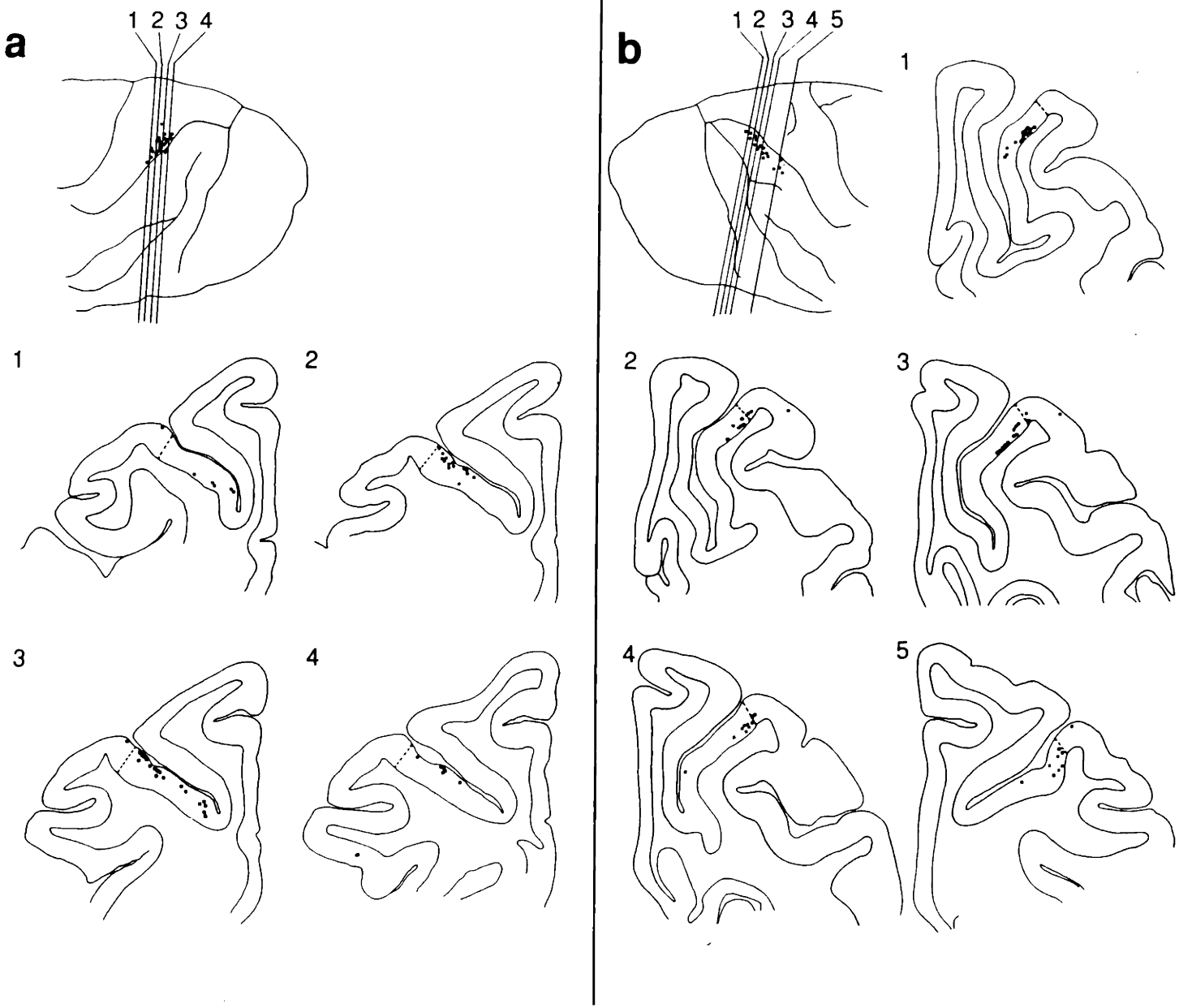



Figure 1

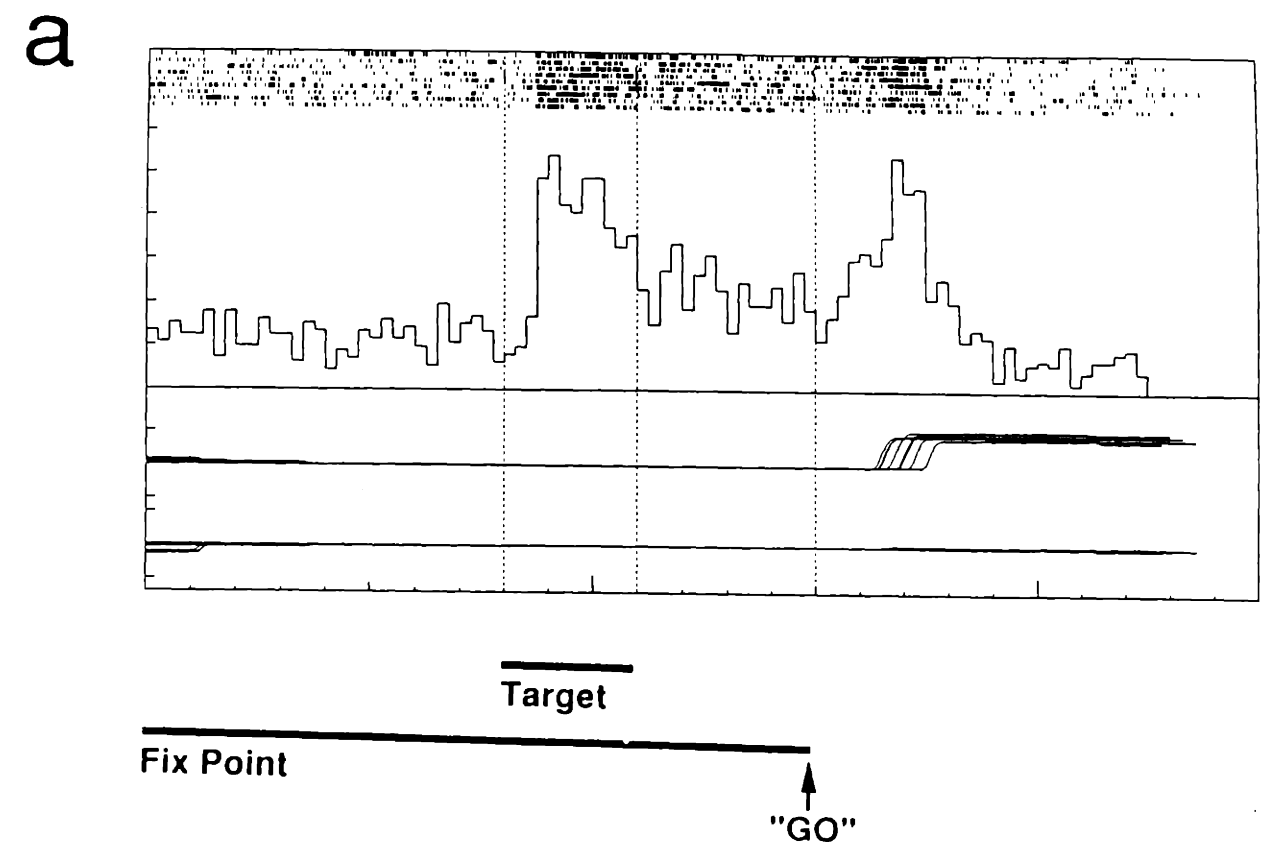

a
Target
Fix Point
"GO"
b
50 imps/sec/div
H
V
15 °/div
100 msec/div
No Target
Fix Point



Figure 2

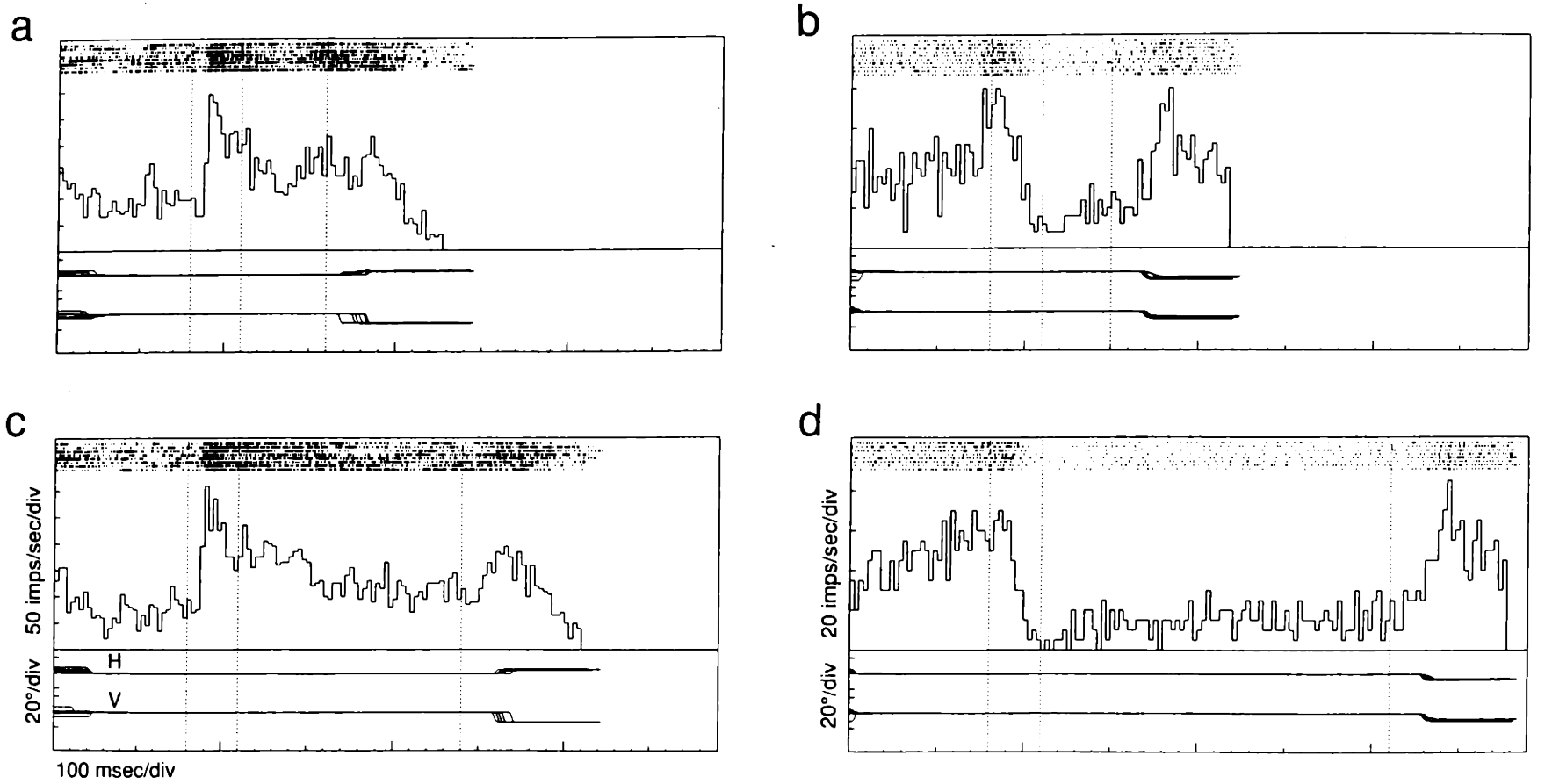

a
b
c
d
50 imps/sec/div
20°/div
H
V
100 msec/div
20 imps/sec/div
20°/div

Figure 3

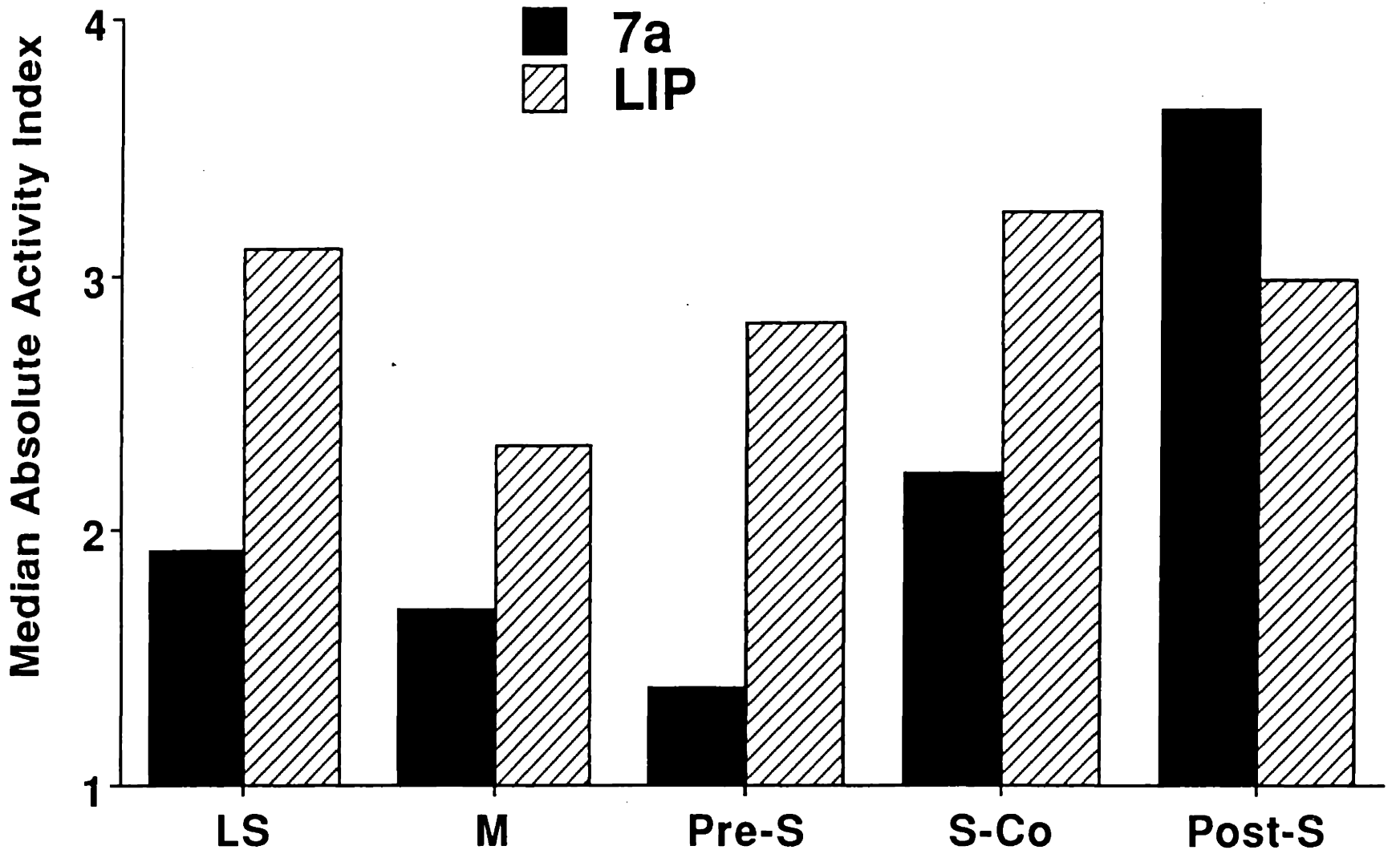

Median Absolute Activity Index
4
3
2
1
7a
LIP
LS
M
Pre-S
S-Co
Post-S

Figure 4

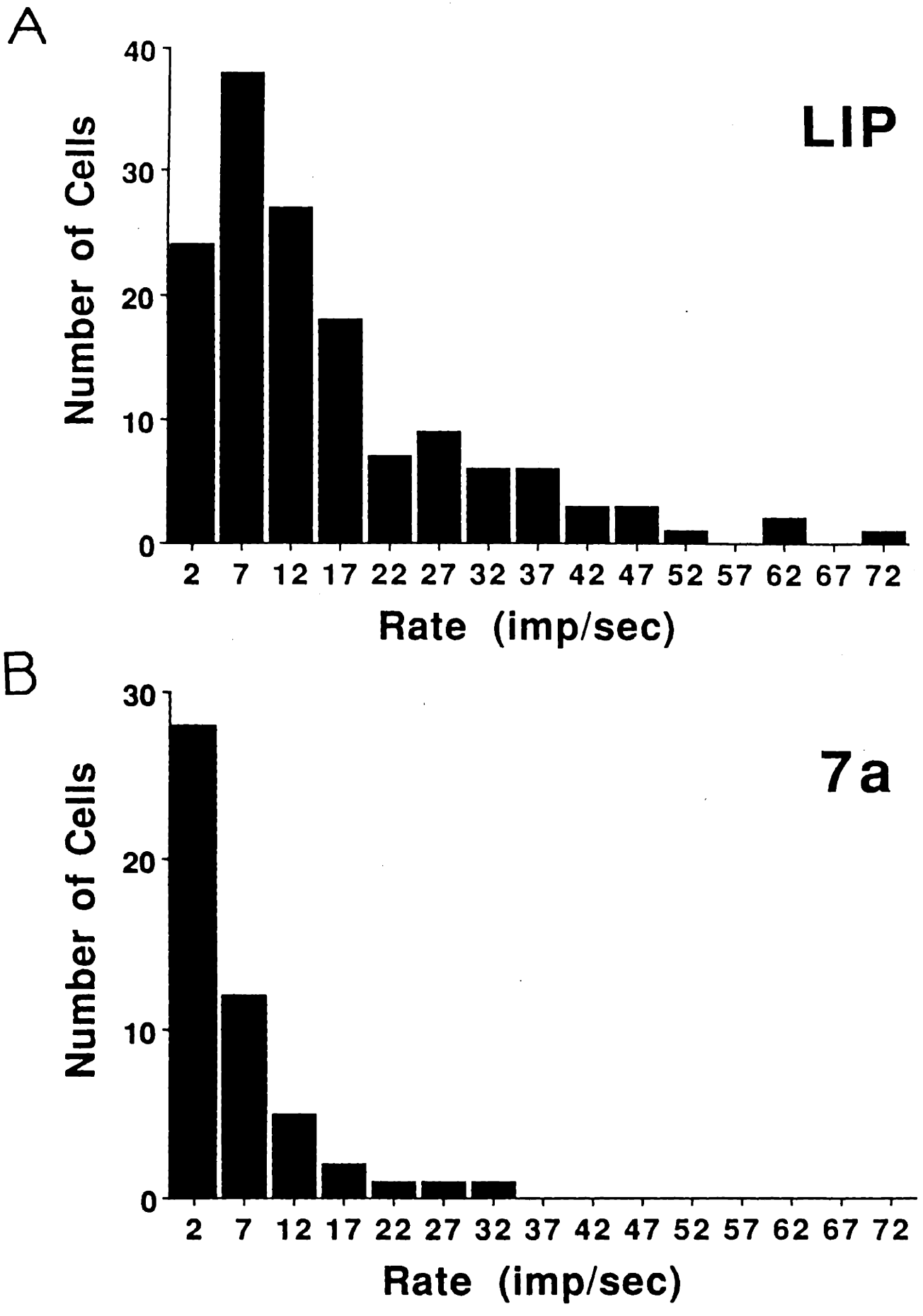

A
LIP
Number of Cells
40
30
20
10
0
2 7 12 17 22 27 32 37 42 47 52 57 62 67 72
Rate (imp/sec)
B
7a
Number of Cells
30
20
10
0
2 7 12 17 22 27 32 37 42 47 52 57 62 67 72
Rate (imp/sec)

Figure 5

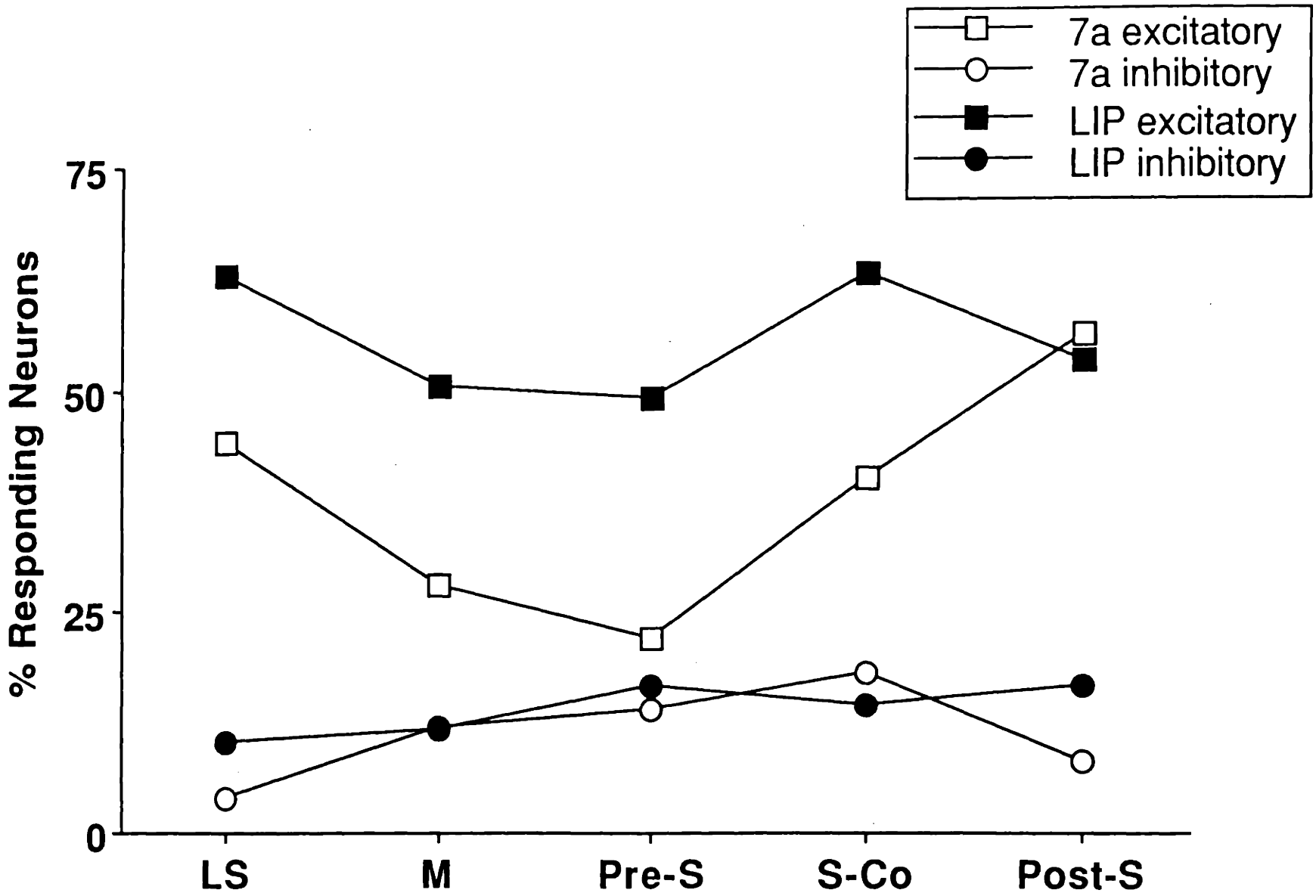

7a excitatory
7a inhibitory
LIP excitatory
LIP inhibitory
% Responding Neurons
75
50
25
0
LS
M
Pre-S
S-Co
Post-S

Figure 6

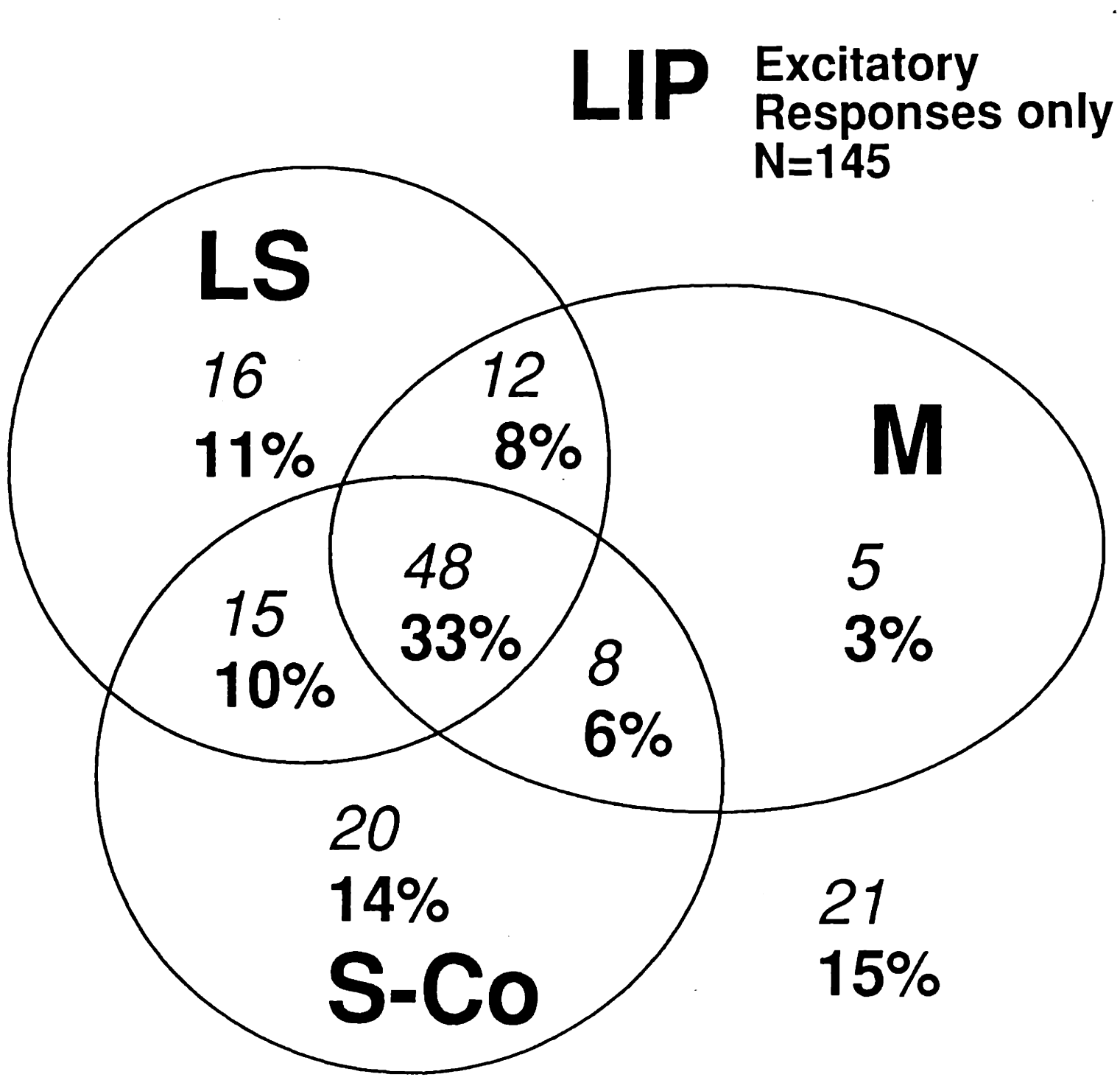
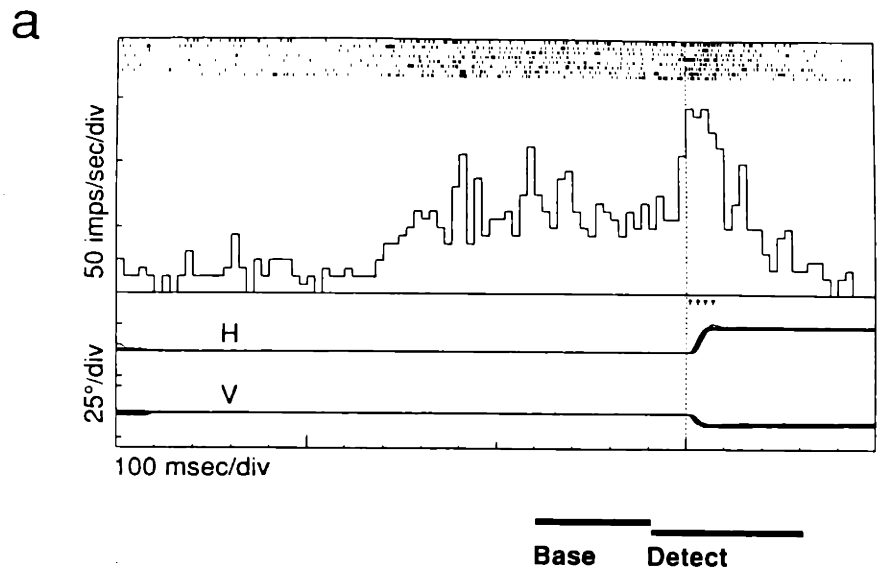
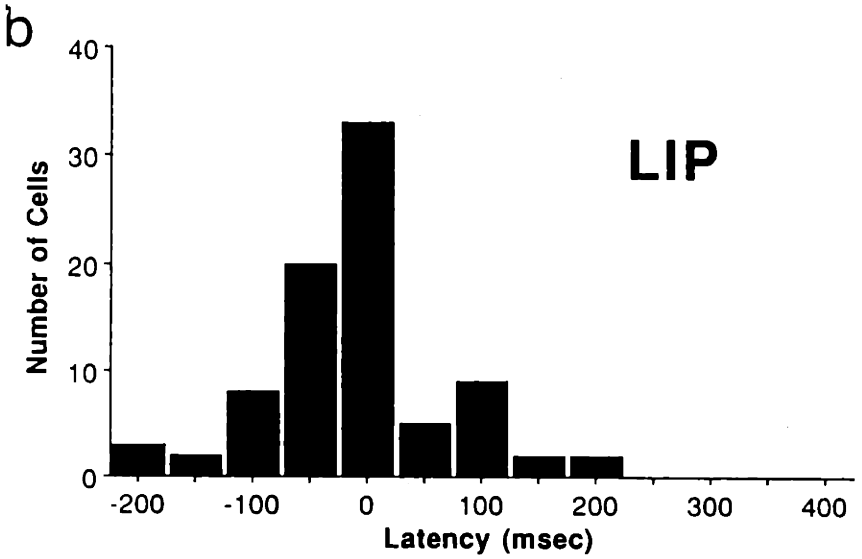

LIP
Excitatory
Responses only
N=145
LS
16
11%
12
8%
M
48
33%
15
10%
5
3%
8
6%
20
14%
S-Co
21
15%

Figure 7


a
50 imps/sec/div
H
V
25°/div
100 msec/div
Base
Detect


b
LIP
Number of Cells
40
30
20
10
0
-200
-100
0
100
200
300
400
Latency (msec)

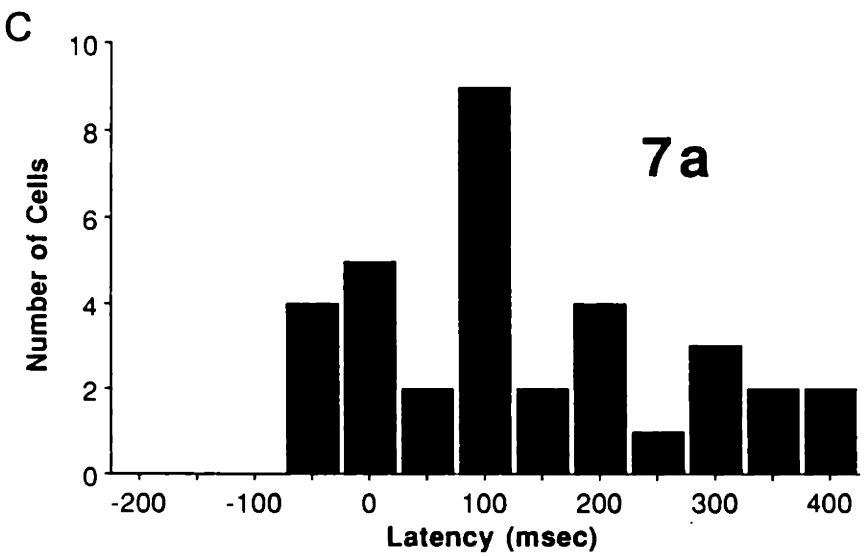
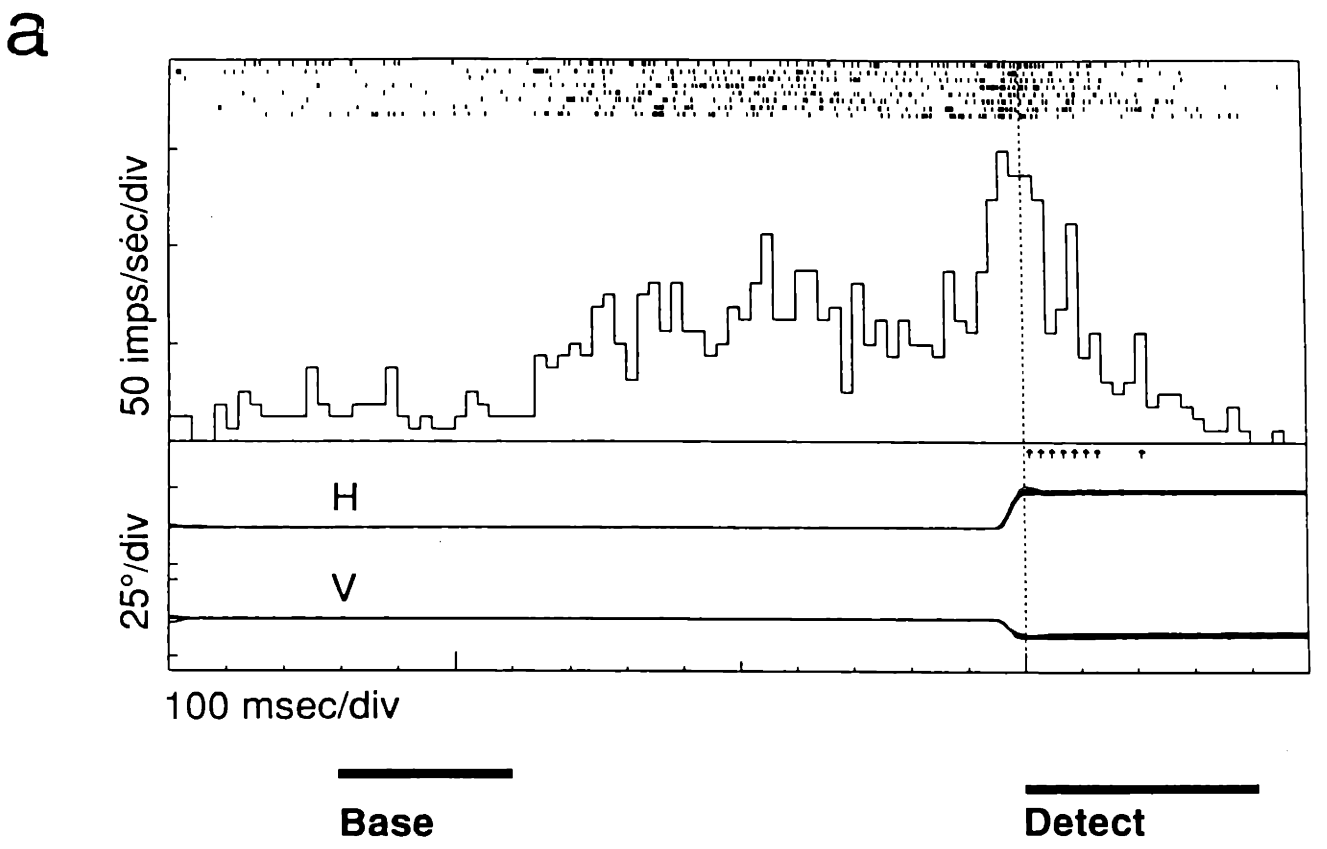

c
7a
Number of Cells
10
8
6
4
2
0
-200
-100
0
100
200
300
400
Latency (msec)

Figure 8


a
50 imps/sec/div
H
V
25°/div
100 msec/div
Base
Detect

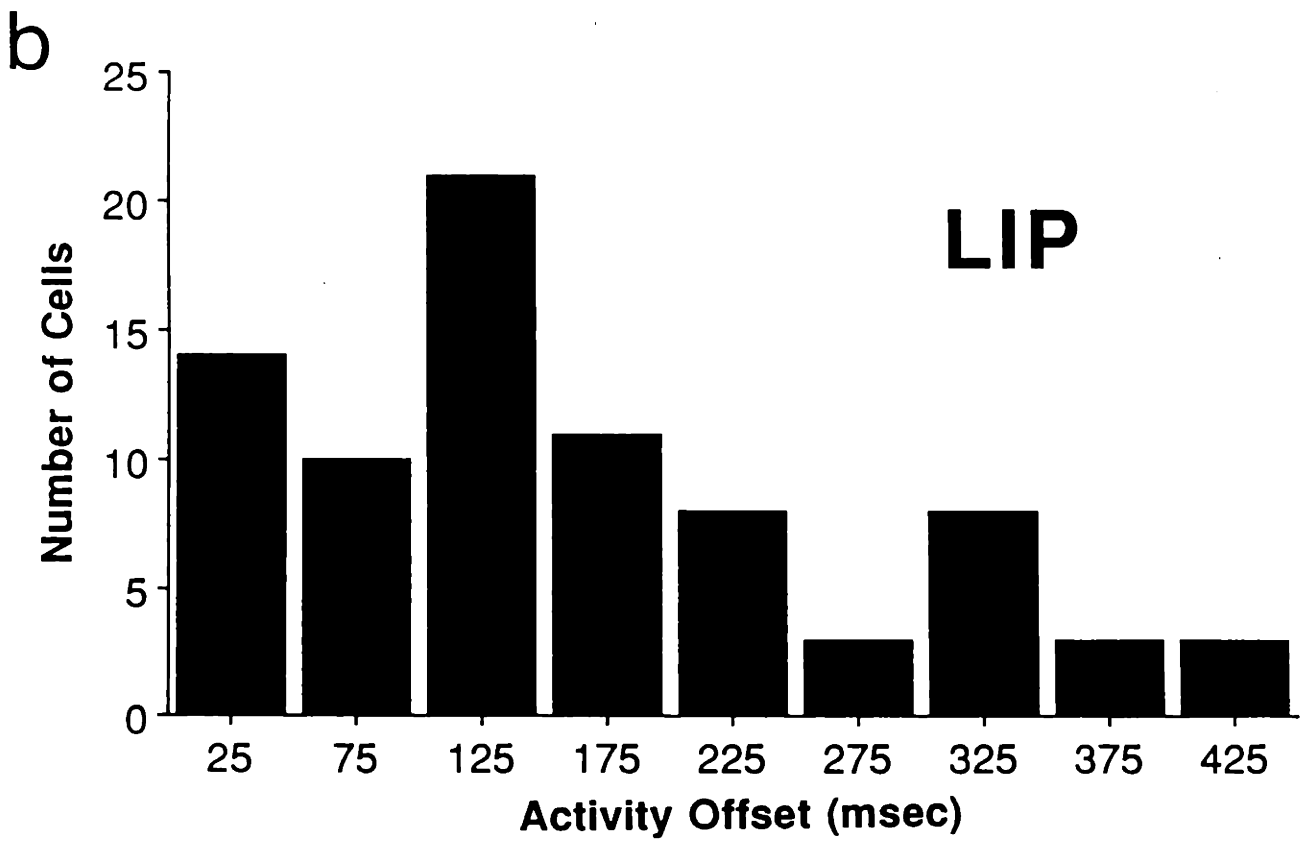

b
LIP
Number of Cells
0
5
10
15
20
25
25
75
125
175
225
275
325
375
425
Activity Offset (msec)

Figure 9

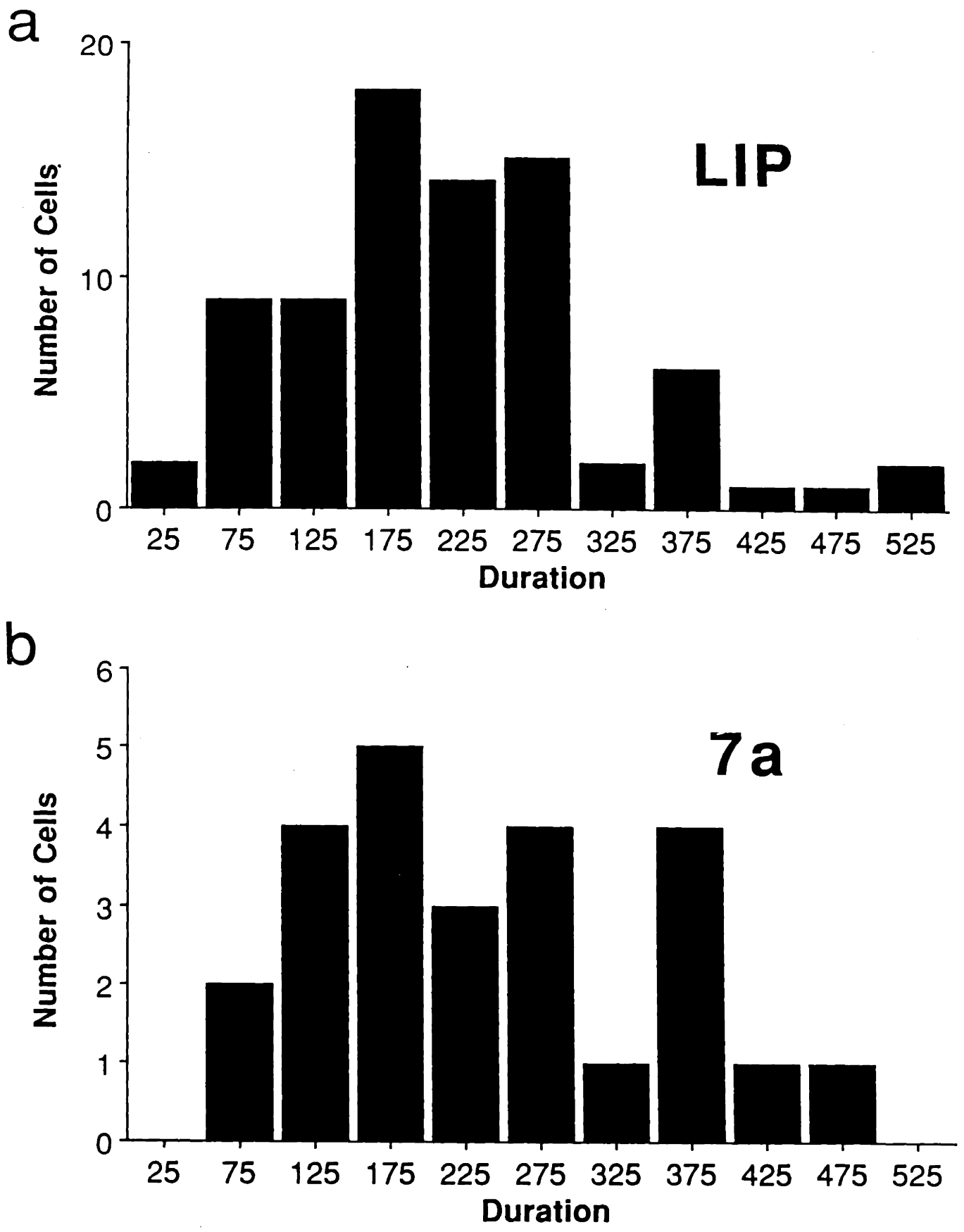
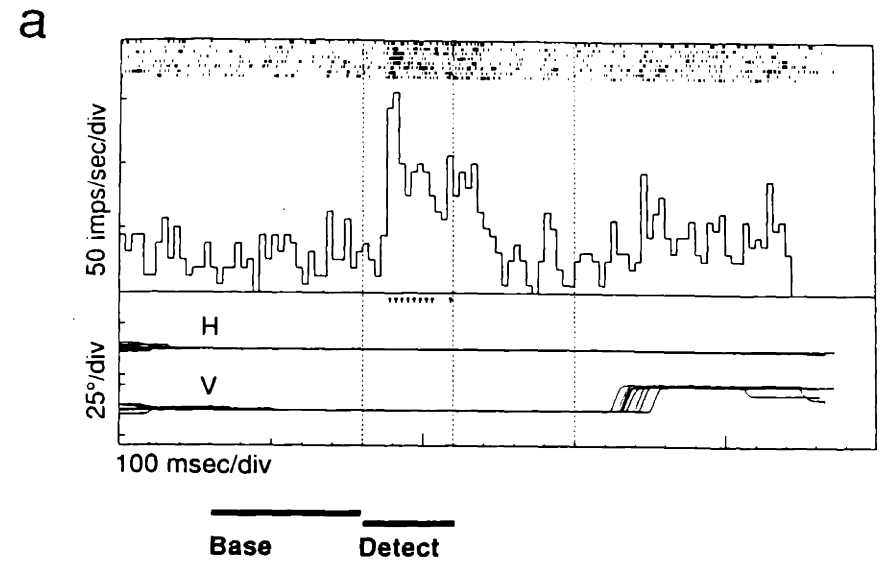
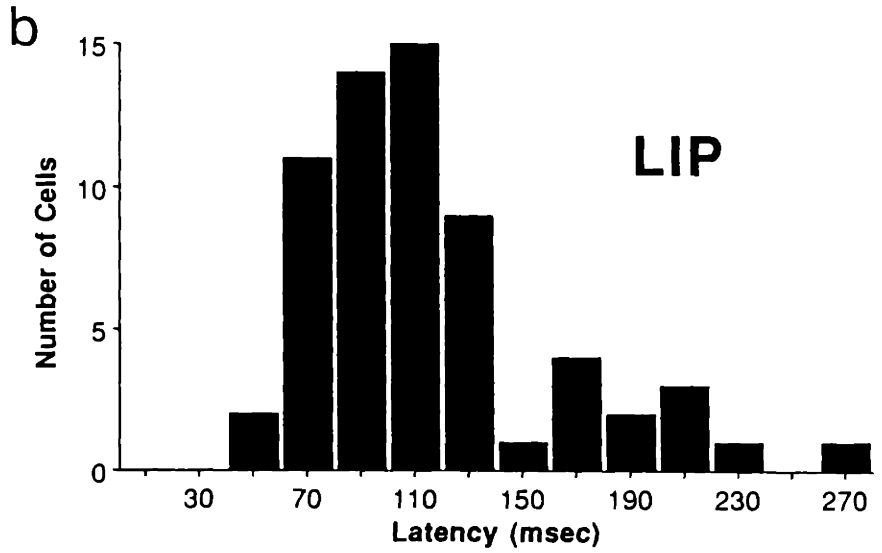

a
20
10
0
Number of Cells
LIP
25
75
125
175
225
275
325
375
425
475
525
Duration
b
6
5
4
3
2
1
0
Number of Cells
7a
25
75
125
175
225
275
325
375
425
475
525
Duration

Figure 10


a
50 imps/sec/div
H
V
25°/div
100 msec/div
Base
Detect


b
LIP
Number of Cells
15
10
5
0
30
70
110
150
190
230
270
Latency (msec)

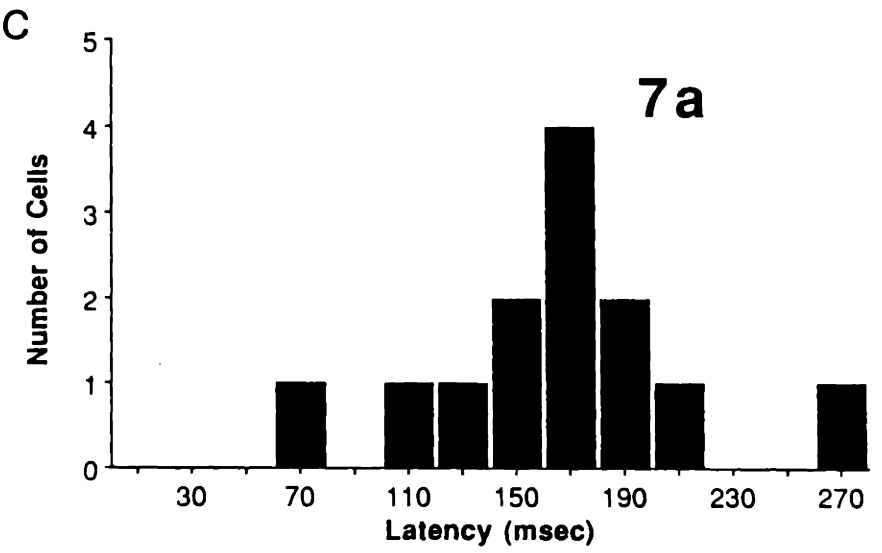

c
7a
Number of Cells
5
4
3
2
1
0
30
70
110
150
190
230
270
Latency (msec)



Figure 11

# Chapter 3

## Visual, motor intention and saccade-related activity in area LIP: spatial characteristics

## SUMMARY

1. Single neurone activity was recorded from the inferior parietal lobule (IPL) of *Macaca mulatta* monkeys while they were performing delayed saccades and related tasks. Temporal characteristics of this activity were presented in chapter 2. Here we focus on the spatial characteristics of the activity. The analysis was based on recordings from 145 neurones. All these neurones were from the lateral intra-parietal area (LIP).

2. Delayed saccades were made in eight directions. Direction tuning curves were calculated for each neurone, during each of the following activity phases that were described in chapter 2: light-sensitive (LS), delay-period memory (M), and saccade-related (S). The last phase was further partitioned into pre-saccadic (Pre-S), saccade-coincident (S-Co), and post-saccadic (Post-S) phases.

3. Width and preferred direction were calculated for each direction tuning curve. We studied the distributions of widths and preferred directions in LIP's neuronal population. In each case we included only neurones that showed clear excitatory activity in the phases in question.

4. Width was defined as the angle over which the response was higher than 50% of its maximal net value. Width distributions were similar for all phases studied. Widths varied widely from neurone to neurone, from very narrow (less than 45 deg) to very wide (close to 360 deg). Median widths were about 90 deg, in all phases.

5. Preferred-direction distributions were also similar for various phases. All directions were represented in each distribution, but contralateral directions were more frequent (e.g., 69% for S-Co).

6. For each neurone, the alignment of the preferred directions of its various phases was determined. Distributions of alignments were calculated (again, phases that were not clearly excitatory were disregarded). On the level of the single neurone, LS, M, and Pre-S were well aligned with each other. S-Co was also aligned with these phases, but less precisely.

7. A set of "narrowly tuned" neurones was selected by imposing a constraint of narrow (width less than 90 deg) LS and S-Co direction tuning. In this set of neurones, the LS and S-Co preferred directions were very well aligned (median 12 deg). The fraction of narrowly

tuned neurones in the population was 40% (25/63). Thus, in a large subpopulation of area LIP units, a fairly precise alignment exists between sensory and motor fields.

8. An additional 82 area LIP neurones were recorded while the monkey performed delayed saccades to 32 targets located on small, medium, and large circles. Preferred directions were calculated for each activity phase of each neurone, separately for each of the 3 circles. Preferred directions of the same phase were well aligned on the different circles. This observation supports the existence of direction preference, not strictly dependent on eccentricity. We also calculated alignment between different phases separately for each circle. The distributions of alignments were similar, indicating that our results are not a peculiarity of the eccentricities used.

9. The post-saccadic activity was not well-aligned with the pre-saccadic phases. The distribution of alignments of the post-saccadic activity with the pre-saccadic phases were flat.

10. We recorded 33 neurones while the monkey was performing back and double saccade paradigms. Neurones in LIP become active in anticipation of a saccade made into their motor field even if no visual stimulation has occurred in their receptive field, that is, these neurones code in motor coordinates.

11. These characteristics of the activity in area LIP suggest that this cortical region is involved in the transformations of visual information for the planning of saccadic eye movements.

## INTRODUCTION

The lateral intra-parietal area (LIP) is a subdivision of the inferior parietal cortex (IPL) originally defined by its strong anatomical connexions to established saccade centers, e.g., the superior colliculus and the frontal eye fields (Andersen et al. 1985a; Lynch et al 1985; reviewed in chapter 1). These anatomical connexions lead to the hypothesis that within the IPL, area LIP is specialised for processing saccades. Here and in the preceding chapter, we investigated the saccade activity in area LIP, in the light of this hypothesis.

An important paradigm in investigating the IPL as well as other saccade-related structures has been the delayed-saccade task (Hikosaka and Wurtz 1983c). Using this paradigm, Andersen and colleagues (1987) showed that both light-sensitive (LS) and saccade-related (S) activities in IPL neurones are distinguishable. Further, Gnadt and Andersen (1988) described a third type of activity, specific to the delay period, called memory (M) because it was presumed to be related to the memory of the location of the target for the forthcoming movement. However, these and other earlier studies did not explore the distribution of these types of activity within the subdivisions of the IPL. In the preceding chapter we showed, using delayed saccades, that area LIP contains vigorous LS, M, and S-Co activity. In contrast, in neighbouring area 7a, another major part of the IPL, these types of activity are weaker in delayed saccades, with the exception of the post-saccadic activity. Moreover, we showed that the majority of area LIP neurones that have saccade-related activity become active before the saccade, while in area 7a pre-saccadic neurones are only a small minority. Thus the hypothesis that area LIP is involved in saccades is corroborated.

In the present chapter we study the spatial characteristics of LIP neurones' activity. We find that the LS, M and S components of activity are all direction-tuned. At the single cell level, these three components are generally aligned with one another. In special double saccade tests we found that the M activity is coded in motor, not sensory, coordinates, suggesting that this activity is related to the planning of saccadic eye movements.

## METHODS

The general framework of the experiment has been described in the Methods section of the preceding chapter. Here we add information specific to the present chapter.

### Delayed saccades to eight locations

The nine target stimuli were usually positioned 15 degrees apart, on an imaginary grid centered on the fixation point. A grid was more suitable than a circle for other studies carried out in parallel on these neurones. We directly compared the responses of 15 neurones in the standard task to the responses obtained when the targets were placed on a circle with 15 or 20 deg radius. In both conditions, responses were similar.

The end points of the saccades were usually not identical to the locations of the targets. This is typical of saccades to remembered locations. We have studied the performance of monkeys in memory saccades in detail (see chapter 8). The main finding of relevance here was that there was an "up-shift" in the end points of memory saccades: they consistently end above the location in which the target had been presented. Saccades directed down are usually hypometric, while saccades directed upward are hypermetric.

We wished to examine whether the results of the present analysis depend on the differences between the target locations and the actual end points of the saccades. Therefore, for 25 neurones we carried out the analysis described in the rest of this chapter in parallel for both the locations of the targets and the locations of the actual end points of the saccades, and compared the two sets of data in detail. The results of the two sets were similar. In the rest of this chapter we define the direction of the saccade as the direction of the target.

### Delayed saccades to 32 locations

An additional group of 82 neurones was recorded from the second hemisphere of the second monkey in a complementary study, examining the activity fields at a higher grain of 32 locations. The criteria for classifying the neurones to area LIP were those described in

the Methods section of chapter 2. The delayed saccade paradigm was the same as described above, except for the location of the targets: in three distinct blocks of trials targets were placed in directions $q_i = 45i$ ( i=1,...,8), on circles of radii 7.5 deg, 15 deg, and 22.5 deg respectively (sometimes the radii were, instead, 5 deg , 15 deg, and 25 deg). In the fourth block targets were placed on a 15 deg circle, in directions 45i + 22.5 deg. The order of the blocks was varied from one neurone to another.

**Definition of the activity phases**

For the convenience of the reader, we reiterate here the activity phases used in this chapter, defined in the preceding chapter. (In a few neurones the times of the phases were slightly changed, to fit their patterns of activity.) (1) Background, 300-700 ms from "fixation attained"; (2) light-sensitive (LS), 75-275 ms from target onset; (3) memory (M), 200-400 ms from target offset; (4) pre-saccadic activity (Pre-S), 200 to 25 ms *before* the beginning of the saccade; (5) saccade-coincident (S-Co), 25 ms before the saccade to 75 ms after the beginning of the saccade; (6) post-saccadic (Post-S), 200-500 ms after the beginning of the saccade. The last three phases are based on alignments of the trials on the beginning of the saccade.

**Double-saccade and back-saccade tasks**

The double-saccade and back-saccade tasks (Mays and Sparks 1980a) were designed along similar lines to the delayed saccade task (for a description of the delayed saccade task, see Methods section of the chapter 2). The first part of a trial was identical in all tasks: a fixation spot was turned on, and the monkey had to foveate it within 1 s. "Fixation attained" was defined as the time-point in which the eye entered a specified window around the fixation spot. If the monkey failed to fixate the spot within the given 1 s, the trial was aborted, declared a "miss", and an inter-trial interval was begun.

In the double saccade task, 1 s after "fixation attained" the fixation spot was extinguished, and at the same time the first peripheral target spot was flashed for 60 ms; simultaneously with the offset of this first target spot, a second target spot appeared, also for 60 ms. The extinction

of the fixation spot served as a "go" signal for the saccade. Since the latency of the first saccade was always greater than 120 ms, both saccades were made in complete darkness. Within 500 ms of fixation spot offset, the monkey had to make a first saccade to the location of the first target. Then, within 1000 ms but not before 100 ms, a second saccade had to be made to the location of the second target. Following the second saccade, the monkey had to keep his eye at the location of the second target for an additional 300 msec. If the monkey fulfilled all these conditions, the trial came to a successful end (a "hit") and the animal received a reward, a drop of apple juice. If a trial had reached the "fixation attained" stage but failed to satisfy any of the subsequent conditions, the trial was aborted and declared an "error". (In some cases these timings were slightly varied).

In the most frequent arrangement of target positions, 8 classes of trials were randomly interleaved. In the first class, an up stimulus, (x,y) = (0,15), was followed by an up-and-right stimulus (15,15). In the second class, a right stimulus (15,0) was followed by up-and-right. The other classes consisted of the analogous paths in the other quadrants.

In the back saccade task the fixation spot was extinguished 800 ms after "fixation attained", and at the same time one peripheral target spot was flashed on the screen for 100 ms. Here, too, the offset of the fixation spot served as a "go" signal for the saccade. Since the saccadic latency was longer than the life-time of the target spot, all movements were made in the dark. Within 500 ms of fixation spot offset, the monkey had to make a first saccade to the location of the first target. Then, within 1000 ms, but not before 100 ms, a second saccade had to be made back to the location of the initial fixation spot. Following the second saccade, the monkey had to keep his eye inside the fixation point window for an additional 300 ms (again, these are typical timings). Fulfillment of all these conditions led to declaring the trial a "hit" and to rewarding the monkey; otherwise (if the "fixation attained" stage has already been reached) the trial was aborted and declared an "error". A typical run consisted of two pseudorandomly interleaved classes of trials. The peripheral stimulus appeared in these classes in opposite positions, e.g., down (0,-15) in one class, up (0,15) in the other. (Sometimes these were pseudorandomly interleaved with two additional classes, in which the fixation spot would reappear - facilitating the animal's task.)

The spatial windows used in double saccades and back saccades were similar to those used in the delayed saccades (see chapter 2).

**Direction tuning**

A direction tuning curve is defined as eight points in a polar plot, $(r_i, q_i)$, i=1,...,8, characterized by the following two conditions. (1) The directions of the points are 45 deg apart: $q_i = 45 \cdot i$, where 0 deg is horizontal contralateral, and 90 deg is upward. (2) The distance of the point from the origin, $r_i$, is proportional to the neurone's rate of activity in the period to which the tuning curve relates. Examples of direction tuning curves are given in figures 2 and 4.

The width of a direction tuning curve was defined as the angle over which the net activity was at least 50% its maximum. In more detail, the following procedure was applied: the points of the tuning curve were connected with linear segments (see figure 2). A threshold rate was defined as $r_{thr} = bck + 0.5 \cdot (r_{max} - bck)$ where $r_{max} = max \{r_1,...,r_8\}$, and bck is the average background rate. The width of the direction tuning curve was defined as the length of the unit circle sector(s) $\{ \alpha \mid -180 \le \alpha \le 180$ deg and $r(\alpha) \ge r_{thr} \}$.

Parametric curve-fitting has been used in cortical physiology to evaluate tuning-curve width (and preferred direction), applying various families of curves (e.g., Bruce and Goldberg, 1985; Georgopolous et al., 1982). Since the tuning curves we obtained had highly variable shapes (see, for instance, figures 2 and 4), we favoured a model-free approach.

The following algorithm was used to evaluate the preferred direction of a polar tuning curve (e.g., figure 2). To every line through the origin in direction $\alpha$, we set $S(\alpha) = \Sigma\, d^2(r_i, q_i, \alpha)$. Here $S(\alpha)$ is the sum of squared distances from the i'th point in the graph $(r_i, q_i)$, i=1,...,8 to the line: $d(r_i, q_i, \alpha) = r_i^2 \cdot \sin^2(q_i - \alpha)$. Since $\alpha$ is orientation, i.e., $S(180+\alpha) = S(\alpha)$, we can assume $0 \le \alpha \le 180$. We determined the $\alpha$ for which $S(\alpha)$ was minimal. To decide between $\alpha$ and $180+\alpha$, we formed the sum $S_p(\alpha) = \Sigma\, p(r_i, q_i, \alpha)$ of the (signed) projections of the points of the graph on direction $\alpha$: $p(r_i, q_i, \alpha) = r_i \cdot \cos(q_i - \alpha)$. The preferred direction was defined as a if $S_p(\alpha) \ge 0$, otherwise $180+\alpha$.

The reason we have implemented this algorithm rather than the more conventional center of mass (cf. Batschelet 1981), was that some direction tuning curves were bi-modal: in addition to the preferred direction a, there was activity above background also in direction 180+a. In such a situation the vector sum strongly fluctuates and does not reflect the cell's directionality, while our estimation of a remains robust. Note that bi-modal direction tuning curves were not typical, but occurred often enough to merit introducing this algorithm.

Statistically the estimation of a is unbiased by the fact that we always sample the same set of 8 directions; e.g., given the random 8 points ($r_i$, $q_i$), i=1,...,8 where $q_i = 45 \cdot i$, the estimated a's will be uniformly distributed, and not tend to cluster close to the sampled directions 45•i.

**Direction tuning of inhibitory responses**

In order to estimate the 'preferred direction' of inhibitory responses, the same procedure as in excitatory responses was applied, not to the spike rate, but, instead, to the inverse of the spike rate, or to the ratio background / spike rate. Care was taken to avoid extreme values, resulting from spike rates very close to zero. This substitution produced reasonable estimates for the directionality, but was too crude for estimating other parameters (such as width).

# RESULTS

## Visual and movement fields

Most LIP neurones are not active in all delayed saccades, but only in trials directed to certain parts of space. Figures 1 and 3 illustrate two LIP neurones active when a saccade is made (figure 1) in an up-and-right, up, up-and-left, left, or left-and-down direction, and (figure 3) in a right-and-down direction. If neurones are to contribute to spatial processing, their activity cannot be the same in all locations. Clearly, the LIP neurones depicted in figures 1 and 3 satisfy this requirement.

The three phases of activity described in chapter 2 - light sensitive (LS), delay-period memory (M), and saccade-related (S) - can be discerned in figure 1 in 5 of the 8 directions investigated. However, the relative intensities of each phase vary from one direction to another; for instance, the memory activity is almost as strong as LS or S-Co in leftward saccades, but is barely above background in the upward direction. The direction tuning of these phases is similar, but not identical.

Figure 2 illustrates direction tuning curves obtained for each phase of activity from the data plotted in figure 1. The bottom parts of figure 2 are polar graphs, i.e., the distance to each point in the graph from the origin is proportional to the average spike rate measured for saccades whose direction was the same as the direction of the point on the graph. Two curves in figure 2, Pre-S and S-Co, cannot be directly compared to figure 1. In these phases, an interval is marked in each trial with respect to the beginning of the saccade (described in detail in the Methods section). The latency of the saccade varies from trial to trial. Hence to directly convey the direction-tuning curves for Pre-S and S-Co, the trials in figure 1 must be shifted so that they are all aligned on the beginning of the saccade. The preferred direction for each tuning curve is indicated by the straight line emanating from the origin (see Methods for the details of this computation).

The direction tuning of the neurone depicted in figure 2 is very broad: in the S-Co phase, this neurone responds over a range of more than 180 degrees. The LS tuning curve is almost as broad; the M and Pre-S tuning curves are narrower. Note that the direction tuning curves, in all phases of the activity, are approximately aligned. More

specifically, the M and Pre-S tuning curves overlap each other almost precisely. The LS tuning curve is also similar in preferred directions to M and Pre-S (9 and 17 degs difference, respectively). The S-Co tuning curve, however, is different, particularly in the upward direction; and the S-Co preferred direction is less well aligned with those of LS, M, and Pre-s (31, 48 and 40 degs difference, respectively).

Figure 4 shows direction tuning curves of the neurone of figure 3. This neurone is clearly different from the one depicted in figures 1 and 2. The direction tuning of this neurone is much narrower, spanning primarily one direction, and the preferred direction is nearly the same for LS, M, and S-Co, thus resulting in an almost perfect alignment.

**Distribution of widths of tuning curves**

The width of a tuning curve was defined as the angle over which the net activity was at least 50% its maximum (see Methods for details). Figure 5 displays the distribution of widths for the S-Co phase. Included in this distribution are 91 LIP neurones with clear excitatory activity (S-Co activity index 2.0 or greater, see Methods section of chapter 2). Observed width values ranged widely - from 26 degs to 313 degs. One quarter of the units were broad - with width greater than 130 deg. For instance, the width of the S-Co phase in the unit displayed in figures 1 and 2 was 142 degrees. One quarter of the units were narrow - having width less than 69 deg; e.g., the width of the pre-saccadic activity of the unit of figures 3 and 4 was 47 deg wide. The remaining half of the units had width between 69 and 130 degrees - the sample median was 90 degrees, and mean ± sd were 105 ± 68. Therefore, a typical S-Co field spans roughly one quadrant.

The width distributions of the other phases were likewise calculated. The distributions were similar to the S-Co activity. The medians of the memory and pre-saccadic periods were slightly smaller (75, 69 deg respectively), and of the post-saccadic period slightly larger (103 deg).

The width of a phase, as defined here (see Methods), is normalised to the neurone's maximal level of activity in the phase under consideration. An alternative normalisation would be to the overall maximal activity of the neurone, in any phase. The maximal activity in M and Pre-S is somewhat lower than in LS and S-Co (chapter 2).

Hence, widths defined by this alternative normalisation would be somewhat narrower for M and Pre-S.

The 8-target paradigm we employed allowed a sampling resolution of 45 deg. Therefore, units with very narrow might be under-represented, because of sample aliasing. The excellent alignment found for narrow units may suggest, however, that such aliasing does not often occur. However, we also ran a further sample of 82 LIP neurones (isolated from the second hemisphere of the second animal) in which we sampled the tuning every 22.5 deg (and at eccentricities other than 15 deg). This analysis, described below, revealed no very narrow units, so we feel confident in our analysis based on a 45 deg sampling.

**Distribution of preferred directions**

A "preferred direction" was calculated for each tuning curve (i.e., for each neurone, in each phase with clear excitatory activity). Figures 2 and 4 show examples of tuning curves and the preferred directions assigned to them. Thus a neurone could have several preferred directions, e.g., on related to its LS and one to its S-Co tuning.

Figure 6 shows histograms of the preferred directions for the LS and S-Co phases. Only neurones with clear excitatory activity in LS (top part) or S-Co (bottom part) were included in the histograms. The shapes of the two histograms are very similar. Virtually all directions are represented; however, most of the neurones, 71% (65/91) in the LS phase, 69% (63/91) in the S-Co phase, point in contralateral directions. In the other phases, likewise, all directions were represented, but most neurones were contralateral: 62% (45/73) in M; 69% (49/71) in Pre-S; and 56% (43/77) for Post-S.

We calculated preferred directions also for inhibitory responses. Clear inhibitory responses were required for inclusion in the analysis. (A clear inhibitory response was defined as activity index of -2.0 or lower, see Methods section of chapter 2). During LS and M, most inhibitory responses were directed toward the contralateral hemifield: 73% (11/15) for LS and 71% (12/17) for M. However, around the time of the saccade this trend reversed, and most inhibitory responses showed ipsilateral preferred directions: Pre-S, 46% (11/24) contralateral; S-Co, only 33% (7/21) contralateral; Post-S, 38% (9/24) contralateral. Therefore, the saccade-related activity, but not the LS,

appears to act in a "push-pull" fashion.

A few neurones showed, in some phases, excitation in opposite directions ("bi-modal tuning"). Usually the response in the opposite direction was weaker than the response in the preferred direction.

**Alignments of the preferred directions of different activity phases**

We define the alignment of two activity phases in one neurone as the angle between the preferred directions (the smaller angle, in the range 0-180 deg). Figure 7 shows distributions of alignments for several pairs of phases. Only neurones whose activity in both relevant phases was clearly excitatory were included in the analysis.

Figure 7 shows that the directions of LS, M, Pre-S, and S-Co, are (at least roughly) aligned. However, these phases break down into two groups. The alignments of the first three phases, LS, M, and Pre-S, are very good: the median alignment of LS and M was 19 deg, N=61; for LS and Pre-S, 22 deg, N=56; for M and Pre-S, 14 deg, N=52. However, the alignments of each of these three periods with S-Co is less accurate: the median alignment of LS and S-Co was 40 deg, N=68; M and S-Co had median 31 deg, N=56; Pre-S and S-Co, median 28 deg, N=60. For an example of this trend, note that the preferred LS, M, and Pre-S directions of the neurone illustrated in figures 1 and 2 match each other better than the preferred direction of S-Co.

The less precise alignment between LS, M and Pre-S with S-Co is not the result of a "drift" in the direction of the activity that accumulates with the passage of time: although the Pre-S and S-Co phases are much closer in time than LS to S-Co, the alignment of Pre-S with S-Co is worse than that of Pre-S with LS.

A small group of neurones, 14% (9/63), with clear excitatory activity in both LS and S-Co, had opposite preferred directions in these two phases. These neurones can be seen as a discrete group in figure 7.

**Units with narrow fields**

We now investigate alignments between activity phases when the sample is confined to neurones in which the matched phases not only have clear excitatory activity (that is, activity indices greater than or equal 2.0), but also narrow direction tuning. We call a direction tuning

"narrow" if its width is, at most, 90 degs. Our motivation for this selection is that neurones with extremely broad fields may be less suitable for spatial processing than neurones with somewhat narrower fields.

The alignments of LS, M, and Pre-S in this smaller sample are even tighter than in the total sample. For LS and M, the median alignment is 6 deg; the sample contains 46% (28/61) of the total number of units with excitatory activity in both periods. For LS and Pre-S, the median is 10 deg, and the sample size 46% (26/56). For M and Pre-S, the median 8 deg, sample size 48% (25/52).

The main finding here is that the discrepancy between the preferred directions of LS, M, and Pre-S, on the one hand, and the preferred direction of S-Co on the other hand, all but disappears. Figure 8 displays the histogram of alignments for neurones with excitatory activity and narrow fields in both LS and S-Co. The histogram shows a much better alignment of these phases as compared to figure 7. The median alignment is 12 deg (*vs.* 40 deg in figure 7). Figure 8 is based on a sample whose size is 37% (25/68) of that in figure 7.

The results of the present section are illustrated on a single neurone level in figures 1 and 3: figure 1 depicts a neurone with wider fields, but less precise alignments, than the neurone of figure 3.

**The direction tuning curve reflects the response field**

We have extensively mapped the response fields of an additional group of 82 neurones. Memory-guided saccades were made to 32 target locations, in 4 blocks of trials. Three blocks contained targets positioned, respectively, on small, medium, and large imaginary circles. The radii of these circles were usually 7.5, 15, and 22.5 degrees, respectively; but sometimes the small circle was 5 degrees, and the large circle 25 degrees. In all these circles, targets were placed in the 8 standard directions (integral multiples of 45 degrees). On the fourth block of trials, targets were placed on a circle of 15 degree radius, rotated 22.5 degrees with respect to the standard directions.

Figure 9 illustrates the intensity of the LS and S-Co responses of one neurone at these 32 target locations. Both LS and S-Co activities prefer the down-and-right direction. The preferred directions are similar in all three circles.

Neither the average intensity of activity in area LIP, nor fraction of LIP neurones showing clear excitatory responses, varied with eccentricity. In each phase, both parameters were similar in each of the three eccentricities tested. The results were similar to those presented in figures 4 and 6 of the preceding chapter.

For each of the 4 blocks of trials of each neurone we have calculated a direction tuning curve and assigned to it a preferred direction. Each block was analysed separately, using the same algorithms as in the rest of this study. For each phase, we then calculated the alignment of the preferred directions derived from the different eccentricities.

The main result is that the preferred directions are largely invariant of saccade size. More specifically, similar estimates for preferred directions were obtained for each of the three target circles. Figure 10 illustrates the results for the LS phase. Forty neurones showed excitatory responses (that is, activity index at least 2.0) in both small and medium-sized circles. The median alignment is 17 degrees. Forty-three neurones showed excitatory responses in both medium and large circles. The medium alignment in this case is 15 degrees. Good alignment for the different eccentricities was observed also in the other phases.

Figure 11 shows that alignments between different phases also do not depend on target eccentricity. The figure presents the alignments of the LS and S-Co phases, calculated separately for each eccentricity. The distributions are similar, as are their median values (26 to 28 degrees). Hence the results presented in this paper are not a peculiarity of the target eccentricities we used.

We also compared the preferred directions calculated separately from the two blocks of trials with targets on a 15 degree radius circle; one block with the standard directions, the other block with targets rotated by 22.5 degrees with respect to the standard. In the example of figure 9, the maximal activity is reached in trials in a non-standard direction (-67.5 degrees). Nevertheless, both blocks of trials, to standard and rotated directions, gave quite close estimates for the neuron's preferred directions. The LS phase, for example, is -67 degrees in the standard block, and -86 degrees in the block of rotated targets. On the population level the preferred directions of both blocks were, similarly, generally aligned. For instance, in the LS phase 44 neurones were active in both blocks, and the median 'alignment' was 17 degrees; in other phases the estimates of difference of preferred directions were

also similar. Hence 8 targets are generally sufficient to capture the neurone's preferred direction, at least in the level of precision applied in this paper.

**Alignments of the post-saccadic phase**

Figure 12 shows the alignment of the LS and Post-S phases. The histogram is clearly flat, leading to the conclusion that, over the whole population, LS and Post-S preferred directions are uncorrelated. Figure 13 shows a neurone whose activity from the LS to S-Co phases is strictly tuned to the down-and-right direction. The alignment of the LS and S-Co preferred directions in this neurone is almost perfect (1 degree). Nevertheless, the pronounced post-saccadic activity of this neurone is directed down and down-and-left, resulting in an LS to Post-S difference of preferred directions of 63 degrees. The post-saccadic activity of this neurone is a static eye position signal; this was confirmed in another run (not shown), in which the monkey had to fixate, for 2 seconds, each of the 9 stimulus positions of figure 13. When fixating the down-and-left or down positions, this neurone emitted a sustained discharge. We conclude that the flat distribution of LS and Post-S alignments depicted in figure 12 may result from several processes occurring simultaneously in the post-saccadic period, related not only to the completed eye movement, but also to the eye-position, and probably, in some neurones, also to the subsequent eye movement, as will now be described.

Figure 14 shows an example of a neurone with nearly opposite Pre-S and Post-S directions. The increase in the activity following down-going saccades occurs at about the same time as the decrease that follows upward saccades. We suggest that in some such neurones the post-saccadic activity represents the intention of the monkey to saccade back to the fixation point; hence in fig. 14 the post-saccadic activity is in the direction opposite to the LS, memory and pre-saccadic activity. We investigated this hypothesis in this and other neurones specifically using the "back saccade" paradigm discussed below.

The S activity of many neurones is peri-saccadic, that is, though starting before or simultaneously with the saccade, the burst continues well after the saccade is completed (chapter 2). Strong S activity, outlasting the saccade, can be seen figure 14, in directions up, and up-

and-left. Clearly, such long S activity can contribute to post-saccadic spike counts. Our choice of Post-S interval starting 200 ms after the beginning of the saccade, was meant to reduce the contribution of such slowly-decaying S activity. Nevertheless, these spikes do occur after the saccade, and they constitute a process that is aligned in direction with the presaccadic activity. This process is, of course, very different from the one occurring in the down direction, illustrating, again, the complexity of the post-saccadic activity.

Note that, since we recorded neither eye position nor neuronal activity during the intertrial interval (from about 500 ms after the end of the saccade to the target until the beginning of the next trial), understanding the nature of the post-saccadic activity requires further work. Post-saccadic activity may reflect a variety of processes, including eye position signals and intention to saccade back to the fixation point in anticipation of the next trial.

**Activity related to the intended movement**

We used the double-saccade and back-saccade paradigms (Hallet and Lightstone 1976a, b; Mays and Sparks 1980) to investigate whether LIP neurones code in "motor coordinates": do these neurones become active if a saccade is planned into their motor field even if no visual target falls within their receptive field?

A detailed description of the double saccade paradigm is provided in the Methods section. In short, the initial fixation spot is replaced by a brief presentation of two peripheral targets, one after the other; the monkey must saccade first to the location of the first target, and then directly to the location of the second target. Although no explicit delay is required, the targets are extinguished during the latency of the first saccade, and thus both movements are made in complete darkness. The second saccade is made in a direction in which no retinal stimulation occurred; hence some transformation of coordinates must have occurred.

Figure 15 illustrates the LS and S-Co fields of the neurone whose activity in the double-saccade paradigm is illustrated in figure 16. This neurone has vigorous S activity, but almost no LS activity (also no M activity). The S-Co activity spans mainly the right-to-down quadrant, but some excitatory response is evoked in all directions (the S-Co tuning width is 120 degrees).

Figure 16 illustrates the activity of the same neurone in the double-saccade task. Two pairs of saccade directions are displayed: rightward and upward saccades (figures 16a, b), and downward and leftward saccades (figures 16c, d). Within each pair, one direction is preferred (that is, it is in the S-Co field), and the other direction is non-preferred. The preferred directions are those of the first saccade (figures 16a, c) or the second (figures 16b, d).

The key result is that in each of the four panels of figure 16, the activity is clearly related to the movement in the preferred directions. This is consistent with a motor coordinate frame.

We have tested 25 neurones in the double-saccade paradigms; 11 neurones showed activity clearly consistent with the hypothesis that they code in motor coordinates. Only one neurone clearly did not code in motor coordinates. Although the remaining neurones were consistent with motor coordinates, the data were difficult to interpret. Several factors complicate the interpretation of the double-saccade paradigm in the remaining neurones. The main factor is that many neurones have wide tuning curves and are thus active for both saccades. Therefore, in order to get clear-cut results, we employed the back saccade paradigm. (See also chapter 5.)

Figure 17a,b illustrates the back saccade paradigm (again, a detailed description is provided in the Methods section). The initial fixation spot is replaced by a brief presentation of a peripheral target; the monkey must first saccade to the location of this target, and then saccade back to the initial fixation position. Although no explicit delay is required, the target is extinguished during the period prior to the first saccade, and thus both movements are made in complete darkness. The essential point is that no retinal stimulation occurs in this trial in the direction of the second saccade.

Figure 17 illustrates the activity of an LIP neurone in the back saccade paradigm. The response of the same neurone to the delayed saccade task was displayed in figure 14. Figure 14 shows that this neurone has visual, memory and saccade-related activity in the upward direction, while post-saccadically the neurone is active after saccades in the downward direction. Figures 17c,d,e depict a back-saccade sequence in which the target is in the upward direction, that is, in the response field of the neurone. In this case the target is followed by a discharge that continues through the upward saccade. About 200

msec after the end of the first saccade the activity declines, in anticipation of the downward saccade, and remains low until the completion of the trial.

Figures 17f,g,h show that a target in the downward direction evokes a very different pattern of activity. The presentation of the target is followed by a subtle inhibition (figure 17f), and the activity remains low until the first saccade (figure 17g). As soon as the downward saccade is completed, however, the level of activity becomes elevated (figure 17g), and is sustained until after the second, upward saccade (figure 17h). Since no visual stimulus was presented in the upward direction in this trial, the sustained activity is not visual; it is related to the intention to make a movement into the motor field. Hence, this neurone codes in a motor coordinate frame.

The back-saccade experiment illustrated in figure 17 offers a clue to the nature of the post-saccadic activity of the neurone depicted in figure 14. We suggested (in the section on post-saccadic activity) that the post-saccadic activity of this neurone may be related to a saccade made in the intertrial interval, returning to the fixation point in anticipation of the start of the next trial. Some support for this conjecture is presented in figure 17. In the back saccade task, the animal is required to look back to the fixation point, in the duration of the trial. If the trial was truncated after the first saccade, the cell would have pre-saccadic activity for upward saccades and post-saccadic activity for downward saccades. Hence, it would show the same pattern of activity that was found for the single saccade task illustrated in figure 14.

We tested 11 neurones using the back-saccade paradigm. Five neurones had activity clearly related to the intended movement in these trials. Three neurones had weak activity consistent with the intended movement. Three neurones were hard to interpret (e.g., too large response fields). None of these neurones had activity clearly inconsistent with the direction of the intended movement.

## DISCUSSION

Three major properties of single neurone activity in LIP have been described in the present chapter. The first was spatial tuning: each phase of activity was found to have direction tuning (i.e., to have responses restricted to only certain parts of space. The second was alignment: in the same neurone, the preferred directions of LS, M, Pre-S and S-Co periods were usually aligned. The third property was coding in motor coordinates: neurones become active in anticipation of saccades planned into their motor field even if there is no visual stimulation in their receptive field.

### Direction tuning; alignment

Relative to earlier stations of the visual system, spatial tuning in area LIP neurones is broad: the median width at 50% maximal activity is about 90 deg. Similar widths were reported in the frontal eye fields: Bruce and Goldberg (1985) calculated a parameter $T_d$, where $2T_d$ is roughly the width at 60% maximum activity. Their average value of $2T_d$ was 91 deg for presaccadic neurones. Note, however, that neurones with a very narrow direction tuning could have been misrepresented by aliasing, caused by the 45 degrees sampling bin we used. However, we do not believe this was a problem, since (a) the alignment of units with narrow fields was especially good, and (b) a separate population of 82 units was sampled at 22.5 deg, and we obtained essentially the same results.

For model neural networks, two types of spatial coding schemes have been suggested. In local coding schemes each unit has a small response field, and each point in space is coded by one unit. Hinton et al. (1986) suggested that a more efficient spatial tuning scheme would have units with large response fields, with each point of space represented by a set of units ("coarse coding"). The argument for coarse coding holds also for biological systems. In the superior colliculus there is experimental evidence for the existence of a coarse coding scheme (Lee et al. 1988). In area 7a there are large visual receptive fields, and coarse coding of visual location has been postulated (Zipser and Andersen, 1988). Hence it is reasonable to assume that in LIP, too, precise population-level coding of the saccade target is achieved by

coarse coding on the single-neurone level.

In view of the broad directional tuning, it is significant that there is such good alignment between LS, M, and Pre-S, and between these three and S-Co if the sample is confined to the "narrowly-tuned" cells. Thus, an accurate linkage of visual and motor-related direction representations exists in a large subpopulation of neurones in area LIP.

Together, these findings corroborate the hypothesis that LIP is involved in spatial aspects of sensorimotor processing for saccades to visual targets.

**Post-saccadic activity**

This study was not designed to examine the post-saccadic activity; in particular, we usually recorded the neural activity and eye position only for 500 ms after the saccade, during which the eye remained stationary. We did not monitor (or impose any requirements on) the behaviour of the animal during the subsequent 500-1500 ms inter-trial interval. However, we did analyze carefully the activity in the first 500 ms after the saccade and feel that several interesting points can be made.

The post-saccadic activity in LIP is strong. It may have important functions, and should not be considered as "noise" that accompanies the pre-saccadic activity. This is better illustrated in area 7a, in which there is strong activity only during the post-saccadic phase (chapter 2).

The post-saccadic activity in some neurones represents a tonic eye position signal (see figure 13, and chapter 4). In some neurones, the post-saccadic activity mirrors pre-saccadic activity in the opposite direction (figure 14). For some of these neurones, the post-saccadic activity may reflect the intention of the monkey to saccade, at the end of the trial, back to the fixation point; note that this return saccade is in the neuron's preferred direction. The results of the back saccade task in some neurones support this proposal.

Bruce and Goldberg (1985) reported a similar pattern of activity in some FEF neurones. Bruce (1988) has suggested an alternative explanation for this pattern of opposite directions; the post-saccadic activity is presumed to represent an efferent copy that is subtracted from the pre-saccadic activity to yield a retinotopic representation invariant of eye position. However, three factors seem inconsistent

with the application of such a proposal to area LIP. First, eye position strongly modulates the visual and saccade-related activity in area LIP, which would interfere with the proposed subtraction scheme (chapter 4). Second, the neurones having opposite pre-saccadic and post-saccadic directions are only a minority in area LIP. More commonly, the discharge occurs during all phases of the saccade, and the pre-saccadic and post-saccadic preferred directions are not opposite. Third, the inhibition Bruce and Goldberg (1985) report at (or immediately following) the saccade is not conspicuous in LIP. The vector subtraction hypothesis is further discussed in chapter 5.

One possible role for postsaccadic activity in areas LIP and 7a is that of updating an internal representation of eye position. Such a representation would presumably be necessary for both oculomotor and visual functions. In order to programme the next eye movement correctly, it is likely that the brain needs to know where the eye is in the orbit (the mechanics of the oculomotor plant are such that different commands are needed to produce identical oculocentric saccades from different eye positions). Moreover, in order to make sense of the series of "snapshots" of the world it receives, one after each saccade, the brain must know where the eye was pointing when the snapshot was "taken". Both oculomotor function and spatial vision may be impaired after PPC lesions (see chapter 1); loss of postsaccadic signals may in part explain such deficits.

**Motor coordinates**

The double and back saccade paradigms used in these experiments suggest that saccade-related (and memory) activity in LIP cells is not coded in retinal coordinates. Cells fire for saccades in their preferred directions regardless of whether a visual stimulus has or has not fallen in their receptive fields.

Further, cells fire in relation to saccades made in a particular oculocentric direction, regardless of where the eye is in the orbit. They do not code for saccades to given locations in craniotopic space. (However, most LIP cells' activity is modulated by eye position and we suggest that the population activity in LIP could encode saccades to locations in head-centred space; see chapter 4.)

Neurones exhibit memory and presaccadic activity before the

saccade in their preferred direction; if this is the second in a sequence of movements, cells become active only after the first saccade is complete. Together with the data obtained using novel "change of plan" (chapter 6) and delayed (memory) double saccade (chapter 5) paradigms, this suggests that LIP encodes the forthcoming intended saccade. Memory and presaccadic activity does not occur until it is appropriate for the monkey's next behaviour, by and large.

**Overview of the neural activity in area LIP**

The following general points can be made about the activity of area LIP neurones based primarily on this and the preceding chapter. First, in the delayed saccade, LIP neurones show three phases of activity (LS, M, S). These phases may or may not occur in individual neurones; most neurones show activity in more than one phase. Second, most LIP neurones with S activity are pre-saccadic. In contrast, in neighbouring area 7a the pre-saccadic neurones are a minority. Third, the activity is spatially tuned. Tuning is wide, typically 90 degrees width at half the maximal rate. Fourth, the preferred directions of the different phases of the same neurone, up to and including the saccade, are approximately aligned. The alignment is good between the pre-saccadic phases (LS, M, Pre-S), and somewhat less precise between each of these and S-Co. Fifth, in neurones with relatively narrow tuning in LS and S-Co, the alignment of the preferred directions of all phases, from LS through S-Co, is much more accurate. Sixth, post-saccadic activity, though strong, is not aligned with the previous phases and probably reflects several different processes. Seventh, activity is related to the intended saccade: it can be evoked without visual stimulation in the retinal receptive field, if the next planned saccade is directed into the movement field. Finally, activity in all phases (LS, M, S) is modulated by eye position. The activity can be described as a gain field, dependent on eye position, that multiplies 'canonical' direction and movement fields, both invariant of eye position. Gain fields are typically planar. The gradients of the gain fields of the different phases in the same neurone are typically aligned. They are also aligned with the preferred LS, M, and S directions (chapter 4).

These findings support the notion that area LIP is involved in representation of space, in visual localization, in visuomotor transformations, and the planning of saccades.

## FIGURE LEGENDS

**Figure 1:**

Activity of an area LIP neurone for delayed saccades made in eight directions, 45 deg apart. Each panel illustrates the trials made in the direction the panel occupies relative to the center of the figure. Shown in each panel, from the top, are the spike rasters, where each horizontal trace represents a trial, and each tick marks the time of occurrence of a spike; the resulting histogram; and the horizontal and vertical eye position traces of the various trials, superimposed. The vertical dotted lines denote, from the left, the onset and offset of the target, and the offset of fixation spot. Trials are aligned on the sensory events (note variable saccadic latencies).

**Figure 2:**

Direction tuning curves of each phase of the activity, obtained for the area LIP neurone illustrated in figure 1. The data are plotted twice, in rectangular coordinates (top panels) and in polar coordinates (lower panels). The straight lines radiating from the center of each polar plot represent the calculated best direction for each time slice of activity. The plotted phases are background (dotted), LS (solid), M (dashed), Pre-S (dash-dot pattern in left side panels), S-Co (dash-dot pattern in right side panels).

**Figure 3:**

Activity of another area LIP neurone in delayed saccades made in eight directions, 45 deg apart. These plots are in a similar format as figure 1. This neurone shows a narrower tuning than the neurone in figure 1.

**Figure 4:**

Direction tuning curves of each phase of the activity, obtained for the area LIP neurone illustrated in figure 3, and plotted in the same format as figure 2.

**Figure 5:**

Distribution of the width of the S-Co activity tuning curves. Width was calculated for 91 area LIP neurones with clear excitatory S-Co activity. The median width is 90 degrees.

**Figure 6:**

Distribution of the preferred directions of the LS activity (upper panel), and the S-Co activity (lower panel) of the area LIP neurones with excitatory activity in the respective phases. Each neurone was placed in a 45 degrees wide bin, centred around one of the eight cardinal directions. The number of neurones with a given preferred direction is indicated by the radius of the line in that direction. 0 degrees denotes horizontal contralateral, 90 degrees denotes the up direction.

**Figure 7:**

Distributions of the alignments between phases of activity in LIP neurons. The alignment of two phases in the activity of an individual neurone is defined as the difference between the preferred directions of these two phases.

**Figure 8:**

Distributions of the alignments between the LS and S-Co preferred directions in individual area LIP neurones with both clear excitatory activity and narrow tuning (width less than or equal 90 degrees) in both LS and S-Co phases.

**Figure 9:**

Activity of an area LIP neurone in memory saccades made to 32 targets. Targets are arranged on three concentric circles, of 7.5, 15, and 22.5 degrees radii, in the 8 standard directions (45 degree multiples). On the 15 degree circles targets are placed 22.5 degree apart. The intensity

of the LS and S-Co activities (left and right bars, respectively) are sketched. The calibration bar at the bottom represents 80 impulses per sec.

**Figure 10:**

Alignments of the preferred LS directions in circles of different eccentricities.

**Figure 11:**

Alignments of the preferred LS and S-Co directions, calculated separately for circles of 3 different eccentricities.

**Figure 12:**

Distributions of the alignments between the LS and Post-S preferred directions in individual area LIP neurones with clear excitatory activity in both phases.

**Figure 13:**

Activity of an area LIP neurone in which the post-saccadic activity is poorly aligned with the LS activity and is probably primarily an eye position signal. Data are in the same format as in figure 1, except that the trials are aligned on the onset of the saccade (denoted by the vertical dotted lines).

**Figure 14:**

Activity of an area LIP neurone in which there is sustained post-saccadic activity in a direction opposite to the LS activity. Data are in the same format as in figure 13.

**Figure 15:**

Direction tuning curves of an area LIP neurone that is mainly saccade-related, with little LS or M activity. The data is plotted twice, in rectangular coordinates (top panel) and in polar coordinates (lower

panel). The plotted phases are background (dotted), LS (thin), and S-Co (thick trace).

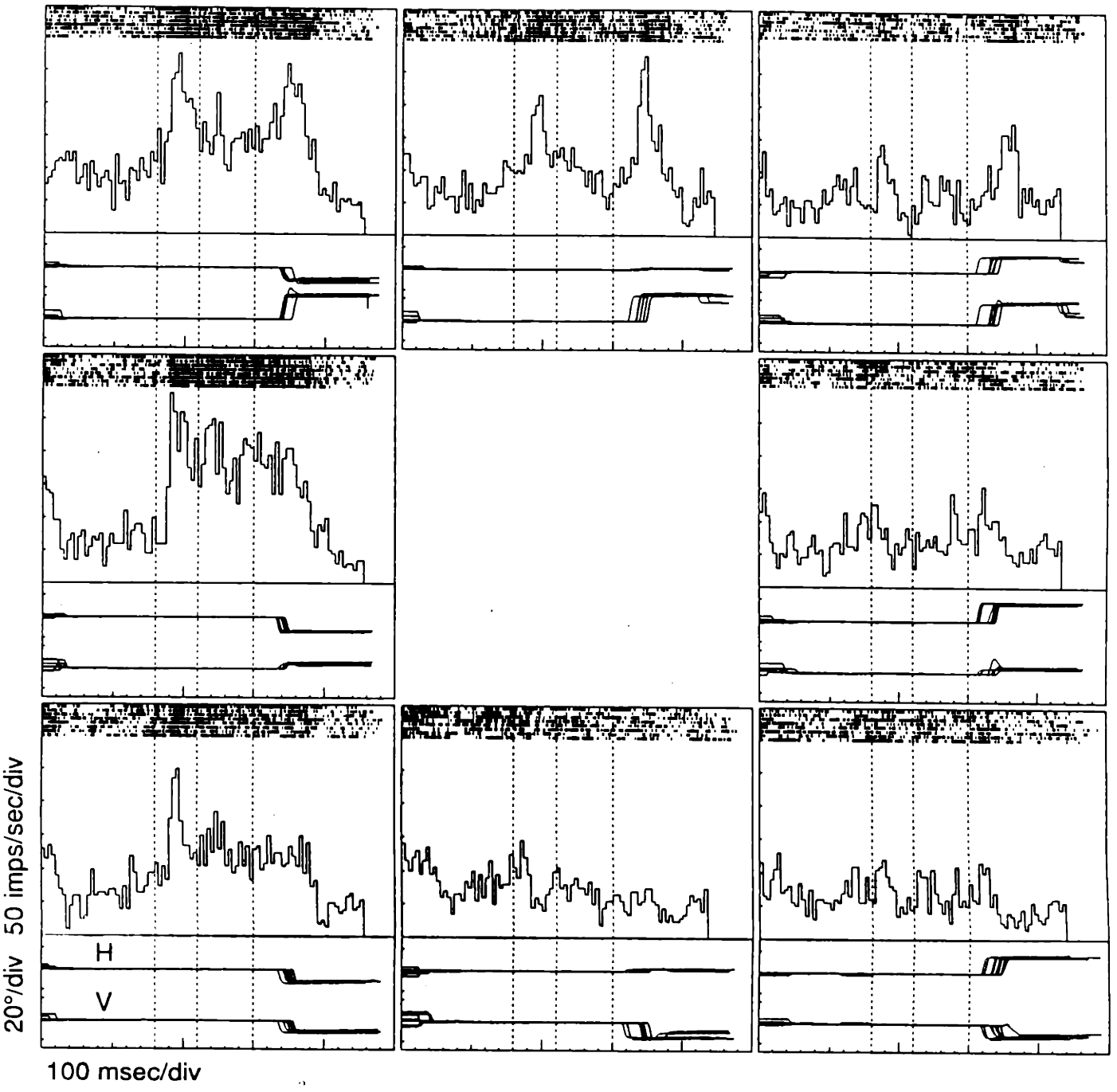
**Figure 16:**

Activity of the same LIP neurone as in figure 15, when tested in the double saccade paradigm. In figure 16a and c, the neurone is active for the first (retinotopic) saccade. In figure 16b and d, it is active for the second saccade. The neurone clearly is active when the forthcoming saccade is in its preferred direction. Note that in figure 16b and d the retinal location of the second stimulus is outside the neurone's motor field, and yet it is still active for the second saccade. This is consistent with the neurone coding in a motor and not a retinotopic coordinate frame. Vertical dotted lines represent end of first saccade (panels a,c) and beginning of second saccade (panels b,d). Shown in each panel are the spike raster and histogram, and the vertical and horizontal eye position traces.

**Figure 17:**

The back saccade paradigm. (a,b) Scheme of the two saccades in the task. The first saccade is to the (single) target, the second saccade is made in the dark back to the location of the original fixation point. (c-h) Activity in the back-saccade task of the same LIP neurone as in figure 14. The preferred direction of this neurone, for the LS, M, and S phases, is upward. Hence, in the top row of panels, the visual stimulation and the first movement are in the preferred direction, and the second movement is in the opposite, non-preferred direction. In the bottom row of panels, the visual stimulation and the first saccade are in the non-preferred direction, but the second saccade is in the preferred direction. Panels c,f are aligned on the sensory stimuli. First dotted vertical line denotes offset of fixation spot and simultaneous onset of target. Second dotted line represents target offset. Panels d,g are aligned on the beginning of the first saccade, and the dotted line denotes the time the first saccade begins. Panels e,h are aligned on the beginning of the second saccade, and the dotted line denotes the time the second saccade begins. Shown in each panel, from the top, are the spike rasters, where each horizontal trace represents a trial, and each

tick within a line marks the time of occurrence of a spike; the resulting histogram; and the horizontal and vertical eye position traces of the various trials, superimposed.

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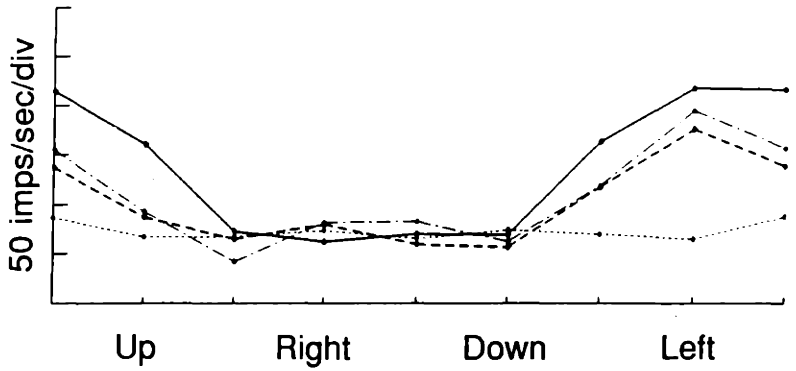
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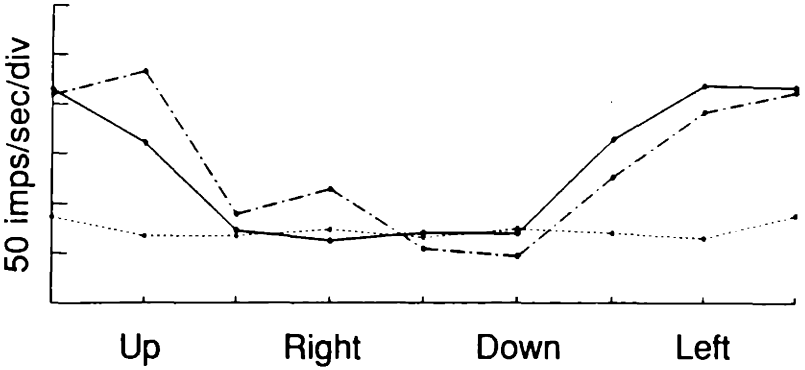
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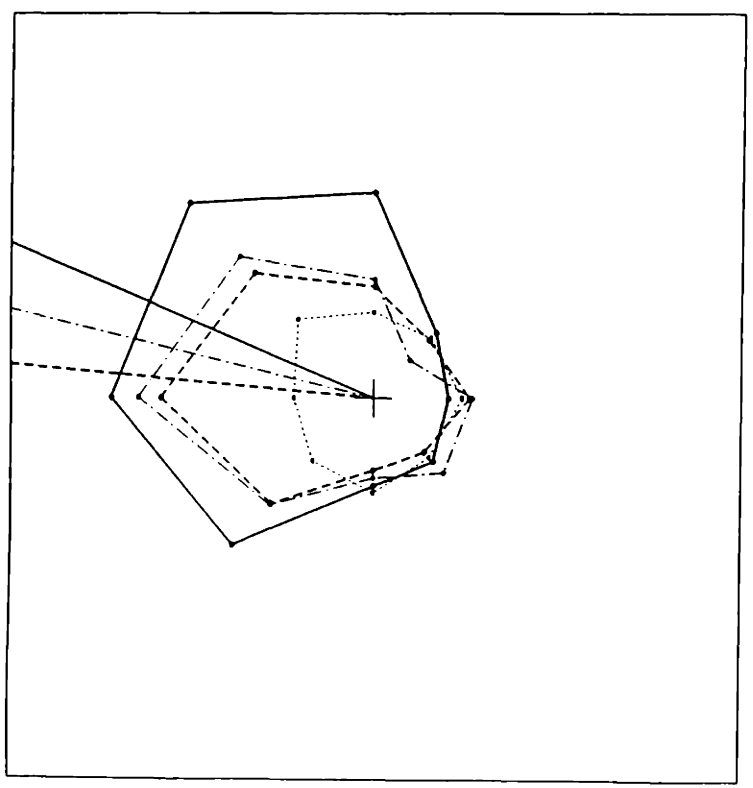

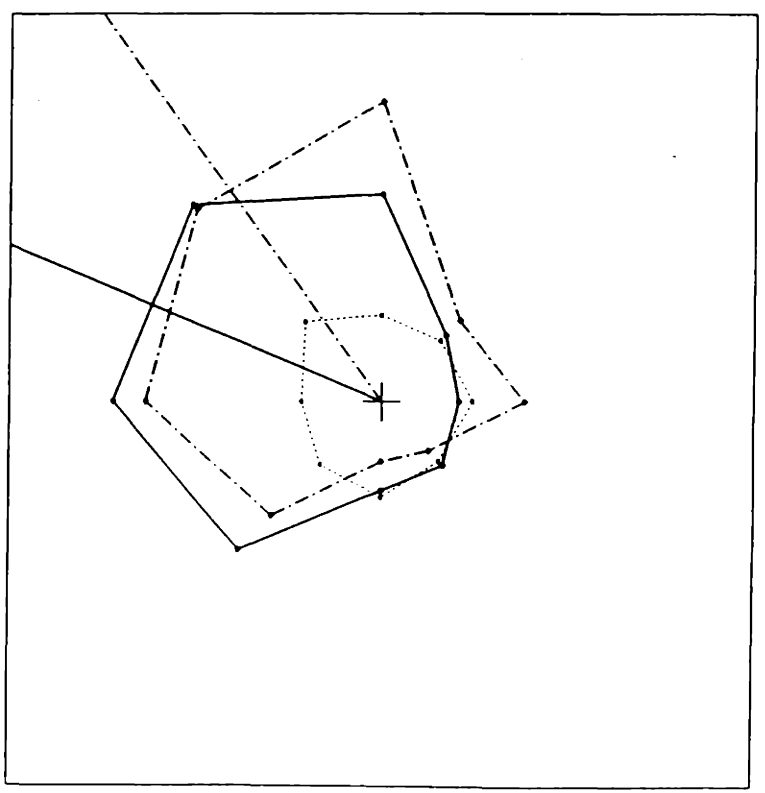

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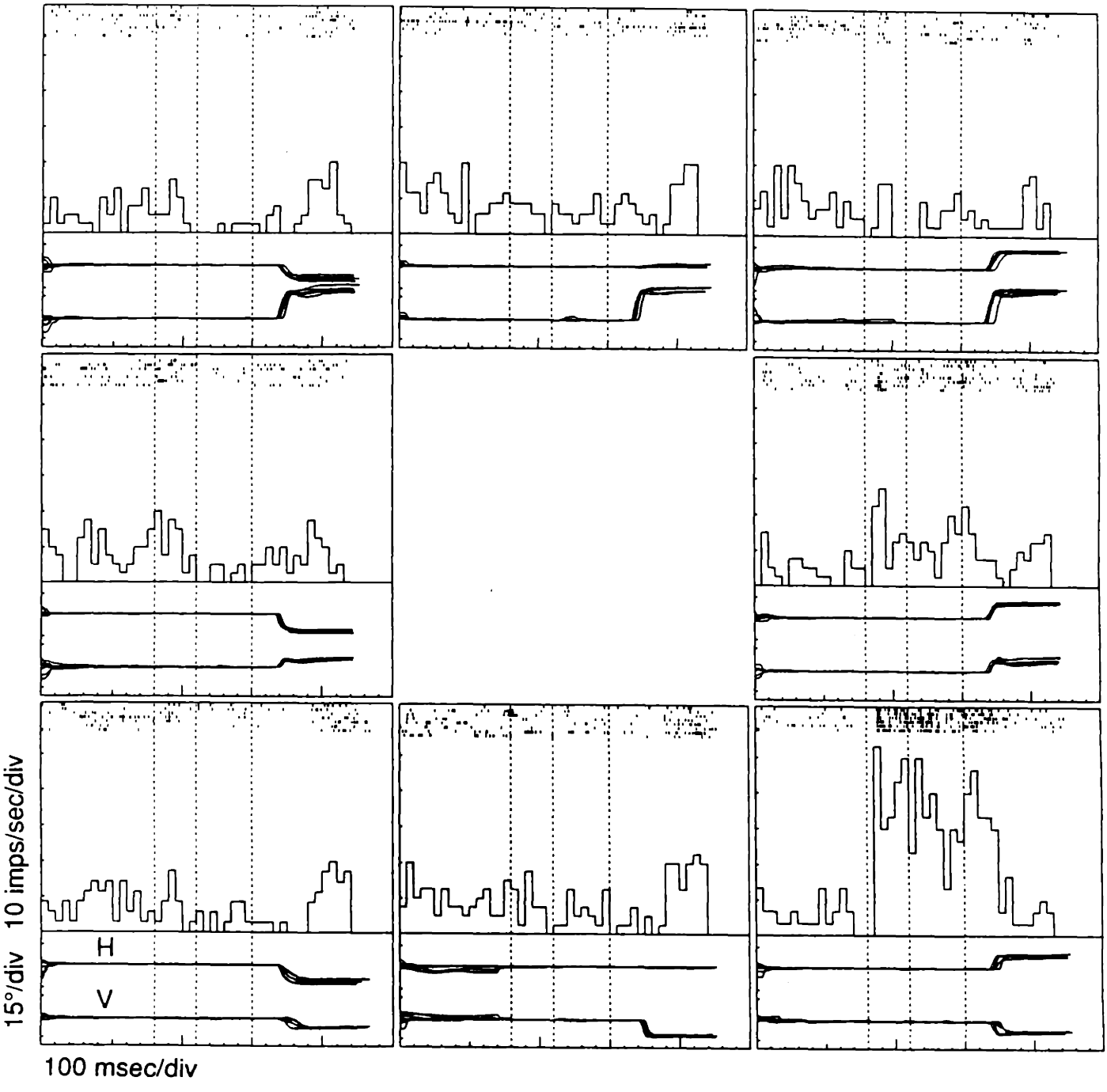


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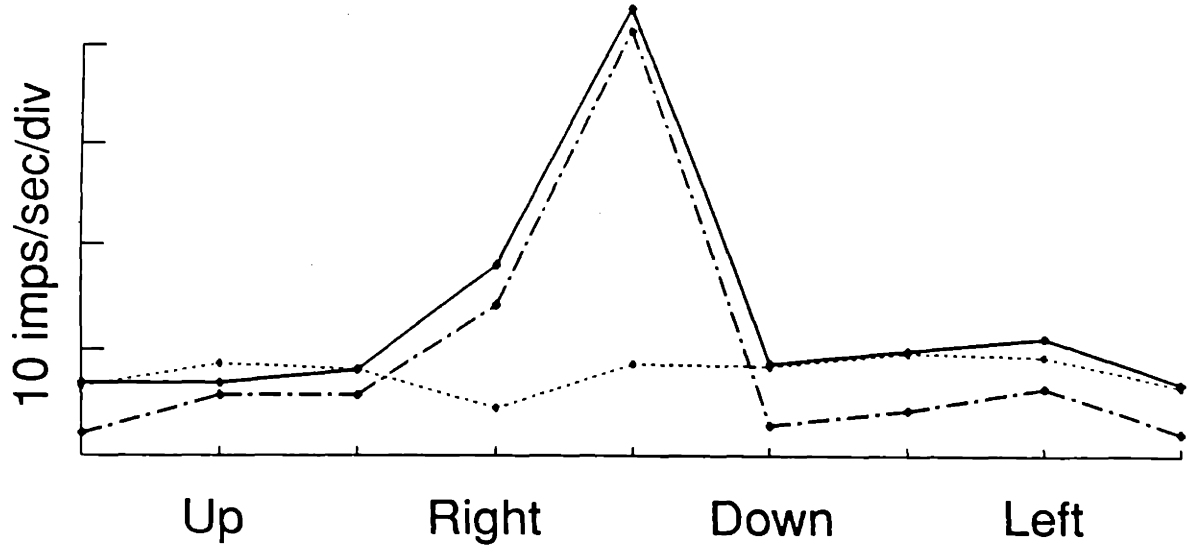


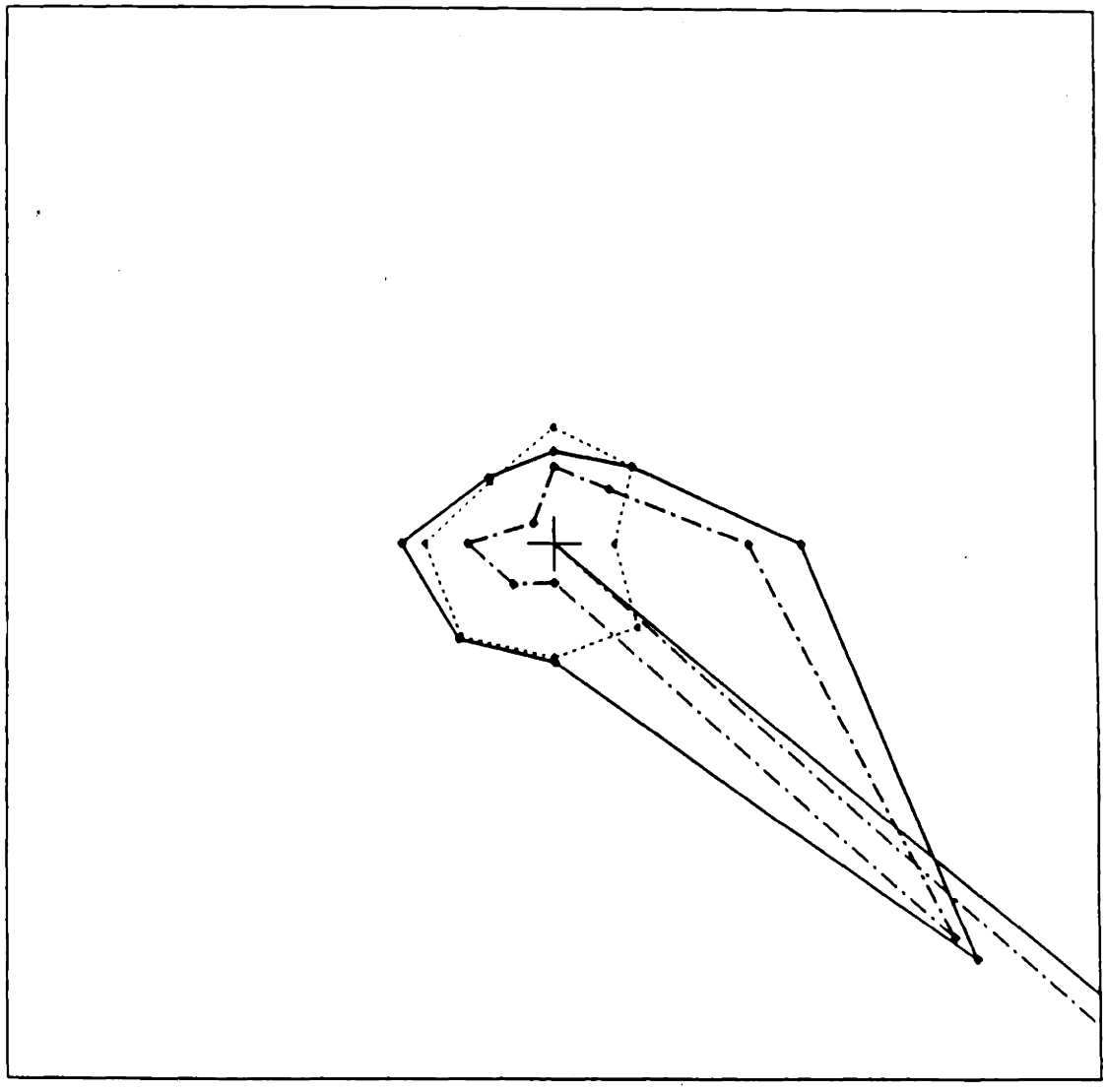



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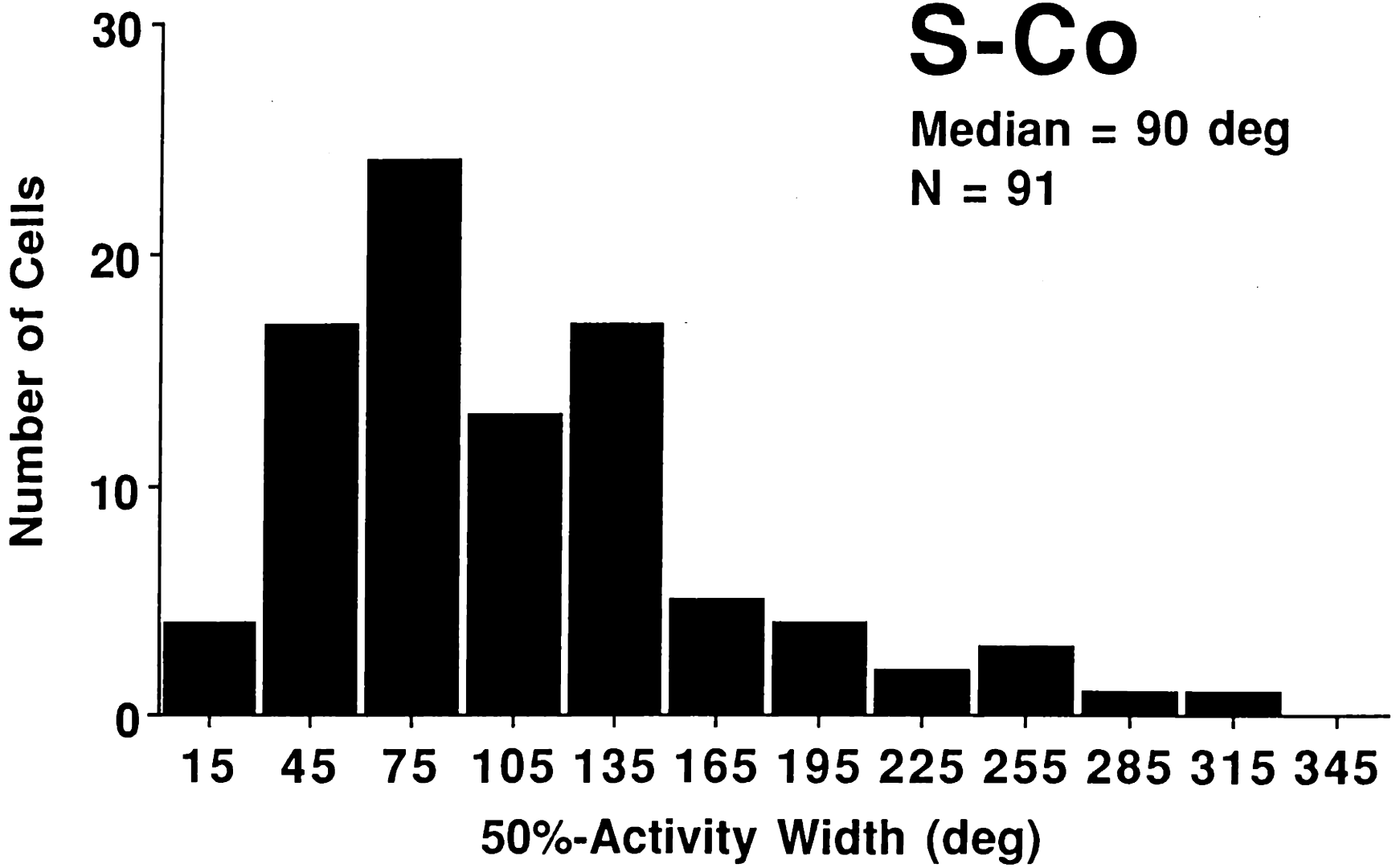
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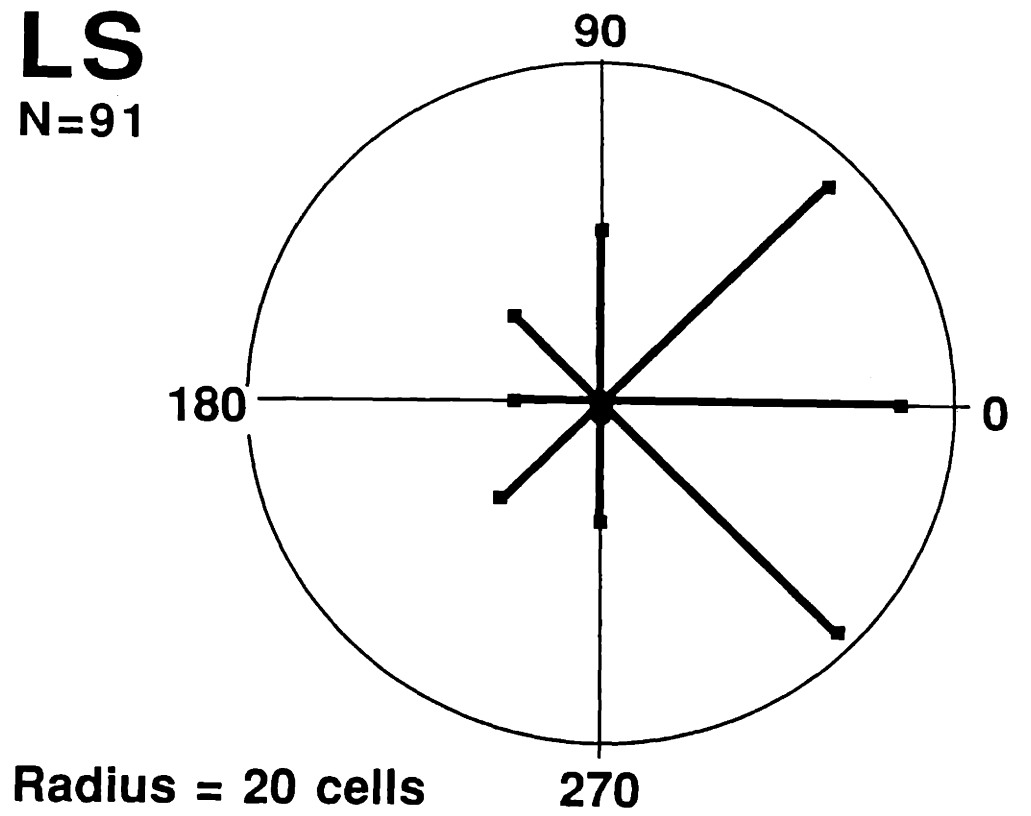
Figure 5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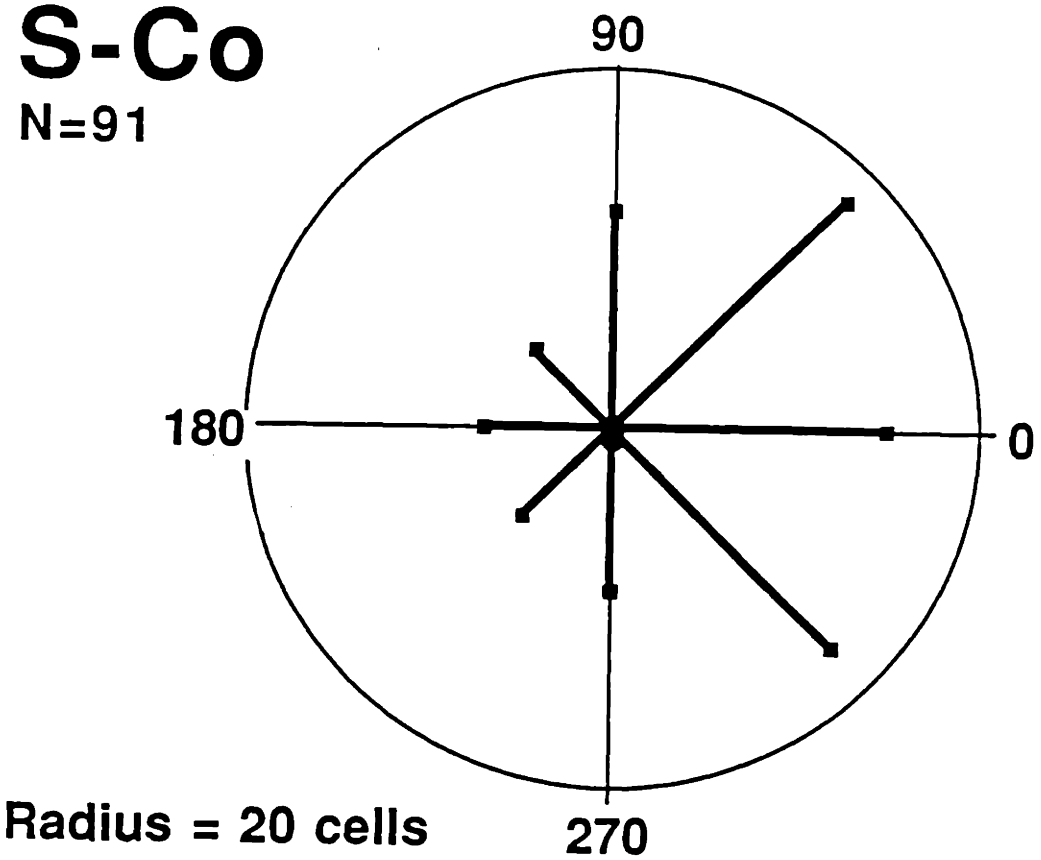
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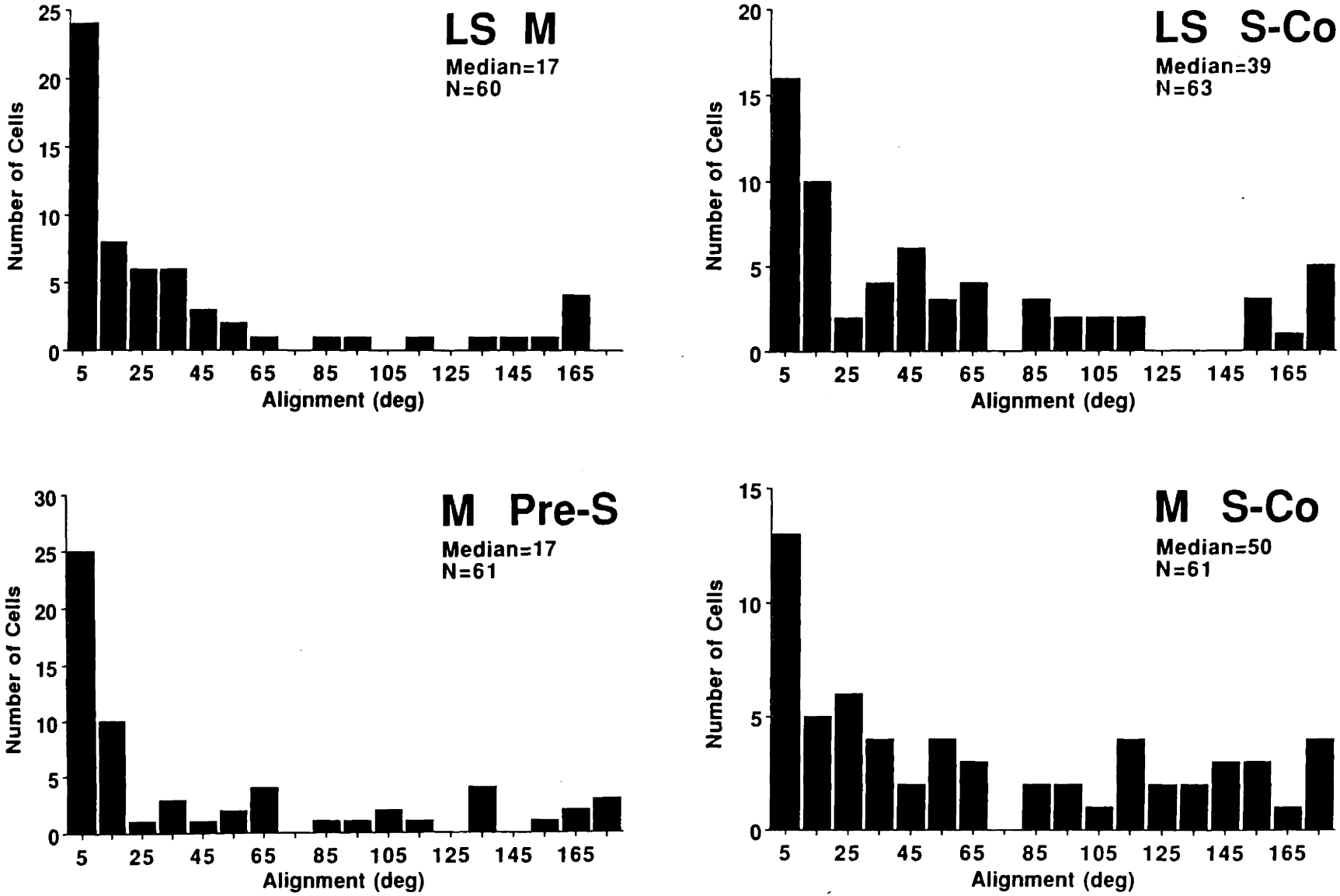
Radius = 20 cells



Figure 6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Number of Cells
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M S-Co
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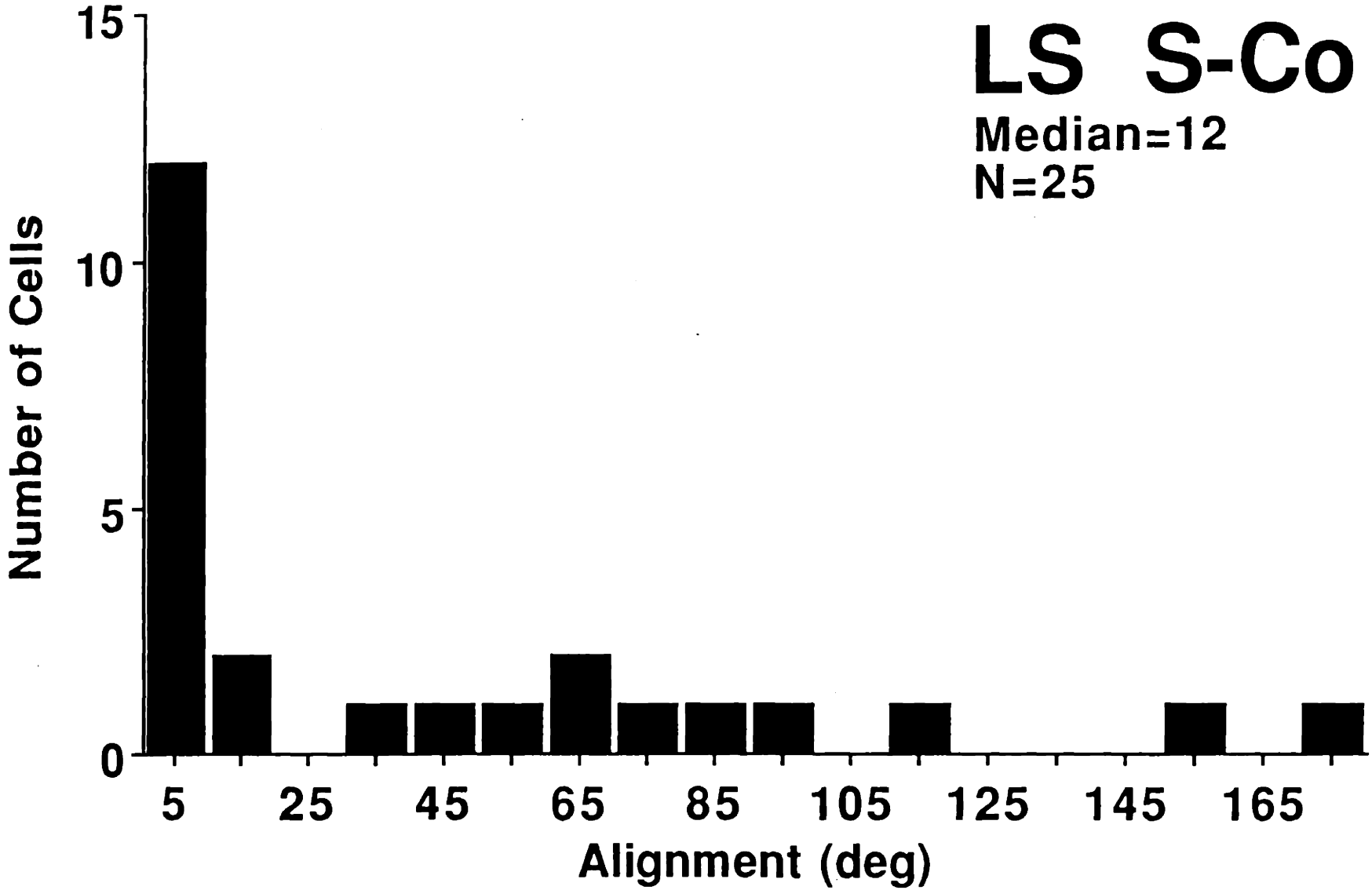
Number of Cells
Alignment (deg)



Figure 7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Alignment (deg)

Figure 8

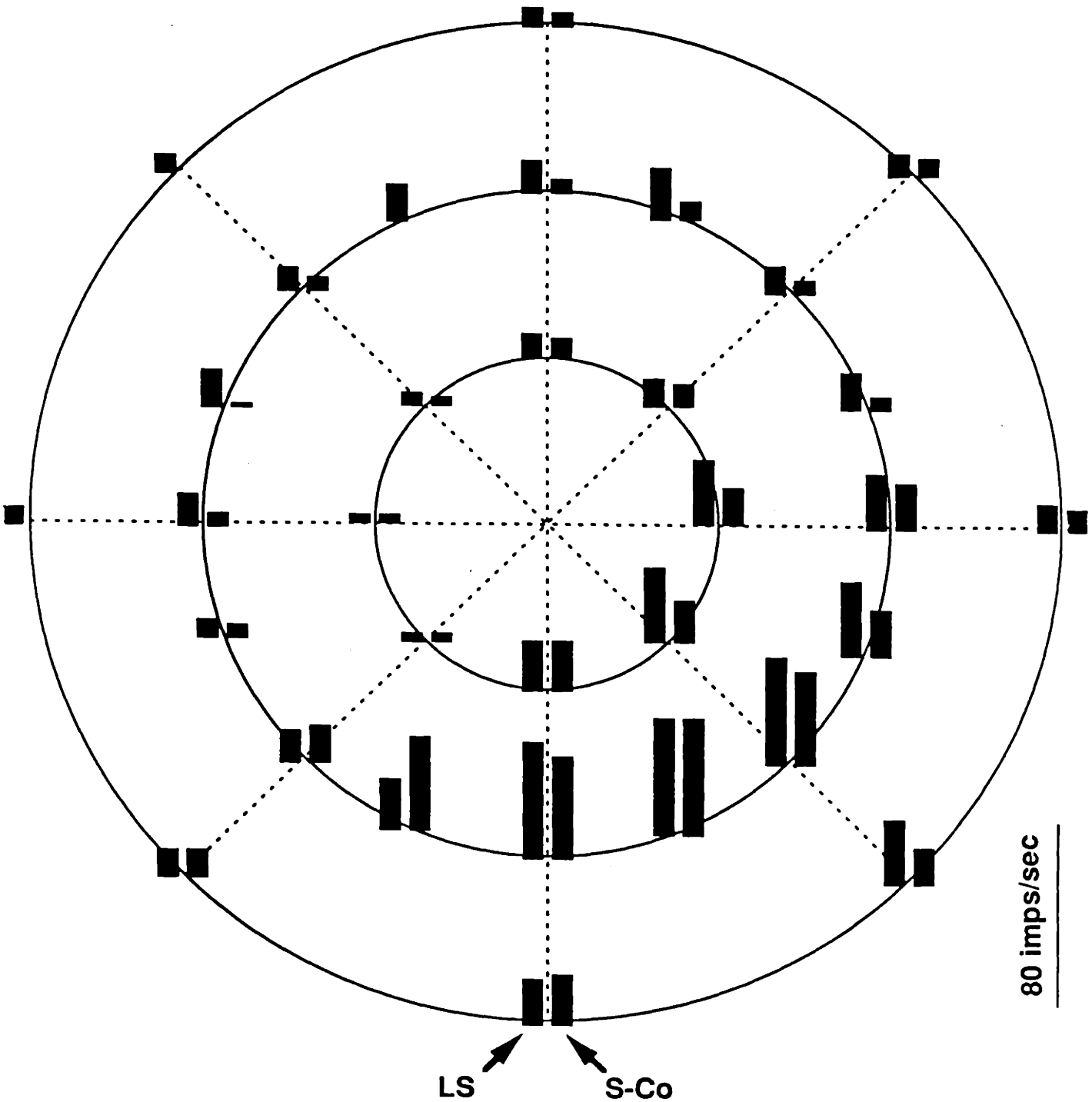
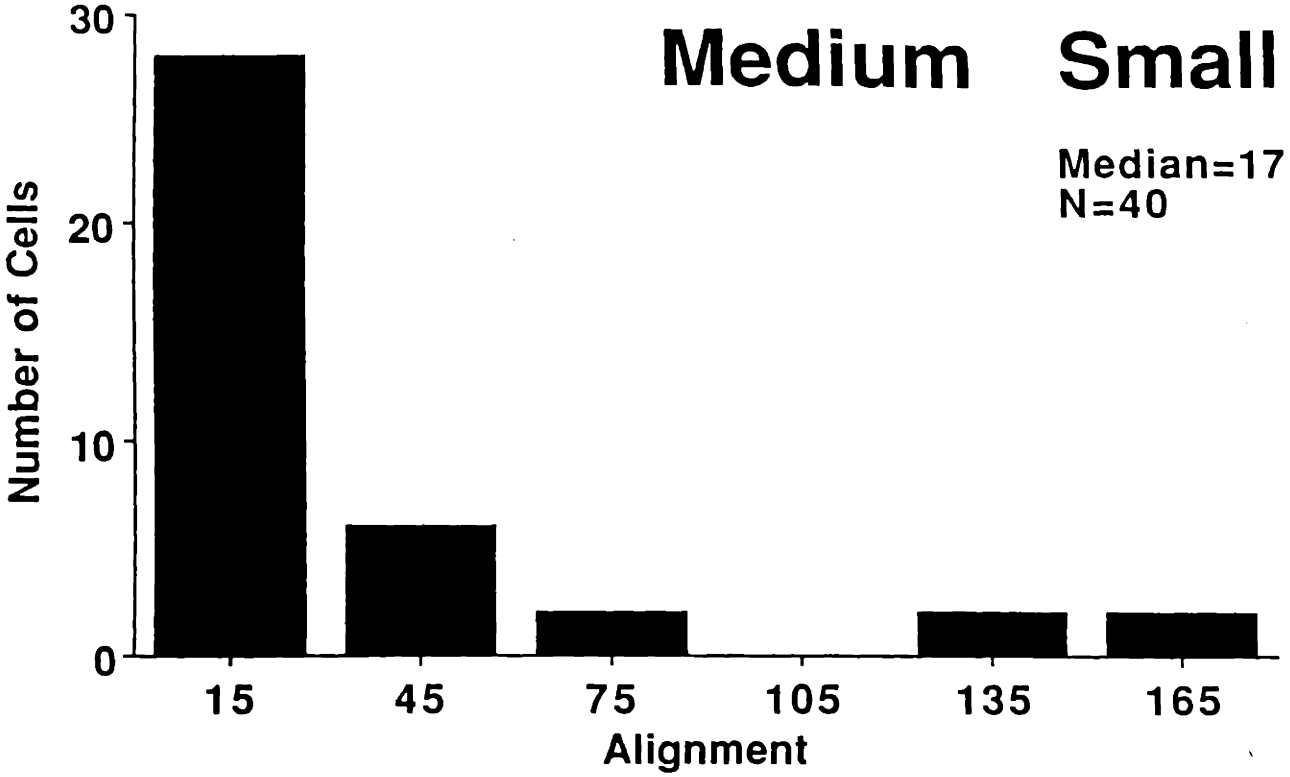





Figure 9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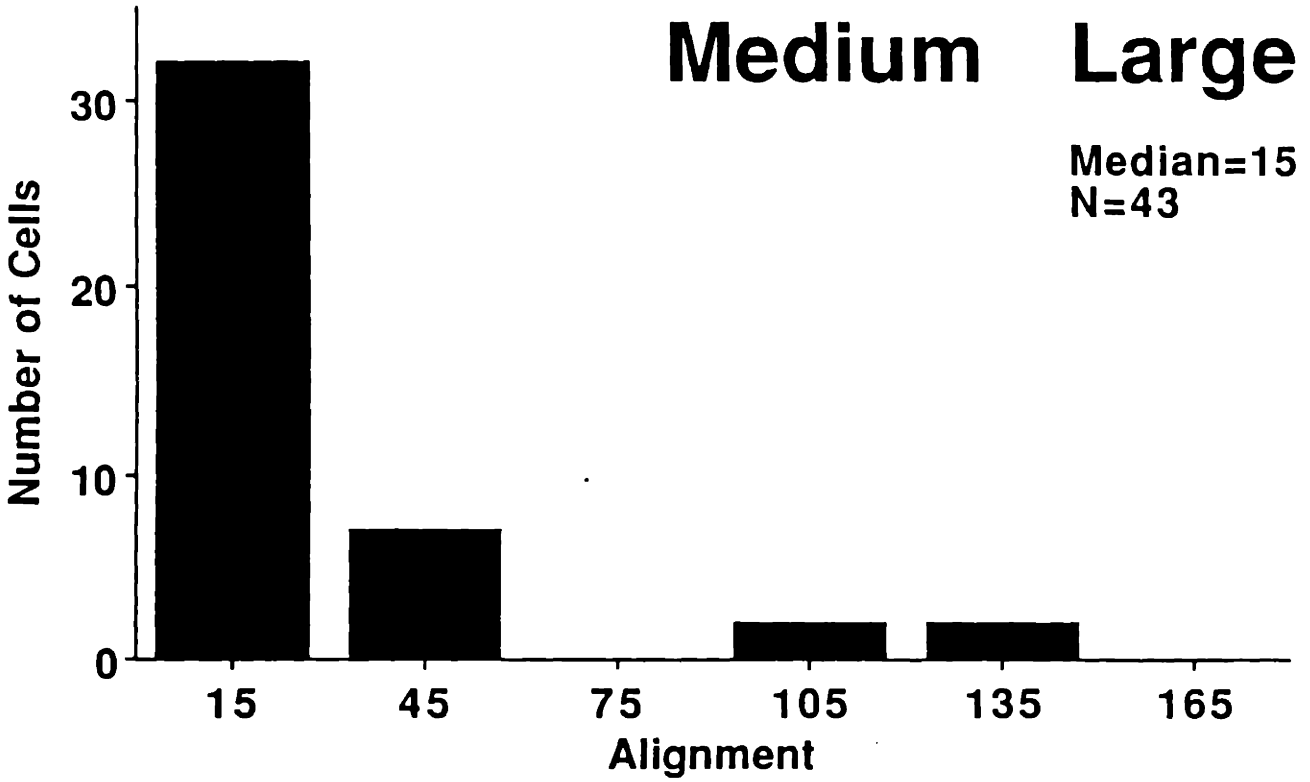
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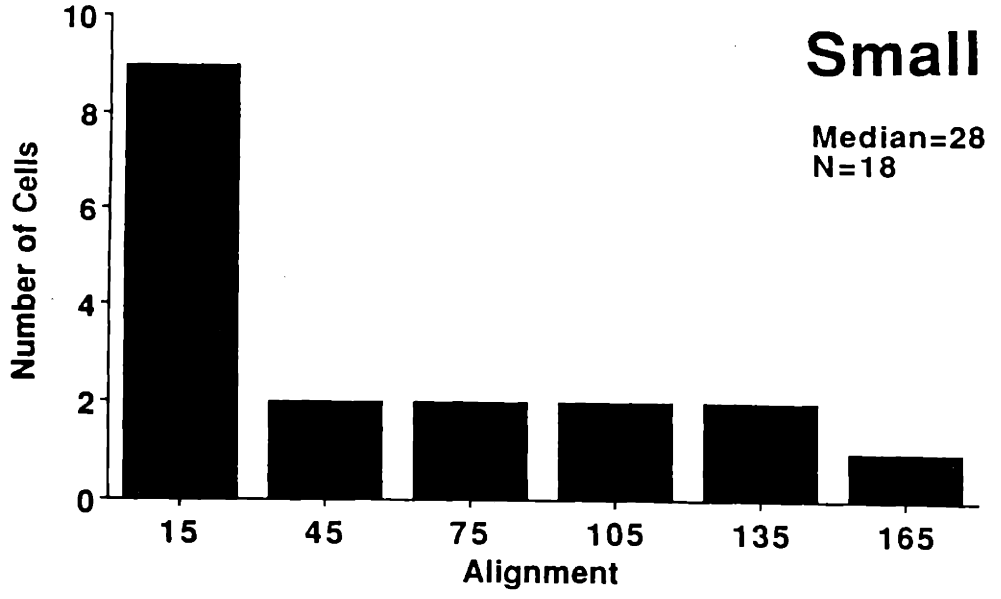
Figure 10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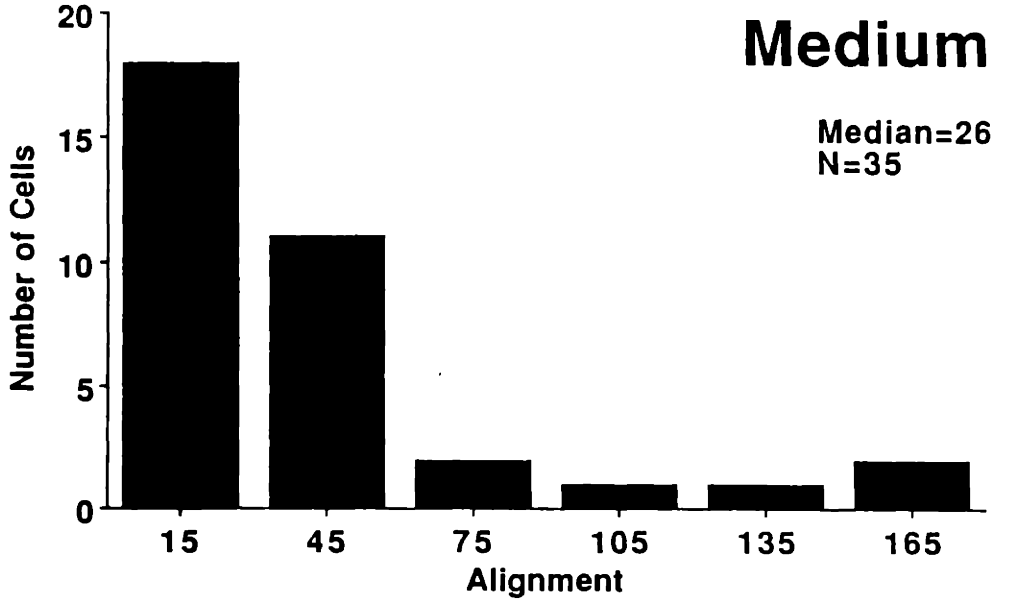
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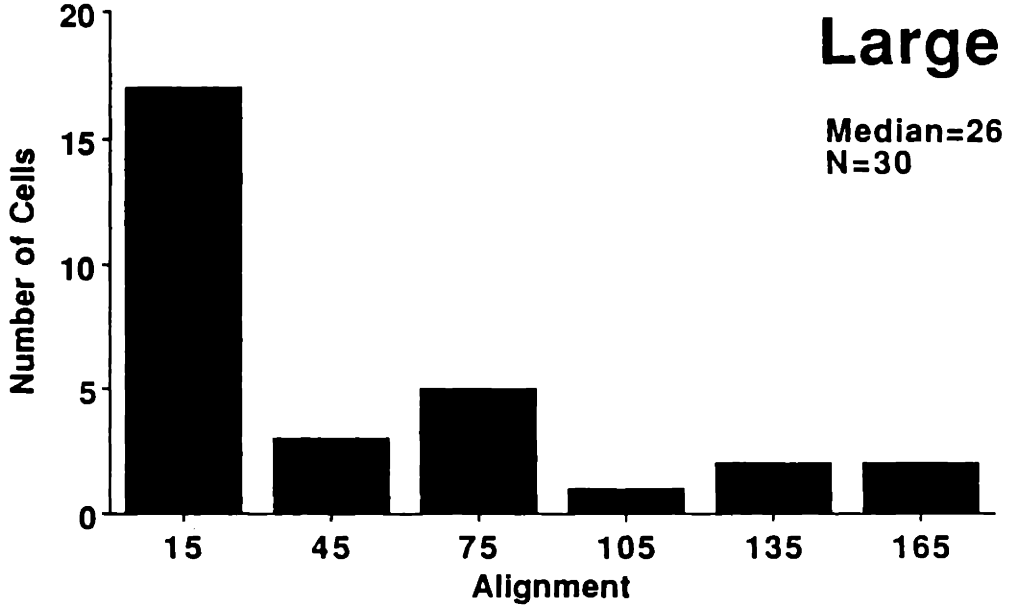
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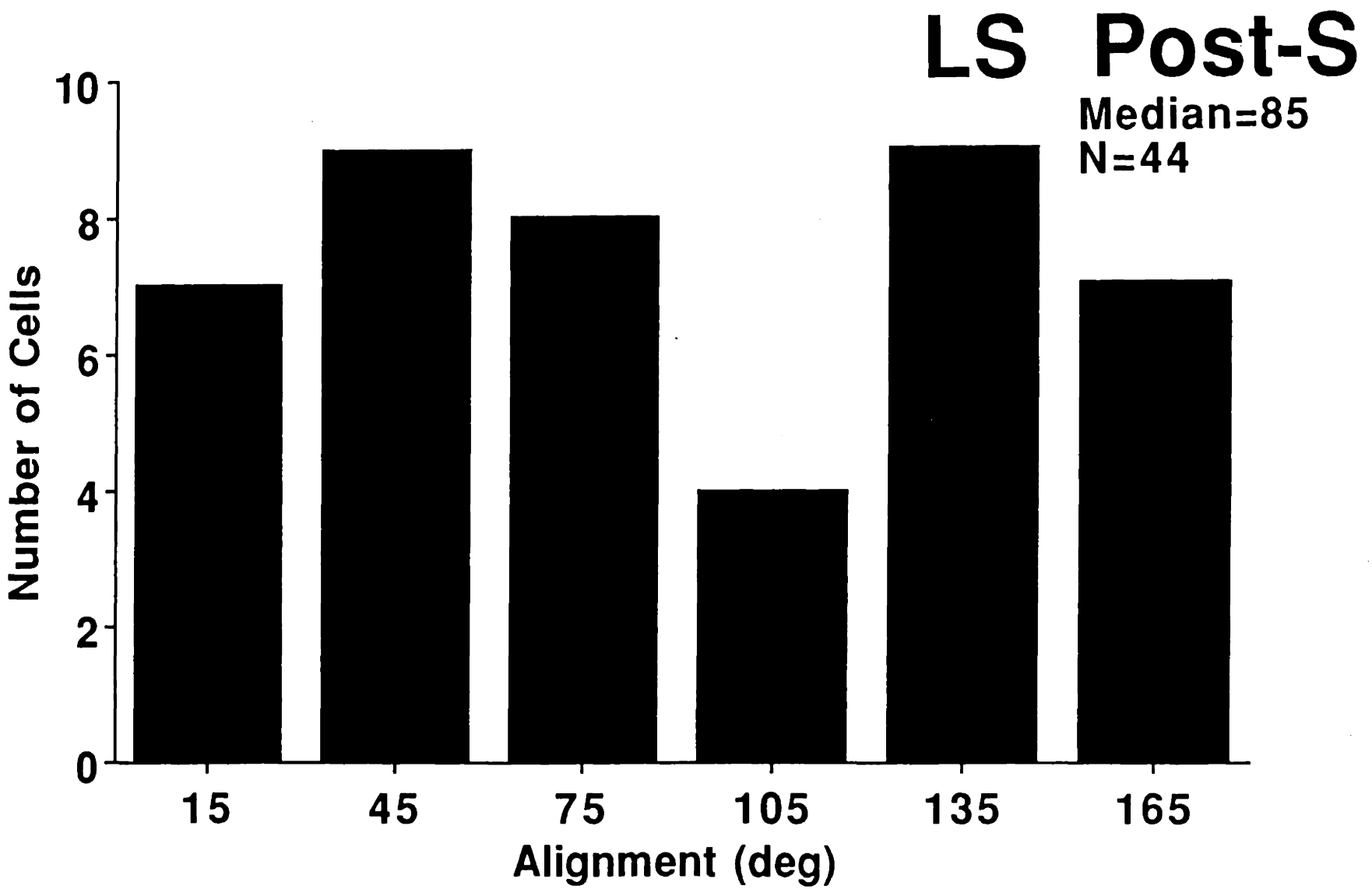
Alignment



Figure 11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Alignment (deg)

Figure 12

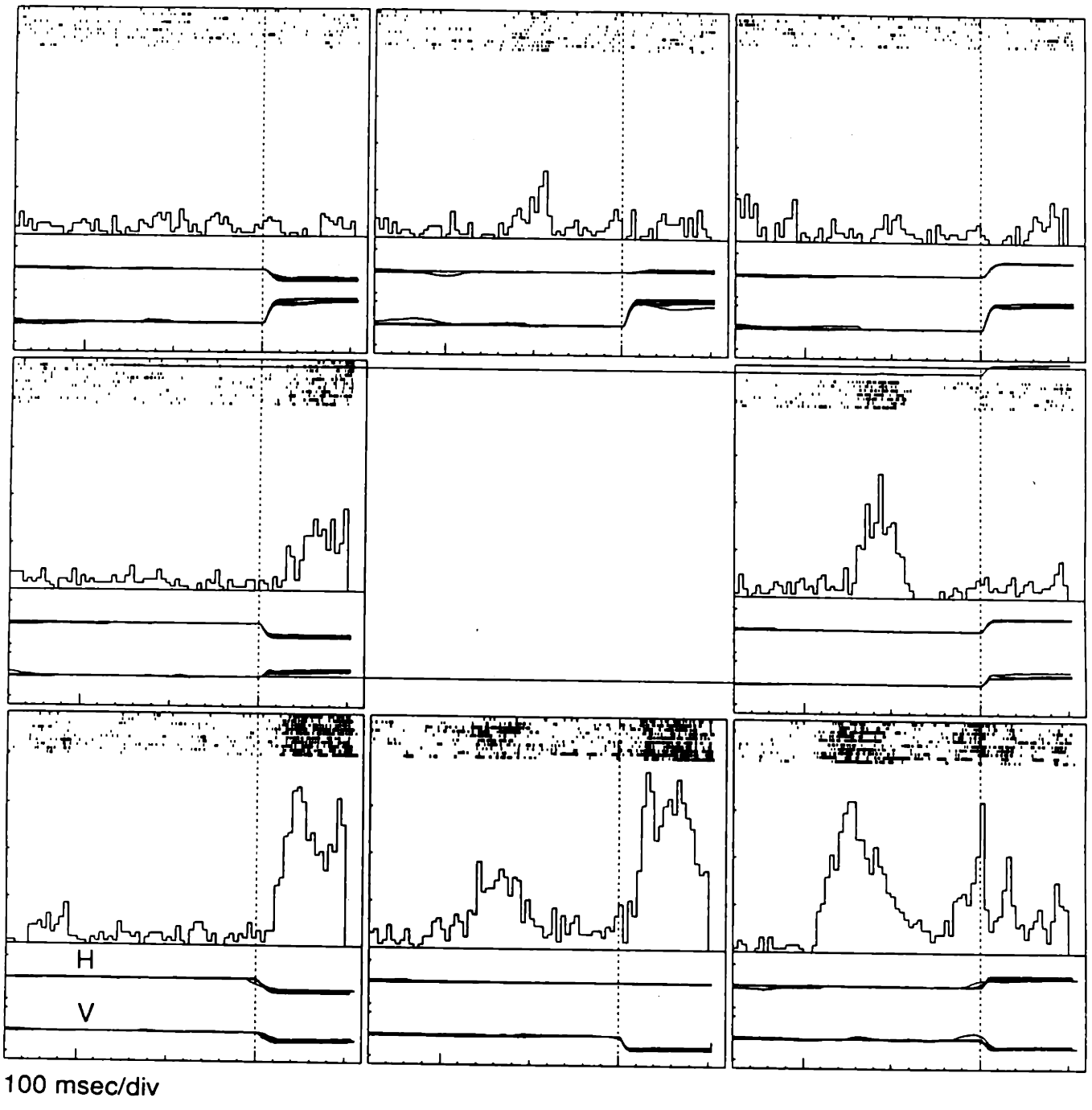





Figure 13

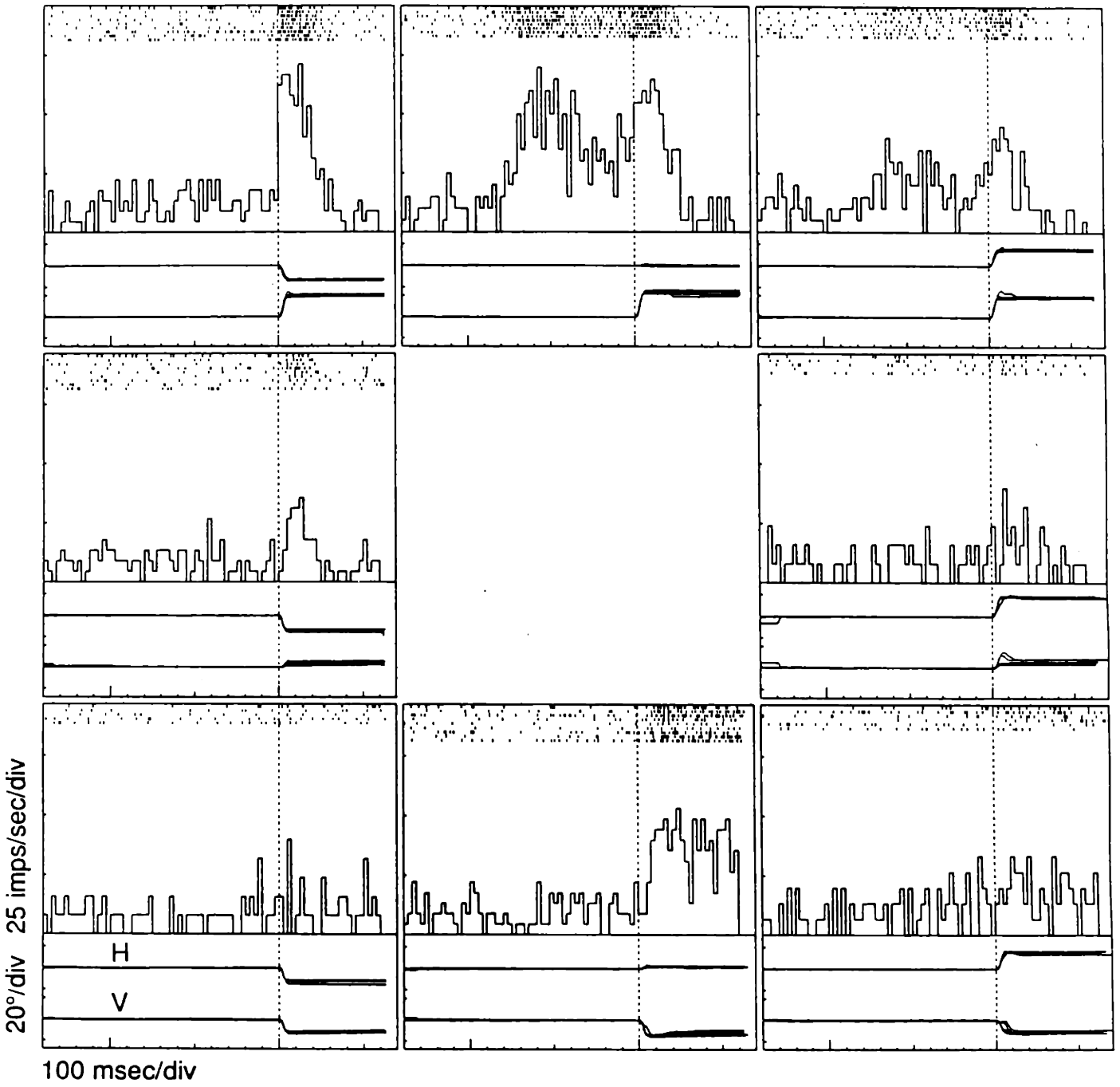
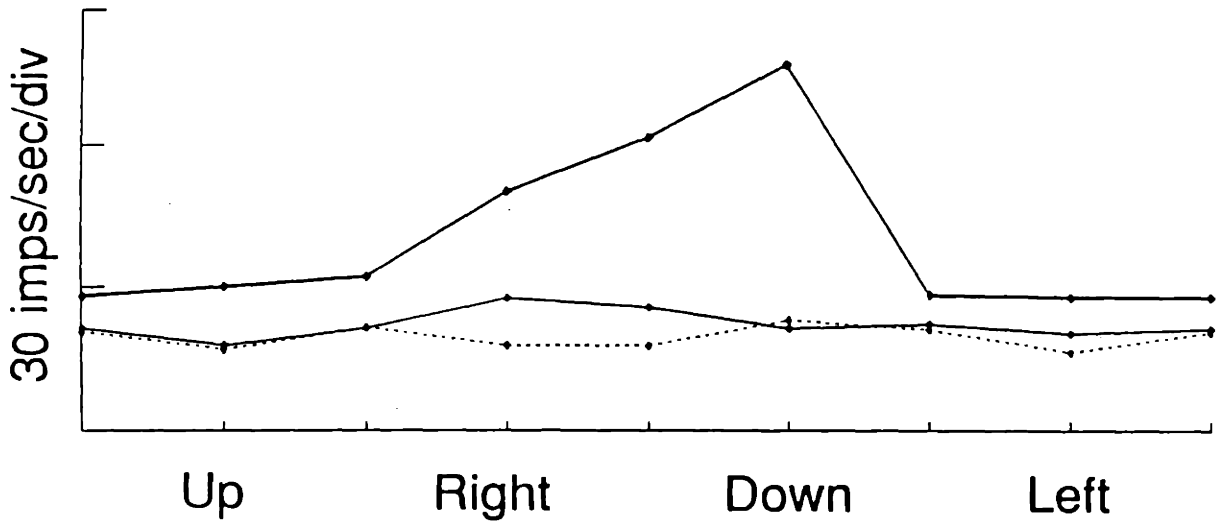





Figure 14



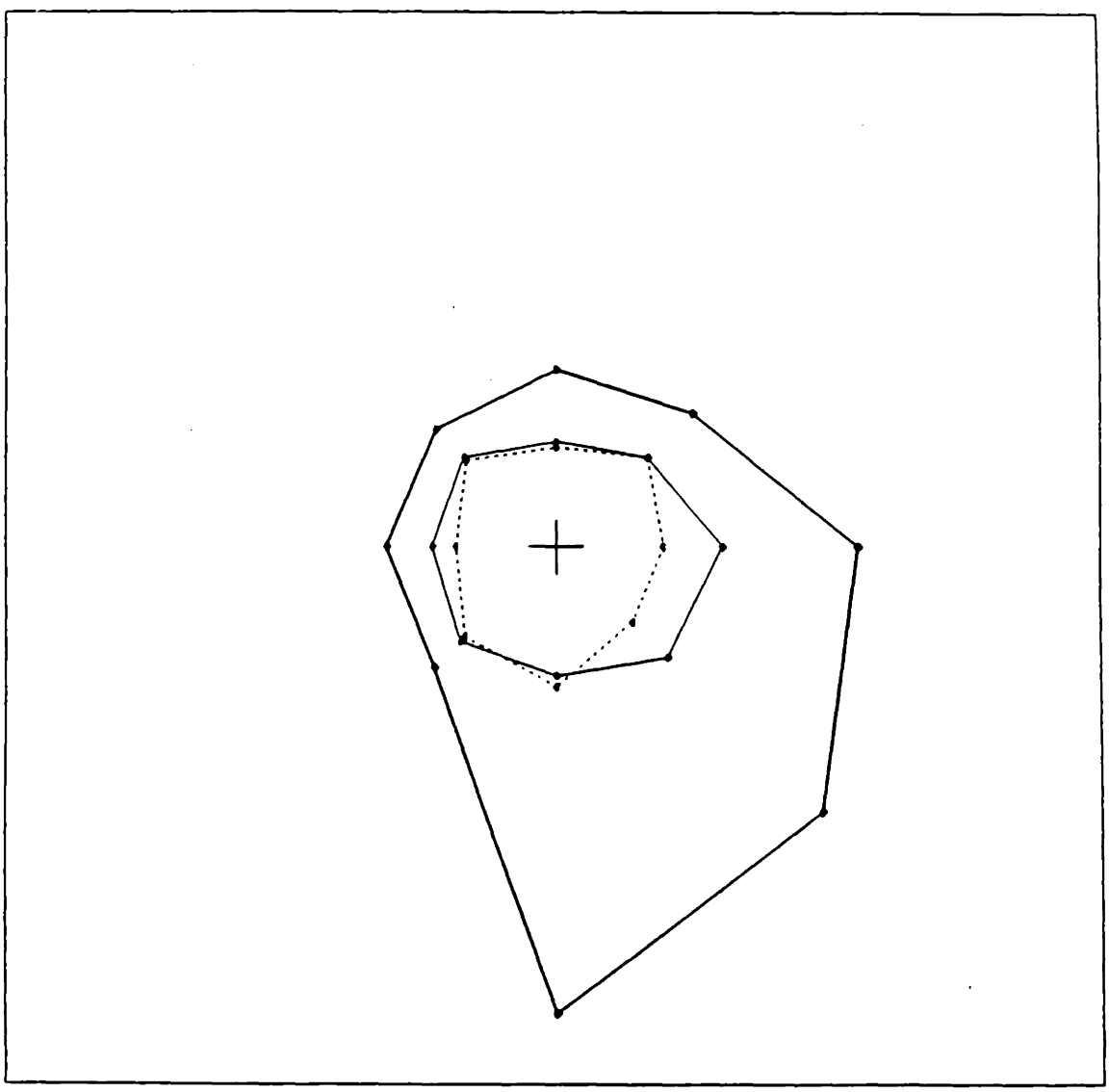





Figure 15

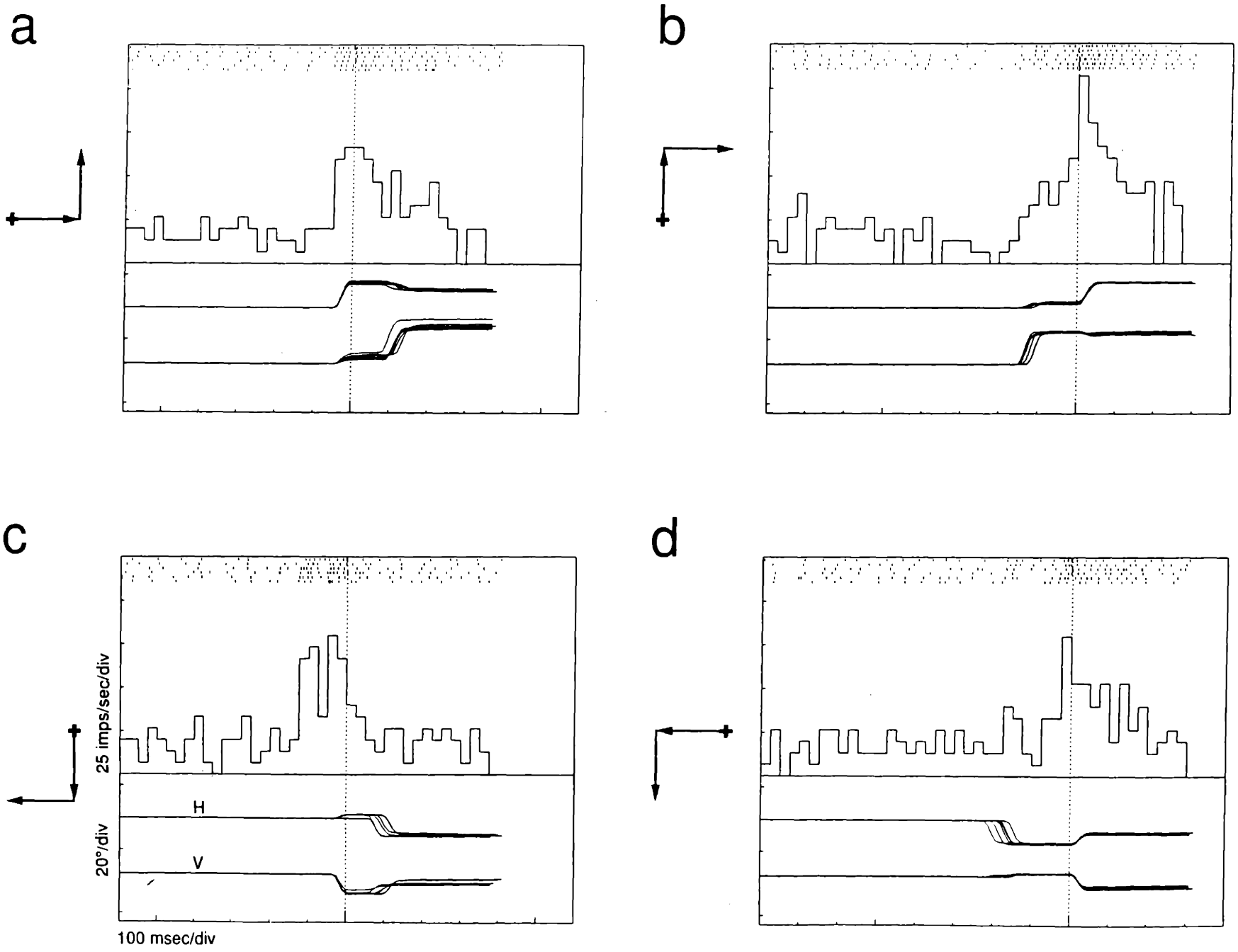



Figure 16

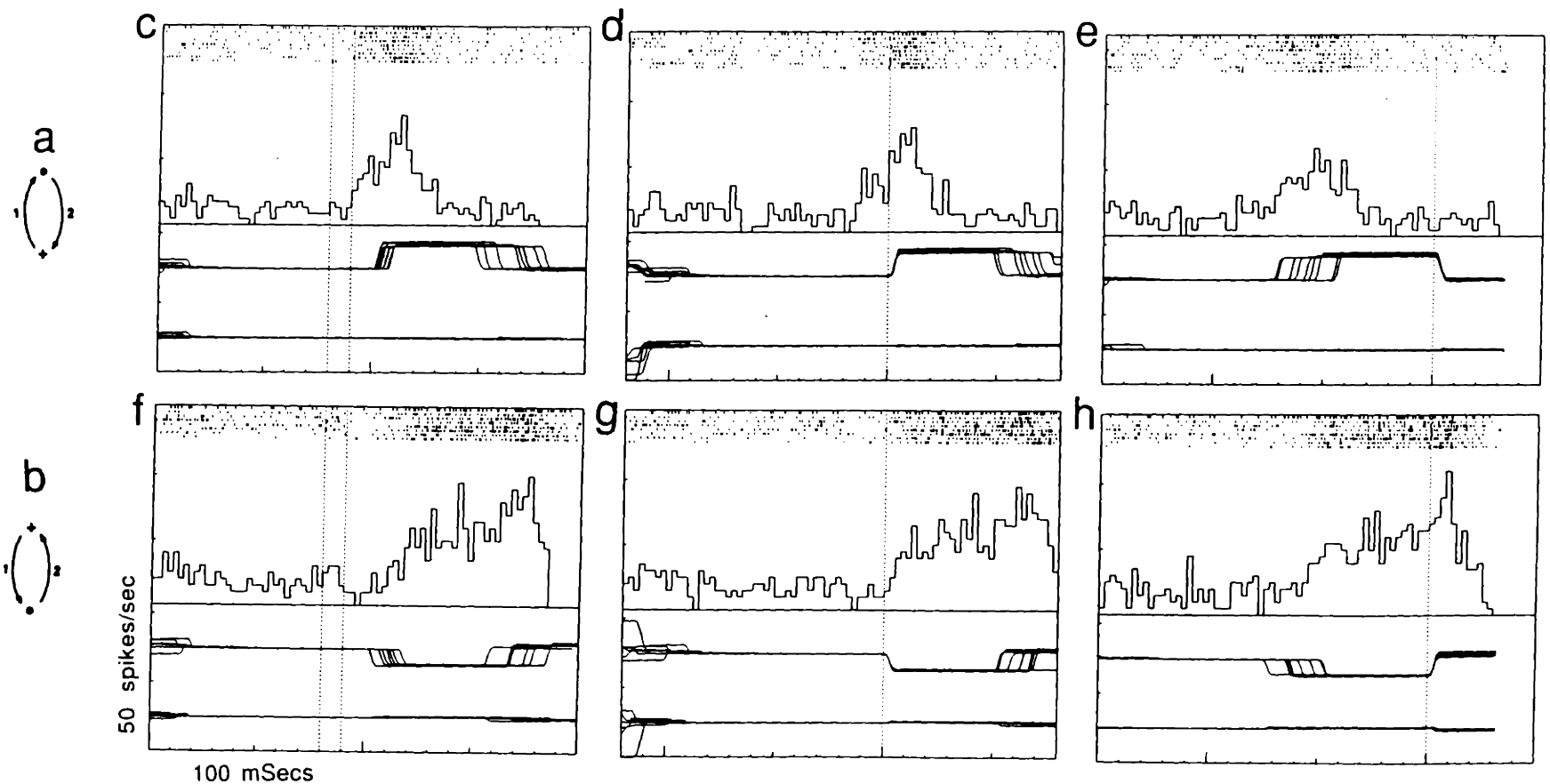



Figure 17

# Chapter 4

## Eye position effects on the visual, motor intention and saccade-related activity in areas 7a and LIP

## SUMMARY

We studied the effect of eye position on the light-sensitive, memory, and saccade-related activities of neurones of the lateral intraparietal area (LIP) and area 7a in the posterior parietal cortex of rhesus monkeys. A majority of the cells showed significant effects of eye position, for each of the three types of response. The direction tuning of the light-sensitive, memory and saccade responses did not change with eye position but the magnitude of the response did. Since previous work showed a similar effect for the light-sensitive response of area 7a neurones (Andersen & Mountcastle, 1983; Andersen et al., 1985b), the present results indicate that this modulating effect of eye position may be a general one, as it is found in three types of responses in two cortical areas. Gain fields were mapped by measuring the effect of eye position on the magnitude of the response at nine different eye positions for each neurone. The gain fields were usually planar or largely planar for all three types of response in both areas, indicating that the magnitude of the response usually varies linearly with both horizontal and vertical eye position. A similar observation was made previously for the gain fields of the light-sensitive response of area 7a neurones (Andersen et al., 1985b). Although gain fields sloped in all directions for the population of cells, the gain field slopes of the light-sensitive, memory and saccade responses for individual cells were usually similar. It is proposed that these eye position effects play an important role in making coordinate transformations for visually guided movement.

## INTRODUCTION

One of the fundamental problems in programming movements under visual guidance is how to link the inherently different coordinate systems used at the input and output stages. The visual inputs are derived from images on the retinas and are cast in retinal coordinates. Due to a point-to-point mapping at the lower levels of the visual pathway, this retinotopic representation is maintained in many brain structures (e.g., see Van Essen 1985). On the other hand, movements must be made to locations in space with respect to the body and therefore it is likely that the motor outputs encode movements in body-centred coordinates (e.g., see Jeannerod 1991).

An area of the primate brain likely to be involved in these coordinate transformations is the posterior parietal cortex. The posterior parietal cortex of both monkeys and humans has been implicated through lesion studies as playing a crucial role in spatial perception and movement under visual guidance (for review, see chapter 1; Critchley 1953; Andersen 1987; Stein 1989; Husain 1991). In particular, human patients with posterior parietal lesions exhibit misreaching to visual locations despite having no overt visual field defects. Similar results are seen in monkeys and suggest that the deficit is a result of coordinate transformation disruption rather than a primary perception defect (for review, see chapter 1; Critchley 1953; Andersen 1987; Stein 1989; Husain 1991). Interestingly, lesions to the posterior parietal cortex produce deficits that are typically specific to saccades made to visual targets and not to saccades made on verbal command or to auditory or somatosensory stimuli (see chapter 1, for review).

Here we focus on coordinate transformations for visually guided saccadic eye movements in rhesus monkeys. The saccade system is simpler than other motor systems, including those involved in moving the limbs, and therefore is easier to study. The number of muscles involved is fewer; there is a constant load or inertia for the eyeball; and the eye and orbit can be considered a single joint. The coordinate transformation problem remains fundamentally the same, however: visual targets for saccades are provided in retinal coordinates, while the motor commands must specify the desired location of the eyes in the orbits.

In previous studies it has been found that eye position and retinal position signals in area 7a interact in a manner appropriate for encoding the location of visual stimuli in head-centered coordinates (Andersen, et al., 1985b; Andersen & Zipser, 1988). In particular, although the interactions between the two signals were non-linear and complex, two general consistencies were identified in the data. The first observation was that while the visual receptive fields remained retinotopic, the evoked visual response was modulated by eye position. The second observation was that the effect of eye position on the total response of the cell varied linearly as a function of both horizontal and vertical eye position for retinotopically identical stimuli. The plots of the effect of varying eye position, with constant retinal position, were referred to as *gain fields*, and a majority of area 7a gain fields were found to be *planar* or to have significant planar components.

In computational studies (Zipser & Andersen, 1988; Andersen & Zipser, 1988; Mazzoni et al., 1991a, b), three layered neural network models were trained to transform eye position and retinal position inputs, such as those converging on area 7a, to output locations in head-centered coordinates. These models were found to have middle layer "hidden" units with response features similar to those found in area 7a neurones (retinotopic receptive fields and eye position gain fields). These studies suggest that the units recorded in area 7a could form (part of) a distributed network underlying the representation of visual targets in head-centred space.

In the present experiments we directly compare, in the same animals, the effects of eye position on the visual, memory, and saccade responses in areas LIP and 7a. We confirm the results previously recorded for eye position effects on the visual responses of area 7a cells and find that the same effects operate for all three responses in both cortical fields. These results suggest that area LIP may play a role in processing the coordinate transformations required for saccadic eye movements. They also suggest that the same algorithm for coordinate transformation may be used by both areas 7a and LIP.

## METHODS

Single cell recordings were made in awake, behaving monkeys trained in eye movement tasks. Recordings were made from three hemispheres of two Rhesus monkeys. Eye position was measured by the scleral search coil technique, which involves recording the induced current in a coil, surgically implanted on the sclera of the eye, as it moves in a magnetic field (Robinson, 1963; Judge et al., 1980).

The experiments were performed in a light-tight chamber, and the animal was monitored with a remote infrared camera and infrared light source. The visual stimuli and fixation point were spots of light 0.5 degrees in diameter, back-projected on a large projection screen. The tangent screen was located 57 cm from the animal's eyes. Three projectors, with electronic shutters and x,y galvanometers, were under computer control and were used to project the visual stimuli and fixation point. Stimulus intensities were 45 candella/$m^2$ against a totally dark background. Optical screens under computer control were used to adjust the luminescence of the stimuli so that they were always of the same value, measured at the eye of the monkey, independent of screen location. Since it was found for monkey M13 that the small changes in luminescence with screen location had no effect on the activity of the area 7a and LIP neurones, this control was not used for monkey M33. The computer corrected for screen tangent errors to ensure that visual stimuli could be positioned at identical retinal eccentricities regardless of eye position.

### Memory saccade task

In the basic paradigm the animal was required to make saccadic eye movements from different orbital positions to the remembered location in the dark. The change in visual, memory and saccade activity for equal amplitude eye movements was measured for neurones in two different cortical fields (areas LIP and 7a). The task was designed to test for visual, memory and saccade responses in one trial. Additionally, it was used to rule out possible visual artifacts contributing to the apparent eye position effects on the saccade response. Such artifacts could arise either from the onset of a visual target that triggers eye movement or from movement in contours of

the visual background through the cells' receptive fields during the eye movement.

The animals were trained to make saccades to remembered locations in total darkness. Figure 1 illustrates the task: after a randomly interleaved intertrial interval of 500 to 1500 msec, a fixation light appeared at the location on the screen corresponding to straight ahead fixation (0,0). "Straight ahead" is defined by a line perpendicular to the coronal plane of the monkey, intersecting the plane at a position equidistant between the two eyes. The animal had 1 second to fixate the stimulus, for the trial to begin. Fixation was indicated by the eye position recordings and was monitored by the computer, which required the eye to be fixated on the fixation point for a continuous period of 100 msec before the trial could begin. If the animal did not fixate the stimulus, a "miss" was recorded and the trial sequence was presented over again after a new intertrial interval. If it did fixate, after either 300 msec (23% of the cells) or 800 msec (77% of the cells) a second stimulus flashed pseudorandomly at one of 8 locations at angle increments of 45 degrees. The screen locations of the targets were located on an imaginary square grid at (-15,15), (0,15), (15,15), (-15,0), (15,0), (-15,-15), (0,-15), and (15,-15) measured in degrees of visual angle. Since the diagonal saccades were slightly longer, for 15 neurones the saccade targets were presented on both a circle and a square. Although the amplitudes were all identical on the circle, no significant difference in direction tuning between the circular and square patterns was noted. This result is likely due to the fact that the amplitude tuning of area LIP and 7a saccade responses are broad, and the visual receptive fields are very large (see chapter 3). The stimulus was only present for 300 msec after which it was extinguished and the animal was required to remember its spatial location. Following a 400 msec (33% of the cells) or 700 msec (67% of the cells) delay the initial fixation light also went off, which commanded the animal to make an eye movement to the remembered location of the flashed target. If the animal broke fixation during the waiting period, the trial was registered an "error," the animal did not receive a reward, and the trial sequence began again. After the fixation point went off, the animal had 500 msec to fixate the remembered target location. If the animal succeeded and maintained steady fixation at the remembered location for 500 msec, it received a drop of juice as reward.

The memory saccade task ensured that the saccade response did not result from either the target, since it had been removed for a long period before the saccade, or from the visual background, since the saccade was made in total darkness. To ensure that the response did not result from the offset of the fixation point, one of the nine classes of each run consisted of a control, shown in figure 1B. In this control, no saccade target is presented and the animal's task is to maintain fixation at the fixation point while it is extinguished for 500 msec. No cells in this analysis showed any response to the offset of the fixation target and are similar to the one in figure 1B.

The electronic windows for maintaining all fixation positions were ± 10 degrees in animal M13 and a range of widths, usually from ±1.5 to 15 degrees, in animal M33. If the animal's eye did not move to gaze within the window of space centered on the test location, the trial was an error. In M33, ±1.5 degree windows were used for saccades to visual targets and the larger windows were used for the memory saccades. Such large windows were used in the memory task because there is a systematic distortion of eye movements to remembered targets for both macaques and humans, with upward saccades typically being hypermetric and downward saccades typically hypometric (chapter 8). We have not found it possible to reduce this distortion even after training an animal on smaller windows for several months (chapter 8). In animal M33 we generally used ±7.5, ±10, ±12.5, or ±15 degree windows depending on the difficulty of the task.

### Training

Under general anesthesia and sterile surgical conditions, an acrylic skull cap for immobilizing the head and an eye coil for eye position recording were implanted. Training began a week after surgery and initially consisted of having the animal learn to fixate the fixation target with the head fixed. Next the animal learned to fixate at different orbital positions and to saccade to the onset of a saccade target which occurred simultaneously with the offset of the fixation target. Finally, the animal was trained to withhold the response for longer periods as described in the memory saccade task outlined above.

**Recording**

Once training was complete, a second surgery was performed in which a recording chamber was mounted over Brodmann's areas 5 and 7 in the posterior parietal cortex. Electrode penetrations were made into area 7a on the gyral surface of the inferior parietal lobule and either down the bank of the intraparietal sulcus into area LIP or through area 5 into area LIP. Before each daily experimental session, the eye movement recording system was calibrated by having the animal fixate 9 positions each separated by 20 degrees on an imaginary grid array centred on straight-ahead fixation. Slopes and intercepts for horizontal and vertical eye position were generated in DAC units from the calibration trials and were entered into the data collection program for setting the eye position windows. Recording sessions typically lasted up to 6 hours daily including rest periods, and typically 3 to 5 cells were isolated and studied in detail on a given day.

When a cell was isolated, the direction tuning was measured using the memory saccade task from orbital position (0,0) (Fig. 1c). Eight directions and the no-movement control were presented as 9 classes in a random block design and 8 to 10 responses were collected for each class (Fig. 1c). The results of this test determined the best directions of the visual, memory, and saccade responses (greatest neuronal response measured in number of action potentials). The three responses generally had the same best-direction tuning (chapter 3).

The next, and most crucial, test consisted of presenting the memory task in the best direction of the cell, but from nine different orbital positions (see figures 1d and 5). In each case a 15 degree saccade was made (in the best direction) from nine different orbital positions spaced 15 degrees apart on a 3 by 3 imaginary grid centered on 0,0. This test determined the effect of eye position on the visual, memory and saccade responses for the best direction of the neurone. The pattern of activity obtained when initial eye position was varied, while maintaining all other parameters constant, is referred to as a *gain field*.

If we were able to maintain recording for long enough periods, additional tasks were administered. For many cells the gain field mapping experiment was repeated for other memory-saccade directions. In some cells we tested all eight directions at the best and

worst eye positions. In many cells we were able to measure the eye position activity alone by requiring the animal to fixate for 2.5 seconds at nine different locations on the screen (Fig. 3). The eye-position only task used a 3X3 grid with 15 degree spacings centered on (0,0). In some cells the visual field was mapped by having the animal maintain fixation at a fixation target while ignoring stimuli flashed at different locations in the visual field.

**Histology**

In the last few weeks of the experiment involving monkey M13, lesions were made at the end of penetrations in both hemispheres by passing small DC currents through the recording electrode at different depths along the electrode tract. At the conclusion of the experiments M13 was given an overdose of sodium pentobarbital and then perfused transcardially with heparinzed saline, followed by buffered formalin. Guide wires were lowered into the brain at selected chamber coordinates immediately after the animal was sacrificed. The wires were used as landmarks for blocking the posterior parietal cortex and for determining the approximate locations of recording tracks that were made early in the recordings. Lesions were not made at the early recording sites since typically the lesions are only visible for about six weeks after they are made. Good agreement was found between the locations of the guide wires and the coordinates of the actual lesions, indicating that the early recording locations, predicted from the coordinate system of the microdrive, appeared to be accurate.

Sections were made at 30 micron thickness with sections stained alternately with thionin for cytoarchitecture and with the Gallyas method for myeloarchitecture (Gallyas, 1979).

For monkey M13, area LIP was identified by myeloarchitectural and physiological criteria. The majority of area LIP is identified by the densely myelinated area on the posterior aspect of the lateral bank of the intraparietal sulcus. This densely myelinated region is approximately 10 mm long in the anterior-posterior dimension of the sulcus and 3 to 4 mm wide in the dorsal-ventral axis (Ungerleider & Desimone, 1986; Andersen et al., 1990). Ungerleider and Desimone (1986) have referred to this densely myelinated zone as VIP*. Area LIP continues 1 to 2 mm dorsal to the densely myelinated area (Blatt et al.,

1990) and was identified on physiological grounds. Area LIP neurones have much brisker responses both during the visual stimulus and the delay period, and generally have shorter latency saccade responses than 7a neurones (chapter 2) . Although there is local grouping of receptive fields according to retinotopic location, the overall organization of area LIP is complex and does not conform to a simple, continuous retinotopic map (Blatt et al., 1990). Only one hemisphere was recorded from in monkey 33 and this animal is presently being employed in experiments. The location of area LIP was determined in this animal based on physiological criteria and the recording depths in the sulcus (see chapter 2 for details).

**Data analysis**

Activity printouts of the gain fields were made for each cell and were used to choose time windows for the data analysis. Windows for the analysis of firing frequency were placed around different periods in the task. In a typical trial the visual stimulus was delivered at 800 msec after onset of the fixation spot for a duration of 300 msec. Memory periods after the offset of the target were 400 or 700 msec at which time the fixation light turned off, initiating the saccade. Typical windows for the data analysis were 300 to 800 msec for the background activity measured at the beginning of the trial, 900 to 1200 msec for the visual response, 1200 to 1500 msec in the 400 msec waiting period, and 1300 to 1800 msec for the 700 msec waiting period. Saccade windows were typically 1600 to 1900 for the 400 msec waiting period trials and 1900 to 2200 for the 700 msec trials. Windows were adjusted slightly on a cell by cell basis to take into account differences in response latency or duration. Care was taken to ensure that the memory period did not include the activity peak associated with the visual response, which fell off rapidly after the offset of the visual target. In tests in which the visual stimulus used to map visual fields was the same as the saccade target, and in which the animal was trained not to saccade to the target, the visual response typically decayed to baseline within 100 msec. Only one set of windows was used on all 9 classes of each gain field test.

The activity rates for the visual, memory and saccade periods were computed both as total activity during the time period and with the background rate subtracted from the total rate. The background rate was typically computed from the time window spanning 300-800 msec

from the beginning of the trial, i.e., before the onset of the saccade target. For the saccade response the background rate was measured during the memory period just before the saccade, rather than at the beginning of the trial, since we were interested in the increase in activity that occurred above the memory response. Occasionally there was a late saccade response and the memory response continued through what would normally be the saccade period. The saccade response appears to add to the memory response and this is why we use the period just before the saccade as a background measure. An analysis program extracted the action potentials that occurred during the chosen time periods, computed the average frequency of firing for each of these periods, and produced a file with these values for statistical analysis.

The statistical analysis used conventional linear regression techniques to partition the variability into components dependent on X and Y eye positions and residual "pure error" and "lack-of-fit" components for statistical testing (Kleinbaum and Kupper, 1978, Netter and Wasserman, 1983). The effects of horizontal and vertical eye position were assumed to be additive and non-interacting. Since all observations for each neurone fell into 9 groups, estimates of pure error variability are comparable to "within group" variability and were obtained in order to determine goodness-of-fit to the planar model.

The sum-of-squares lack-of-fit was calculated as the difference between the sum-of-squares of the model data and the sum-of-squares of the pure error. The F ratio was computed from the ratio of mean-square lack-of-fit divided by the mean-square pure error. In other words, the error of the model should be approximately equal to the pure error if the planar model is valid. If the model error is significantly greater than the pure error, the planar model is not the best model to fit the data. In order to determine whether there was a significant planar component to the data, an $r^2$ value (ratio of explained variation to total variation) was computed and used to test the significance of the sample correlation coefficient as an estimate of the population correlation coefficient. Coefficients for horizontal and vertical slope and Z axis intercept (the intercept of the plane on the Z axis) were computed as part of the regression analysis. The direction of the gradient of the planar component is defined as the direction of greatest positive slope and was computed by taking the inverse tangent

of the ratio of the vertical and horizontal slopes of the plane. The best directions of the light-sensitive, memory, and saccade responses were computed as described in chapter 3. The axis of symmetry was the direction of a regression line through a polar plot of the responses which gave the smallest value for the sum of the squares of the differences between the line and the data points (Fig. 3).

# RESULTS

## Database

Recordings were made from 3 hemispheres of 2 rhesus monkeys. 409 cells were studied in quantitative experiments under computer control. Many of these cells were used to examine other saccade parameters and are reported elsewhere in this thesis. For 126 cells, eye position effects on visual, memory and saccade responses were measured. However, in 35 of these neurones only 5 eye positions were studied and these cells were not subsequently used for more detailed statistical analysis. The ninety-one remaining cells had gain fields mapped at 9 eye positions and these cells form the basis of this study. Thirty of these cells were recorded from monkey M13 and 61 cells were recorded from monkey M33. For monkey M13, 21 cells were recorded from area LIP and 11 from area 7a and for monkey M33, 34 cells were from area LIP and 25 from area 7a. In all, 55 neurones of the sample were from area LIP and 36 were from area 7a. No major differences in eye position effects on the visual, memory, or saccade responses were seen for the two cortical fields. It should be noted that most area 7a saccade responses are postsaccadic (82%) whereas over half (72%) of the area LIP responses were presaccadic (chapter 2). Also area LIP memory, saccade, and visual responses were stronger than those recorded for area 7a (chapter 2).

## Responses of area LIP and 7a neurones

Neurones from areas LIP and 7a exhibited three basic types of activity in the memory saccade paradigm: light-sensitive (LS), memory (M) and saccade (S) related responses. Figure 1A is a typical example of activity, in this case for an area LIP neurone. There is a visual response that begins after the onset of the stimulus, then prolonged activity in the delay period, and finally a second peak of activity occurring at the time of the saccade. Since the saccade is made in total darkness the saccade-related response cannot be an artifact of visual stimulation. For 12 neurones, tests were made in both a lighted (1 candella/$m^2$) and dark test chamber. No appreciable differences were found in the responses under these two conditions.

To control for the possible artifact that the response could be related to the offset of the fixation point, a control class was used. In this control class, illustrated in figure 1B, no saccade target is flashed in the visual field before the offset of the fixation target. The animal had been trained not to make an eye movement if no target is given, but rather to maintain fixation at the remembered location of the fixation target. The target reappears 500 msec later. The eye position trace in figure 1B shows that the animal did not move his eyes and the spike histogram indicates that there was no response to the offset of the fixation point. No cells used in this study showed any response to the fixation target offset. A second indication that the response is not an artifact of fixation target offset is the observation that the saccade responses are almost always direction tuned; a simple offset response would not depend on the direction of the programmed eye movement.

Figure 2 shows why the activity in the delay period is believed to be memory-related. The response continues as long as the animal withholds its saccade response. In other experiments we have shown that this memory activity is coded in motor coordinates and therefore reflects the intent of the animal to make an eye movement of a particular direction and amplitude.

Figure 3 shows an example of direction tuning for LS, M and S activity in an area LIP neurone. Note that all three responses are greatest when the animal saccades up. An extensive quantitative study (chapter 3) has shown that in most cases the best directions of the three responses are similar for single area LIP and 7a neurones.

**Eye position effects**

Many neurones with LS, M, or S responses also had a tonic background activity that was related to eye position. Fourteen cells had only eye position-related activity and were not used in this analysis. These cells were interesting nonetheless because their activity varied linearly with eye position.

Figure 4 shows the activity of such a cell from area LIP in a task in which the animal was required to fixate for 2.5 seconds at nine different eye positions arranged on a 3X3 imaginary grid with 20 degree spacings and centred on straight ahead. As indicated in the figure, the activity of

the neurone varied monotonically with increased activity for more rightward fixations. Activity varied from 25 spikes/sec to almost 100 spikes/sec over the 30 degree range of eye positions. This cell did not have LS, M, or S activity but the eye position-related activity was inhibited during saccades of any direction or length.

**Gain fields**

The effect of eye position on LS, M, and S activity was analysed by having the animal perform the delayed saccade task for different directions at different eye positions. Figure 5 shows the effects of eye position on direction tuning for the saccade response. The peak of the direction tuning curve does not change with eye position; only the magnitude of the response is affected. The same observation was made for the LS and M responses. In all, 56 neurones were examined at more than one direction and all showed results consistent with those illustrated in Figure 5. These results confirm previous studies of the effects of eye position on the visual responses of area 7a neurones which showed that the visual fields remained retinotopic while the magnitude of the activity varied with eye position (Andersen et al. 1985, Andersen and Zipser 1988).

By examining delayed saccades made in the same direction from several different initial eye positions, we were able to map the cells' gain fields--the change in the magnitude of the LS, M, and S responses corresponding to change in eye position. The direction that gave the best saccade response, determined from the direction tuning test, was used in mapping the gain field. For most cells, the LS, M, and S best-directions were similar (chapter 3). Delayed saccades of the same direction and 15 degrees in amplitude were made from 9 orbital positions with 15 degree spacings on an imaginary 3X3 grid centred on straight ahead. Figure 6 shows an example of a cell that responded best for saccades 15 degrees down. On the left are plots of the actual eye movement records for the nine classes and on the right are the corresponding saccade responses. The saccade activity varies linearly in both the horizontal and vertical dimensions and a plane can be fit to the gain field. Planar behaviour was common for the gain fields of the LS, M, and S responses for cells from areas 7a and LIP. These results confirm previous findings that the gain fields for the LS responses for area 7a are planar (Andersen et al., 1985b; Andersen and Zipser, 1988).

Although the saccade direction and amplitude varied by small amounts with eye position, these variations had negligible effect on the cell's responses because the motor fields of these neurones are so large, typically averaging about 90° in diameter for a reduction to 50% of maximum activity (chapter 3).

**Quantitative analysis of gain fields**

Linear regression techniques were used to determine if a plane was a good model for the gain fields of areas LIP and 7a. Regression analysis on the LS, M, and S responses used two measures of activity. The first was a measure of the evoked response and was computed by subtracting the background activity from the total activity of the response period. For the LS and M responses the background activity value was measured at the beginning of the trial, whereas the S activity was taken during the delay period just prior to the saccade. The other analysis used total activity during the test period without subtracting the background. The same basic results were recorded, using either measure, for the population of cells. Because the results were essentially the same, only activity without background subtraction is shown in subsequent figures. Eye-position related activity was also tested for the planar model by analysing the change in background activity with eye position. The background activity for the eye position analysis was measured prior to the onset of the saccade target.

The analysis revealed four types of gain fields. Planar gain fields (P) were those that had significant planar components ($P<.05$) and no significant lack-of-fit ($P>.05$). For this category the planar model is the best possible fit to the data. The gain field on the left in figure 7 is for a saccade response from a cell with a planar gain field. Planar component gain fields (PC) had significant planar components but also demonstrated a significant lack-of-fit. A portion of the variance of these gain fields could be accounted for by a plane; however, a simple linear model was not the best fit to the data. The data in the middle of figure 7 is from a planar component gain field for a saccade response. The non-planar gain fields (NO) had no significant planar component but a significant lack-of-fit, indicating that while the activity did vary significantly with eye position, there was no planar component to the variation. The histograms to the right in figure 7 illustrate a non-

planar gain field for a saccade response. The fourth classification was the no gain fields (NG) which had both no significant planar component and no significant lack-of-fit; that is, there was no significant effect of eye position on the responses.

Table 1A shows the results of the regression analysis for all cells with and without background subtraction. The main result is that most cells that have significant gain fields for LS, M, or S responses show planar or planar component behaviour. From 22% to 53% of the cells showed no significant gain field, depending on the category, with an average of 34% over all categories. Table 1B recomputes percentages after excluding those cells with no gain fields. Most of these remaining neurones fall into the planar and planar component categories with very few in the no planar component category. For example, for saccade responses without background subtraction, 49% of the cells showed planar gain fields and an additional 41% had planar components, with only 10% having non-planar gain fields.

An interesting question is what percentages of P, PC, NO and NG classes would we have encountered from a random distribution. The statistical analysis, with $P<.05$ as a measure of significance, would predict that 90.25% of the cells would be NG, 4.75% would be NO, 4.75% would be P, and only .25% would be PC for a random distribution. We tested this hypothesis by generating 100 different random data files with background activity randomly distributed between 0 and 10 spikes/sec and the responses (without background subtraction) randomly distributed between 0 and 30 spikes/sec. When these random data files were processed with the same analysis programs as were used on the real data, 93% were found to be NG (compared to 90.25 predicted), 5% NO (4.75 predicted), 2% P (4.75% predicted), and 0% PC (.25% predicted). These percentages from the random number simulation are entered in the last column of Table 1a for direct comparison with the recording data.

Table 2 shows the percentages of planar, planar component, and no planar component gain field types by cortical field. Inspection of this table shows no appreciable differences between areas 7a and LIP.

The gradient directions for LS, M, and S activities were compared for area LIP and 7a neurones. As indicated in Figure 8, all three types of responses produced gain fields with gradients fairly evenly distributed in all directions. There did not appear to be a bias toward the contralateral or ipsilateral visual field. Also, no appreciable difference

was noted between areas LIP and 7a.

The slopes and intercepts of the gain fields (calculated without background subtraction) are illustrated in Figures 9 and 10 and the means, medians, and other statistics are listed in Table 3. In general, the intercepts were larger for area LIP (Figure 9) as well as the slopes (Figure 10), indicating a larger response for area LIP. Although the background activity is also higher in area LIP (chapter 2), it accounted for only a portion of the difference.

At first glance, the intercept and slope figures appear low, but this is due to the fact that the firing rate is averaged over a period of time. Often the response rate will peak at over 100 spikes/sec, but these peaks are usually quite transient, and the averaged rate, which includes the time of the peak, is usually much lower.

Using the data from Table 3, a quantitative measure of the overall effect of eye position on the LS, M, and S responses was calculated. The minimum and maximum activities along the horizontal and vertical axes of the gain fields were calculated by multiplying the mean slope by 15 degrees and subtracting and adding it to the mean intercept respectively. A measure of percentage modulation was calculated as 100 ( 1 - min/max): a value of 50% would mean that the activity varied by 50% of the maximum activity over an eye position range of 30 degrees. Modulation values varied over a range of 30% to 47% and are shown in Table 3B. The modulation values were slightly higher for area 7a, possibly due to the fact that the background rate was higher in LIP and these modulation values were calculated without background subtraction. The overall average modulation was 42%.

**Co-variation of LS, M, and S responses for single cells**

For single cells, the light-sensitive, memory, and saccade responses usually varied together as a function of eye position. Figure 11 shows an area LIP cell that gives a large response in both the LS and S periods when the animal fixated left and up, and a relatively smaller response for both when the animal fixated to the right and up.

Figure 12 shows entire planar gain fields for the light-sensitive, saccade and memory responses of a single neurone. The inner circle diameters are proportional to the evoked activity and the outer circle diameters to the total activity. Thus, the widths of the annuli are

proportional to the component of activity contributed by the eye position input. Note that all three planes have similar gradients, i.e., directions of steepest positive slope.

The histograms in Figure 13 display the differences in the gradient directions for the light sensitive and saccade (panel A), light-sensitive and memory (panel B), and memory and saccade (panel C) responses (without background subtraction) of area 7a and LIP neurones. Both gain fields of a comparison had to be planar or have a planar component for a cell to enter into this analysis. The differences in gradient directions were generally found to be small for all three comparisons for single cells. Thus it can be concluded that the eye position input to single cells in area 7a and LIP produces the same effects on the magnitudes of the light-sensitive, memory, and saccade responses. Changes in eye position will increase or decrease in LS, M, and S activity together in single neurones.

# DISCUSSION

The results indicate that eye position has a significant effect on light-sensitive, memory, and saccade responses in both areas 7a and LIP. Two-thirds of the cells tested showed a statistically significant effect of eye position on these responses. The direction tuning of the light-sensitive, memory, and saccade responses did not change but the magnitude of the response did. For all three types of responses in both areas the gain fields were usually planar or had significant planar components. The eye position signals were also usually planar. At the single cell level, the effect of eye position was usually the same for all the responses; that is, the changes in the magnitudes of the light-sensitive, memory, and saccade responses usually covaried with eye position.

Neurones in areas 7a and LIP had similar properties for the parameters examined in this study. Neurones from both areas in each animal exhibited light-sensitive, memory, and saccade responses. For both areas, the best direction remained the same but the magnitude of the responses varied with eye position. Both areas showed a predominance of planar gain fields. The planar gain fields had similar gradient directions for the two areas. The only major difference was that area LIP intercepts and slopes were much larger, indicating that the visual, memory, and saccade responses were greater for area LIP. In a separate study using the same general population of cells from monkeys M13 and M33, we also found that the saccade responses of area LIP neurones were presaccadic in over half of the recordings whereas the saccade responses were almost always post-saccadic for area 7a neurones (chapter 2).

## Controls

The most important control is one that rules out the possibility that the visual background could influence the response of the neurones at different eye positions. For example, at a particular eye position a contour of the test chamber might fall within the receptive field of a neurone and influence the excitability of the cell to the visual target stimulus. Likewise, during eye movements from some initial eye positions, the eye might sweep across stimuli in the background that

evoke a response. To rule out these possibilities the experiments were done in total darkness, eliminating any visual background. An additional control, in which the animal made no eye movement with offset of the fixation point when no saccade target was previously presented, ruled out the possibility that the saccade response could result from the offset of the fixation target.

In earlier experiments on the effects of eye position on visual responses of area 7a neurones, an additional control was performed in the light using prisms (Andersen et al. 1985; Andersen and Zipser 1988). In these experiments the monkey was required to fixate at different eye positions by looking through prisms of variable diopter values and polarity. Neither the fixation point nor the visual test stimulus was moved on the screen; rather the animal fixated on the fixation point from different angles of gaze through the prisms. As a result, the visual background was always retinotopically the same at the different eye positions, yet the visual response still varied with eye position.

A second potential problem is that the visual stimulus may fall on slightly different locations on the retina at different eye positions. These errors could result from errors in positioning the test stimulus, errors in fixation accuracy, or torsions of the eyes during fixation. The positions of the test stimuli were calculated and adjusted under computer control to eliminate tangent errors that would normally result from using a flat screen. Errors due to improper fixation or torsion were small, usually under one degree of visual angle under the present conditions. The direction tuning of the receptive fields and motor fields of the neurones in this sample were very broad, averaging about 90 degrees for a 50% reduction in activity for visual or motor responses in areas 7a and LIP (chapter 3). There is a smooth variation of sensitivity between neighbouring points in the receptive and motor fields and thus errors of one degree would have little effect on the response of the cells. Moreover, when the entire visual receptive field was mapped at best and worst eye positions for area 7a neurones, it was often found that at the worst eye position the cell was completely unresponsive, regardless of where in the visual field the stimulus was presented (see figure 6, Andersen and Zipser, 1988).

Because a tangent screen was used, we were concerned that stimuli would be presented at slightly different depths depending on the screen

location of the stimulus and the point of fixation. It could be argued that small disparities or small differences in vergence could account for these results. In fact, Sakata et al. (1983) have found effects of depth on the eye position activity which suggest that the cells are coding fixation position in three dimensions. However, the tuning with depth was very broad in their experiments, typically varying continuously from 10 to 160 cm. The small differences in vergence due to the use of a tangent screen would have a negligible effect according to these data. Andersen and Mountcastle (1983) compared responses with the animal fixating at different angles of gaze in which the fixation depth and relative depth of the test visual stimulus were the same. They found that the angle of gaze under these conditions still had a major influence on the response of area 7a neurones to visual stimuli.

Another potential source of error could arise from the fact that the intensity of the stimulus varies slightly when delivered to different locations on the screen. In the experiments with monkey 13, the test stimulus intensity was maintained under computer control and calibrated so that it was always of the same intensity, regardless of screen position, measured at the animal's eye. In the second monkey the intensity was not adjusted and results were similar, suggesting that any small difference in the intensity of the stimulus was not a factor.

A last possible (although unlikely) artifact is that vertical disparities may account for the effects of eye position. Vertical disparities would be small at the screen distance used in these experiments. More importantly though, there were large eye position effects for fixations along the vertical midline, where vertical disparities would not be a factor (see figure 11, Andersen and Mountcastle 1983).

**Relation to previous studies**

Modulation of visual responses by eye position was first reported in the intralaminar nuclei of the thalamus (Schlag et al., 1980) and superior colliculus of the cat (Peck et al., 1980), although the nature of the modulation was not determined. Andersen and Mountcastle (1983) showed a modulation of the visual responses of area 7a cells by eye position. This study reported effects for both stationary stimuli and stimuli moving at a constant velocity. Andersen et al. (1985a) were the first to show that the visual receptive fields of area 7a neurones remained retinotopic but the magnitude of the response was gated by eye position. These studies also first demonstrated the planar gain fields for the visual responses of area 7a neurones. Galleti et al. (1991) have observed gaze-dependent neurones in area V6 (on the anterior bank of the parieto-occipital sulcus - an area which connects with other parietal regions such as LIP and area 7a, and area V3a). They also report visual and saccade-related activity in this area. Unfortunately, their study was rather qualitative, and the possibility of modulation of visual and saccade-related activity by eye position was not investigated. In a recent study (Galletti and Battaglini, 1989) of area V3A, a similar modulation of visual responses by eye position was found, including the presence of planar gain fields. Since area V3A provides input to area LIP (Andersen et al., 1990), it is possible that the eye position effects are initially produced in this area or an area even earlier in extrastriate visual cortex, although it is also possible that they are generated independently in several brain regions. Yin and Mountcastle (1977) and Mann et al., (1988) have noted a modulation of saccade responses from two eye positions in area 7a and the supplementary eye fields of monkey respectively. From these previous results and from the present results, it can be concluded that modulation of visual and saccadic signals by eye position is quite common in the primate and cat brain. In several cases in which this modulation has been examined carefully, the receptive and motor fields have been found to remain in retinotopic coordinates, but the magnitude of the response to be modified by eye position. Furthermore, the effect of eye position has been found to be generally linear for both horizontal and vertical positions, producing planar gain fields. These results suggest that the method of interaction of eye and retinal position described here *may*

be common to those regions of the brain that combine these signals. If the interactions of these signals are used for coordinate transformations from retinal to head- or body-centered coordinates, then the results also suggest that the same algorithm *may* be used for coordinate transformations in several brain areas.

**Distributed coding**

A recent computational study (Zipser & Andersen, 1988) has demonstrated that the angle-of-gaze effect on the visual responses of neurones in area 7a could subserve a distributed representation of visual object location in head-centred space. Single neurones with receptive fields restricted to certain locations in craniotopic space are *not* required for the brain to represent such information. Similarly, that the presaccadic responses of LIP neurones show a formally identical angle-of-gaze effect suggests that a similar, distributed representation may underlie the ability of primates to make saccades to targets defined in craniotopic space (see also Goodman and Andersen 1989).

**Models of saccade generation**

Two general hypotheses for the programming have been proposed, the "foveation hypothesis" and the "spatial hypothesis". They are discussed below. Recently, a third hypothesis, which shares some features of both the previous ones, has been proposed. This "vector subtraction" hypothesis (Bruce 1988, 1990; Goldberg and Bruce 1990) is discussed in chapter 5.

Foveation hypothesis

About twenty years ago a "foveation" hypothesis for the production of saccades was proposed (Schiller and Koerner, 1971; Robinson, 1972). In essence it was suggested that the retinal error (i.e., the distance and direction of a visual target from the fovea) directly specified the motor error (the eye movement vector required to foveate the target). This intuitively appealing hypothesis was made even more attractive by then recent discoveries about the superior colliculus (SC). The superficial layers of the SC contain a retinotopic map (Cynander and

Berman, 1972), therefore the retinal error is represented by the locus of visually-triggered activity in these layers. An orderly retinotopic motor map of saccades had been found in the deeper layers by microstimulation (Schiller and Koerner, 1971; Robinson, 1972). It was proposed that activated neurones in the superficial visual layers activated, relatively directly, the subjacent part of the deeper layers of SC. These layers contain a "motor map" of visual space, in register with the overlying visual map, such that activity in a given part of it would cause a saccade that would foveate the region of visual space currently represented in the overlying region of the visual map. Subsequent recording studies have confirmed that the deeper layers do indeed contain a motor map (reviewed in Sparks, 1986).

Although it is attractive, problems with the Foveation Hypothesis have become apparent over the last twenty years. These I briefly enumerate below:

1. Shebilske (1977) and Skavenski (1976) showed that humans perceptually localise visual targets in non-retinal coordinates.

2. Hallet and Lightstone (1976a, b) showed that humans can make saccades to targets localised "spatially" . (Spatial is the term generally used in the literature to refer to a non-retinal, head- or body-centred frame of reference.)

3. Mays and Sparks (1980a) showed that monkeys can make a saccade that requires the association of eye as well as retinal position information.

4. Mays and Sparks (1980b) also showed that the discharge of overlying visual cells in the superficial layers is neither necessary nor sufficient for the activation of subjacent pre-saccadic cells.

5. Superficial visual cells discharge within 60 ms of target onset, whereas deeper presaccadic cells start to burst 100-130 ms later, *c.*20 ms before the saccade (Sparks, 1986). 100 ms would be an inordinately long time for direct superficial-to-deep signal transmission.

6. There is no anatomical evidence for the necessary superficial-to-deep linkage (reviewed in Sparks, 1986).

7. Ablation of SC leads to relatively small deficits in visually-guided saccades (reaction times increase modestly; velocity and accuracy decrease slightly: Albano and Wurtz, 1982, Butler et al., 1983, Schiller et al., 1980), so SC cannot be *essential* for such saccades. (However, these results and those of Hikosaka and Wurtz (1983, 1985) suggest that normally SC *participates* in the generation of such saccades.)

Points 4-7 above deal with the specific anatomical instantiation proposed for the hypothesis. However, points 2 and 3 clearly show that the basic hypothesis is no longer tenable. Point 1 also suggests that it is not tenable.

Spatial Hypothesis

In most current models of visual saccade generation (e.g., Robinson, 1975; Zee et al. 1976) the saccade is programmed in spatial coordinates. At its simplest, the hypothesis says (a) the target is localised in head-centred space by linear summation of retinal and eye position signals; (b) after a delay (*c.* 0.2 s), the current eye position - which *need not* be the same as that from which the target was seen - is subtracted from the target position signal to generate a motor error which specifies the correct saccade to foveate the target. This model accounts for many of the problems that flawed the foveation hypothesis.

It was reasoned that this hypothesis predicted that there should be neurones in the brain that fired before saccades that brought the eye to a specific position in the orbit, regardless of the starting position of the eye, and similarly that stimulation of brain regions containing such cells should evoke "goal directed" saccades (i.e., saccades that brought the eye to a specific orbital location). Such neurones and such sites have rarely been reported. (Goal-directed presaccadic and/or eye position-independent visual activity has been found in the postarcuate cortex (Gentilucci et al., 1983), the central thalamus (Schlag and Schlag-Rey, 1984), and the dorsomedial frontal cortex (Mann et al., 1988)). This has led some to doubt the validity of the hypothesis (e.g., Bruce 1988). However, the present results, together with computer simulation studies (Goodman and Andersen, 1989), suggest that the craniotopic representation required by spatial models of saccades may be a distributed one.

**Summary**

The results of the study reported here show that the direction tuning of visual, memory and saccade responses in two cortical fields of the posterior parietal cortex are not altered significantly by eye postion but that the magnitude of the responses are. The degree of modulation of these responses is usually linear for changes in both horizontal and vertical eye position. The fact that single posterior parietal cells never have receptive fields for restricted locations in head-centred space independent of eye position suggests that the code for spatial location is distributed. The coding of spatial location could, in theory, remain distributed throughout the visual and oculomotor systems and only be explicit in the behaviour of moving the eyes.

## TABLE LEGENDS

**Table 1:**

A) Numbers and percentages of gain fields that fell into the four classes defined by the statistics of the two-dimensional regression analysis. Gain fields are listed in the columns for the light-sensitive, saccade, eye position, and wait (memory) responses. W indicates that the firing rates used to compute the gain fields were "with" background subtraction and W/O indicates that the firing rates were "without" background subtraction. The eye position gain fields are calculated from the background rates. The rows show the percentage and number of cells in the different categories. P is for "planar" gain fields (regression $P<.05$, lack-of-fit $P>.05$), PC is for "planar-component" (regression $P<.05$, lack-of-fit $P<.05$), NO is for "no-planar-component" (regression $P>.05$, lack-of-fit $P<.05$), and NG is for "no-gain-field" (regression $P>.05$, lack-of-fit $P>.05$). The bottom row shows the total number of neurones for each column. The table in part B is the same as A, but with the percentages recomputed after taking out those gain fields that had no gain field (NG). The number of gain fields remaining for response class after subtracting the NG category is listed in the bottom (N) row. The number of cells with NG varied by a small amount depending on whether or not background activity was subtracted, leading to different numbers within a class. For instance, 26 saccade cells with background subtraction were NG and only 20 were NG without subtraction, resulting in Ns of 65 and 71, respectively.

**Table 2:**

A) The percentages of area LIP cells with significant gain fields that fell into the planar, planar-component and no-planar-component categories. The numbers of each type of gain field are listed in the bottom row. W indicates gain fields calculated from firing rates "with" background subtraction and W/O indicates gain fields calculated from firing rates "without" background subtraction. B) The same as (A) but for area 7a neurones. Note that there does not appear to be any significant differences between areas LIP and 7a in the types (P, PC, NO) of gain fields for the light-sensitive (LS), saccade (SAC), eye position

(EYE), or memory (WAIT) responses.

**Table 3:**

A) Statistical data on the intercepts and slopes of the LS, M, and S gain fields for areas 7a and LIP. All data are taken from P and PC gain fields without background subtraction listed in Table 2. The slopes listed all had significant regressions. S.D., standard deviation; S.E., standard error; N, number of gain fields. B) The percent modulation of the LS, M and S activities over a 30 degree range of horizontal (X) or vertical (y) eye positions. The modulation was calculated as 100(1-minimum response/maximum response).

## FIGURE LEGENDS

**Figure 1:**

A) Illustration of the memory saccade task showing the sequence of events. The baseline period represents the time prior to the onset of the fixation light and was always 800 msec long. The saccade target appeared next for 300 msec followed by a 400 or 700 msec delay (memory period, a 400 msec period is illustrated in this figure). Following the memory period, the fixation light is turned off commanding the animal to make a saccade to the remembered location of the saccade target in total darkness. The histogram shows activity from an area LIP neurone during the baseline, light sensitive (LS), memory (mem) and saccade periods. Firing rates were determined during these epochs; the method of measurement of spike rate is detailed in the text. Below the histogram are traces of the horizontal eye position indicating the time at which the animal made a saccade 15 degrees to the left. For horizontal eye position traces in all figures, down corresponds to leftward eye movements and up to rightward eye movements. B) Control task to show that the saccade response was not a result of the offset of the fixation target. The fixation light goes off for 500 msec beginning at 1500 msec after the initiation of the trail. The animal is trained not to make an eye movement if no saccade target is presented prior to the offset of the fixation point. The histogram indicates that the cell does not respond to the offset of the fixation target and the eye trace indicates that the animal did not make an eye movement during the holding period when the fixation point is extinguished. C) Task which tests for the direction selectivity of the light sensitive, memory, and saccade responses. Each computer run consisted of 8 classes of memory saccades, each calling for an eye movement in a different direction, and a control class (illustrated in B); the 9 classes were presented in random block design for 8 to 10 trails in each class. The axes indicate screen coordinates in degrees of visual angle. D) Test for determining the gain fields. Once the best-direction of a neurone has been determined by the test in (C), memory saccades are made in that best direction, but from 9 different initial eye positions.

**Figure 2:**

Memory saccade task with different delays demonstrating the memory character of the activity during the delay. Delays are 200 msec (panel A), 1000 msec (B), and 1300 msec (C). The rasters show the actual neural activity that is used to make the histograms. The period between the first two dotted vertical lines represents the time the saccade target is present and the period between the second and third lines is the delay period. The fixation light goes off coincident with the third dotted vertical line. Both horizontal (H) and vertical (V) eye position traces are shown. In this experiment the saccade target appeared 15 degrees to the left. There is a vertical component in the leftward eye movement; this upward component for horizontal eye movements is common for saccades to remembered locations made in the dark (see chapter 8).

**Figure 3:**

A) Histograms for remembered saccades made in eight different directions. The delay period was 400 msec. Note that the light-sensitive, memory and saccade related activities all have approximately the same best-directions (up).

B) A polar plot comparing the best-direction tuning for the light-sensitive and saccade responses. The upper graph shows the numerical values for the spontaneous, light-sensitive, and saccade activities. The lower graph is a polar plot of these values with the radius proportional to the actual activity and the direction corresponding to the direction of the visual target for the light-sensitive and spontaneous activity measures, and the actual direction of the remembered saccade for the saccade activity measure. The solid straight line indicates the calculated best direction of the light-sensitive response and the dotted line the best direction of the saccade response.

C) Same as in (B), but comparing the light-sensitive and memory responses.

**Figure 4:**

Eye position related activity for fixations at nine different eye positions. The dotted vertical line represents the onset of the trail 100 msec after the animal's eye position is continuously within the eye position window. Fixations are at the locations indicated by the coordinates to the left of each histogram. Note that the variation of activity with eye position approximates a plane with increased activity for more rightward fixations.

**Figure 5:**

Direction tuning of the saccade response for saccades made from 6 different initial eye positions. Note that the magnitude of the response changes with eye position, but the best-direction of the response does not.

**Figure 6:**

A) Eye position recordings for saccades made 15 degrees downward from 9 different initial eye positions. Each dot of the eye movement trace represents an analog-to-digital sample; the sampling rate was 500 Hz. The movements are displayed on a graph of visual angle in screen coordinates.

B) Histograms of the evoked activity resulting from the saccades made in (A). Each histogram is positioned to correspond to the initial orbital position from which the saccades were made. The histograms are made from spike rasters that have been aligned to the beginning of the eye movement. The dotted line in each histogram represents the beginning of the saccadic eye movement, determined by the method of Usui and Amidror (1982). This area LIP neurone had activity beginning prior to the beginning of the eye movement. Note that the gain field is planar, with better responses for eye positions located down and to the right.

**Figure 7:**

Examples of planar (left panel), planar component (middle panel) and non-planar (right panel) saccade gain fields. The histograms have no had the background activity subtracted. The dotted vertical line for each histogram indicates the time of onset of the saccade, determined by the method of Usui and Amidror, and all spike rasters that form the histograms were synchronized to the beginning of the eye movement. Planar gain fields have significant regressions ($P<.05$) with no significant lack-of-fit ($P>.05$), planar component gain fields have significant regressions with significant lack-of-fit, and non-planar gain fields have no significant regressions but significant lack-of-fit. Below each gain field example is the percentage of cells that have planar, planar component or non-planar gain fields for the saccade, light sensitive and memory responses. These percentages were computed using firing rates without background subtraction.

**Figure 8:**

The direction of the gain field gradients for the light sensitive (A), memory (B), and saccade (C) gain fields for are 7a and area LIP neurones. Contralateral is to the right. Note that there is a fairly even distribution of directions for all three types of gain fields in both areas. The gradients were derived from gain fields using firing rates without background subtraction. Plots are from cells listed in Table 2.

**Figure 9:**

Intercepts for light sensitive (A), memory (B) and saccade (C) gain fields for area 7a and area LIP neurones. The intercepts were calculated from gain fields using firing rates without background subtraction. Note that the area LIP neurones have larger intercepts overall compared to area 7a neurones. The medians, means, standard deviations and standard errors for the data in these histograms are contained in Table 3.

**Figure 10:**

Horizontal and vertical slopes for the light-sensitive (A), memory (B), and saccade (C) gain fields for area 7a and LIP neurones. The slopes were calculated from gain fields using firing rates without background subtraction. Only slopes that were statistically significant are plotted. The slopes for area LIP neurones are slightly larger than for area 7a neurones. The medians, means, standard deviations and standard errors for the data in these histograms are contained in Table 3. The gain fields plotted were the same as those shown in Table 2. The numbers plotted are lower than in Table 2 because often a planar gain field was significant only in the vertical or only in the horizontal slope. In this figure only significant horizontal or vertical slopes are plotted.

**Figure 11:**

The responses of an area LIP neurone for eye movements made 15 degrees down and left from (-20,20) initial eye position (left panel) and from (20,20) initial eye position. Note that both the light-sensitive and saccade responses are larger for eye position (-20,20).

**Figure 12:**

Light sensitive, saccade and wait (memory) gain fields for a single area LIP neurone. These data were all derived from the same memory saccade. The inner circle diameters are proportional to the evoked activity (total activity minus background) and the outer circle diameters are proportional to the total activity. Each pair of circles is positioned with respect to its initial eye position within the gain field. Note that the gradient direction for all three planar gain fields are very similar.

**Figure 13:**

Differences in angle between LS and S (A), LS and M (B), and M and S (C) gradients for single area 7a and LIP neurones. The gradient directions of the planar gain fields from the three epochs of the activity of single cells are subtracted and the absolute value of the difference is used for the histograms. Only gain fields that are planar or planar-component were analysed. The number of cells in the histograms is smaller than that in Table 2 because both gain fields being compared in individual cells had to be statistically significant to be plotted. Note that regardless of which two epochs are compared, the differences tend to be small, indicating that the planar gain fields for all three epochs in single cells tend to have the same gradient direction.

## Table 1

A) **Total of All Cells**
**N = 91**

| | LS | | SAC | | EYE | MEMORY | | Random Distribution Simulation |
|---|---|---|---|---|---|---|---|---|
| | W | W/O | W | W/O | | W | W/O | |
| P | 22% (20) | 29% (26) | 31% (28) | 38% (35) | 37% (34) | 34% (31) | 32% (29) | 2% (2) |
| PC | 13% (12) | 35% (32) | 29% (26) | 32% (29) | 26% (24) | 10% (9) | 24% (22) | 0% (0) |
| NO | 12% (11) | 11% (10) | 12% (11) | 8% (7) | 6% (5) | 12% (11) | 8% (7) | 5% (5) |
| NG | 53% (48) | 25% (23) | 29% (26) | 22% (20) | 31% (28) | 44% (40) | 36% (33) | 93% (93) |
| N | 91 | 91 | 91 | 91 | 91 | 91 | 91 | 100 |

B) **All Cells Excluding NG**

| | LS | | SAC | | EYE | MEMORY | |
|---|---|---|---|---|---|---|---|
| | W | W/O | W | W/O | | W | W/O |
| P | 47% (20) | 38% (26) | 43% (28) | 49% (35) | 54% (34) | 61% (31) | 50% (29) |
| PC | 28% (12) | 47% (32) | 40% (26) | 41% (29) | 38% (24) | 18% (9) | 38% (22) |
| NO | 25% (11) | 15% (10) | 17% (11) | 10% (7) | 8% (5) | 21% (11) | 12% (7) |
| N | 43 | 68 | 65 | 71 | 63 | 51 | 58 |

Table 2

A) **LIP % All Cells Excluding NG**

| | LS | | SAC | | EYE | MEMORY | |
|---|---|---|---|---|---|---|---|
| | W | W/O | W | W/O | | W | W/O |
| P | 41% (11) | 50% (21) | 48% (19) | 51% (21) | 57% (21) | 68% (19) | 54% (20) |
| PC | 30% (8) | 36% (15) | 35% (14) | 42% (17) | 35% (13) | 21% (6) | 38% (14) |
| NO | 29% (8) | 14% (6) | 17% (7) | 7% (3) | 8% (3) | 11% (3) | 8 (3) |
| N | 27 | 42 | 40 | 41 | 37 | 28 | 37 |

B) **7a % All Cells Excluding NG**

| | LS | | SAC | | EYE | MEMORY | |
|---|---|---|---|---|---|---|---|
| | W | W/O | W | W/O | | W | W/O |
| P | 56% (9) | 20% (5) | 36% (9) | 47% (14) | 50% (13) | 52% (12) | 43% (9) |
| PC | 25% (4) | 65% (17) | 48% (12) | 40% (12) | 42% (11) | 13% (3) | 38% (8) |
| NO | 19% (3) | 15% (4) | 16% (4) | 13% (4) | 8% (2) | 35% (8) | 19% (4) |
| N | 16 | 26 | 25 | 30 | 26 | 23 | 21 |

Table 3

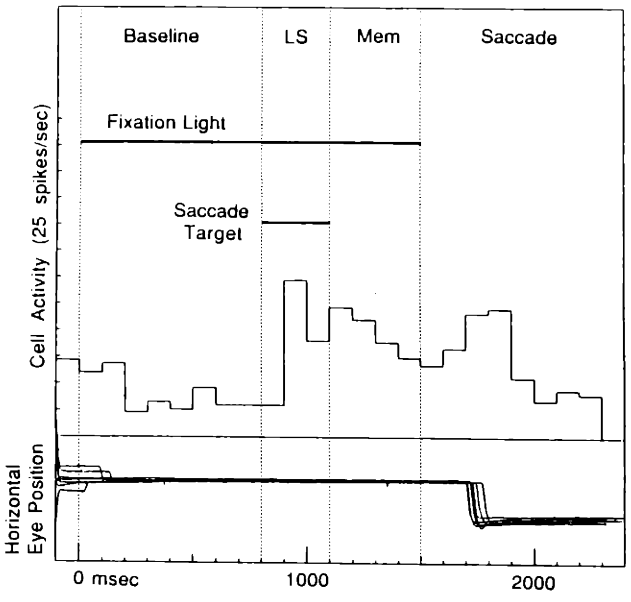
A) Intercepts and Slopes

| | Median | Mean | S.D. | S.E. | N |
|---|---|---|---|---|---|
| **Intercepts** | | | | | |
| 7a LS lateral | 8.37 | 11.296 | 8.758 | 1.867 | 22 |
| 7a M lateral | 7.17 | 8.995 | 7.846 | 1.903 | 17 |
| 7a S intercept | 9.04 | 13.237 | 11.184 | 2.193 | 26 |
| LIP LS | 15.40 | 25.171 | 40.276 | 6.713 | 36 |
| LIP M lateral | 13.77 | 24.263 | 32.653 | 5.6 | 34 |
| LIP S intercept | 16.39 | 21.674 | 15.963 | 2.59 | 38 |
| **X-Slope** | | | | | |
| 7a LS | .12 | .188 | .145 | .037 | 15 |
| 7a M | .16 | .184 | .146 | .044 | 11 |
| 7a S | .16 | .200 | .166 | .035 | 22 |
| LIP LS | .26 | .294 | .160 | .033 | 23 |
| LIP M | .17 | .271 | .267 | .058 | 21 |
| LIP S | .24 | .299 | .225 | .045 | 25 |
| **Y-Slope** | | | | | |
| 7a LS | .19 | .169 | .075 | .018 | 17 |
| 7a M | .165 | .17 | .116 | .037 | 10 |
| 7a S | .23 | .27 | .264 | .076 | 12 |
| LIP LS | .21 | .338 | .351 | .073 | 23 |
| LIP M | .18 | .285 | .243 | .053 | 21 |
| LIP S | .175 | .27 | .327 | .062 | 28 |

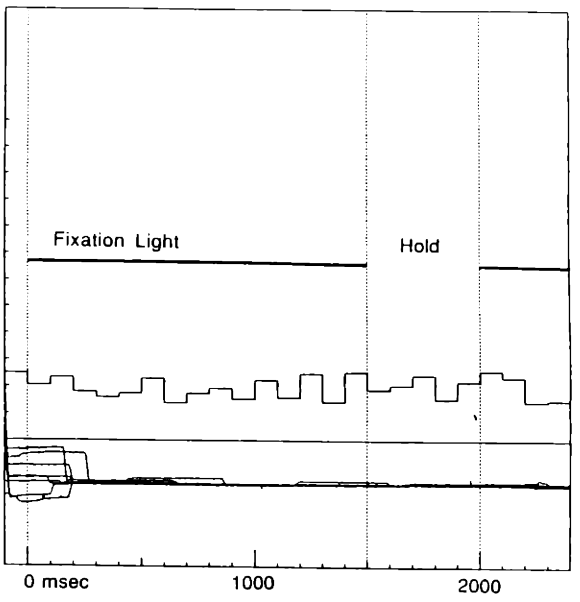
**Table 3**
**B)**

| | Percent Modulation | |
|---|---|---|
| | X | Y |
| 7a LS | 40% | 37% |
| 7a M | 47% | 44% |
| 7a S | 37% | 47% |
| LIP LS | 30% | 34% |
| LIP M | 29% | 31% |
| LIP S | 34% | 31% |

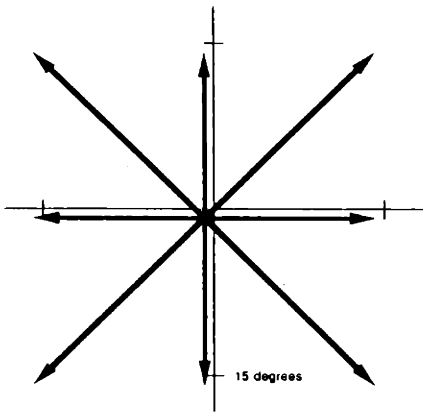
A) Memory Saccade Task




B) Control Task




C) Saccade Direction Test




D) Gain Field Test

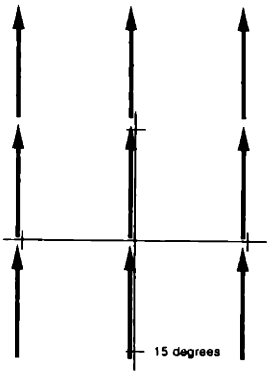
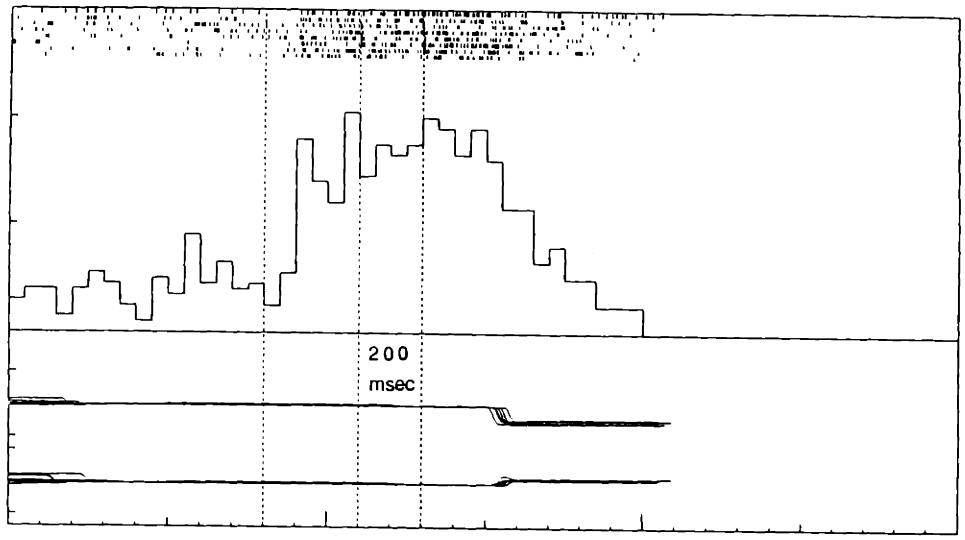
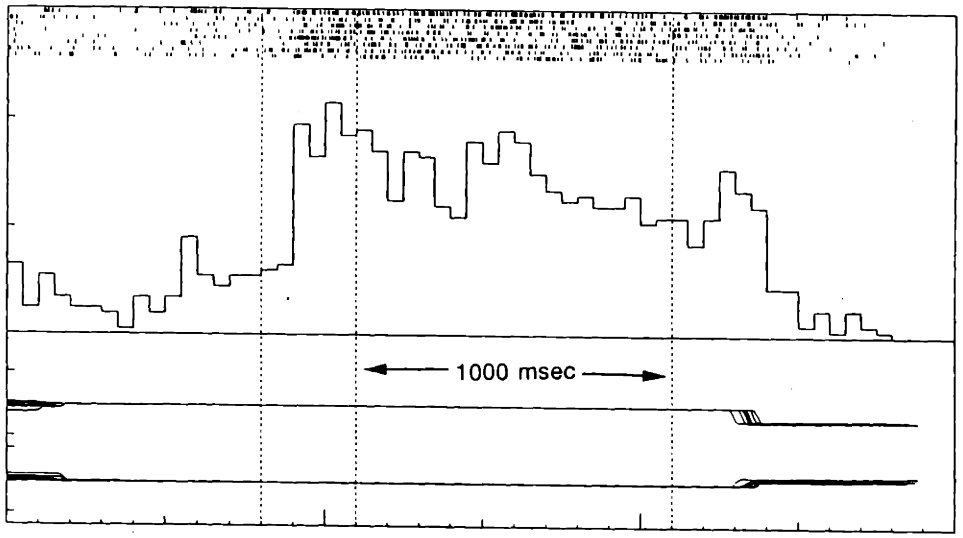



Figure 1

A) 200 msec Delay




B) 1000 msec Delay




C) 1300 msec Delay

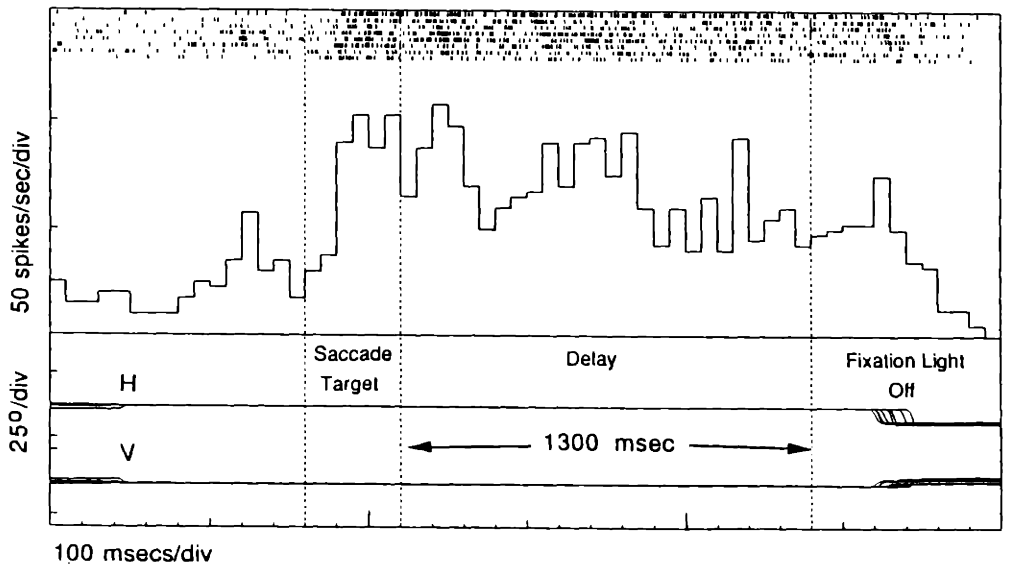
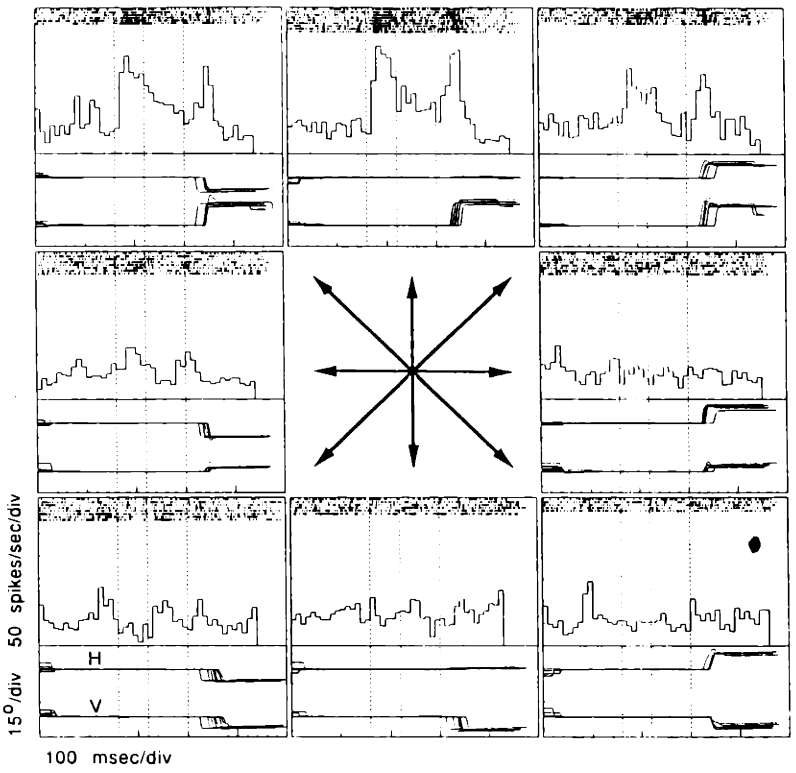
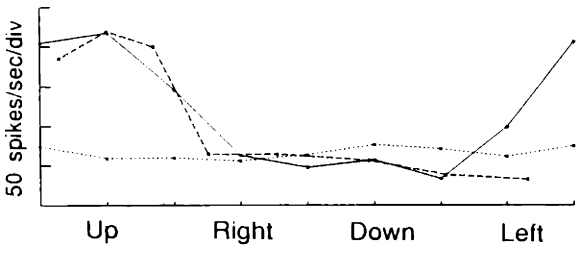


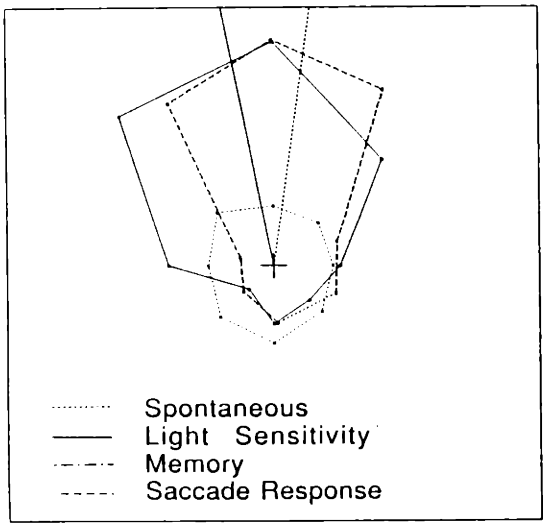

Figure 2

a) Saccade Direction Histograms

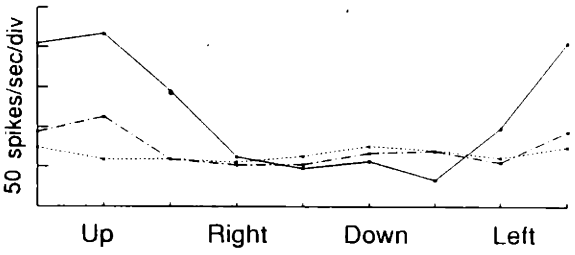



b) Light Sensitive and Saccade Polar Plots




c) Light Sensitive and Memory Polar Plots



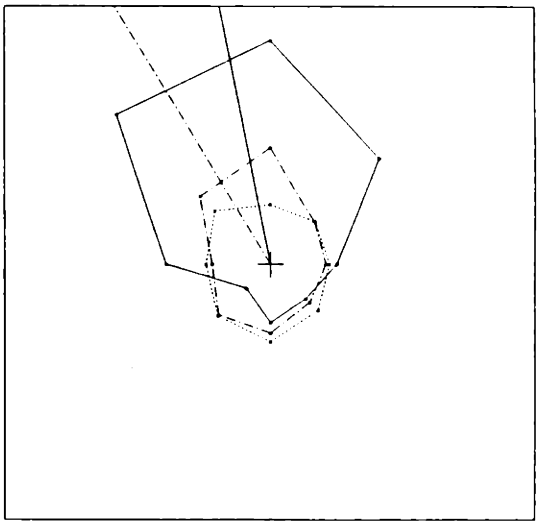





Figure 3

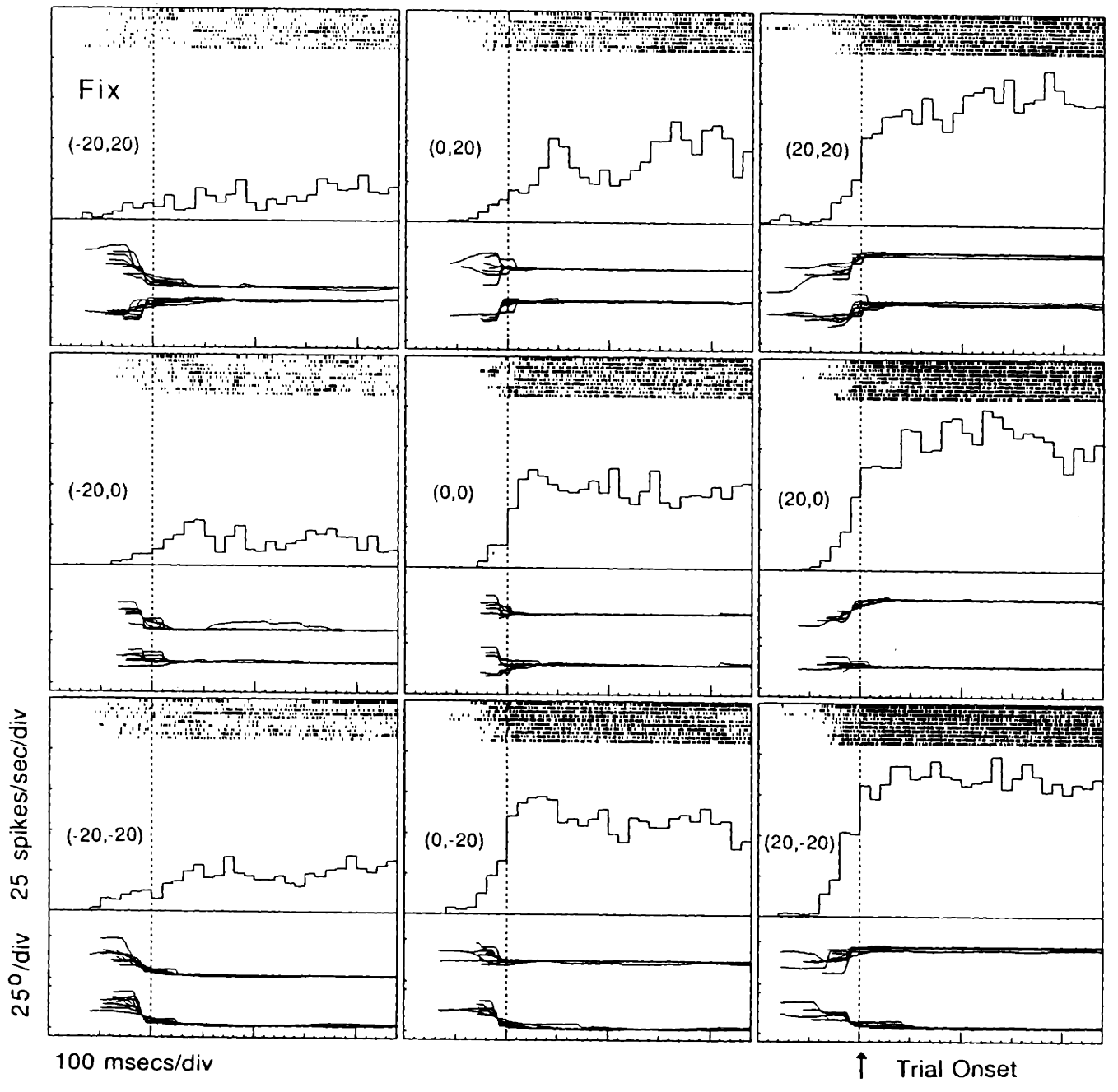

Fix
(-20,20)
(0,20)
(20,20)
(-20,0)
(0,0)
(20,0)
(-20,-20)
(0,-20)
(20,-20)
25 spikes/sec/div
25°/div
100 msecs/div
Trial Onset

Figure 4

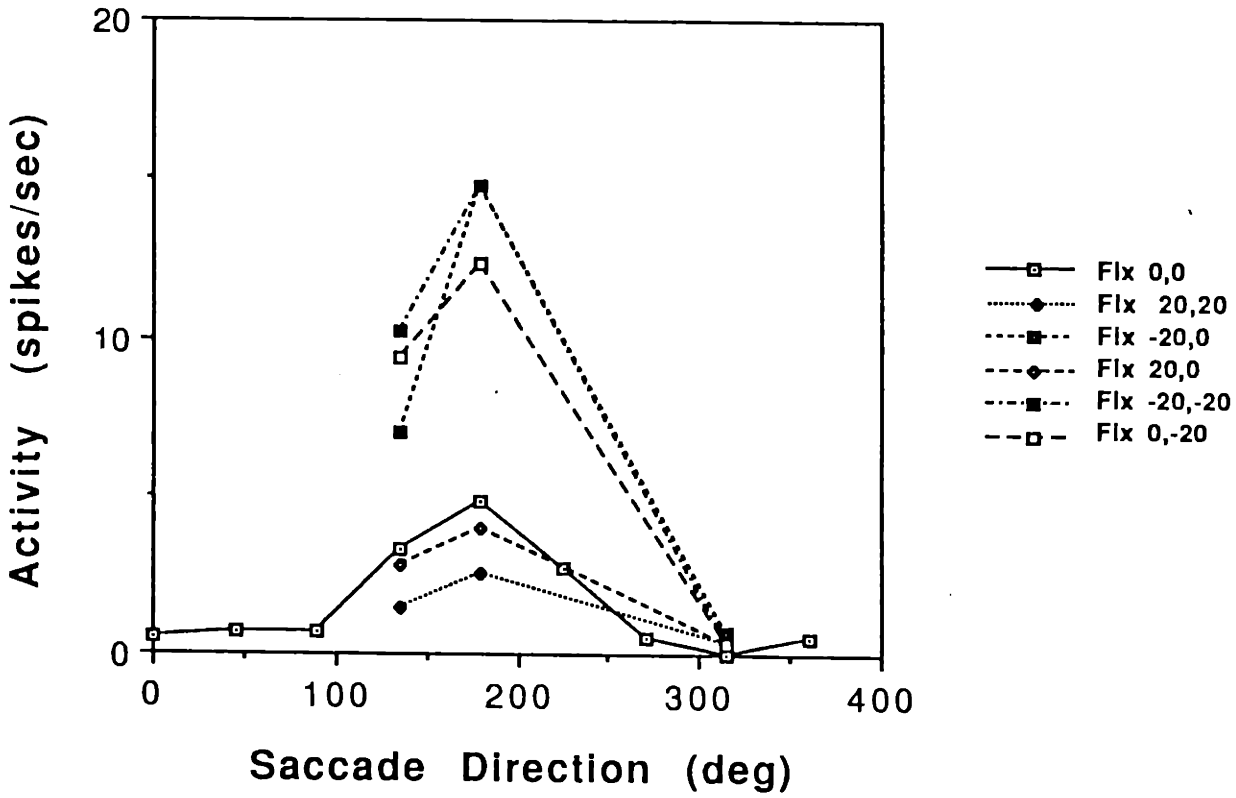
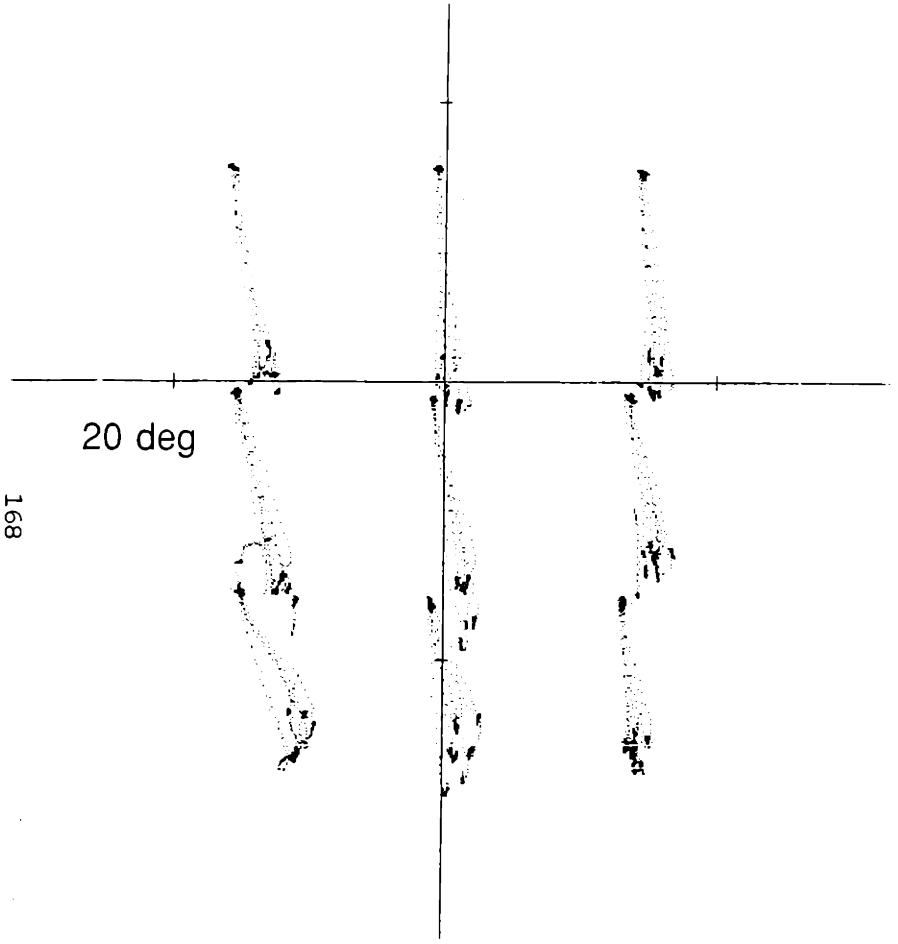

20
10
0
0
100
200
300
400
Activity (spikes/sec)
Saccade Direction (deg)
Fix 0,0
Fix 20,20
Fix -20,0
Fix 20,0
Fix -20,-20
Fix 0,-20

Figure 5

A) Eye Movements




B) Gain Field

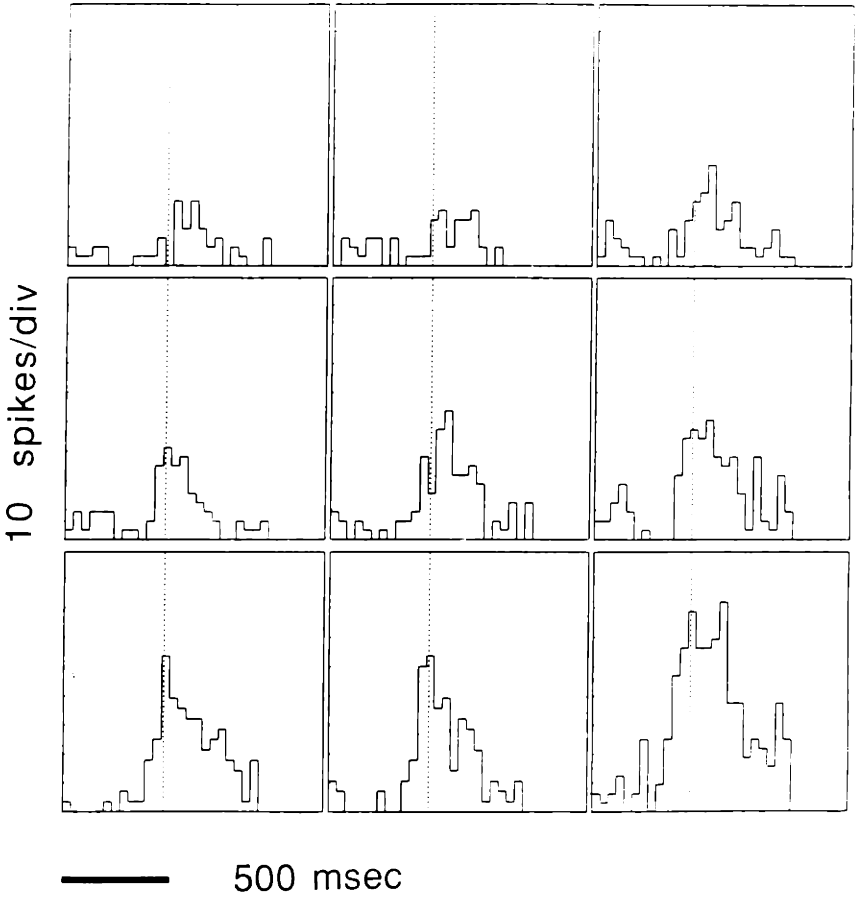
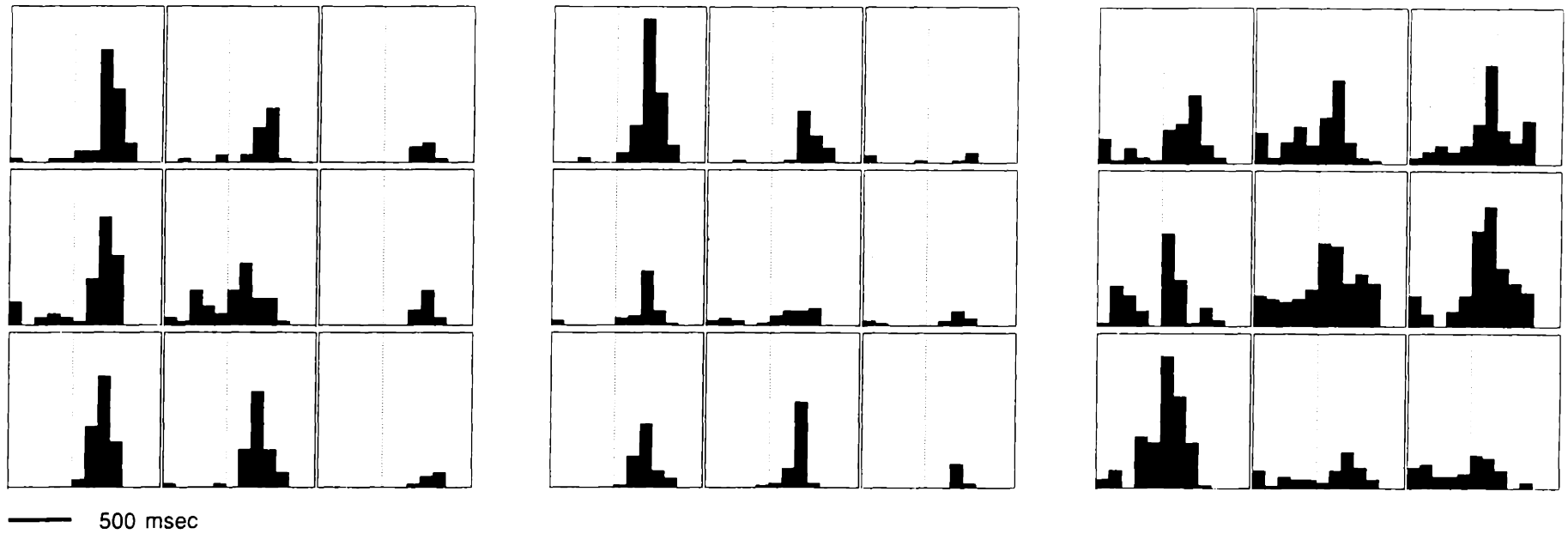



Figure 6

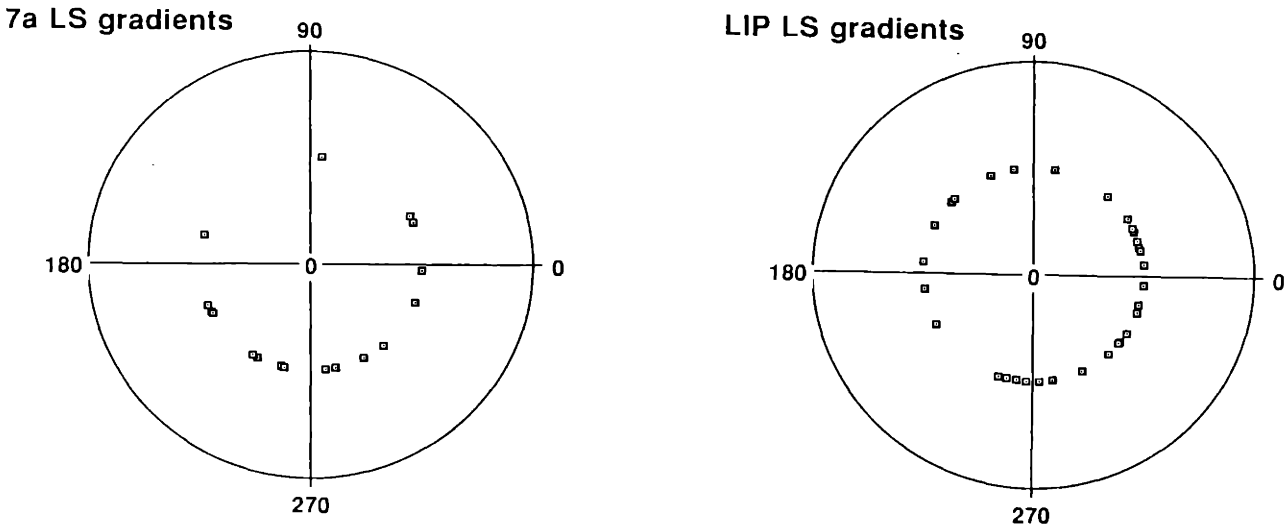
| | | | |
|---|---|---|---|
| Regression | $p < .05$ | $p < .05$ | $p > .05$ |
| Lack-of-fit | $p > .05$ | $p < .05$ | $p < .05$ |



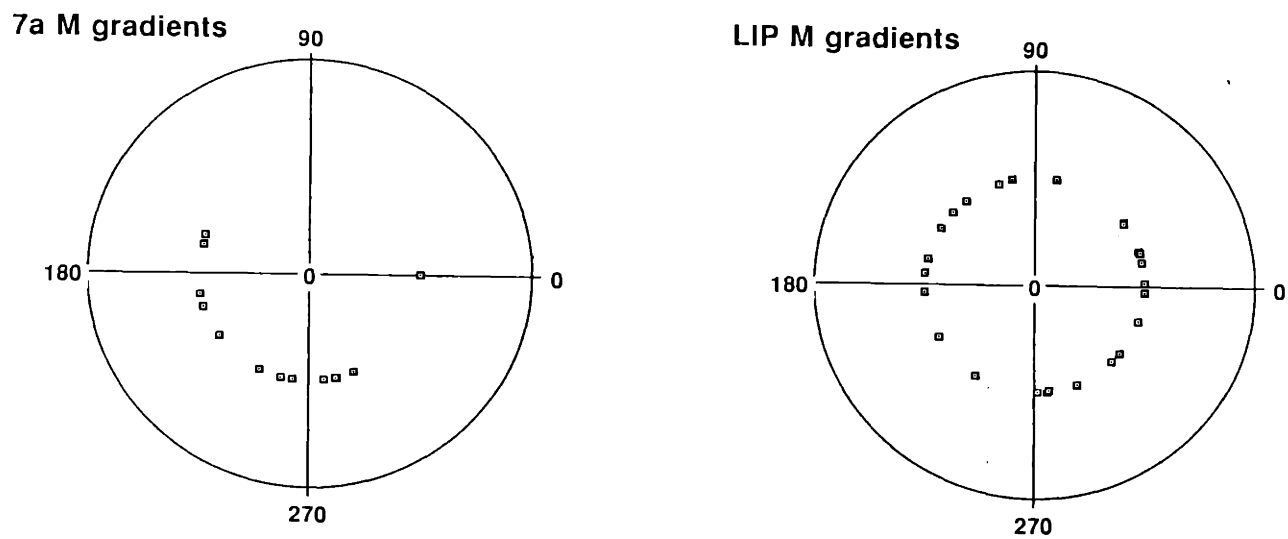

| | Plane | Planar Component | No Plane |
|---|---|---|---|
| SAC | 49% | 41% | 10% |
| LS | 38% | 47% | 15% |
| WAIT | 50% | 38% | 12% |

Figure 7

a)


7a LS gradients
90
180
0
0
270
LIP LS gradients
90
180
0
0
270

b)


7a M gradients
90
180
0
0
270
LIP M gradients
90
180
0
0
270

c)

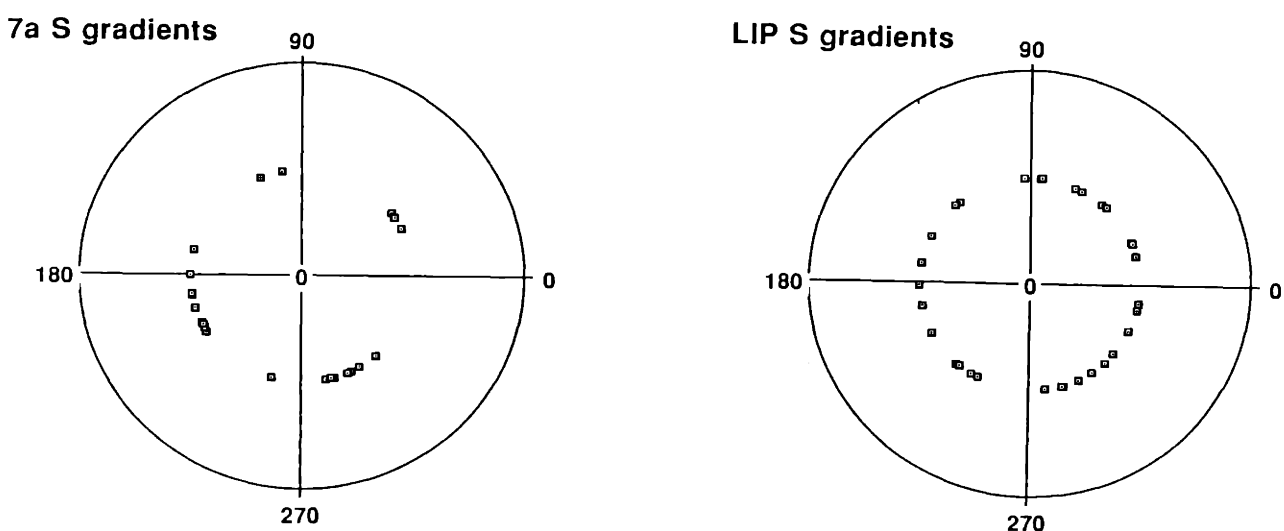
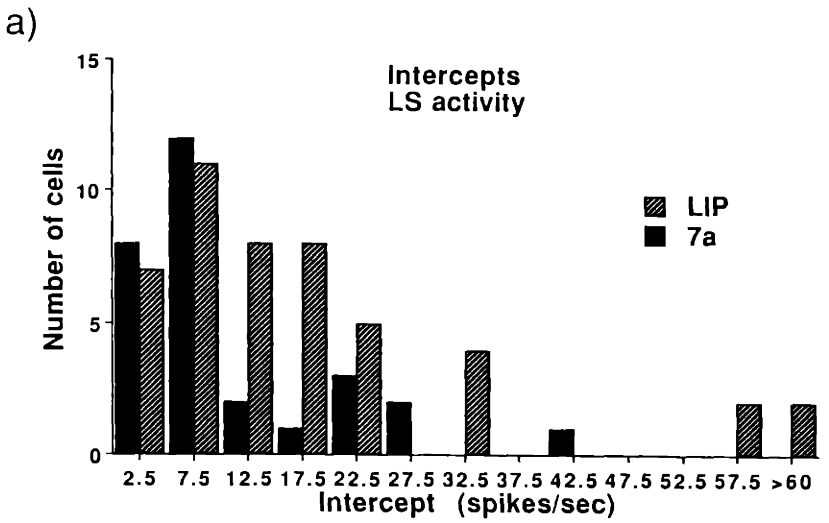
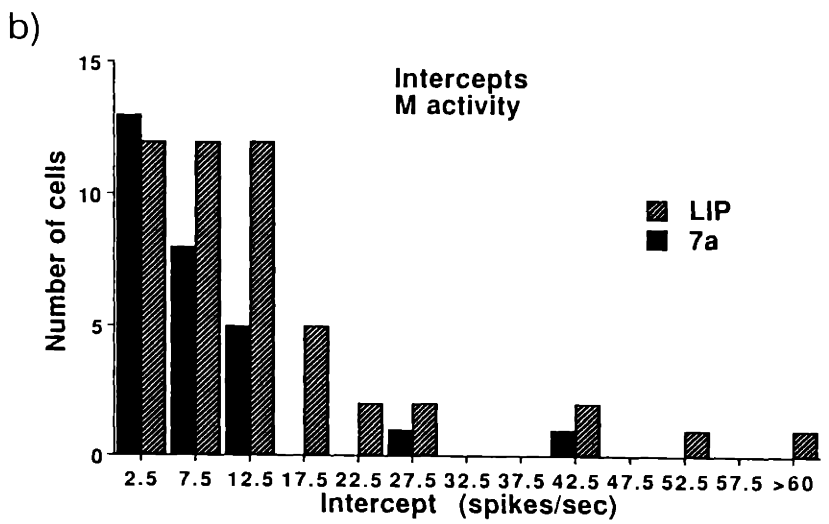

7a S gradients
90
180
0
0
270
LIP S gradients
90
180
0
0
270



Figure 8


a)
Intercepts
LS activity
Number of cells
15
10
5
0
LIP
7a
2.5 7.5 12.5 17.5 22.5 27.5 32.5 37.5 42.5 47.5 52.5 57.5 >60
Intercept (spikes/sec)


b)
Intercepts
M activity
Number of cells
15
10
5
0
LIP
7a
2.5 7.5 12.5 17.5 22.5 27.5 32.5 37.5 42.5 47.5 52.5 57.5 >60
Intercept (spikes/sec)

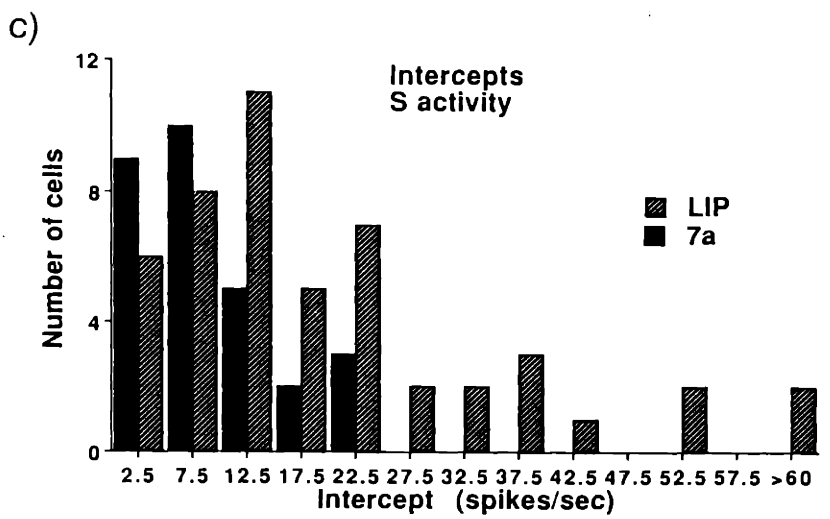

c)
Intercepts
S activity
Number of cells
12
8
4
0
LIP
7a
2.5 7.5 12.5 17.5 22.5 27.5 32.5 37.5 42.5 47.5 52.5 57.5 >60
Intercept (spikes/sec)



Figure 9

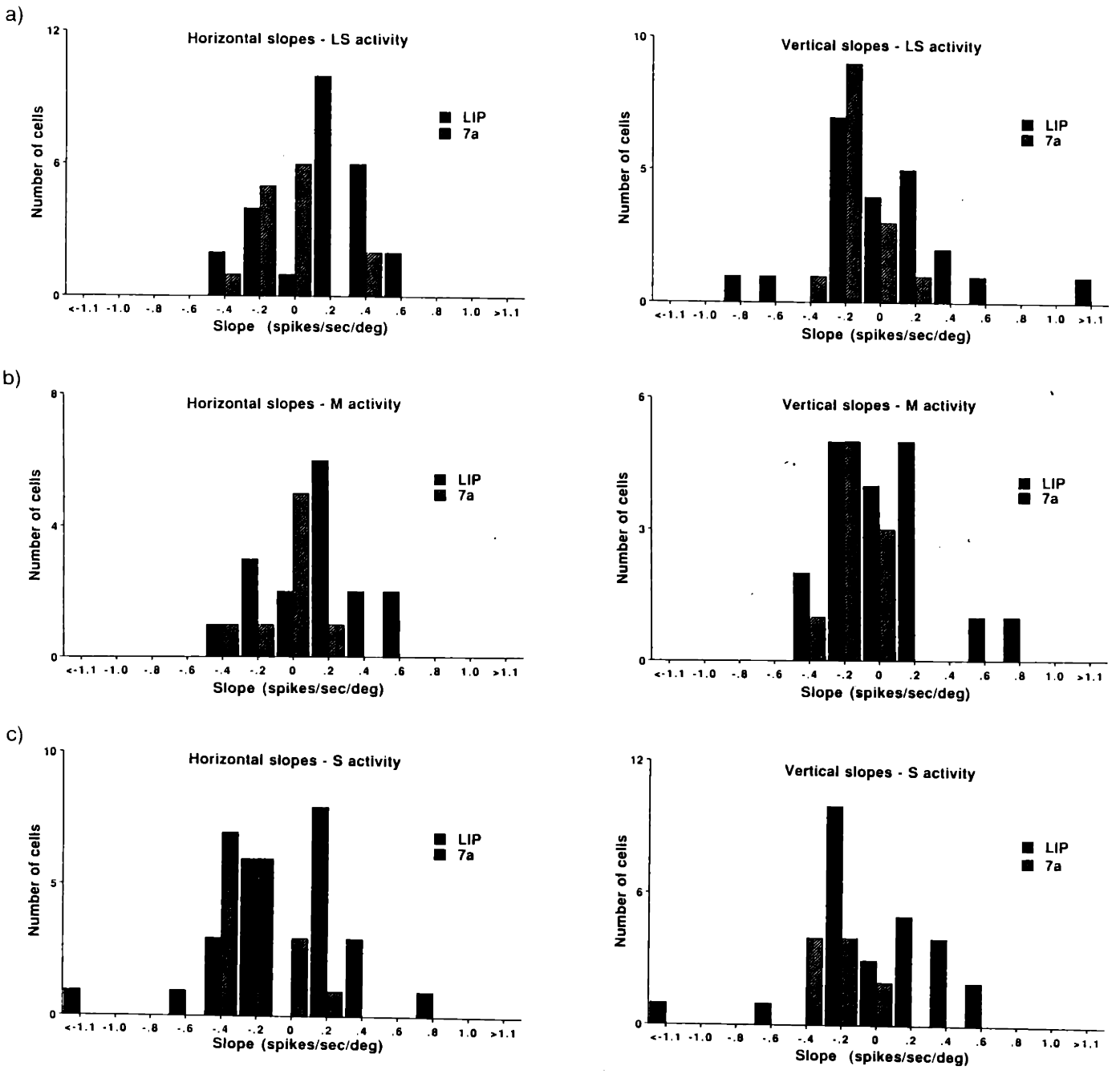
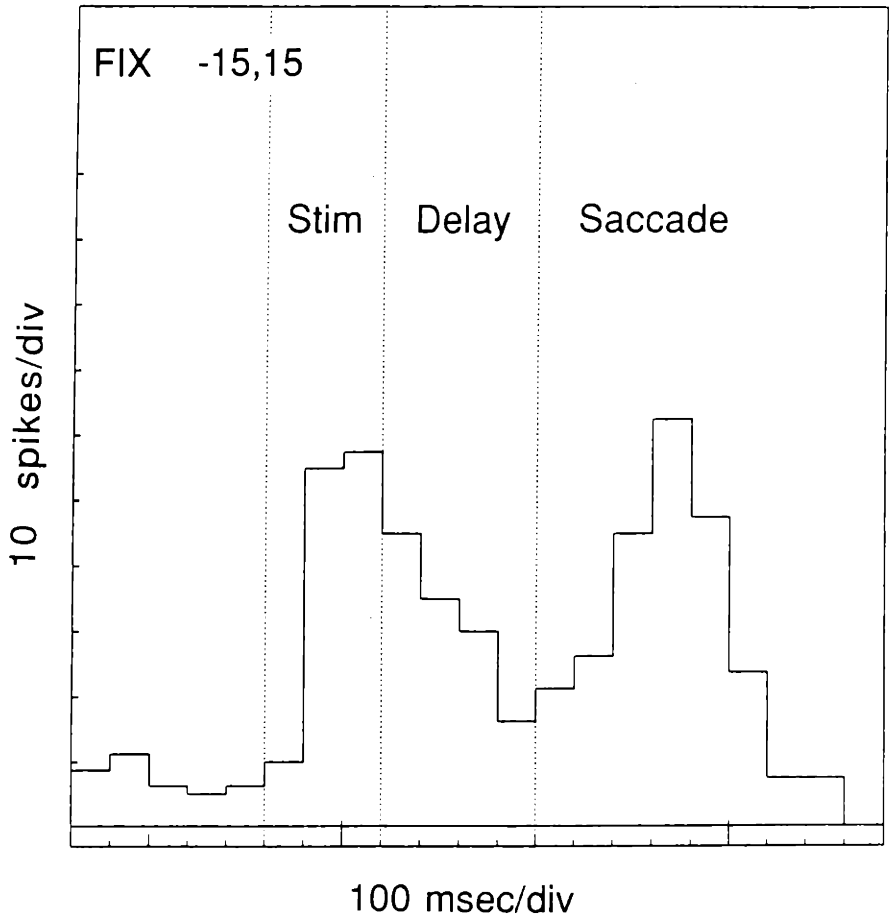

a)
Horizontal slopes - LS activity
Vertical slopes - LS activity
b)
Horizontal slopes - M activity
Vertical slopes - M activity
c)
Horizontal slopes - S activity
Vertical slopes - S activity
Number of cells
Slope (spikes/sec/deg)
LIP
7a
<-1.1 -1.0 -.8 -.6 -.4 -.2 0 .2 .4 .6 .8 1.0 >1.1

Figure 10


FIX -15,15
Stim
Delay
Saccade
10 spikes/div
100 msec/div

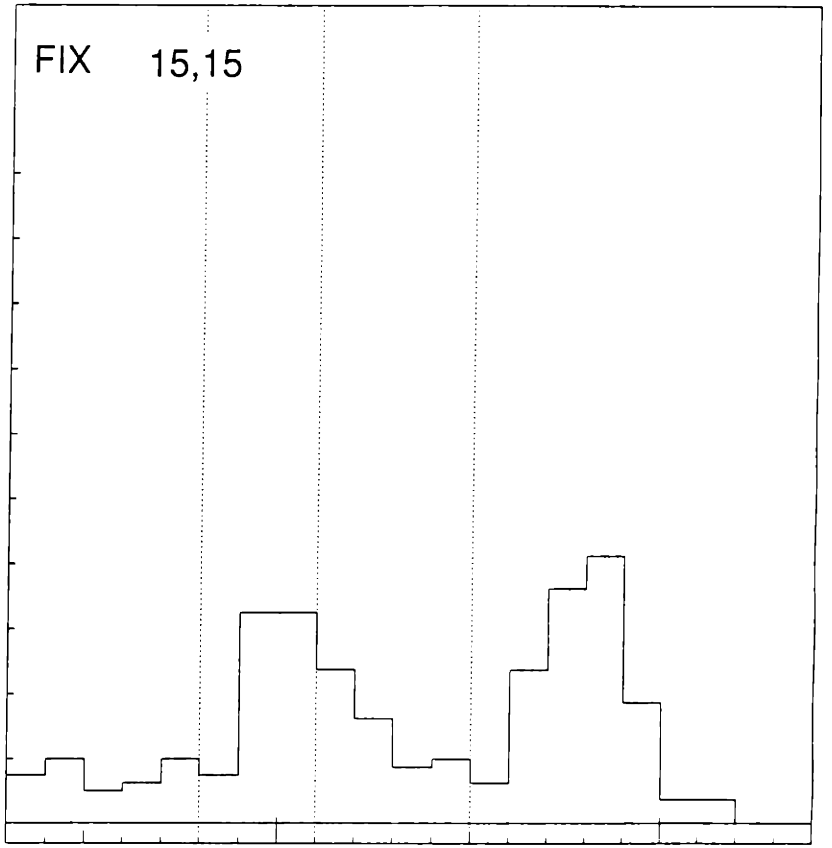
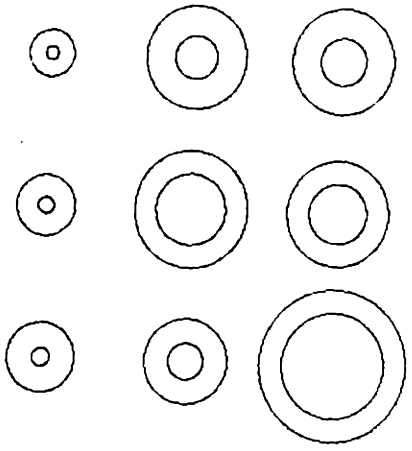
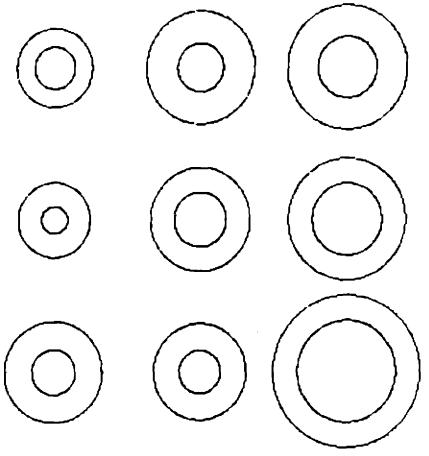

FIX 15,15

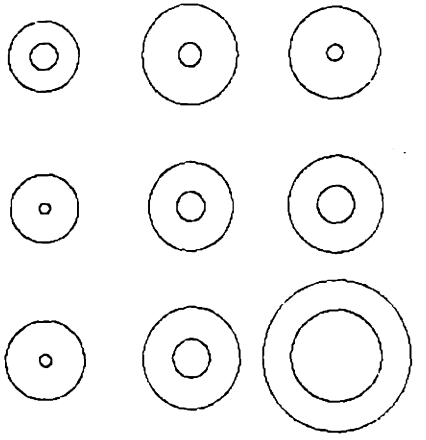
Figure 11



Light Sensitivity



Saccade



Wait

Figure 12

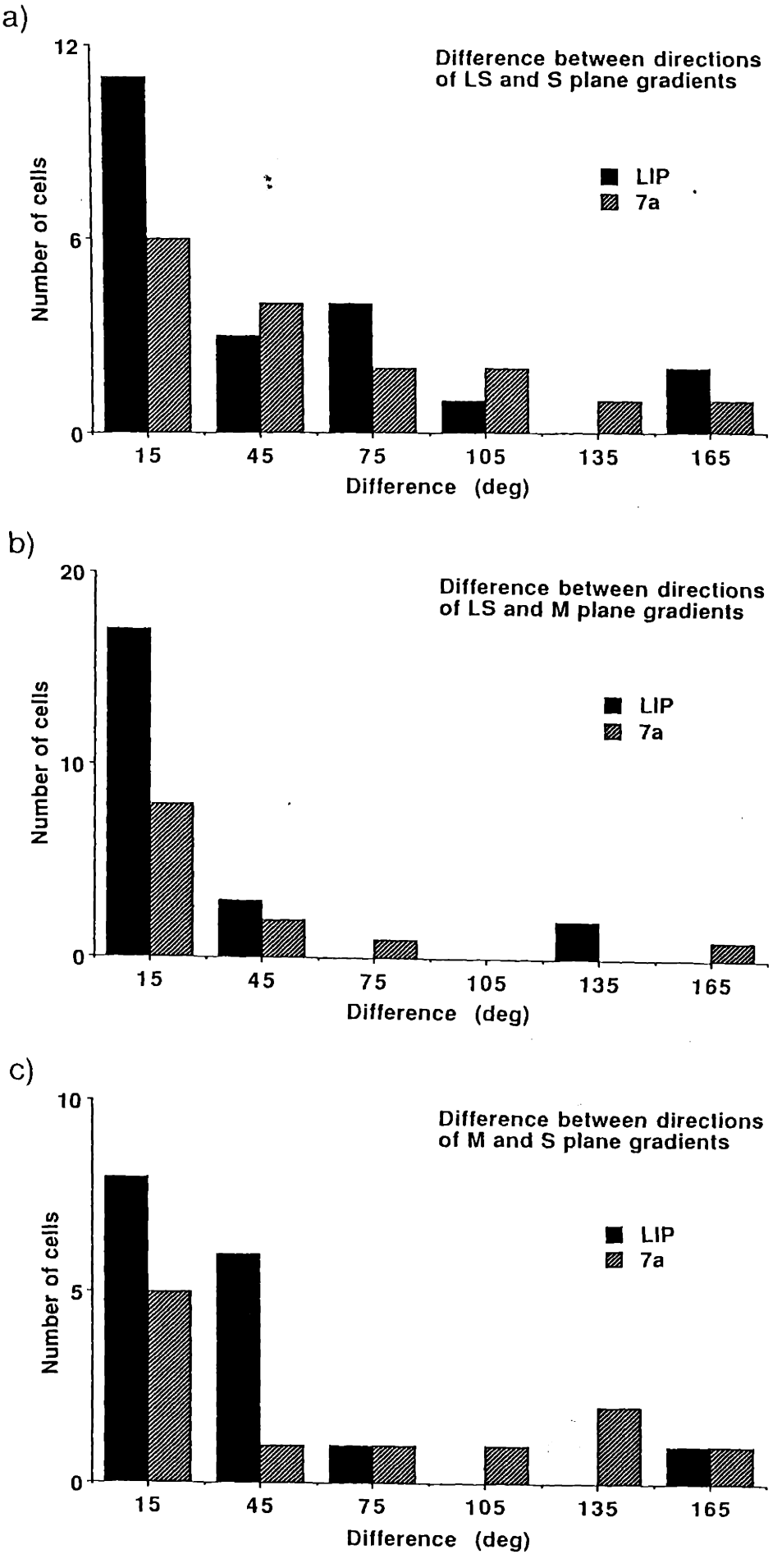

a)
Difference between directions
of LS and S plane gradients
LIP
7a
Number of cells
12
6
0
15
45
75
105
135
165
Difference (deg)
b)
Difference between directions
of LS and M plane gradients
LIP
7a
Number of cells
20
10
0
15
45
75
105
135
165
Difference (deg)
c)
Difference between directions
of M and S plane gradients
LIP
7a
Number of cells
10
5
0
15
45
75
105
135
165
Difference (deg)



Figure 13

# Chapter 5

## Motor intention activity in area LIP during a delayed double saccade task

## SUMMARY

A useful paradigm in the study of the saccadic system has been the double saccade. However, visually-evoked and saccade-related activity in cortical areas such as LIP is often long-lasting, thus the interpretation of physiological studies may be a little problematic. In order to achieve clearer temporal separation of the various phases of activity in this paradigm, we introduced the delayed double saccade (DDS). In the DDS task, a memory (M) period of several hundred milliseconds is imposed between the presentation of the targets and the eye movements. Thus visually-evoked or light-sensitive (LS), memory/motor intention (M), and saccade-related (S) activities may be distinguished. The delay period allowed us to investigate how area LIP might be involved in the coding of sequences of saccades.

The results support our hypothesis that M activity in LIP generally reflects the next intended saccade in a sequence of saccades. Typically, a neurone only becomes active during the memory period of a delayed double saccade trial if the first saccade is to be made in its preferred direction. Thus even if the second target were flashed in the receptive field, it does not evoke M activity. Similarly, the cell only becomes active after the first saccade, if the second saccade is in its preferred direction.

We have also shown the the "visual" responses of some LIP neurones are behaviourally-contingent.

Finally, we provide further evidence that individual LIP neurones carry an oculocentric saccade vector signal and do not code for saccadic end-points in craniotopic space. However, this vector signal is modulated by eye position; on a population level, LIP neurones can encode saccades craniotopically (see chapter 4).

## INTRODUCTION

A useful paradigm in the study of the saccadic system has been the double saccade (Hallet and Lightstone 1976a, b; Mays and Sparks 1980a; chapter 3). In the double saccade task, two targets are flashed sequentially. The timings of the targets are such that both have been extinguished before the first saccade is initiated. The subject must saccade to the spatial locations of the targets in the order in which they were presented. A spatially accurate second saccade cannot be made simply on information derived from the retinal stimulus of the second target. Thus, most importantly the task has been used to demonstrate behaviourally that saccades are not simply retinotopically coded (see chapter 3 for discussion).

We (chapter 3) and others (Mays and Sparks 1980a; Bruce and Goldberg 1990) have used double saccades in electrophysiological experiments to distinguish activity corresponding to retinal and saccade vectors. In particular we have shown that saccade-related activity in area LIP reflects the vector of the next intended saccade, and not a retinal vector nor a "goal-directed" saccade (chapter 3).

One difficulty in analysing the activity of LIP (and frontal eye fields, FEF) neurones in the "traditional" double saccade paradigm is that visual and saccade-related bursts of activity typically persist for many tens of milliseconds (see chapter 2). Consequently, the visual and saccade responses may overlap in time; therefore it is often difficult to determine the nature of neural activity in double saccade trials. In order to try to circumvent this problem, we introduced a variant on the standard double saccade task. In the "delayed double saccade" (DDS), the two targets are flashed briefly, as in a traditional double saccade, but the fixation point remains on for a further 500 ms after the targets are flashed. Thus a memory (M) period of 500 ms is imposed between the offset of the second target and the "go" signal for the saccades. Consequently, the saccades are made in the dark to the remembered locations of the targets. In particular, it allows visually-evoked or light-sensitive (LS) and saccade-related (S) activities to be clearly distinguished, and, moreover, reveals any memory/motor planning (M) activity.

A major objective of this study was to further test our hypothesis that M activity in area LIP neurones reflects the next intended saccade

(see chapter 3). We predicted that a neurone should only be active during the memory period of a memory double saccade trial if the next saccade were to be made in its preferred direction. Thus even if the second target were flashed in the receptive field, it should not evoke M activity. The cell should only become active after the first saccade, if the second saccade were in its preferred direction.

An alternative hypothesis might be that LIP contains activity related to a sequence of saccades. Were this the case, we should expect to observe M activity after the first or second target is flashed in the receptive field, as long as one of the two saccades were in the neurone's preferred direction.

Another possibility would be that the *retinal* vector of the second target is present. Were this the case, we should expect to observe M activity after the second target is flashed in the receptive field.

Our results in general support our hypothesis that M activity in LIP reflects the next intended saccade. The retinal vector of the second target is usually either not present or suppressed.

Second, we were interested in investigating the possibility that sensory responses in LIP might be behaviourally-contingent. We found some evidence for context-dependent visual responses in LIP.

Third, we confirmed our previous finding (chapter 3) that LIP neurones code in motor coordinates. Memory/motor planning activity reflects the oculocentric vector of the forthcoming saccade. LIP neurones do not fire before saccades that drive the eye to specific orbital locations. Moreover, firing is not dependent on a visual stimulus being presented within the receptive field.

# METHODS

The experiments described in this chapter were conducted in parallel with others described elsewhere in this thesis. Basic methods (animal care, surgery, eye movement and neuronal activity recording) are described in detail in earlier chapters. The animal was trained on the delayed double saccade task after he had mastered the basic memory saccade task.

## Delayed double saccade tasks

We developed the delayed double saccade (DDS) from the "traditional" double saccade (DS) paradigm (Hallet and Lightstone, 1976a, b; Mays and Sparks 1980; chapter 3). It is essentially similar to the DS task, except that there is a delay or memory period imposed between the presentation of the targets and the saccades.

As in all our paradigms, the trial began with the presentation of a fixation spot (for DDS trials, always directly ahead of the monkey at screen position 0,0) which the monkey had to foveate within one second. "Fixation attained" was defined as the time at which the eye entered a specified window (typically 2 deg) around the fixation spot. If the monkey failed to fixate the spot within the given one s, the trial was aborted, declared a "miss", and an inter-trial interval was begun. The monkey had to maintain fixation on the central fixation spot for as long as it was present (1200 ms from "fixation attained").

500 ms after "fixation attained" the first peripheral target spot was flashed for 50 ms; 100 ms after the offset of this first target spot, a second target spot appeared, also for 50 ms. The extinction of the fixation spot, 500 ms after the offset of the second target, served as a "go" signal for the saccades. Thus a delay period was imposed between the presentation of the targets and the saccadic responses. Within 500 ms of fixation spot offset, the monkey had to make a first saccade to the remembered location of the first target. Then, within 500 ms but not before 100 ms, a second saccade had to be made to the remembered location of the second target. Following the second saccade, the monkey had to keep his eye at the location of the second target for an additional 100 ms. If the monkey fulfilled all these conditions, the trial came to a successful end (a "hit") and the animal received a reward, a

drop of apple juice. If a trial had reached the "fixation attained" stage but failed to satisfy any of the subsequent conditions, the trial was aborted and declared an "error".

Fig. 1c illustrates the sequence of events in the task, and the response of a typical LIP neurone. Both targets are presented while the monkey maintains fixation on the fixation spot. Only after the fixation spot is extinguished may he move his eyes.

Typically four classes of trials were pseudorandomly interleaved. In the first class (see fig. 1a), the first target was presented 20 deg from the fixation spot, and the second at 10 deg, in the same direction (e.g., -20, -20 then -10, -10). Both stimuli were in the receptive field of the unit. In the second class (see fig 1b) the targets were presented at the same eccentricities in the other direction (e.g., 20, 20 then 10, 10). Thus neither fell in the receptive field. In the third (fig. 1c) and fourth (fig. 1d) classes, the targets were presented at 10 deg on either side of the fixation spot, in opposite directions (e.g., -10, -10 then 10, 10; and 10, 10 then -10, -10). In the third class, the first, but not the second, stimulus fell in the receptive field. In the fourth class, the second, but not the first, stimulus fell in the receptive field. Occasionally, targets were presented at different eccentricities, but always in an analogous spatial distribution to that described above.

In classes 1 and 3, the first saccade is made in the preferred direction of the neurone. In classes 2 and 4, the second saccade is in the preferred direction.

In some cases, we pseudorandomly interleaved an additional four classes of standard memory saccade trials, to the same four target locations (e.g., -20, -20; -10, -10; 10, 10; 20, 20).

The spatial windows used in DDS trials were similar to those used in our other experiments: a 2 deg window about the fixation spot and, typically, a 20 deg window about the targets (because saccades in the DDS trials showed similar spatial distortions to memory saccades - see chapter 8 - which is to be expected since the saccades in DDS trials are "memory" saccades).

The target directions were chosen such that one was in the preferred direction of the neurone under investigation, and, of course, the other at 180 deg to this. This spatial arrangement of targets usually ensured that only targets and saccades in one of the two directions would evoke clear neural activity. In our earlier studies (see chapter 3) with standard

DS trials, we had typically used targets arranged at 90 deg to one another. Since LIP neurones are typically broadly tuned (width-at-half-height of about 90 deg; see chapter 3), it was sometimes a little difficult to distinguish activity related to the first and second saccades. We believe this may also have been a problem with others' studies using the DS paradigm (e.g., Goldberg and Bruce, 1990).

**Experimental procedure and data collection**

Once a unit had been isolated, we conducted a run of standard memory saccades in eight directions. Thus we determined the neurone's preferred and least preferred directions (typically 180 deg apart), and whether it showed clear memory activity. For DDS experiments, the two target directions were chosen such that one was preferred and one at 180 deg to this (non-preferred). Other studies described elsewhere in this thesis were also conducted on some of these units. Not all eligible units were tested in the DDS paradigm.

Data was collected in "runs"; a run is a sequence of trials of pseudorandomly interleaved classes. We typically collected at least 8-10 trials in each class.

There was an intertrial interval (pseudorandomly varied from 500 to 2000 ms) during which the collection program accomplished book-keeping and data display tasks.

**Data analysis**

Action potentials from isolated single units were sampled at 10 KHz and stored by the laboratory computer. In off-line analysis, the firing rates of the unit during different phases of the task were computed. The phases were: BG (background): from 100 ms after start of trial to the onset of the first stimulus at 500 ms; LS1 (first light stimulus): 550 to 650 ms; LS2 (second light stimulus): 700 to 800 ms; M (memory): from 800 to 1200 ms (offset of the fixation spot). We also aligned the trials on the onset of the first saccade (see chapter 2 for details of this alignment process) in order to the determine firing related to it (phase S1: from 25 ms before to 75 ms after saccade onset). A similar phase, S2, was determined by aligning trials on the second saccade onset. Finally we determined the activity during the intersaccadic interval (IS). The timings of this phase varied a little as the intersaccadic intervals varied

somewhat. Occasionally the timings of these phases were slightly altered to account for idiosyncrasies of individual neurones.

Paired t tests (alpha level 0.05) were used to compare the levels of activity (mean firing rate) in phases within a class, e.g., is the M activity significantly different from the BG activity? Unpaired t tests (separate estimates of sample variances, alpha level 0.05) were used to compare the levels of activity in phases in different classes.

**Allocation of units to area LIP**

Units were assigned to LIP on the grounds of depth of recording, of location of electrode within the chamber, and of their physiological characteristics (see chapters 2 and 4 for details). The animal is currently being used in physiological experiments; on completion of these studies he will be sacrificed and the recording sites reconstructed using standard histological techniques (see chapters 2 and 4).

# RESULTS

## Database

We isolated and recorded from 43 neurones from one hemisphere while the monkey was performing the DDS task. Since we were also conducting related experiments in parallel with those reported here (see elsewhere in this thesis), other eligible units were not tested in the DDS paradigm.

## Experimental issues

1) Does M activity in LIP reflect only the next in a sequence of saccades?

Our main objective in this experiment was to investigate the role of area LIP in the coding of sequences of saccades. Our hypothesis, based on previous experiments reported chapter 3, was that M activity reflects only the next in a sequence of saccades. From this hypothesis, we can make several predictions of the behaviour of area LIP neurones in the various classes of DDS trials. These are outlined in the section on "question 1" below.

We also were able to address an additional question:

2) Does a stimulus, if it falls in the receptive field of the cell, always evoke LS activity, or may the response to it be context-dependent?

Finally, we confirmed our previous finding (chapter 3) that coding in LIP is oculocentric: neurones fire for saccades of a certain vector, and not for any saccade that brings the eye to a specific orbital position (as would be the case if single units in LIP encoded craniotopically).

## Question 1: Does M activity in LIP reflect only the next in a sequence of saccades?

In other studies (see chapters 3, 6 and 7), we have shown that LIP neurones seem to encode the motor vector of the next saccade. M activity seems to be in motor coordinates; it reflects the vector of the forthcoming saccade. A major goal of these experiments was to

determine whether M activity in LIP reflects more than the first in a sequence of saccades. Naturally, we would expect a unit with M activity to be active after the first stimulus fell into its receptive field (rf) (classes 1 and 3). However, if only the second stimulus fell into the rf (class 4), we would expect (if LIP does indeed only encode the next saccade in a sequence) to observe no M activity before the first saccade. However, we would expect the neurone to be active in the IS interval, after the first (non-preferred) saccade and before the second (preferred) saccade. Similarly, we would predict that a neurone should only become active after the first saccade in class 2.

If, on the other hand, LIP encodes both saccades, we would expect M activity both when the stimulus falls first (classes 1 and 3) and second (class 4) in its rf. Also, since the M activity in an LIP neurone reflects a motor intention and can be evoked without a stimulus ever falling within the rf (see chapter 3), we might also expect to observe M activity in class 2.

The long M period between the disappearance of the targets and the execution of the movements allows these different possible coding schemes to be differentiated experimentally.

A) Does the first stimulus, if it falls in the receptive field of the cell, evoke memory activity?

The relevant class is 3, in which only the first target is presented in the receptive field. This is tested by comparing the M activity with the BG activity.

Fig. 1c shows the response of an LIP neurone in such trials. The first stimulus falls within the receptive field. There is clear sustained M activity during the delay period before the first saccade is made.

Note that we also expect that the first target will evoke M activity in class 1 trials, but in theory this activity could be evoked by the second target (which also falls in the receptive field). Fig 1a shows the response of the same neurone in class 1. There is indeed clear M activity.

19 units showed M activity in response to the first stimulus in class 3.

B) Does the second stimulus, if it falls in the receptive field of the cell, evoke memory activity?

The relevant class is 4, in which only the second target is presented in the receptive field (see fig. 1d). This is tested by comparing the M activity with the BG activity.

Fig 1d illustrates the response of the same LIP neurone in class 4 trials. The second stimulus falls within the receptive field, and produces only a transient burst of activity. The neurone is not tonically active during the delay period (as it is if this stimulus is presented first in the sequence - see A above and fig.s 1 a and c). 12/19 units showed this pattern of activity, i.e., no memory if the preferred stimulus is presented second, but memory if it is presented first.

These results are in accord with our hypothesis that LIP encodes only the next intended saccade.

However, 7/19 units showed significant M activity following the preferred stimulus, whether it was presented first or second. Fig 2d is an example of such a neurone. In general, M activity in class 4 seemed to wane with time. In two of these neurones, the M response to the stimulus when presented second was significantly less than when it is presented first.

M activity after the second target is flashed in the receptive field might represent the *retinal* vector of the second target. The results in (C) below suggest that such activity cannot represent the second *saccade* vector.

C) Do neurones show M activity for the second saccade, even if no stimulus falls within their rf?

We have shown that M activity may be evoked in LIP even in the absence of a stimulus falling within the rf of a cell (see chapter 3). In class 2 trials, neither stimulus falls within the rf, but the second saccade is made in the cell's preferred direction. If LIP encodes both saccades in the sequence, one might therefore expect to observe M activity (before the first saccade) in class 2 trials. This is tested by comparing the M activity with the BG activity.

Figures 1b and 2b show results typical of *all* LIP units: no M activity during class 2 trials. This result is in accord with our hypothesis that

LIP encodes only the *next* saccade in a sequence.

D) If the second saccade is in the preferred direction of the neurone, does the cell become active after the first saccade?

If LIP does encode the next saccade, we would expect a unit to become active *after* the first saccade in the non-preferred direction, before the second saccade in the preferred direction (i.e., during the IS period). This should be the case whether (as in class 4) or not (class 2) a visual stimulus ever falls within its rf. The relevant classes are 2 and 4. This is tested by comparing the IS (intersaccadic) activity with the BG activity.

In fig 1a, c are illustrated the responses of an area LIP unit in DDS trials in which the second saccade is in its preferred direction. There is a clear elevation of activity after the first saccade (in a non-preferred direction) before the second. A second example of such activity is given in fig 3. Again we observed activity after the first saccade, before and during the second saccade, despite the fact that no stimulus was presented within the rf of the unit.

14 units showed clear evidence of such activity. This is the case regardless of whether the second stimulus appears within the receptive field (as in class 4) or not (as in class 2). However, since some cells show long-lasting bursts of saccade-related activity and postsaccadic signals (discussed in chapter 2), it was not possible to test for such activity in all units.

In sum, these experiments in general support our hypothesis that activity in area LIP reflects only the next saccade to be made.

**Question 2: Does a stimulus, if it falls in the receptive field of the cell, always evoke LS activity, or may the response to it be context-dependent?**

The relevant class is 4, in which only the second target is presented in the receptive field. This was tested by comparing the LS2 activity with the BG activity.

Fig 1d illustrates the response of an LIP neurone in such trials. The

second stimulus fell within the receptive field, and produced only a transient burst of activity. 22 units showed such LS2 activity.

However, in 8 cells, the response to the second stimulus was "absent" or suppressed, even though it fell within the receptive field. An example of such a (lack of) response is shown in Fig 4b: target 2 falls within the rf but fails to evoke a significant response. In Fig 4a, we can see the activity of the same neurone in class 3: the same stimulus, when presented first, clearly evokes a response.

In two cells, the response to the preferred stimulus was attenuated if it was the second rather than the first in a sequence. This was tested by comparing LS1 activity from the class 3 with LS2 activity from class 4.

Therefore, in 10/32 neurones, the "visual" response appeared to be at least somewhat contingent on extraretinal factors, in this case whether or not the target indicated the next saccade.

**Is there a "goal-directed" representation of saccades within LIP?**

The above results suggest that LIP neurones code in motor coordinates: they are active before saccades of a specific vector. Another possibility is that they fire for saccades to a specific location in craniotopic space (see chapters 3 and 4). Such a coding scheme would predict that an LIP neurone should be active for any saccade that brought the eye to a specific orbital location. If this were the case, one would expect to see similar activity for the second saccade in classes 1 and 4, since the end point is the same in each class. Similar activity (but of course different from classes 1 and 4) would be expected in classes 2 and 3 (which share a *different* common end point). We found no evidence for such "goal-directed" activity (in accord with our previous results - see chapter 3). This can be seen in fig's 1 and 2: in both, activity for the second saccade in (a) and (d) should be similar in each class. Also, activity for the second saccade in (b) and (c) should be similar in each class. This is clearly not the case.

**Summary of results**

The most important result of this experiment was that many (12/19) LIP neurones have M activity when the first stimulus falls in their receptive field (therefore indicating that the first saccade will be made in the preferred direction of the unit), but not when only the second stimulus is flashed in the receptive field.

We have also shown that LIP neurones become active after the first saccade (if it is in the non-preferred direction) before the second saccade (in the preferred direction). This is true even if neither stimulus falls within the receptive field. Thus M activity in LIP is not dependent on stimulation of the receptive field. LIP units seem to code in motor coordinates (as suggested by our earlier DS experiments - see chapter 3). They become active before saccades into their motor fields.

These results strongly support the notion that M activity in LIP generally reflects the plan for the next saccade, and not for a sequence of saccades.

We have also shown that the strength of the response to a stimulus may depend on the temporal sequence of events (and thus its behavioural significance): the response to an identical stimulus within the receptive field is weaker or absent (in 10/32 units) if it is the second, rather than the first, in a sequence (if the other stimulus is outside the receptive field). We suggest that this is a result of the behavioural significance of the stimulus: when presented first it signifies the next saccade, whereas when second it signifies the second saccade (see above).

We have also confirmed our previous findings (chapter 3) that LIP neurones do not fire before saccades to a specific goal in craniotopic space, regardless of the vector of the movement. Activity in LIP reflects the oculocentric (motor) vector of the forthcoming saccade.

# DISCUSSION

This experiment was primarily designed to address the question: does M activity in LIP reflect only the next in a sequence of saccades? We have shown that memory activity in most LIP cells reflects only the next saccade in a DDS sequence. When the second saccade is to be made into a cell's motor field, the cell becomes active after the first saccade. This is further support for our hypothesis that LIP encodes the next intended saccade. Activity related to the second saccade does not become manifest in LIP until after the first saccade is made.

Our paradigm also allowed us to address some other issues of the role of LIP in the coding of saccades:

Does a stimulus, if it falls in the receptive field of the cell, always evoke a visual response (LS activity)? Although this appears to be true for the majority of LIP cells, in some the response to a stimulus, if it is the second in the sequence, is attenuated or absent. This suggests that the behavioural significance of the stimulus in part determines the "visual" response to it of some LIP neurones.

We have also confirmed our earlier findings (chapter 3) that saccade-related activity in single units in area LIP reflects the (oculocentric) vector of the next intended saccade, and not a retinal vector nor a "goal-directed" saccade (to a craniotopically defined location).

## Further evidence that area LIP encodes the next intended saccade

A major objective of this study was to test further the hypothesis that M activity in area LIP neurones reflects the next intended saccade. We predicted that a neurone should only be active during the memory period of a delayed double saccade trial if the next saccade were to be made in its preferred direction. Thus even if the second target were flashed in the receptive field, it should not evoke M activity. The cell should only become active *after* the first saccade, if the second saccade were in its preferred direction. Our results in general confirm these predictions (see fig 1).

It is also clear from these experiments (and others described in chapter 3) that LIP neurones become active before saccades into their motor fields, even in the absence of a visual stimulus falling in their

receptive field (see figures 1b, 2b, 3).

The present results therefore support our hypothesis that M activity in many LIP neurones reflects the next intended saccade.

**Implications for the "vector subtraction" model of saccade generation**

The results of double saccade experiments have been generally interpreted as strong evidence that saccades are coded craniotopically (e.g., Andersen and Gnadt 1989; Mays and Sparks 1980a; Robinson 1973). However, Goldberg and colleagues have challenged this interpretation (Bruce 1988 1990; Goldberg and Bruce 1990). They have pointed out that a spatially accurate second saccade may be made in the double saccade paradigm if the vector of the first saccade is subtracted from the retinal vector of the second target. Thus they envisage that there is a continually remapped retinotopic representation underlying the programming of saccades. They reject the commonly held notion that a spatially accurate second saccade is evidence for craniotopic encoding of saccades. They maintain that both areas FEF (Goldberg and Bruce 1990) and LIP (Goldberg et al. 1989) show evidence for such a vector subtraction operation. They claim that both necessary signals are present in LIP and FEF. We agree that, in LIP, some neurones do carry a postsaccadic signal related to the first saccade (this is the one of the two required vectors). However, do neurones carry a signal of the retinal vector of the second target, at the appropriate time, for the vector subtraction to be carried out? Although Goldberg and colleagues have not been explicit about how such a subtraction is to be effected, presumably a signal carrying the second retinal vector should be present at the same time as the postsaccadic signal of the first saccade, so that the vector subtraction may be carried out to yield the correct second saccade vector. It seems reasonable, therefore, for the retinal vector signal to be present from the offset of the second target until the first saccade is made, i.e., it should be manifest during the memory period.

We find little evidence to support this hypothesis in LIP. Presentation of the second target within the receptive field during a DDS trial typically evokes only a transient response. In some cases there is no response at all. Thus for the majority of cells the visual

response to the second target is transient or entirely absent, and therefore is not available when the postsaccadic signal appears after the first saccade. It is difficult to envision how the vector subtraction is carried out if one of the two vectors in not present at the appropriate time.

However, in 7 cells we have found significant M responses to the second target (see fig 2d). It is thus possible that these cells carry a signal necessary for the subtraction-vector hypothesis. However, since these cells also have M activity when the target is presented first in the sequence, another signal would be necessary to disambiguate the M signal (i.e., to what does it refer? The first saccade plan? The second target retinal vector?).

We also noted that, in general, memory evoked by the second target is less robust than that evoked by the first target (e.g., the M activity in fig 2d is clearly waning with time and is weaker than that in fig 2c). It is possible that if we had imposed a longer delay period, the M activity evoked by the second target would have decayed to baseline, whereas the M activity evoked by the first saccade would have remained strong (we have previously demonstrated (chapter 2) that the memory activity in delayed saccades may persist for well over a second).

We have reported elsewhere that the visual, memory and saccade-related activity of neurones in areas 7a and LIP is influenced by eye position (see chapter 4). Goldberg et al. (1989) have recently replicated this finding. Since the firing rate of LIP neurones for identical retinal stimuli, or identical saccades, varies with initial eye position, activity representing such vectors must also vary with eye position. This too presents considerable difficulty for the vector subtraction hypothesis.

Computer simulations (Goodman and Andersen 1989) suggest that a population of neurones carrying such oculocentric signals modulated by initial eye position could subserve a distributed representation of the desired saccade in craniotopic coordinates (see chapter 4), as required by currently influential models of saccade generation (e.g., Robinson 1973).

Note that there is an important distinction between the issues of craniotopic encoding of saccades on the level of single units (for which we find no evidence in LIP) and on the level of populations of units (for which there is evidence in LIP - see chapter 4).

### Context-dependent visual responses

We noted that visual responses were absent or attenuated in some units when the "correct" visual stimulus was presented second in the double target sequence in DDS trials (see fig 4b). When the same target to be presented first in the sequence it evokes a response (as expected, of course) (see fig 4a). In these units, the visual response seemed to be context-dependent. Whether the stimulus is presented first (and therefore indicates the forthcoming saccade), or second, alters (or "gates") the "visual" response.

These findings are reminiscent of the observations of many workers in other higher order motor regions of the brain, where "sensory" responses to stimuli are typically only observed when the stimuli were cues to move. For instance, Godschalk et al. (1985) observed visual responses in the premotor cortex only if the stimuli cued an arm movement. Such transient, motor-contingent, sensory responses are discussed in detail in the "Motor Set" section of chapter 10.

### Coding sequences of saccades

That LIP activity, in general, seems to encode only the next saccade in a sequence (of two, in the present case) makes some sense, if one considers that it might be issuing general premotor commands to "downstream" premotor structures such as the superior colliculus (SC). If only one saccade is specified in the pattern of activity in LIP, then this may be "read" simply and unambiguously by the SC. If, however, LIP were to simultaneously encode the vectors of both saccades in a double saccade trial, then the SC could not simply read the pattern of activity in LIP. It is possible that a saccade representing a vector average of the two encoded in LIP would be elicited. It is thought that the SC encodes saccades in a topographic motor map in its deeper layers (see Schiller 1984; Sparks 1986, for reviews) and that a saccade is coded by the weighted average of the vector contributions of each neurone that is active in the motor layers (Lee et al. 1988). If two sites in this map are electrically stimulated at the same time, a saccade that is the weighted average of the two that would have been elicited by stimulation of each site individually is evoked (Robinson 1972). Schiller et al. (1979) have shown that such averaging occurs if one electrode is in the SC and one

in the FEF. It is known that stimulation of LIP evokes saccades (Shibutani et al. 1984; Kurylo and Skavenski 1991; Thier, pers. com.). Two-site stimulation in LIP also evokes a "vector average" saccade (Thier, pers. com.).

It is of interest that activity in other motor areas such as primary motor cortex (Thach 1978), cerebellum (Thach 1978), globus pallidus (Brotchie 1989) and superior colliculus (Mays and Sparks 1980a) also seems to encode only the next in a sequence of movements to be made. However, the present results in a sense merely "push back" the representation of a sequence of saccades. Recent neurological studies may shed some light on this issue. Pierrot-Deseilligny and coworkers (1991b) have recently reported that patients with PPC and frontal lesions (probably including the frontal eye fields), but not those with supplementary motor cortical (SMA) damage, are impaired in the production of single memory saccades. However, these authors report that SMA-lesioned patients are impaired in the production of sequences of memory saccades (Gaymard et al. 1990).

Both human (Penfield and Welsh 1949, 1951; Melamed and Larsen 1979; Orgogozo and Larsen 1979, Fox et al. 1985) and monkey (Woolsey et al. 1952; Brinkman and Porter 1979, Schlag and Schlag-Rey 1985, 1987; Schall, 1991a, b) studies suggest that the SMA may contain a third cortical eye field, the supplementary eye fields (SEF) (see Schall 1991c and Goldberg and Segraves, 1989, for reviews). SEF has connexions with FEF, IPL - specifically LIP (Huerta and Kaas 1990; Parthasarathy, pers. com.), deep layers of the SC and oculomotor regions of the brainstem (reviewed in Schall 91c). The SMA has in general been implicated in higher order aspects of motor planning (see Goldberg, 1985, for a review). Of particular interest here is that regional cerebral blood flow increases in SMA in man during complex, volitional movements, but not simple ones (Orgozo and Larsen 1979; Roland et al. 1980). Dick et al. (1986) have reported a patient with SMA damage who was impaired in the production of sequences of limb movements, but not simple movements. Moreover, when subjects are required to imagine - without performing - a complex sequence of movements, regional cerebral blood flow increases there (Ingvar and Philipson 1977, Roland et al. 1980). Thus it is an attractive possibility that SEF is involved in the planning of sequences of saccades.

## LEGENDS

**Figure 1:**

The response of a typical LIP neurone in the four classes of the DDS paradigm.

(a) Class 1: Both stimuli appear within the receptive field of the neurone. The first saccade is made in the preferred direction of the cell; the second in the opposite direction. The task is schematically illustrated at the top of the panel. In the lower part of the panel are shown the sequence of events and the neuronal activity and eye movement behaviour. Onset and offset times for the targets and the fixation light are marked by vertical dotted lines (and also schematically at the bottom of figure 1c). Shown, from the top, are the spike rasters from individual trials, the resultant histograms, and the vertical and horizontal eye position traces.

(b) Class 2: Neither stimulus appears within the receptive field.

(c) Class 3: The first but not the second stimulus appears within the receptive field.

(d) Class 4: The second but not the first stimulus appears within the receptive field. The tasks and data for classes 2, 3 and 4 are presented as for class 1.

The receptive and motor fields of this cell are down-and-left. This cell is relatively more active for more eccentric targets and larger saccades. Thus the first (relatively more eccentric) stimulus in class 1 evokes more activity than the (relatively less eccentric) first stimulus in class 3 or the second in class 4. Similarly, there is greater activity in the intersaccadic interval in class 4 (when the monkey is preparing to make a large down-and-left saccade) than in class 2 (when he is preparing to make a small down-and-left saccade).

**Figure 2:**

The response of an LIP neurone in the four classes of the DDS paradigm. The data and tasks are presented as in fig. 1. See text for discussion.

**Figure 3:**

The response of an LIP neurone in class 2 trials. Neither stimulus falls in the receptive field. The neurone only becomes active after the first saccade (in the non-preferred direction), before the second saccade. This LIP neurone codes in motor coordinates. It exhibits sustained activity before a saccade in its preferred direction, even in the absence of a visual stimulus ever falling within its receptive field. The data and task are presented as in fig. 1

**Figure 4:**

The response of an LIP neurone that shows a motor-contingent visual response. In (a) target 1 falls within the receptive field and evokes a brief response. In (b) the same stimulus is presented as target 2, and evokes no significant response. See text for discussion. The data and task are presented as in fig. 1

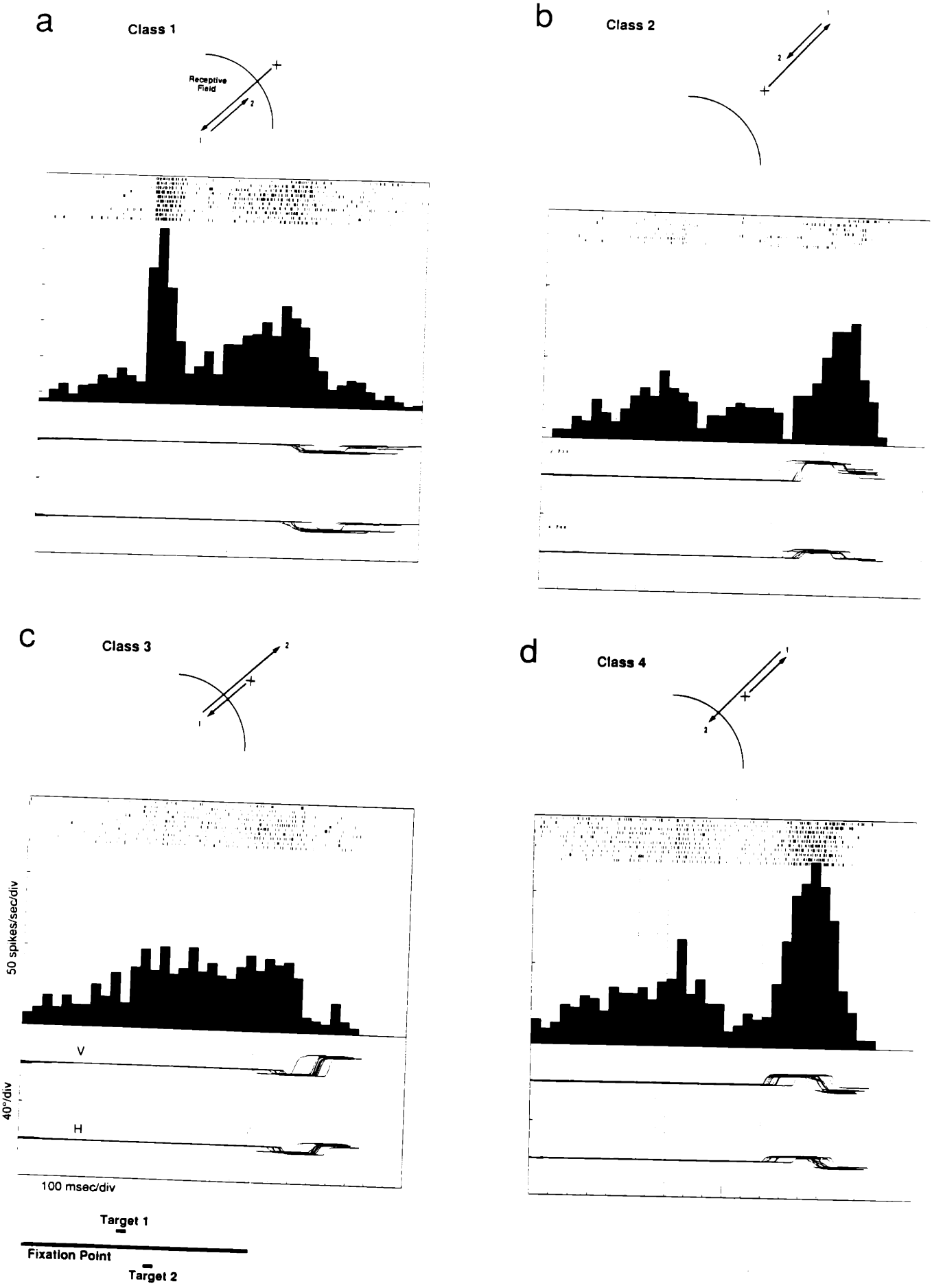

a
Class 1
Receptive Field
b
Class 2
c
Class 3
d
Class 4
50 spikes/sec/div
V
H
40°/div
100 msec/div
Target 1
Fixation Point
Target 2

Figure 1

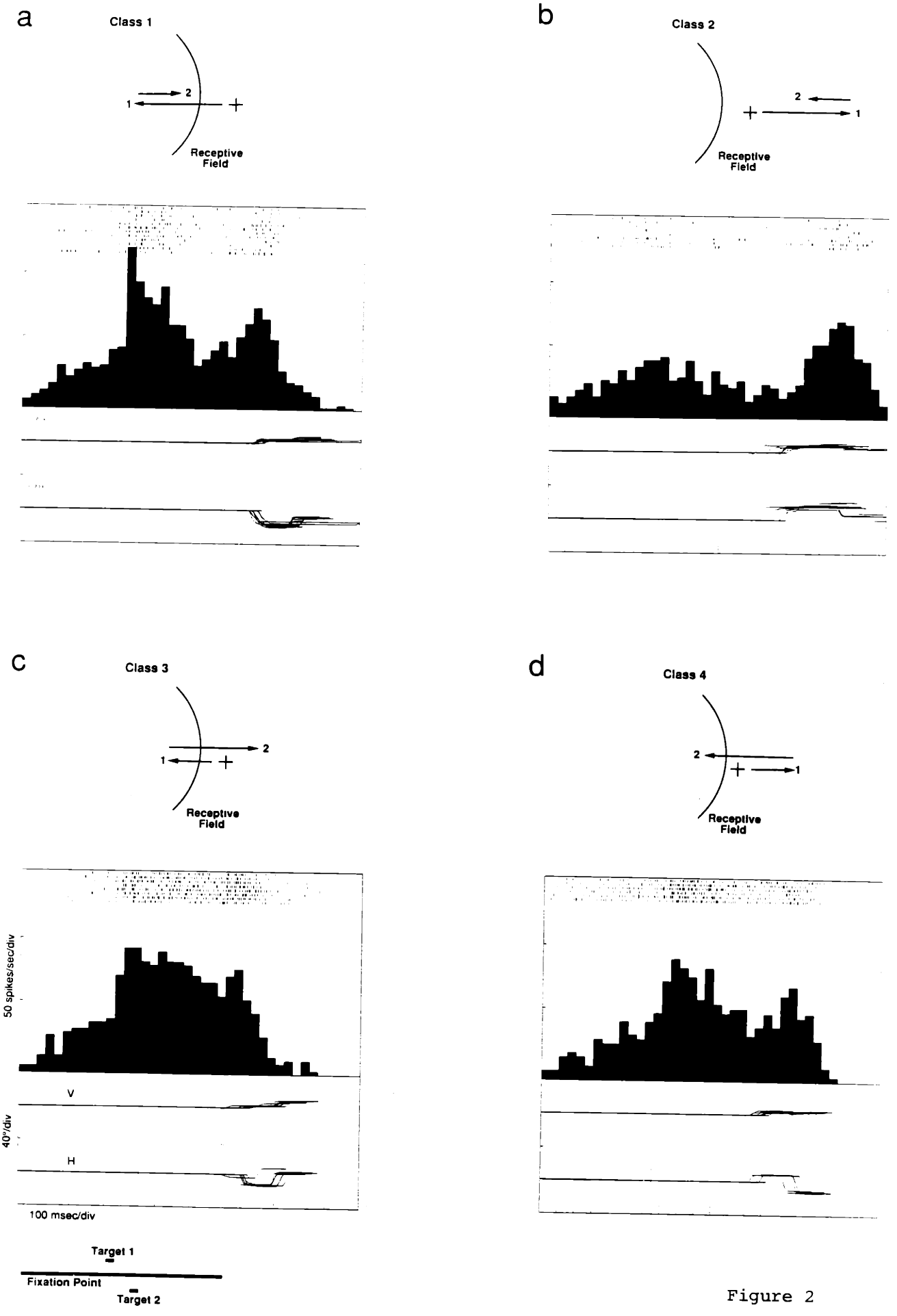

a
Class 1
2
1
Receptive Field
b
Class 2
2
1
Receptive Field
c
Class 3
2
1
Receptive Field
50 spikes/sec/div
V
40°/div
H
100 msec/div
Target 1
Fixation Point
Target 2
d
Class 4
2
1
Receptive Field

Figure 2

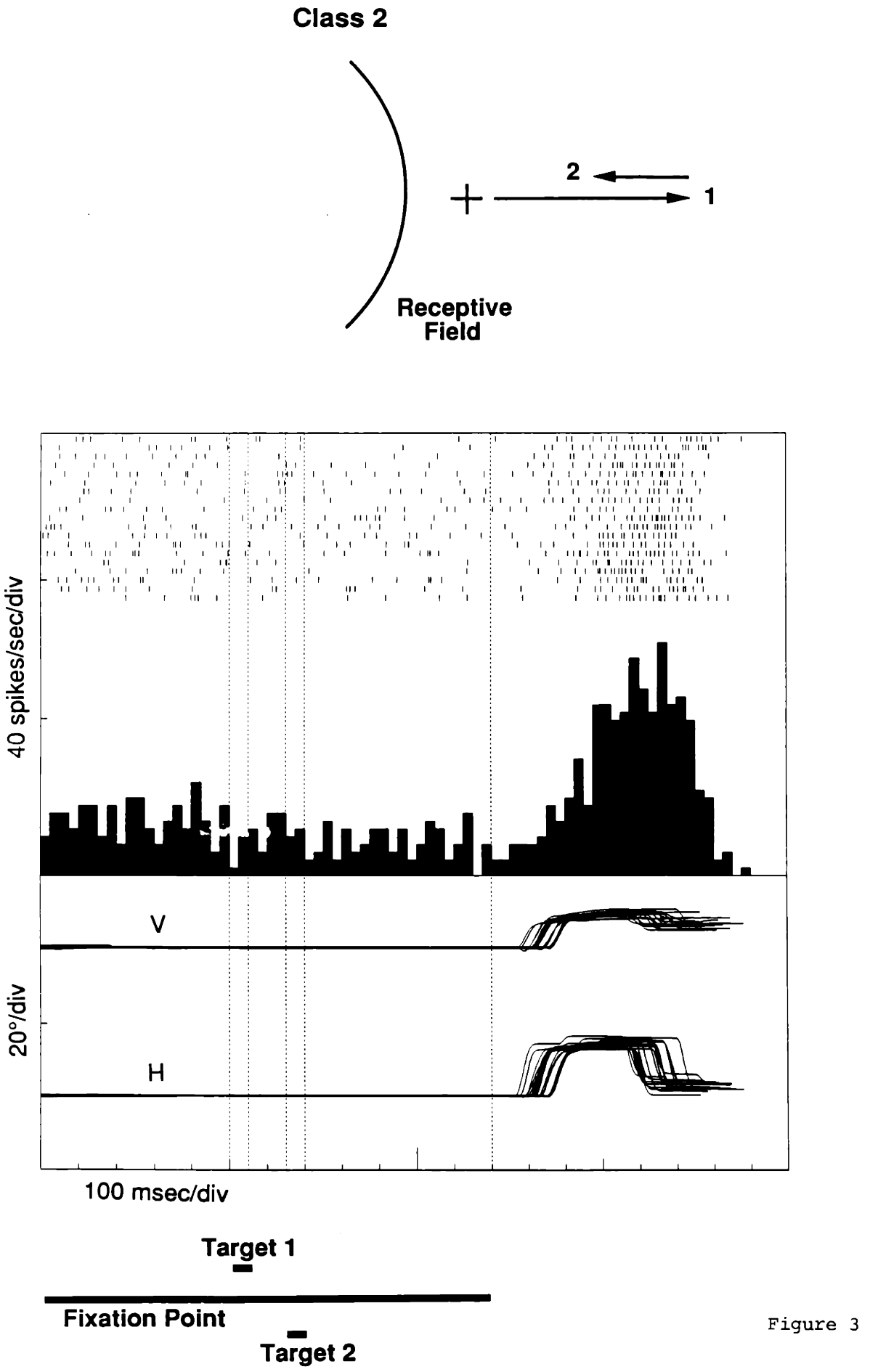

Class 2
2
1
Receptive Field
40 spikes/sec/div
V
H
20°/div
100 msec/div
Target 1
Fixation Point
Target 2

Figure 3

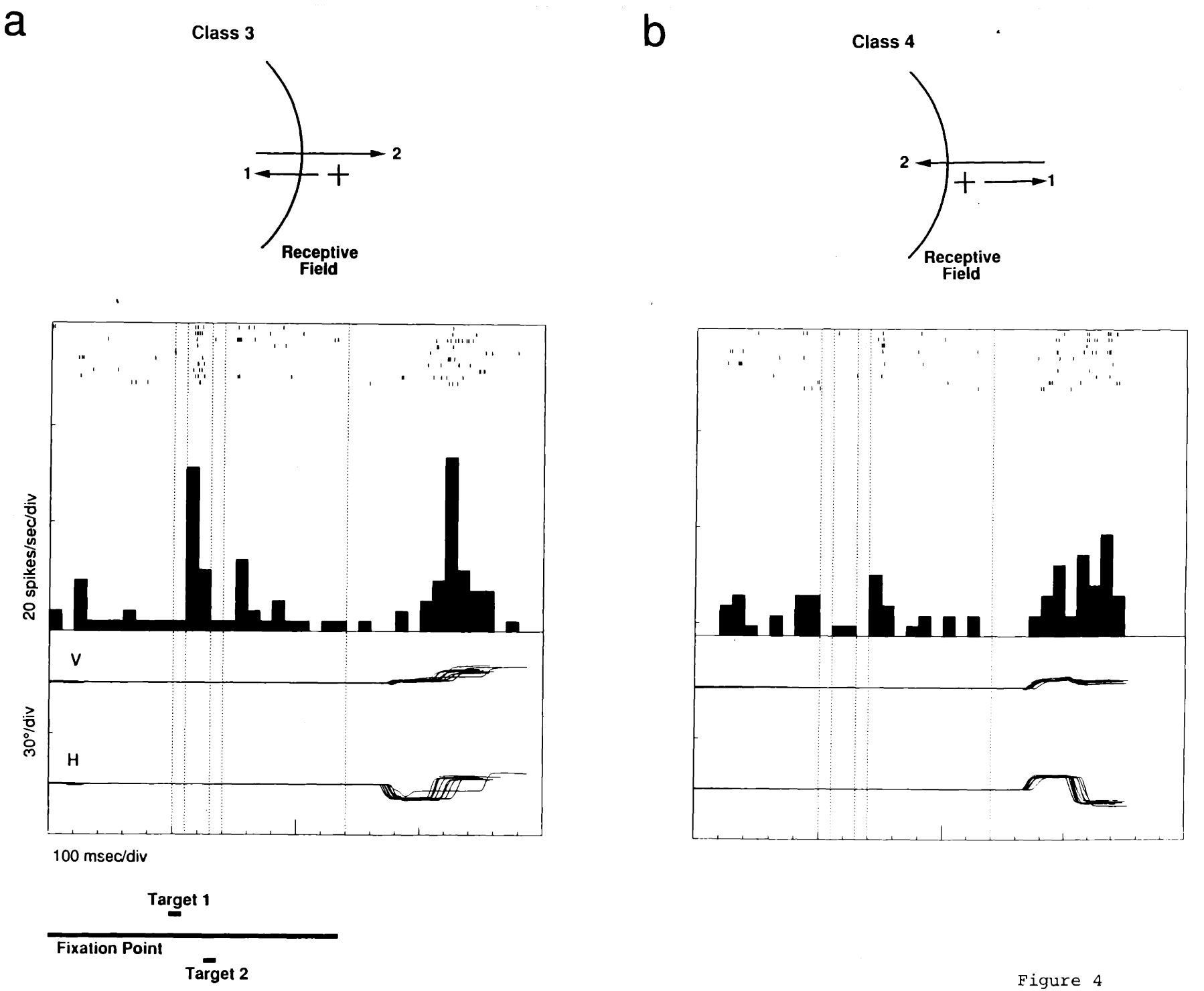

a
Class 3
2
1
Receptive Field
20 spikes/sec/div
V
30°/div
H
100 msec/div
Target 1
Fixation Point
Target 2
b
Class 4
2
1
Receptive Field

Figure 4

# Chapter 6

## Motor intention activity in area LIP during a change of motor plan task

## SUMMARY

Using the delayed saccade paradigm, we have shown that many area LIP neurones manifest "memory" (M) activity which persists from the offset of the visual target until the "go" signal for the saccade. We have suggested that this spatially specific "memory" activity reflects the monkey's intention to make the next saccade into the motor field of the neurone (chapter 3). On the basis of double saccade (chapter 3) and back saccade (chapter 3) tasks, we have demonstrated that LIP cells code in motor coordinates: they become active if a saccade is planned into their motor field, even it no visual target ever falls within their receptive field. Moreover, the results of back saccade (chapter 3) and delayed double saccade (chapter 5) experiments suggest that the sustained (M) activity seen in LIP cells in the absence of visual stimulation and in anticipation of overt behaviour reflects the monkey's *intention* to make the next saccade into its motor field. The M activity is *not* a sensory memory; it reflects the vector of the forthcoming saccade.

We reasoned that if this activity did indeed reflect the monkey's motor plan, then alterations of this plan, even in the absence of overt behaviour, should be manifest in altered LIP activity. We report here the results of experiments using a "change of motor plan" paradigm designed to test this hypothesis. In this paradigm, one, two or three targets were presented sequentially during the fixation period. The monkey did not know how many, nor which, targets would be presented, as the different trial types were pseudorandomly interleaved. He presumably planned to saccade to the first target when it appeared, and then changed his plan if a subsequent, different, target appeared. We were thus able to correlate changes in motor plan with alterations in single unit activity in LIP.

The results support our conjecture that neuronal activity in LIP reflects the monkey's intention to make the next saccade.

## INTRODUCTION

Studies described in previous chapters (2-4) have revealed that many LIP neurones are active in the three basic phases of the delayed saccade task: they show bursts of activity related to the visual stimulus (light-sensitive or LS) and to the saccade (S), and "memory" (M) activity which persists from the offset of the visual target until the "go" signal for the saccade. Fig 1a illustrates the memory saccade task, and the response of a typical LIP neurone recorded during the task. The target was flashed for 300 ms, followed by a 400 ms delay period before the fixation spot was extinguished and the saccade could be made. The unit exhibits a burst of activity when the target is presented within its receptive field, and remains active during the memory period (during which there is no peripheral visual stimulus and the monkey's eyes are steady on the fixation spot). It bursts for a second time with the saccade (to the remembered location of the target), and activity subsequently declines to baseline. We have suggested that the spatially specific "memory" activity reflects the monkey's intention to make the next saccade (chapter 3). On the basis of double saccade and back saccade tasks (chapter 3), we have demonstrated that LIP cells code in motor coordinates: they become active if a saccade is planned into their motor field, even it no visual target ever falls within their receptive field. The M activity is *not* a sensory memory. Moreover, the results of back saccade (chapter 3) and delayed double saccade (chapter 5) experiments suggest that the sustained (M) activity observed in LIP cells in the absence of visual stimulation and in anticipation of overt behaviour reflects the monkey's *intention* to make the next saccade into its motor field.

We reasoned that if this activity did indeed reflect the monkey's motor plan, then alterations of this plan, even in the absence of overt behaviour, should be manifest in altered LIP activity. We report here the results of experiments using a "change of motor plan" paradigm designed to test this hypothesis. In this paradigm, one, two or three targets were presented sequentially during the fixation period. The monkey did not know how many, nor which, targets would be presented, as the different trial types were pseudorandomly interleaved. He presumably planned to saccade to the first target when it appeared, and then changed his plan if a subsequent, different, target

appeared. We were thus able to correlate changes in motor plan with alterations in single unit activity in LIP.

The results support our conjecture that neuronal activity in LIP reflects the monkey's intention to make the next saccade.

## METHODS

### Training and change of plan paradigm

Two adult male rhesus (*M. mulatta*) monkeys (5 and 4 Kg) were used in this study. They were prepared for chronic recording experiments as described in detail elsewhere in this thesis (chapters 2, 4). Eye movements were recorded using the scleral search coil technique. (Robinson 1963, Judge et al 1980). The monkeys were initially trained to fixate stationary spots of light, then to perform visually guided saccades, and then to make memory saccades. This training and the memory saccade paradigm are described in detail elsewhere in this thesis (chapter 2). Fig 1a illustrates the memory saccade task, and the response of a typical LIP neurone recorded during the task. The target was flashed for 300 ms, followed by a 400 ms (or sometimes longer) delay period before the fixation spot was extinguished and the saccade could be made. In fig 1a the stimulus (target A) fell in the receptive field of the cell, evoking clear LS, M and S activity. In fig. 1b, the stimulus (target B) was presented outside the receptive field. It evoked essentially no activity in the neurone.

After the monkey had mastered the delayed saccade task, we trained him on a "change of motor plan" (CP) paradigm. In the basic version of the CP task, we presented two targets (each for 300 ms), separated by a memory period of 400 ms. 400 ms after offset of the second target, the fixation spot was extinguished. The monkey was rewarded for holding his gaze steady on the fixation point throughout the trial from "fixation achieved" until it was extinguished (the "go" signal), and then making a saccade within 500 ms to the location in which the *second* target had appeared. The electronic window around the fixation spot was usually a 2 deg square; that around the target location typically a 15 deg square (to accommodate the systematic spatial errors seen in saccades made to memory targets - see chapter 8). Figures 1c, d illustrate the temporal sequence of events, and the activity of the same LIP neurone recorded during the task. In fig. 1c target A (which falls in the receptive field) is followed by target B (at 180 deg. to A). In fig. 1d the sequence of targets is B then A. Typically the targets were presented at 15 deg from the straight ahead fixation point, and were arranged 180 (or occasionally 90 or 135) deg. apart.

Once the monkey had mastered this task, CP trials were pseudorandomly interleaved with normal delayed saccade trials. During later training periods and all recording sessions at least four classes of trials were interleaved (class 1: target A alone; class 2: B alone; class 3: A then B; class 4: B then A). Thus the monkey did not know how many targets would appear in a trial. If A appeared, he presumably planned a saccade to location A; if the trial happened to be a CP trial, he would have to change his plan once B was presented. Since the trials were pseudorandomly interleaved, and both monkeys almost always performed at 90-100% correct, we believe this was the strategy they used.

We pseudorandomly interleaved four further classes of trials in our studies of some neurones. In two classes, a second target appeared during the fixation period, but in these classes it was the same as the first target (class 5: A then A; class 6: B then B). In these trials the first plan formulated by the monkey was indeed the correct one. The second target therefore did not serve to change the monkey's plan. These classes serve as a control: they demonstrated that the second target's appearance was not interpreted by the monkey as a spatially non-specific signal to saccade to change his plan and saccade to the other (non-presented) target. This task is illustrated in figures 1e and f (along with the responses of a typical neurone).

In the final two classes we presented three targets in sequence during the fixation period (class 7: A then B then A; class 8: B then A then B). In these trials the monkey was rewarded for looking to the last target to appear; thus he presumably changed his plan twice as he was not aware how many targets would appear in the trial. Figures 1g and h illustrate this task and the response of a typical LIP neurone.

The timings of the onsets and offsets of the stimuli were varied somewhat during the course of the experiments (although this had no effects on the results); typical values (after "fixation achieved") were: first stimulus on, 700 ms; first stimulus off, 1000 ms; fixation off (classes 1 and 2) or second stimulus on (classes 3-8), 1400 ms; second stimulus off (classes 3-8), 1700 ms; fixation off (classes 3-6) or third stimulus on (classes 7 and 8), 2100 ms; third stimulus off (classes 7 and 8), 2400 ms; fixation off (classes 7 and 8), 2800 ms.

**Experimental procedure and data collection**

Once a unit had been isolated, we conducted a run of standard memory saccades in eight directions. Thus we determined the neurone's preferred and least preferred directions (typically 180 deg apart), and whether it showed clear memory activity. If the unit had clear memory activity and spatial tuning, we then conducted a run of CP trials (interleaved, of course, with standard delayed saccades, as described above). The two target locations were chosen such that one was preferred and one non-preferred. Other studies described elsewhere in this thesis were also conducted on some of these units. Not all eligible units were tested in the CP paradigm.

Data was collected in "runs"; a run is a sequence of trials of pseudorandomly interleaved classes. We typically collected at least 8-10 trials in each class.

There was an intertrial interval (pseudorandomly varied from 500 to 2000 ms) during which the collection program accomplished book-keeping and data display tasks.

**Data analysis**

Action potentials from isolated single units were sampled at 10 KHz and stored by the laboratory computer. In off-line analysis, the firing rates of the unit during different phases of the task were computed. The phases basically corresponded to the timings of the stimuli: BG (background): from 100 ms after start of trial ("fixation achieved") to the onset of the first stimulus; LS1: from onset to offset of the first target; M1 (first memory) from offset of the first target to onset of the second; LS2: from onset to offset of the second target; M2 from offset of the second target to onset of the third (when a third target was presented), *or* from offset of the second target to offset of the fixation spot (when only two targets were presented); LS3: from onset to offset of the third target; M3: from offset of the third target to offset of the fixation spot.

Paired t tests (alpha level 0.05) were used to test for differing levels of activity (mean firing rates) in different memory phases.

**Allocation of units to area LIP**

Units were assigned to LIP on the grounds of depth of recording, of location of electrode within the chamber, and of their physiological characteristics (see chapters 2 and 4 for details). Both animals are currently being used in physiological experiments; on completion of these studies the animals will be sacrificed and the recording sites reconstructed using standard histological techniques (chapters 2 and 4).

# RESULTS

## Database

We report here data from 88 single units isolated from two hemispheres of one monkey and one hemisphere of a second while the animals were performing the change of plan (CP) task. The units were selected according to the following criteria: first, assignation to LIP (as described in the methods section); second, presence of clear, spatially specific, memory/motor intention activity in delayed saccade tasks. Since we were also conducting related experiments in parallel with those reported here (discussed elsewhere in this thesis), not all the eligible units that we isolated were tested in the CP paradigm.

## Activity of area LIP neurones in delayed saccade tasks

We have previously reported (chapters 2 and 4) that the delayed saccade task allows us to distinguish three basic phases of activity in LIP cells: visual (LS), motor intention/memory (M), and saccade-related (S). Fig 1a illustrates the activity of a typical LIP cell while the monkey was performing the delayed saccade task. There is a visual response that begins after the onset of the stimulus in the receptive field, then prolonged, sustained activity during the delay period (during which there is no target present in the receptive field, and the monkey is not making any eye movements), and finally a second peak of activity occurring at the time of the saccade. Since the saccade is made is darkness to the remembered location of the target, the saccade-related response cannot be an artifact of visual stimulation. These findings have been described in detail in chapter 2.

Not all LIP neurones show all three phases of activity. In this chpter we further investigated the response of units that exhibited clear M activity.

Fig 1a and b illustrate another key aspect of LIP neurones' responses: they are spatially tuned. In fig 1a, target A is presented (15 deg. above the fixation spot), and the neurone clearly shows LS, M and S activity. However, when target B is presented (15 deg. below the fixation spot), the cell has negligible activity in any of the phases of the trial. The LS,

M and S fields of any given neurone are typically broad (*c.* 90 deg width at half-maximal activity) but aligned with one another. These findings have been described in detail elsewhere (chapter 3). To be selected for further study in the present experiments, units had to show spatially selective M responses (the vast majority of LIP neurones were sufficiently narrowly tuned to meet this criterion).

**Change of plan results: predictions**

On the basis of double saccade and back saccade tasks (chapter 3) we have demonstrated that LIP cells code in motor coordinates: they become active if a saccade is planned into their motor field, even it no visual target ever falls within their receptive field. Moreover, the results of back saccade (chapter 3) and delayed double saccade (chapter 5) experiments suggest that the sustained (M) activity seen in LIP cells in the absence of both visual stimulation and overt behaviour reflects the monkey's *intention* to make the next saccade into its motor field. M activity is not a sensory memory.

We reasoned that if this activity did indeed reflect the monkey's motor plan, then alterations of this plan, even in the absence of overt behaviour, should be manifested in altered LIP activity. The CP paradigm was designed to test this hypothesis. The key aspect to these experiments was that the monkey did not know how many targets would be presented during the fixation period. If target A appeared, he presumably planned a saccade to it, since he did not know whether a second target would appear or not. On those trials in which a second target B *was* subsequently presented, he had to change his plan and instead plan to saccade to B. Our prediction was that a preferred target (let us say A) would evoke sustained M activity either until a saccade to the location A was made (in standard delayed saccade trials) *or* until a non-preferred target (say B) was presented during the fixation period (A then B CP trials). This presentation of B was expected to clearly reduce the elevated level of activity induced by A earlier in the trial, since the monkey had changed his plan from "saccade to A" to "saccade to B". Thus the first memory period (M1) would contain significantly more activity than the second (M2). Conversely, on those CP trials in which A was flashed after B (B then A CP trials), we expected the neurone only to become active following the onset of the second target. We

expected the activity to persist until the saccade to location A was made, of course. Thus M2 would contain significantly more activity than M1.

Similar arguments apply to the other four classes of CP trials. A then A trials: we predicted that both M1 and M2 would show elevated levels of activity. B then B trials: neither M1 nor M2 should show elevated levels of activity. A then B then A trials: high levels of activity in M1 and M3, low levels in M2. B then A then B trials: high levels of activity in M2, low levels in M1 and M3.

**Change of plan results: an example**

Fig 1 illustrates the paradigm, and shows the response of a typical area LIP neurone recorded during the task. Fig 1a shows that target A evoked a clear memory period activity, whereas target B did not (fig 1b). In fig 1c we see the response on the neurone in a change of plan task. Initially target A evokes a sustained response, which we suggest reflects the monkey's intention to saccade to A when the fixation spot is extinguished (as in fig 1a). However, whilst he is waiting, target B appears, thus indicating to the monkey that he must change his plan and saccade to B. The eye movement traces indicate that this is what he does, after the fixation point is extinguished (he continues to fixate it for as long as it is present, thus changes in firing rate cannot be attributed to eye movements). We can see that target B appears to "cancel" the sustained memory planning activity evoked by target A. The clear activity present during the first memory period (M1) is absent in the second (M2). Conversely, in those trials in which target B is followed by target A the neurone shows the opposite pattern of memory period activity (fig 1d): Target B evokes no memory planning activity (period M1). However, when target A appears, indicating that the monkey must change his plan and saccade to A not B, sustained activity is evoked (period M2).

We also used four further classes of trials in our studies of some neurones. In two classes, a second target appeared during the memory period, but in these classes it was the same as the first target (A then A, or B then B). In these trials the first plan formulated by the monkey was indeed the correct one. The second target therefore did not serve to change the monkey's plan. These classes serve as a control: they demonstrate that the second target's appearance is not interpreted by the monkey as a spatially non-specific signal to saccade to the non-

presented target. This task is illustrated in figures 1e and f. Note that the appearance of the second target does not substantially alter the memory activity in either class of trial (firing rates during M1 and M2 are similar).

In the final two classes we presented three targets in sequence during the memory period (A then B then A, or B then A then B). In these trials the monkey was rewarded for looking to the last target to appear (as always); thus he presumably changed his plan twice as he was not aware how many trials would appear in the trial. Fig 1g and 1h illustrate this task and the response of a typical LIP neurone. In fig 1g we see that target A evokes memory activity (during period M1) which is cancelled by the appearance of B (little activity in M2) only to reappear after A is presented once more (period M3). The converse pattern of activity is observed in Fig 1h, in which the sequence of targets is B A B.

**Change of plan results: quantitative analysis**

In order to test quantitatively the above predictions, we performed paired t tests (two-tailed, alpha level = 0.05) to compare the levels of activity in different memory periods in the trials of a given CP class. Thus we asked the question, is there significantly different activity in M1 and M2? (In A-then-B-A and B-A-B trials, we considered M3 as well). We predicted a positive answer in A-B and B-A trials, and a negative answer in A-A and B-B trials. In A-B-A and B-A-B trials, we predicted that M1 and M3 should be similar to one another, and M2 different from them.

Classes 3 and 4

88 units with significant M activity in either class 1 or class 2 (standard memory saccades) were tested in the CP paradigm. We expected the M activity in these neurones to vary with the monkeys' (presumed) intentions, as outlined above. The most important result is that for 60 (68 %) of these units, activity in M1 and M2 differ significantly as predicted in both A-B and B-A trials (classes 3 and 4). See Fig. 1c and d for the responses of a typical area LIP cell. In 22 units (25% of our sample), the difference in one class was significant and as predicted, but inconsistent with our hypothesis in the other class. For

example, a unit might "fail to switch off" in A-B trials, i.e., M2 activity is not significantly reduced with respect to M1 activity.

The activity of the remaining 6 units (7 % of our sample) in classes 3 and 4 was inconsistent with predictions based on their activity in class 1 and 2 trials.

Thus the activity of a majority of LIP neurones reflects (what we infer are) the monkey's intentions.

Classes 5 and 6

These are the control classes in which the same target (A in class 5, see fig 1e; B in class 6 see fig 1f) is presented twice. In these classes, any M activity evoked by the first target (M1 activity) should be appropriate even after the second target is presented (since the second target does *not* call for a change of plan); therefore we predicted that M2 activity should be the same as M1 activity. We tested 33 units of our population in classes 5 and 6.

In 17 units (52 % of this sample), M1 and M2 activity did *not* differ in either class, as predicted. In a further 9 units (27 % of this sample), M2 activity was *higher* than M1 activity in class 5. This pattern of activity is also in accord with our hypothesis: a further increase in the strength of M activity in the second activity period presumably does not indicate a change in intention; rather it would seem to reflect the animal's increased confidence that he will indeed be making the saccade he had first planned (in response to the first appearance of target A). Indeed, in fig 1e one can discern that M2 activity is a little more prominent than M1 activity for this neurone in class 5. Therefore, in all 26 (79 %) units behaved in accord with our hypothesis.

In 7 units (21 % of this sample), M2 activity did differ "inappropriately" (i.e., not as predicted from our hypothesis) from M1 activity in one of the two classes (in five cells, class 6). However, for no neurones did activity during M1 and M2 differ "inappropriately" in both classes.

Thus the neural activity would, in general, seem to reflect the monkeys' intentions and behaviour during trials of classes 5 and 6: they were not using the second target's appearance as a non-spatial cue to change their plans, and the second cue did not evoke a major change in memory activity.

Classes 7 and 8: Comparison of activity in periods M1 and M3

The sequence of targets in class 7 is A then B then A (in class 8 it is B-A-B); thus the monkey must change his plan twice. In these trials, the original plan turns out to be appropriate: therefore we predicted that activity in M1 and M3 should be similar (and different from that in M2). We tested 34 units from our population in classes 7 and 8.

In 20 units (59 % of this sample), M1 and M3 activity did *not* differ in either class, as predicted. In a further 8 units (23 % of this sample), M3 activity was *higher* than M1 activity in class 7. This pattern of activity is also in accord with our hypothesis: the relatively stronger memory activity in M3 would seem to reflect the animal's increased confidence that he will indeed be making the saccade he has planned. (When a target is presented first in the sequence, there is a certain probability that it a second and even a third might subsequently appear; whereas no new targets ever appear after the third one, so the monkey can be confident that he will execute the saccade he plans to the third target's location). Indeed, in fig 1g, M3 activity is clearly stronger than M1 activity. Therefore, in all, 28 (82 %) units behaved in accord with our hypothesis.

In 6 units (18 % of this sample), M3 activity did differ "inappropriately" from M1 activity in one of the two classes (in three cells, class 8). However, for no neurones did activity during M1 and M3 differ "inappropriately" in both classes.

Classes 7 and 8: Comparison of activity in periods M2 and M3

We predicted that activity should be different in M2 and M3 in these classes (see above). In 21/34 (62 %) of the units in our sample, activity did differ as predicted in both classes.

In 11 (32 %) units, activity was significantly different in M2 and M3 in only one of the two classes. In the remaining two (6 %) units, M2 and M3 were not significantly different in either class.

Classes 7 and 8: Summary

In general, the activity of most LIP neurones during the three memory periods of trials of classes 7 and 8 does vary systemically. In class 7 it is elevated (M1) then low (M2) then elevated once again (M3) (and *vice versa* for class 8), reflecting (what we presume to be) the monkey's changing intentions during the trial.

**Change of plan results: error analysis**

A strong prediction of our hypothesis is that the pattern of M activity during the last M period should reflect the monkey's eventual behaviour. Clearly this is so for most cells analysed above. However, if the monkey were to saccade to the incorrect target, we would expect the activity during the last M period of that trial to be "inappropriate". We should be able to look at the neural activity and *predict* the monkey's response. Unfortunately, both our monkeys were highly overtrained in this task and performed at 90-100% correct. Individual trials did support our prediction, but are not suitable for quantitative analysis.

**Change of plan results: summary**

We have previously shown (chapters 3 and 5) that the "memory" activity exhibited by an LIP neurone reflects the intention to saccade in a certain direction: it is a motor memory or plan, rather than a sensory memory. The present results clearly demonstrate that alterations in the monkey's intentions, even in the absence of overt behaviour, are manifested in altered LIP activity.

# DISCUSSION

On the basis of double saccade and back saccade tasks (chapter 3) we have demonstrated that LIP cells code in motor coordinates: they become active if a saccade is planned into their motor field even if no visual target ever falls within their receptive field. The M activity is *not* a sensory memory. Moreover, the results of back saccade (chapter 3) and delayed double saccade (chapter 5) experiments suggest that the sustained (M) activity seen in LIP cells in the absence of visual stimulation and in anticipation of overt behaviour reflects the monkey's *intention* to make the next saccade into its motor field.

We reasoned that if this activity did indeed reflect the monkey's motor plan, then alterations of this plan, even in the absence of overt behaviour, should be manifested in altered LIP activity. The results presented here strongly suggest that the M activity of LIP cells reflects the next planned movement; alterations of this plan, even in the absence of overt behaviour, were manifest in altered LIP activity. These and other results (reported elsewhere in this thesis) suggest that LIP is involved in the motor planning of saccadic movements.

## Controls

1. The monkeys had to maintain stringent fixation (within 1 deg of the fixation spot) for as long as the fixation spot was present. Thus the alterations in activity during the M period(s) of the trials could not have been due to eye movements.

2. Trials were pseudorandomly interleaved; thus the monkey did not know how many (nor which) targets would be presented. In order to perform nearly flawlessly (as they did), they presumably had to plan to saccade to a target when it was presented, and change their plan if necessary later during the delay period.

3. Classes in which the same target was presented twice (A-A and B-B trials) ensured that the monkeys could not use the appearance of a second target as a non-spatial cue to change their plans.

### Further possible studies

In these experiments we have used visuospatial targets: the final saccade is directed to the remembered location of a target. However, we have shown that LIP activity is not dependent on the presentation of a visual stimulus. For example, an LIP neurone shows activity in the back saccade task (see chapter 3), even though no stimulus falls into its receptive field. This suggests that changes in activity during the delay period should not depend on the presentation of spatial targets. One might predict that an arbitrary, symbolic, central cue (e.g., fixation light turning red) should evoke memory/motor intention activity in a "rightward" neurone, if the monkey had learned that the cue meant "saccade right". If the cue were changed during the delay period (e.g., from red to yellow) so that another saccade was now indicated, one might predict that our "rightward" unit would become silent, as the monkey changed his plan.

Another interesting paradigm would be a delayed anti-saccade task, in which the monkey would be trained to saccade in the opposite direction to that of the peripheral target. Funahashi and Goldman-Rakic (1990) have used such a paradigm in the prefrontal cortex. They report that the majority of cells there show memory activity related to the location of the target, rather than to the forthcoming saccade direction. Kalaska and Crammond (1990) have used an analogous task requiring an arm movement. They report that most cells in area 5 show a transient burst of activity related to the target location, and then sustained memory period activity related to the forthcoming movement direction. The results of our back and double saccade experiments (chapters 3 and 5) suggest that M activity in LIP is likely to reflect the direction of movement, rather than the target location.

### Other change of motor plan study

Wise and colleagues have performed extensive studies of "motor set" (in our terminology, motor set is "motor intention") in the premotor cortex, PMC (for review, see Wise 1985; see "Motor Set" section in chapter 10 for a discussion). Their most important finding is that, for most PMC neurones, the delay period activity is related to the direction of the forthcoming arm movement (the motor set), and not

to the visuospatial cue ("instructional stimulus", IS) indicating which response is required (Wise et al 1983, Weinrich et al 1984).

In a study in which the IS was changed during the delay period, directionally-specific motor set units showed concomitant changes in activity (Wise and Mauritz 1985). These results are similar to those of our "change of plan" study. One difference between their study and ours was that we did not present our targets (IS's) for the whole duration of the delay period. However, Wise and Mauritz (1985) also demonstrated that delay period activity did not depend on the continual presence of the IS, which suggests that the continual presence of the IS's in their change of motor set experiment did *not* account for the change in activity with change in motor plan which they observed.

**Relationship between LIP activity and saccades**

Clearly these results suggest that LIP is involved in the planning of saccades, and rather indirectly in their production. Activity in LIP is not necessarily followed by a saccade. LIP activity may vary in the absence of overt eye movement behaviour. It is possible that LIP projections to superior colliculus (and perhaps to the frontal eye fields) may raise the level of excitation there such that a "trigger" signal can more easily evoke a saccade. In this regard it is interesting that LIP cells often show a saccade-related burst of spikes with a frequency substantially higher than that during the sustained, elevated M activity (e.g., see fig 1a; also fig 3, chapter 3). This burst may serve as part of the trigger signal suggested above.

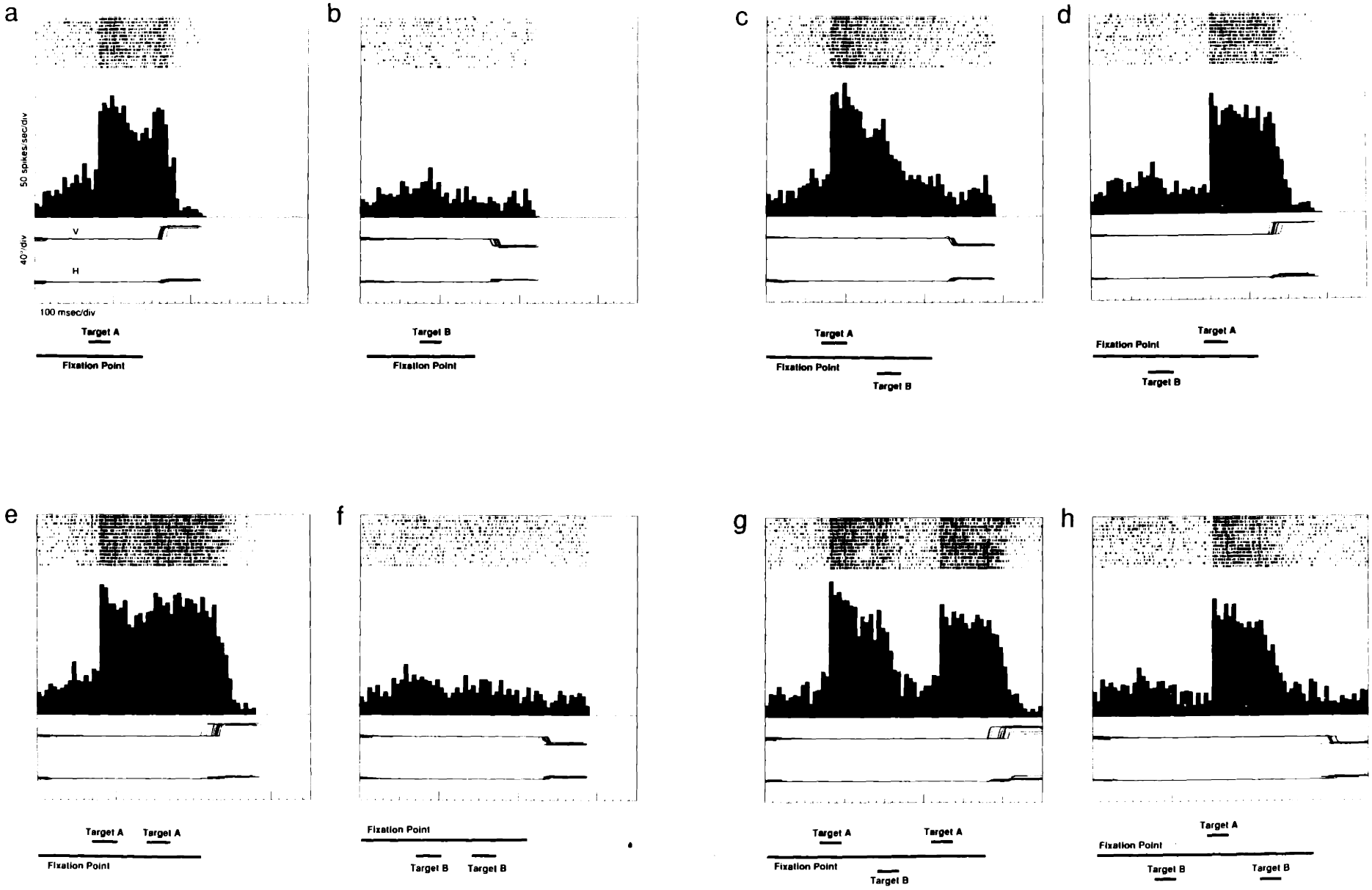
The activity in other high order motor areas typically also has a non-obligate relation to movement (reviewed in Georgopoulos 1991). This is true even of the corticomotoneuronal cells of the primary motor cortex (M1) cells, the "upper motor neurones" of many a neurology textbook. Evarts (1981; 1986), Cheney and Fetz (1980) and Lemon (1988) have shown that the relationship between their firing and muscle activity is conditional and complex. In addition, some M1 neurones fire during an instructed delay period of a delayed response task (e.g., Evarts and Tanji 1976). It is thus perhaps better to think of high order areas in terms of motor planning, and to "consign" the details of execution to lower regions such as the brainstem (for eye

movements - see Wurtz and Goldberg, 1989, for review) and the spinal cord (for limb movements - see Alsternack et al 1981; Georgopoulos and Grillner 1989). See chapter 10 for further discussion of this issue.

## LEGEND

**Figure 1:**

Sequence of events in the change of plan task and the response of an LIP neurone. In each panel, a-h, onset and offset times, for targets and fixation spot, are indicated both in the scheme in the lower part of the panel, and by the dotted vertical lines above. Shown, from the top, are the spike rasters, where each horizontal trace represents a trial, and each tick marks the time of occurrence of a spike; the resulting histogram (bin width 50 ms); and the vertical and horizontal eye position traces of the various trials, superimposed. Trials are aligned on the sensory events (note variable saccadic latencies). (a) Class 1 trials: memory saccade to a preferred target (A). (b) Class 2: memory saccade to non-preferred target (B). Class 3 trials: change of plan, A-B. (d) Class 4 trials: change of plan, B-A. (e) Class 5: no change of plan control, A-A. (f) Class 6: no change of plan control, B-B. (g) Class 7: double change of plan, A-B-A. (h) Class 8: double change of plan, B-A-B. Presentation of A is followed by activity that persists through the following memory period until either a saccade to it's location is made, or until B is presented (indicating that the monkey should change his plan). Target B evokes no memory activity. See text for details.


a
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50 spikes/sec/div
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Figure 1

# Chapter 7

## Motor intention activity in area LIP during saccades to the remembered locations of auditory targets

## SUMMARY

Using a delayed visual saccade paradigm, we have shown that many LIP neurones maintain a sustained discharge after the offset of a target in their receptive field until the "go" signal for the saccade (chapters 2-4). Further experiments (using double, delayed double and back saccades) suggest that this "memory" (M) activity is in motor, not retinal, coordinates (chapters 3 and 5). We have proposed that this M activity may represent the monkey's intention to saccade to the remembered location of the previously presented target. We have used memory saccades to auditory targets to investigate the generality of such activity.

In these experiments we have demonstrated that auditory stimuli - if they serve as cues for saccades - can drive LIP neurones. Furthermore, we have shown that the memory activity of some neurones reflects the monkey's intention to make the next saccade, regardless of the modality of the target. However, we have also demonstrated that certain LIP neurones have modality-specific responses. We suggest that LIP is more intimately involved in the sensorimotor processing underlying visual saccades than auditory ones.

## INTRODUCTION

Using a delayed visual saccade paradigm, we have shown that many LIP neurones maintain a sustained discharge after the offset of a target in their receptive field until the "go" signal for the saccade (chapters 2-4). Further experiments (using double, delayed double and back saccades) suggest that this "memory" (M) activity is in motor, not retinal, coordinates (chapters 3 and 5). We have proposed that this M activity may represent the monkey's intention to saccade to the remembered location of the previously presented target. The change of plan results support our conjecture, as they demonstrate that the M activity changes with the monkey's motor intention, even in the absence of overt behaviour (chapter 6).

In all of the paradigms we have employed thus far, with the exception of the back saccade (chapter 3), saccades have been made to the remembered locations of *visual* targets. However, it is possible to make saccades on the basis of other cues. For example, primates can make fairly accurate saccades to auditory targets (e.g., Jay and Sparks 1984, 1987a, b). We have employed an auditory memory saccade paradigm to investigate the activity of LIP neurones during the planning of such saccades. Is the M activity we have observed during visual memory saccades specific to visual memory targets, or does it represent a more generalised saccade plan? The results of back saccade experiments (in which M activity is evoked before the second saccade, which is made into the motor field without a second target ever being presented) suggest that the latter may indeed be so (chapter 3). Since LIP is not normally responsive to auditory stimuli (Hyvarinen 1982a, b), and it has no direct connections with auditory cortex (Andersen et al. 1990) – in contrast with its heavy visual input from the extrastriate cortex – this might seem a remarkable possibility.

We employed a version of the memory saccade paradigm for the following reasons: first, it allows any sensory response to be clearly separated in time from any motor response (see chapter 2); second, it allows us to observe any M activity that might be evoked.

# METHODS

## Animal surgery and initial training

One adult male rhesus (*M. mulatta*) monkey (5 Kg) was used in this study. He was prepared for chronic recording experiments as described in detail elsewhere in this thesis (chapter 2). Eye movements were recorded using the scleral search coil technique. (Robinson 1963; Judge et al. 1980). He was initially trained to fixate stationary spots of light, then to perform visually guided saccades, and then to make memory saccades. This training and the memory saccade paradigm are described in detail elsewhere in this thesis (chapter 2).

## Auditory memory saccade training

After the monkey had mastered the visual memory saccade task (see chapter 2), we trained him on the auditory saccade task. The auditory stimuli were presented by two small speakers (78 dB at monkey's ear, 150-12000 Hz, broad band noise) mounted 50 cm in front of the monkey, such that one was 15 deg horizontally to the right of the animal's straight ahead gaze position, and the other 15 deg to the left. (Note that we typically presented visual targets at 15 deg eccentricity in our other experiments.) Initially the monkey was trained to look from a central 0.5 deg visual fixation point to one of the targets. The offset of the fixation point coincided with the onset of the peripheral auditory target. Sometimes visual and auditory targets were paired. Once he had mastered this task, we introduced an overlap between the offset of the fixation point and the onset of the target, so that he had to withhold his saccade to the target until the fixation light was extinguished. Finally he was trained on the "true" auditory delayed saccade task, in which the auditory target is presented while the fixation light remained on. Only several hundred ms after the offset on the auditory target was the fixation spot extinguished: the offset of the fixation point served as the "go" signal for the saccade, which was made to the *remembered* location of the auditory target. (In early stages of training on the auditory memory saccade task, visual feedback was sometimes given after the saccade had been made.) Thus the auditory memory saccade task is analogous to our visual delayed

saccade paradigm (chapter 2). All experiments were run in a darkened chamber. Fig. 1 shows the sequence and timing of events in an auditory delayed saccade, and the response of an LIP neurone recorded during the task.

The experiment was controlled by a laboratory computer. Trials of the delayed saccade task were organized in the following fashion (illustrated in figure 1): the appearance of a fixation spot signalled to the monkey the beginning of a trial. The monkey had to fixate the spot within 1 s. The moment the eye foveated the fixation spot was called "fixation onset". If the monkey failed to fixate the spot within the given 1 s, the trial was aborted, declared a "miss", and an inter-trial interval was begun. If the monkey successfully foveated the fixation spot, "fixation achieved" was declared and the trial began. The timings (after "fixation achieved") of the onsets and offsets of the stimuli were: first stimulus on, 750 ms; first stimulus off, 1500 ms; fixation off, 2750 ms.

The electronic window around the fixation spot was a 2 deg square; that around the target location typically a 20 deg square (to accommodate the systematic spatial errors seen in saccades made to memory targets - see chapter 8).

**Auditory-visual change-of-motor-plan task**

We also trained the monkey on a novel auditory-visual change of plan task, analogous to the one described in chapter 6. After the monkey had mastered the auditory delayed saccade task, we trained him on an auditory-visual "change of motor plan" (CPVA) paradigm. In the CPVA task, we presented two targets (each for 750 ms) during the period in which the fixation spot remained illuminated. The timings (after "fixation achieved") of the onsets and offsets of the stimuli were: first stimulus on, 750 ms; first stimulus off, 1500 ms; second stimulus on, 2250 ms; second stimulus off, 3000 ms; fixation off, 3750 ms. The monkey was rewarded for holding his gaze steady on the fixation point until it was extinguished (the "go" signal), and then making a saccade within 1000 ms to the location in which the *second* target had appeared. Fig. 2 illustrates the temporal sequence of events, and the activity of a typical LIP neurone recorded during the task. We pseudorandomly interleaved four classes of trials: (1) first target visual

left, second target auditory right (2) visual right then auditory left (3) auditory left then visual right (4) auditory right then visual left.

Once he had mastered the task, CPVA trials were always pseudorandomly interleaved with normal visual and auditory delayed saccade trials. During later training periods and all recording sessions in which we employed CPVA classes, eight classes of trials were interleaved (the four CPVA classes described above, and auditory and visual memory saccades to the left and right). Thus the monkey did not know how many targets would appear in a trial. If a target (either auditory or visual) appeared to the left, he presumably planned a saccade to it; if the trial happened to be a CPVA trial, he would have to change his plan once the second target (either visual or auditory) was presented to the right. Since the trials were pseudorandomly interleaved, and the monkey almost always performed at 90-100% correct, we believe this was the strategy they used.

**Location of stimuli**

The animal had difficulty reliably distinguishing the direction of auditory targets placed above or below the midline (as did the experimenters!), so we restricted our stimuli to horizontal right and left only. In those runs in which we combined visual and auditory targets, the visual targets were presented 8 deg horizontal to the left or right. We chose 8 deg so that the visual targets (0.5 deg squares) would not be obscured by the speakers. The speaker apparatus was designed so that it could be expeditiously mounted and removed between runs. We always tested our units with other, purely visual memory saccades, in other runs.

**Experimental procedures**

We used auditory delayed saccades to test single units which we had previously determined to be active during horizontal left or right visual memory saccade trials. Trials requiring left and right saccades were pseudorandomly interleaved, often with two additional classes of trials (delayed saccades to *visual* targets presented 8 deg to the left or right of the fixation spot). Sometimes an additional four CPVA classes were interleaved, requiring a change of motor plan (see above).

**Data collection and analysis**

Single units were isolated and their action potentials recorded with glass-coated Pt-Ir electrodes, placed into the cortex by a Chubbuck microdrive (see chapter 2 for details). Spike data were sampled at 10 KHz and eye position data at 500 Hz. These data were analysed off-line.

Trials were divided into different phases: background (BG), from 100 msec after start of trial ("fixation achieved") to 750 ms; stimulus (ST), from 750 to 1500 ms (the duration of the presentation of the auditory or visual target); memory (M), from 1500 ms to 2750 msec (the period from the offset of the target to the offset of the fixation spot); saccade-related (S), for the 500 ms following the offset of the fixation spot. Paired t tests (alpha level = 0.05) were used to determine whether the activity (mean firing rate) in a given phase was significantly different from BG, or another phase. Unpaired t tests (alpha level 0.05, separate estimates of sample variances) were used to compare activity in phases from different classes of trials .

CPVA trials were analysed in a similar fashion. The phases were: background (BG), from 100 ms after start of trial to 750 ms; stimulus 1 (ST1), from 750 to 1500 ms (the duration of the presentation of the first target); memory 1 (M1), from 1500 ms to 2250 ms (the period from the offset of the first target to the onset of the second); stimulus 2 (ST2), from 2250 to 3000 ms (the duration of the presentation of the second target); memory 2 (M2), from 3000 msec to 3750 ms (the period from the offset of the second target to the offset of the fixation spot); saccade-related (S), for the 500 ms following the offset of the fixation spot.

Latencies of sensory responses were measured as described in chapter 2.

**Allocation of units to area LIP**

Units were assigned to LIP on the grounds of depth of recording, of location of electrode within the chamber, and of their physiological characteristics (see chapter 2 for details). The animal is currently being used in physiological experiments; on completion of these studies he will be sacrificed and the recording sites reconstructed using standard histological techniques (chapter 2).

# RESULTS

## Database

We tested 55 neurones from one hemisphere of a rhesus monkey. They were assigned to LIP as described in the methods section. Only neurones which showed activity in left- or rightward visual delayed saccade trials were tested with auditory delayed saccades. Not all eligible units isolated were tested.

## Auditory sensory responses

37 units showed significant response to auditory and/or visual targets. 15 had similar visual and auditory responses (e.g., responded to a left side target of either modality), six had dissimilar responses, four only responded to auditory targets and twelve only to visual targets. 25/55 (45%) neurones showed an auditory sensory response. Of the 25 auditory-sensory units, 11 preferred ipsilateral, 12 contralateral and 2 ipsi- or contralateral stimuli.

Fig. 1 illustrates the response of an LIP neurone in auditory memory saccades. Fig. 3 illustrates the response of an LIP unit in memory saccades made to auditory right (fig. 3a) and visual right (fig. 3b) targets. The responses are very similar.

The latency of auditory responses varied considerably from unit to unit, with a population mean of 139.8 ± 101.4 ms. Typically the visual responses of a neurone were a little faster (for this population, 102.8 ± 52.1 ms). This difference was not significant (paired t test, $p > 0.05$).

## Saccade-related responses

34/55 (62 %) units showed significant saccade-related (S) responses to auditory and/or visual targets. 24 had similar visual and auditory SR responses (e.g., responded to leftward saccades regardless of the modality of the target), two had dissimilar responses, five only responded to auditory saccades and three only to visual saccades. 31/55 (56 %) units had auditory S activity. Of the 31 auditory saccade units, 5 preferred ipsilateral, 16 contralateral and 10 ipsi- or contralateral stimuli.

Figures 1, 3a and 4 illustrate LIP units which fire with remembered saccades to auditory targets.

**Memory activity**

32 units showed significant memory (M) responses during auditory and/or visual memory saccades. 12 had similar visual and auditory M responses, four had dissimilar responses, nine only responded during auditory memory saccades and seven only during visual memory saccades. Of the 25 auditory M units, 5 preferred ipsilateral, 14 contralateral and 6 ipsi- or contralateral stimuli. 25/55 (45 %) units had auditory M activity.

Fig. 4 illustrates the response of an LIP neurone during auditory memory saccades to the right. There is clearly an enhanced level of activity between the offset of the auditory stimulus and the saccade. This unit also responded in the visual memory saccade task (not illustrated).

**Relation of auditory sensory to auditory memory activity**

Of the 25 units that showed significant auditory sensory responses, 11 also had significant M activity. In 9/11 cases this was in the same direction as the sensory response. Similarly, we have previously shown that visual and memory activity is typically aligned during visual memory saccades (chapter 3).

Interestingly, 14/25 (56 %) units exhibiting auditory M responses did not have auditory sensory responses. This pattern of an M response without an antecedent sensory response was only observed in 13/73 (18 %) units during visual memory saccades (chapter 2).

**Inhibitory responses**

We noted a high proportion of inhibitory responses during auditory trials: 10/25 (40 %) sensory; 13/25 (52 %) memory; 15/31 (48 %) saccade-related (these numbers are expressed as a fraction of total number of cells with significant excitatory or inhibitory responses). For visual memory saccades, the proportions of inhibitory responses ranged from 14 to 25 % (see chapter 2).

**Summary of activity during memory saccade tasks**

These results are summarised in table 1. Clearly a substantial number of units respond in both visual and auditory memory saccades. Often the responses are similar in both tasks. This is especially true for the saccade-related activity. However, a considerable proportion of the units exhibit either modality specific responses, or different responses to the two modalities.

In fig. 5 we show the numbers of units with the various possible combinations of auditory responses.

**Change of plan results**

We have previously shown that when a monkey changes his motor plan, activity in LIP reflects these changes (chapter 6). In those experiments, visual targets were used to denote the forthcoming saccades. Here we have shown that auditory targets may also evoke M activity (see above). In preliminary audio-visual change of plan (CPVA) experiments, we have shown that activity in LIP reflected the direction of the next planned saccade; alterations of this plan, even in the absence of eye movements, were reflected in neuronal activity. This was regardless of whether the memory was evoked by visual or auditory targets. Fig. 2 illustrates the response of an LIP unit that shows memory/motor intention activity before rightward saccades. Target B (be it visual or auditory) to the left evokes no memory activity, but the cell becomes active when target A (be it visual or auditory) to the right is represented. The cell remains active until a rightward saccade is made.

We have tested 22 units in the CPVA paradigm. Activity in eight clearly reflected change in plan; activity in a further eight was in partial support of our hypothesis. Cells with strong M activity gave the clearest results in this paradigm. More units need to be tested in this paradigm. One complication is that not all units have similar M activity following auditory and visual targets (see above).

**Parameters of auditory memory saccades**

The peak velocities of 15 deg. auditory and visual memory saccades

were compared by t tests. We compared leftwards and rightward saccades separately. We chose blocks of trials that were performed by the monkey at similar times on the same day of recording. This was because we found a considerable variation in velocity during recording sessions: velocities typically fell towards the end of the session, when we presume the monkey's motivation was lower. Typical results are presented in table 2. In general, auditory M saccades were slower than visual M saccades, but not significantly so.

The velocity profiles of auditory M saccades were similar to those of visual M saccades. Both types of saccades typically have a bell-shaped profile, although occasionally saccades with lower and multiple peaks are observed (see also Traccis et al. 1984).

## DISCUSSION

It appears from this study that auditory stimuli can drive some LIP neurones when they serve as targets for saccades. This is despite the lack of auditory responses from LIP when auditory stimuli have no behavioural significance for the animal (Hyvarinen 1982a, b), and the lack of connexions of LIP with auditory areas (e.g., Andersen et al. 1990).

Furthermore, many LIP neurones are tonically active after offset of the target until the saccade to the remembered location of the auditory target is made. The change of plan results show that the activity of some such cells reflected the next planned movement; alterations of this plan, even in the absence of overt behaviour, were manifested in altered LIP activity. We suggest that these results support our contention that activity in many LIP neurones reflects the monkey's intention to make the next saccade. This activity may be evoked regardless of the cue to move (but see below). Thus an important implication of this study is that some cells in LIP are at least bimodal: they may issue commands for saccades to behaviourally relevant targets, regardless of their modality.

Although we did observe a good number of auditory responses, visual responses were more common (e.g., 33/37 of units with a sensory response were visually-driven, whereas only 25/37 were auditorily-driven). This is in accord with the predominance of visual inputs to LIP (e.g, Andersen et al, 1990). It is also to be expected, given the emphasis on *visuo*-spatial deficits reported after PPC lesions (see below and chapter 1). We also noted a preponderance of contralateral responses.

A sizeable proportion of neurones in LIP appear to have modality-specific responses. This was especially true of the sensory and memory phases of the trials (saccade responses are more often not modality-specific). Kubota (1985) has obtained similar results whilst investigating sustained activity in prefrontal cortex in delayed response tasks: some of his units have modality-specific delay period activity. (He suggests they may activate both the modality specific and non-specific movement cells which he also finds in the prefrontal cortex). Both supramodal and modality-specific problems have been reported following PPC lesions in man (see below). The latter implies the

existence of somewhat separate neuronal mechanisms underlying spatial behaviours in different modalities.

**Controls: pinnae movements**

It is possible that some of the activity we observed is related to pinnae movements. Bruce et al. (1988) have reported that the pinnae tend to orient in the direction of gaze. Interestingly, they found that the tonic orientation of the pinnae was directed towards the direction of gaze, even when the monkey was attending to a sustained peripheral auditory cue. This suggests that the activity we observed in these experiments is unlikely to be due to the orientation of the pinnae. We did not systematically attempt to relate neuronal activity to pinnae movements, but qualitative observations (using our infrared video system) did not suggest any relationship. We plan to place search coils on the pinnae in future experiments to investigate this possibility more thoroughly.

**Controls: saccades are made in the dark**

Experiments were performed in a darkened, light-tight chamber. A dim fixation light was extinguished before the saccades were made. Thus no visual cues were available for target localisation: the saccade was made to the remembered location of an auditory target.

**Relation to earlier studies of auditory saccades**

There have been but few studies of saccades to auditory targets in primates (man: Paulsen and Ewertsen 1967, Zahn et al. 1978, 1979; Konrad et al. 1989; Traccis et al. 1984; Zambarbieri et al. 1981, 1982; Lueck et al. 1990; monkey: Jay and Sparks 1984, 1987a, b). In man, only "standard" (i.e., with no delay period) auditory saccades have been studied. In general, such saccades have been found to be slower, less accurate and to have somewhat longer latencies than comparable visual saccades (e.g., Zahn et al. 1978). Jay and Sparks (1984, 1987a, b) have studied both standard and delayed saccades to auditory targets in monkey. However, in their delayed saccade task (Jay and Sparks 1987a, Fig. 2b), the target remained on, so the monkey was making a saccade to

a target, and not the remembered location of a target (as in our experiments). They report (unpublished, cited in 1987a) that velocities of auditory saccades are lower than visual saccades, and that latencies of saccades to auditory targets near the midline are long (in accord with findings in man - see above).

Jay and Sparks (1987a) recorded in the intermediate layers of the superior colliculus. 12/13 saccade-related burst (SRB) cells fired before saccades to targets of either modality; the remaining cell only fired before saccades to visual targets. 45/59 visual-motor (VM) cells fired before saccades to targets of either modality; 13/59 only fired before saccades to visual targets and 1/59 only fired before saccades to auditory targets. Thus the majority of SC premotor cells fired before saccades to targets of either modality. However, 57/59 VM cells only showed sensory responses to visual targets; the remaining 2 were bimodal.

Jay and Sparks (1987b) also recorded from cells in the deep SC. They report that 122/124 cells tested with both visual and auditory stimuli were bimodal. 71% cells were tonically active, until just after the eye movement in delayed saccade trials. However, as noted above, in their delayed saccade task (Jay and Sparks 1987a, fig. 2b), the target remained on, so the monkey was making a saccade to a target, and not the remembered location of a target (as in our experiments).

Since we have studied saccades to the remembered locations of auditory targets, our results are not strictly comparable to those discussed above. However, we did note that auditory memory saccades were in general a little slower than corresponding visual memory saccades, in accord with the results of previous studies (see above). Velocity profiles were also sometimes multipeaked (as noted by Traccis et al. 1984). We also found both visual and bimodal responses in LIP, as did Jay and Sparks in SC, although they did not report any purely auditory responses.

**Anatomy**

The auditory connexions of PPC have not been studied in detail. There are connexions from area 22/area TA (areas AA1-3 of Pandya and Yeterian 1985) - the auditory association cortex - to area 7 (both the surface and the inferior bank of the IPS (Divac et al, 1977)). Tpt (the temporoparietal junction) receives connexions from parakoniocortex (paAlt) (Pandya and Sanides 1973), considered to be part of the auditory

association cortex (Pandya and Yeterian 1985), and projects on to area 7 (Pandya and Kuypers 1969). There are also connexions from the superior temporal polysensory area of Bruce et al. (1981) to area 7a (Andersen et al. 1990) and LIP (Baizer et al, 1991). Baylis et al. (1987) have reported many auditory responses in single units in the dorsal superior temporal sulcus (areas TS and TAa). Since the various subdivisions of the PPC are densely interconnected (Pandya and Seltzer 1982; Andersen et al. 1990) it seems reasonable to assume that auditory information can gain access to the whole PPC, but indirectly.

**Relation to previous reports of auditory responses in PPC**

Hyvarinen and his colleagues, in their extensive studies of the PPC of awake monkey (reviewed in Hyvarinen 1982a) did not observe any auditory responses in "area 7 proper" (*ibid*, p 116). However, they frequently encountered auditory responses in area Tpt - the temporo-parietal junction (monkey: Pandya and Sanides 1973; man: Galaburda and Sanides 1980). In about 70% of the auditory units encountered, the response varied with the spatial location of the stimulus (Leinonen et al. 1980). Informal testing suggested that Tpt neurones were relatively insensitive to the spectral properties of auditory stimuli. Latencies were usually 15-60 ms, only rarely greater than 100 ms. Some Tpt neurones also responded to somatic stimuli (on the head), and a few to visual and auditory stimuli.

Those Tpt neurones with motor-related activity were mainly active during head, rather than eye or limb, movements (Leinonen et al. 80). Only 4/197 cells had combined auditory and motor-related responses.

An important difference between Hyvarinen and colleagues' experiments and ours was that their monkeys were not trained to perform specific behaviours in response to sensory stimuli. This may explain the difference in numbers of auditorily responsive units reported from the two laboratories. For instance, it is known that motor cortex units will give auditory responses usually only when they serve as a cue to movement (see "Motor Set" section in chapter 10 and below for a discussion of this issue). There may well be a similar relationship between LIP activity and auditory stimuli (see below). However, it is an attractive possibility that Tpt is involved in the

coding of auditory space, much as area 7a seems to code visual space (Andersen et al, 1985b; chapter 4).

Various other authors (Sakata et al. 1973, Koch and Fuster, 1989; Seal et al. 1983) have reported auditory responses in portions of PPC. Interestingly, these authors only found responses to auditory stimuli when they were cues to movement. This is not unexpected as areas of PPC can receive auditory input only via indirect pathways (Hyvarinen 1982a,b; Andersen et al. 1990).

It was beyond the scope of the present study to investigate in depth the auditory responses of PPC. However, the precise role that it plays in such tasks as auditory localisation is worthy of further investigation, especially in the light of some the lesion studies mentioned below. It is intriguing that we recorded several area 7a units that had a purely sensory response in the auditory delayed saccade paradigm. They showed no M nor S activity. It is tempting to speculate that these neurones were involved in the coding of auditory space - or perhaps even in a supramodal representation of extrapersonal space (such purely sensory auditory units tended to have spatially similar visual receptive fields).

**Auditory responses in other non-auditory structures**

That we have found auditory responses in LIP may appear a little difficult to explain. However, we would like to stress that auditory responses have been reported in other areas of the brain that are considered far from being auditory. Prime examples are the premotor cortex (PMC) and the supplementary motor area (SMA) (e.g., SMA and PMC, Tanji 1985; SMA, Tanji and Kurata 1982; PMC, Wise et al. 1983), the prefrontal cortex (e.g., Vaadia et al, unpublished, cited in Evarts et al. 1984, p 76) and other PPC areas (see above). Auditory signals are observed in these areas when auditory stimuli serve as triggers or cues for arm movements - but only rarely when they are behaviourally irrelevant for the animal. We suggest that the auditory signals we have observed in LIP may be of a similar nature.

Similarly, visual responses in the precentral motor areas are also generally motor-contingent (e.g., Godschalk et al. 1985: PMC; Kwan et al, 1981: areas 4 and 6; Kubota and Hamada 1978: area 6). Evarts et al. 1984 suggest that such motor-contingent sensory responses reflect

"motor set".

One further study deserves mention in this discussion, although it is of primary and adjacent auditory cortex. Vaadia et al. (1982) showed that some units responded differently to an identical auditory stimulus, depending on its "meaning". For example, some units only responded to the tone stimulus if it signalled a leftwards movement.

Auditory responses in LIP are may only be observed when the stimulus is a cue for movement, whereas area Tpt may be involved in the coding of auditory space *per se*.

**Relation of auditory sensory to auditory memory activity**

Of the 25 units that showed significant auditory sensory responses, 11 also had significant M activity. In 9/11 cases this was in the same direction as the sensory response. Similarly, we have previously shown that visual and memory activity is typically aligned during visual memory saccades (chapter 3).

Interestingly, 14/25 units exhibiting auditory M responses did not have auditory sensory responses. This pattern of a M response without an antecedent sensory response was only observed in 13/73 units during visual memory saccades (chapter 2). This may reflect a difference in the nature of the sensorimotor processes underlying the production of the two types of movement. Evidence presented in other chapters suggests that LIP may be intimately involved in the sensorimotor coordinate transformations underlying saccades to targets defined visually. This might not be the case for auditory saccades. LIP receives its auditory input "second hand", whereas it serves as a way-station in the processing of visuo-spatial information (Andersen et al. 1990; Baizer et al. 1991; Felleman and Van Essen 1991). Also, auditory saccades appear to be relatively spared, as compared to visual saccades, following parietal lesions in man (see below and chapter 1).

Fuster has noted that the cells in the posterior parietal (Koch and Fuster 1989) and infero-temporal (Fuster 1990) cortices which are active on sample presentation (in haptic and visual short-term memory tasks) are not necessarily those that are active during the ensuing memory period.

Kubota (1985) has reported sustained responses in prefrontal cortex during delayed response tasks. Some of the units have modality-specific delay activity. He also reported responses to movements

triggered by cues of a specific modality. He suggested that modality-specific delay cells may activate both modality-specific and non-specific movement cells. We have observed similar patterns of activity in LIP.

It is possible that processing analogous to that suggested by the results of Fuster and of Kubota may be occurring in LIP: certain cells may represent the auditory target *per se*, and pass this information on to other, motor intention, cells.

### Motor intention neurones

Results from only some of our units support the strong statement of our hypothesis that M activity in LIP neurones reflects the next saccade, regardless of the instructional cue. These units were active during the delay period for saccades elicited by targets of either modality. In some cells, the M activity was modality specific, being evoked by either visual or auditory targets. Similar results have been reported from the prefrontal cortex (Kubota 1985). It would be of interest to examine the M activity of LIP neurones during tasks in which the required saccade was indicated by an arbitrary symbolic cue, such as the fixation light changing colour. Another interesting paradigm would be a delayed antisaccade task. One might expect truly modality-independent "intention" cells to be active before their preferred saccade, regardless of the cue to movement. See chapter 10 for further discussion of possible future experiments.

### Saccade-related responses

It is of interest that of the three phases of activity, stimulus-related, memory and saccade-related, the last has the lowest incidence of modality-specificity. Modality-independent saccade units may help trigger saccades (see chapter 10), or register their occurrence (especially those with postsaccadic activity; see chapter 3).

### Latencies of responses to auditory stimuli

The latencies we observed were about 140 ms. Seal et al. (1983) reported values of 60-80 msec in area 5 (interestingly these values were increased to 120-140 msec in deafferented animals, who showed a

concomitant increase in movement reaction time). The mean latency in primary auditory cortex of behaving monkey has been reported as 26.5 msec (Pfingst and O'Connor, 1981). Visual latencies in this population of LIP neurones were a little over 100 ms. The long latencies reported in PPC are consistent with extensive preprocessing of auditory signals, and the lack of direct connexions of PPC with auditory areas (Hyvarinen 1982a, b; Andersen et al. 1990).

**Monkey lesion studies**

To my knowledge, there is only one report of auditory dysfunction following PPC ablation in monkey. Heilman et al. (1972) reported auditory hemineglect (in association with visual and tactile hemineglect) following a large unilateral excision of PPC. However, it appears that auditory function has rarely been explicitly examined in PPC lesion studies.

**Relation to neurological findings**

Auditory dysfunction *per se* is not commonly reported as a sequel to PPC damage in man or monkey. There is a debate about whether the classic PPC symptoms of neglect and inattention (see chapter 1) may be independently manifest in the auditory domain. In the clinical setting they are most marked and easily tested in the visual domain.

Patients with damage to various brain regions including the PPC may exhibit auditory neglect (reviewed in Heilman and Valenstein 1985). Often this neglect is most clearly demonstrable using bilateral auditory stimuli; patients tend to exhibit extinction, only reacting to the ipsilateral stimulus (Heilman and Valenstein 1970; Bender 1952). Extinction in the auditory domain is rarer and typically milder than visual or tactile extinction (Heilman and Valenstein 1985). Although auditory hemi-inattention is frequently reported in association with visual neglect (Wortis and Pfeffer 1948; Denny-Brown et al. 1952; Battersby et al. 1956; Schott et al. 1966; Dehen & Cambier 1980; Butter et al. 1989), it occasionally occurs in the absence of visual neglect (Bisiach et al. 1984; de la Sayette 89; de Renzi et al. 1984).

The IPL has been implicated in auditory neglect as a result of both human (Pinek et al. 1989; Bisiach et al. 1984, Heilman et al. 1984) and monkey (Heilman et al. 1972) lesion studies. Case 5 of Holmes (1918)

could not localise sounds following biparietal lesions. Moreover, the right hemisphere seems to be more important than the left in auditory spatial functions (Bisiach et al. 1984; de Renzi, 1982). This pattern is like that seen for visual spatial functions. This, and the frequent co-occurrence of auditory and visual spatial deficits, supports the notion of a supramodal representation of space (see Farah et al. 1989 for review). Indeed, Farah et al. (1989) have recently presented evidence that parietal attentional mechanisms seem to operate on a supramodal (at least visual and auditory) spatial representation. However, there are clear dissociations between the two domains (see above; Buchtel and Butter 1988), so one is forced to conclude that the representations of auditory and visual space are at least somewhat separate. See chapter 10 for further discussion of this issue.

Parietal patients are generally able to make saccades to auditory targets although they are unable to make saccades to visual targets (Holmes 1918; Allison et al. 1969).

Thus there is no clear-cut answer to the question of the extent of the role of the PPC in the processing of audio-spatial information, and especially auditory saccades. It is clear from physiological and lesion studies that PPC plays an important role in visuospatial and visuomotor processes. Its appears to have a less vital role in the auditory domain. This is perhaps related to the preeminence of vision in primates' spatial analysis of the world (Welch and Warren, 1986).

### Summary

In these experiments we have demonstrated that auditory stimuli - if they serve as cues for saccades - can drive LIP neurones. Further, we have shown that the M activity of some neurones reflects the monkey's intention to make the next saccade, regardless of the modality of the target. However, we have also demonstrated that certain LIP neurones have modality-specific responses. We suggest that LIP is more intimately involved in the sensorimotor processing underlying visual saccades than auditory ones.

## FIGURE LEGENDS

**Figure 1:**

Sequence of events in a memory saccade task and the response of a typical LIP neurone. Onset and offset times, for both target and fixation spot, are indicated both in the scheme in the lower part of the figure, and by the dotted vertical lines above. Shown, from the top, are the spike rasters, where each horizontal trace represents a trial, and each tick within a line marks the time of occurrence of a spike; the resulting histogram; and the vertical and horizontal eye position traces of the various trials, superimposed. Trials are aligned on the sensory events (note variable saccadic latencies).

**Figure 2:**

Sequence of events in the auditory-visual change of plan task, and response of an LIP neurone. Data are displayed as in Fig. 1. In both parts the first target (B) is presented in a non-preferred location and evokes little activity, but the second target (A) appears in the receptive field and evokes a clear response which persists from after the target offset until the saccade to its remembered location is made. In (a) the first stimulus is an auditory one, and the second visual; in (b) the first is visual and the second auditory. Note the similarity of the pattern of responses, regardless of the modality of the targets.

**Figure 3:**

Activity of an LIP neurone recorded during auditory (panel a) and visual (panel b) memory saccades. Data are displayed as in Fig. 1. Note the similarity of the responses of the cell in both types of memory saccade.

**Figure 4:**

Activity of an LIP neurone recorded during the auditory memory saccade task. Data are displayed as in Fig. 1. This cell exhibits clear memory activity in response to the auditory target, and a presaccadic

burst of activity before the saccade to the remembered location of the target.

**Figure 5:**

The numbers of LIP neurones with responses in the sensory, memory and saccade phases of auditory memory saccades. AS = auditory sensory response. M = memory responses. S = saccade-related response.

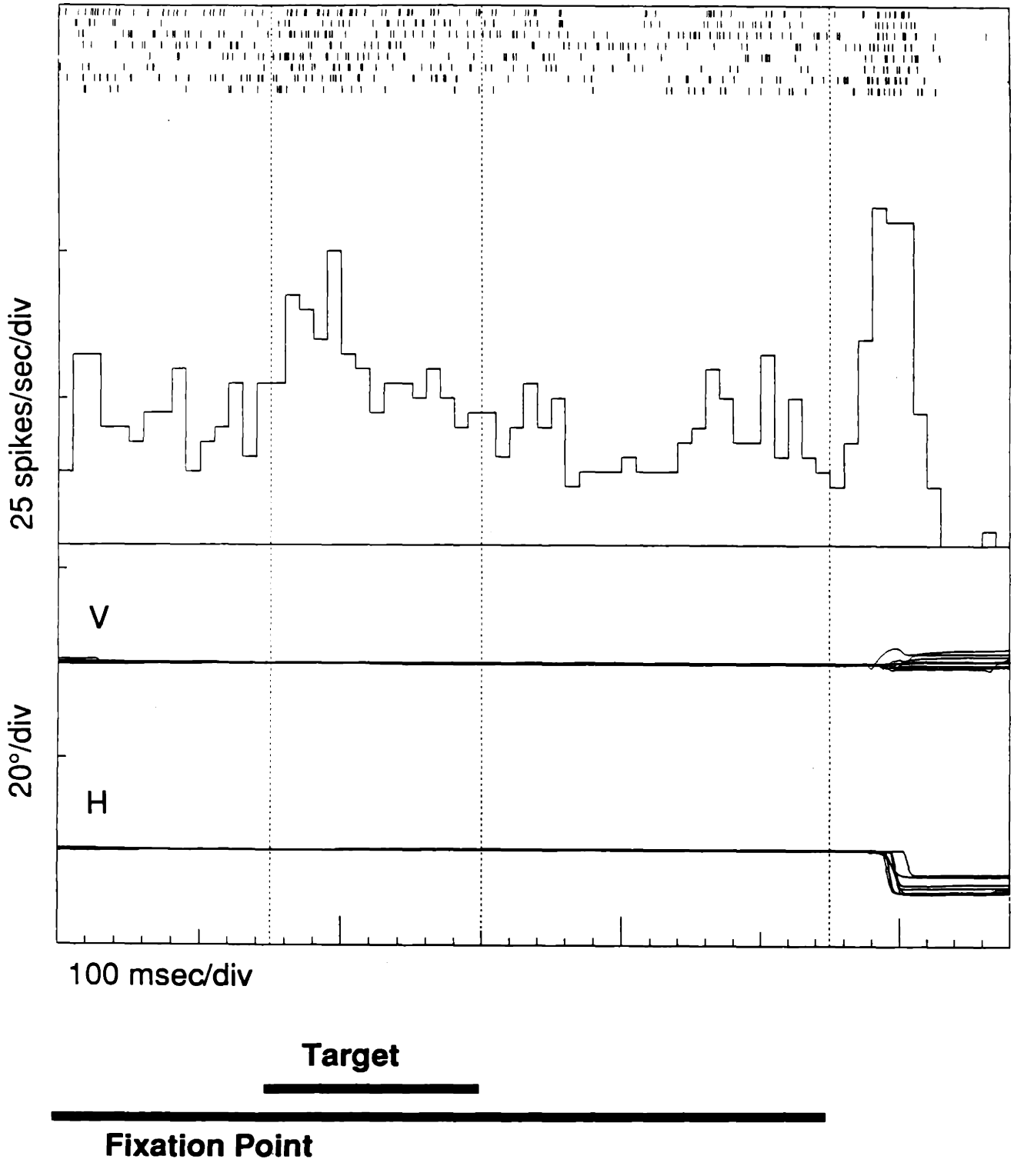
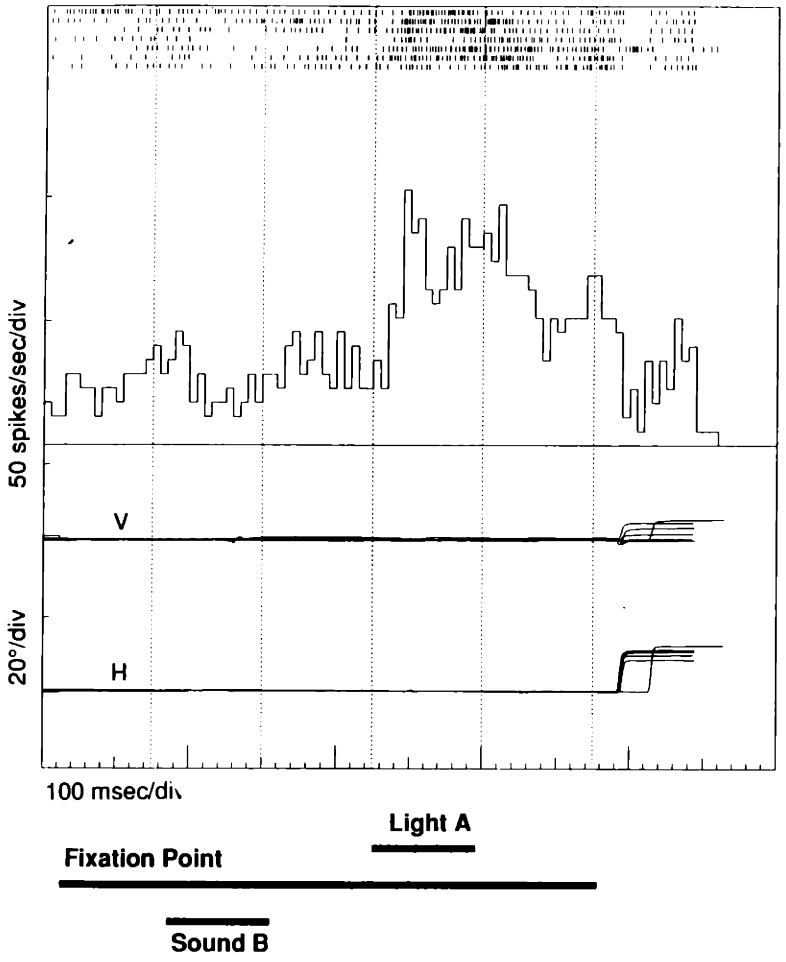

25 spikes/sec/div
V
20°/div
H
100 msec/div
Target
Fixation Point

Figure 1


50 spikes/sec/div
V
20°/div
H
100 msec/div
Light A
Fixation Point
Sound B

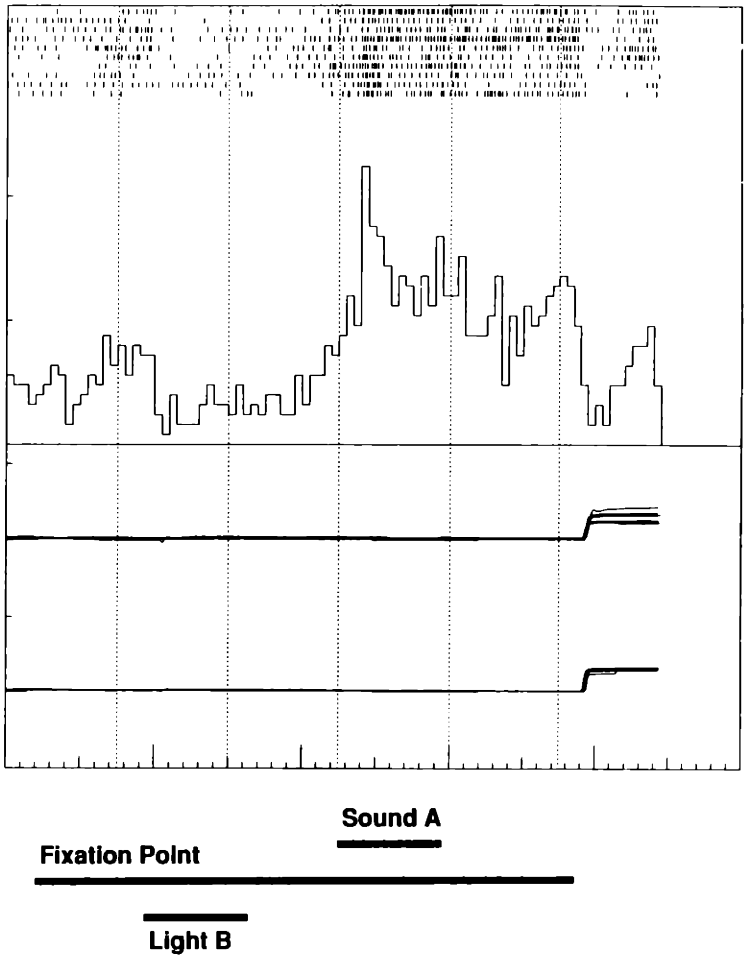

Sound A
Fixation Point
Light B

Figure 2

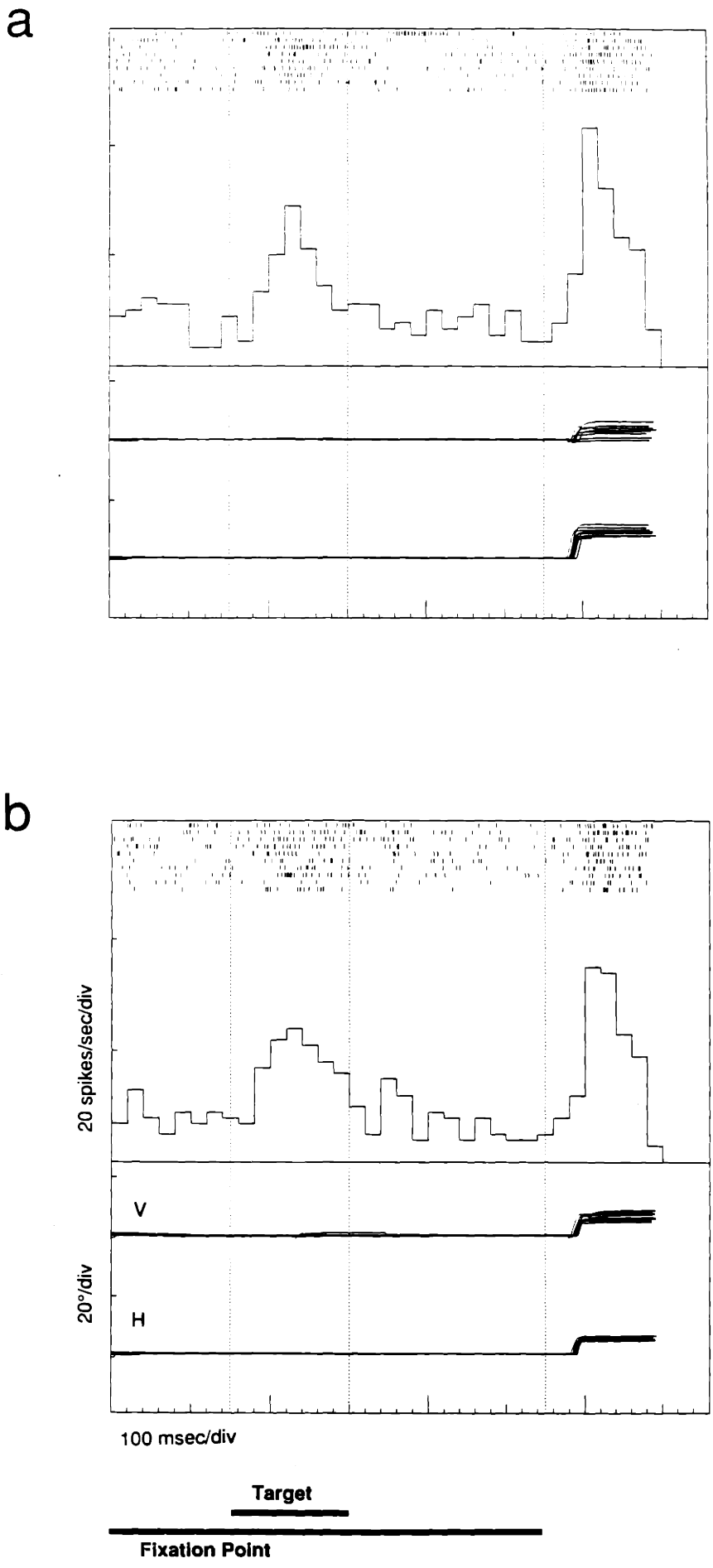

a
b
20 spikes/sec/div
V
20°/div
H
100 msec/div
Target
Fixation Point

Figure 3

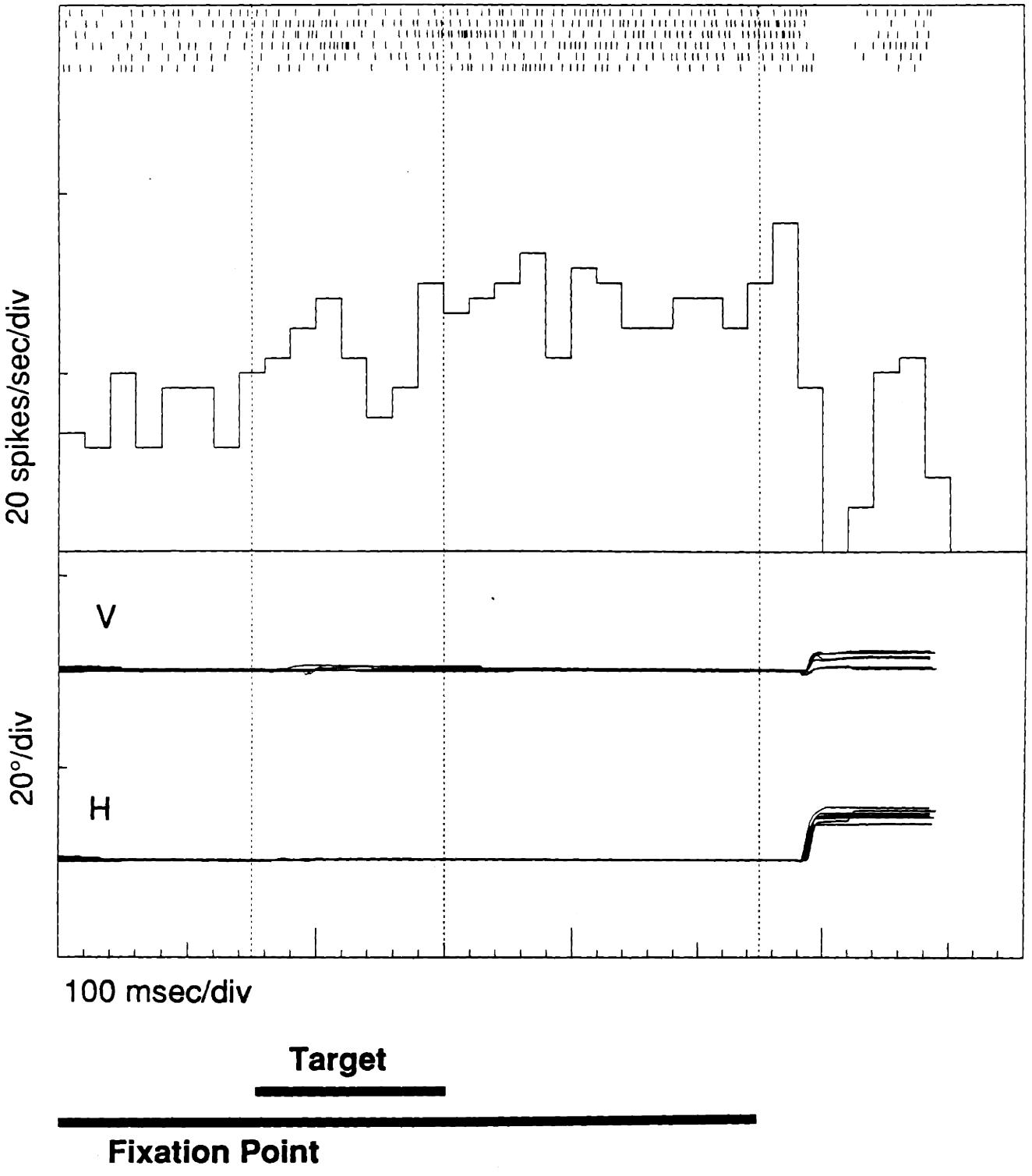

20 spikes/sec/div
V
20°/div
H
100 msec/div
Target
Fixation Point

Figure 4

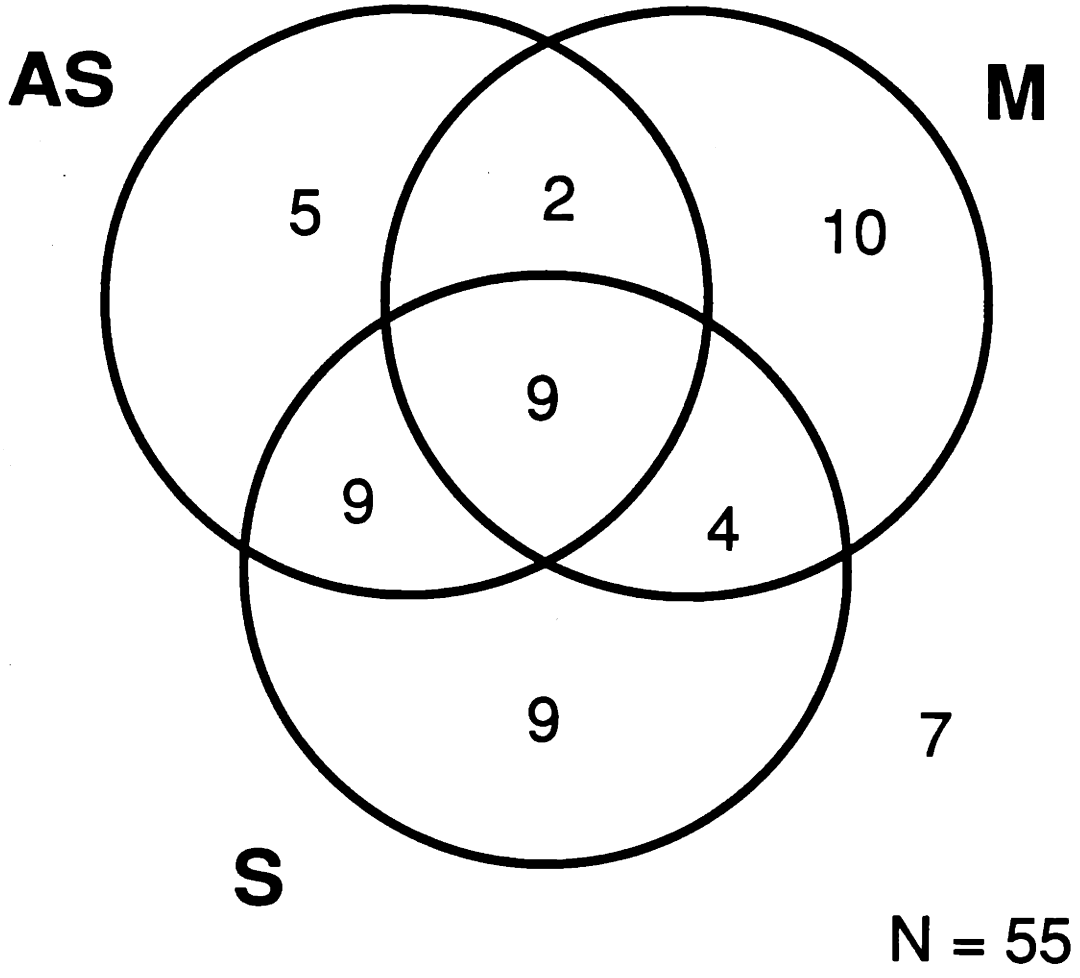



Figure 5

| | A/V - s | A/V - d | A only | V only | Total |
|---|---|---|---|---|---|
| S | 15 (41 %) | 6 (16 %) | 4 (11 %) | 12 (32 %) | 37 (100 %) |
| M | 12 (38 %) | 4 (13 %) | 9 (28 %) | 7 (22 %) | 32 (100 %) |
| S | 24 (71 %) | 2 (6 %) | 5 (15 %) | 3 (9 %) | 34 (100 %) |

**Table 1:** numbers of units exhibiting sensory, memory and saccade responses. A/V - s: similar response in both auditory and visual memory saccade trials. A/V - d: differing but significant responses in auditory and memory saccades trials. A only: response only in auditory memory saccade trials. V only: response only in visual memory saccade trials. S = sensory. M = memory. S = saccade-related.

| | Visual M Saccades | | | Auditory M Saccades | | | |
|---|---|---|---|---|---|---|---|
| | PV | SD | n | PV | SD | n | PV Δ |
| L: | 401.7 | 96.2 | 6 | 286.6 | 139.9 | 5 | 115.1 |
| R: | 319.2 | 40.2 | 6 | 343.3 | 65.5 | 5 | -24.1 |
| L: | 396.3 | 80.6 | 6 | 388.1 | 38.5 | 9 | 8.2 |
| R: | 301.1 | 36.0 | 6 | 258.6 | 34.8 | 9 | 42.5 |
| L: | 322.7 | 69.2 | 10 | 296.6 | 121.1 | 8 | 26.1 |
| R: | 265.9 | 44.0 | 10 | 266.9 | 75.7 | 8 | -1.0 |
| L: | 307.4 | 120.5 | 9 | 256.1 | 101.1 | 8 | 51.3 |
| R: | 284.1 | 53.7 | 10 | 298.2 | 75.7 | 8 | -14.1 |
| L: | 231.9 | 98.4 | 9 | 206.9 | 113.0 | 9 | 28.0 |
| R: | 285.4 | 75.4 | 6 | 281.4 | 57.0 | 9 | 4.1 |

**Table 2:** Typical values of peak velocity (PV) for matched auditory and visual memory (M) saccades. PV values in deg./s. PV Δ = difference in PVs.

# Chapter 8

## The psychophysics of saccades to the remembered locations of visual targets

## SUMMARY

In order to make a saccadic eye movement to a visual target, the brain must transform information from the retinotopic frame of reference of the visual system to that of the oculomotor plant. However, when saccades are made to the remembered location of visual targets, performance deteriorates. For both monkey and human subjects, the imposition of a delay period of only a few hundred ms between the offset of a visual target and the "go" signal for the saccade (offset of the fixation spot) leads to a considerable decrement in performance. Compared to equivalent visual (V) saccades, these memory (M) saccades are slower, have more variable and curved trajectories, and show both constant and variable end point errors. The constant error that we have observed is most intriguing: for all monkey and some of our human subjects, it is an "upshift" of the end point, such that saccades end consistently above the location at which the target had been presented. Although the overall pattern is one of an upshift, the distortions are non-uniformly dependent on direction of saccade. Errors accumulate rapidly over the first 800 ms of delay, and then more slowly. Both eye and head position affect the distortion and other aspects of M saccades. Non-target visual cues markedly improve the performance of such saccades.

## INTRODUCTION

We chose to study the spatial and temporal properties of saccades made to the remembered locations of visual targets for a variety of reasons. The memory (M) saccade paradigm is being used increasingly in neurophysiological (e.g., Chapter 2; Funahashi et al. 1990), psychophysical (Smit et al. 1987; Smit and Van Gisbergen 1990) and even clinical (e.g., Pierrot-Deseilligny et al. 1991b) studies, but there are no comprehensive quantitative studies of M saccades in the literature.

M saccades place different demands on the saccadic system than visually-guided (V) saccades, and the study of M saccades might reveal important properties of the system. How does the brain produce M saccades? It must take retinotopic information and transform it into a spatial representation in memory. This representation might, for example, be of the retinal locus of the stimulus, or of the target location in some other coordinate frame (e.g., head-centred), or of the desired movement vector. The pattern of distortions might give us insight into how the saccadic system programmes M saccades.

We wished to compare directly monkeys and humans in the same paradigm. It is frequently assumed in the vision and oculomotor communities that humans and monkeys are essentially the same, at least in terms of their visual and oculomotor systems. Here we were able to make direct comparisons of the two species. We hope that such an approach will allow for better integration of data from monkey physiological and human perceptual experiments.

Specific issues investigated here included the following:

First, we were interested in quantifying any differences between visual and memory saccades. Any such differences might indicate differences in the sensorimotor transformations underlying the two sorts of movement.

Second, we investigated effects of orbital position. Any differences would suggest a role for orbital position signals in the sensorimotor transformations.

Third, we investigated the effects of head position. Any differences would suggest a role for somatic or vestibular factors in the sensorimotor transformations.

Fourth, we investigated the role of the visual background to look for effects of non-target visual cues on performance (such effects have

been rarely considered in previous studies of the saccadic system).

Fifth, we measured the time course of the accumulation of spatial errors.

# METHODS

## Subjects

Three rhesus monkeys (M02, M13, M88) and five humans (one female, four male; age 18-30) (H50-54) with normal or corrected-to-normal vision were used in these experiments. Eye movements were monitored by the scleral search coil technique (Robinson 1963). In the monkeys, a search coil was surgically implanted in one eye (Judge et al. 1980). For the humans, the coil was embedded in a soft, clear annulus contact lens (Collewijn et al, 1975).

The monkeys were trained in oculomotor tasks (see previous chapters). Two were also used in physiological experiments. Standard animal care and surgical techniques were used (see chapter 2). During experiments, monkeys were head-restrained by a painless head post.

Human subjects were naive to the purpose of the experiments. Once they had been instructed about the task, the contact lens was inserted and the subjects were given five minutes' practice. Data was collected for about 30 minutes. Their heads were fixed by means of a bite bar. Two of the subjects participated in multiple data collection sessions. Informed consent was obtained from each subject, in accordance with guidelines from the Salk Institute Safety Committee.

## Experimental set up

These experiments (involving both human and monkey subjects) were conducted in the same apparatus as that used in the physiological experiments described elsewhere in this thesis. In brief, spots of light 0.5 deg in diameter were back-projected onto a translucent screen 57 cm in front of the subjects. The targets were adjusted to 15 $cd/m^2$. A laboratory computer controlled the position and timing of the stimuli via galvonometer-mounted mirrors and rapid electronic shutters. All experiments were run in a darkened chamber, with the exception of certain control experiments (discussed below) designed to test the effects of a visible background on the observed behaviours.

**Eye movement monitoring**

We monitored eye movements with an accuracy of better than 0.25 deg. with as range of ± 40 from straight ahead. For eye positions that were far from parallel to the magnetic fields, appropriate corrections were applied off-line. Eye position was sampled at 500 Hz, except for monkey M02 (100 Hz). Eye velocities were calculated off-line using a second order differentiating/filtering algorithm (Usui and Amidror 1982). Other saccade parameters were also calculated off-line.

**Monkey training**

Before training and data collection sessions, monkeys were deprived of water overnight. They received their daily fluid ration during training and data collection sessions. Successful behaviours were rewarded by a drop of fruit juice. The experiment was run under computer control.

At the beginning of each training and data collection session, and following any alterations during a session, the monkey was required to maintain fixation (within tight electronic windows) of visual targets presented at various screen locations. This calibration data was retained and used in off-line calibration and analyses.

Monkeys M13 and M88 were initially trained to fixate spots of light, then to saccade to visual targets, and finally to make memory saccades (see chapter 2 for details). In memory saccade trials, targets were presented for 300 ms, followed by delay periods of from 400 to 2000 ms. Monkeys were rewarded for saccading to the remembered location of the target and maintaining fixation in the dark for 500 ms.

In the early phases of training, large windows (about 30 deg) were used and memory and visual saccades were interleaved. Within two weeks, we were able to reduce the size of the windows and present blocks of memory saccades alone. For monkey M13, the final size of the window was ± 10 deg. For M88 it was ± 22 deg in the vertical and ± 18 deg in the horizontal.

Monkey M02 was trained in a quite different fashion. He was trained to pull a lever on detection of the appearance of the fixation spot on the screen. Whilst he maintained fixation of this spot, a peripheral target spot was presented briefly. Following the offset of the

fixation spot, he saccaded to the remembered location of the peripheral target. After this saccade, the target was turned on again, and the monkey had to release the lever in response to a near-threshold dimming of the target. Since the monkey would always look to the target when it reappeared, he received visual feedback at the end of each trial. M13 and M88 received no such feedback.

### Human training

Our monkeys received extensive training over many weeks. In contrast, our human subjects received careful verbal instruction before being fitted with the contact lens. They were given five minutes of practice before data collection. For visual saccades they were instructed to look accurately at the spot of light and to refixate it quickly if it moved. For memory saccades they were told to maintain careful fixation of the first (fixation) target for as long as it was present. They were told that a second target would be presented, but that they could only look to its location after the first spot had been extinguished. They were asked to look to this location as accurately as possible. Verbal feedback of performance was given during training but not data collection.

### Statistical analysis of data

Since we had collected a very large database from our monkeys (each ran more than a thousand trials a day for a few months), and since behaviour was similar from day to day, we selected at random two blocks of trials for each task. These blocks were combined for analysis. One of the blocks was drawn from the early months and one from later months of the experiment. Each block had about 70-140 trials with roughly 6-15 trials for each level of the variables tested. Except were noted, all statistical comparisons are between appropriate tasks performed on the same pair of days.

We used analysis of variance (ANOVA) to test for for differences between multilevel variables. T tests were used to compare group means (including *post hoc* analysis from the ANOVA). Results of *post hoc* analyses were only considered significant at $p < 0.01$ (to avoid type II - false positive - errors). We used the F test to compare group

variances. In a few *post hoc* comparisons we calculated coefficients of linear correlations.

Since our stimuli were 0.5 deg in diameter and since there were small (less than 0.5 deg) differences for equivalent tasks on different days, we only considered statistically significant effects of more than 0.5 deg (since smaller effects might have been due to unknown factors other than our experimental manipulations).

**Eye movement data**

Eye position data was sampled at 500 Hz (100 Hz for monkey M02). In off-line analysis, the laboratory computer calculated the instantaneous tangential velocity. The start of a saccade was defined as the time at which the speed exceed 35 deg/s. The end of the saccade was defined as when the speed fell below 35 deg/s (for humans) or 50 deg/s (for monkeys). The "end of saccade" criterion was adjusted to differentiate between saccades (memory saccades were often found to decelerate slowly) and postsaccadic drift, which followed memory saccades from time to time. The end point of the saccade was defined as the average position for the 50 ms after "end of saccade".

We compared the horizontal and vertical coordinates of the end points of memory saccades with those of visual saccades to the same target locations recorded in the same sessions.

**Experimental issues**

First, we were interested in quantifying any differences between visual and memory saccades. Any such differences might indicate differences in the sensorimotor transformations underlying the two sorts of movement.

Second, we investigated effects of orbital position. Any differences would suggest a role for orbital position signals in the sensorimotor transformations.

Third, we investigated the effects of head position. Any differences would suggest a role for somatic or vestibular factors in the sensorimotor transformations.

Fourth, we investigated the role of the visual background to look for effects of non-target visual cues on performance (such effects have been rarely considered in previous studies of the saccadic system).

Fifth, we measured the time course of the accumulation of spatial errors.

**Basic experimental procedures**

Visual and memory saccades were recorded in eight cardinal directions (up, up-and-left, left, etc.). In a block of trials, the directions of the targets were pseudorandomly interleaved but the eccentricity of the targets was usually held constant (at 10, 15, 20 or 30 deg). In some blocks of trials, 15 deg saccades along the horizontal and vertical meridia were mixed with 21 deg saccades in the diagonal directions. Memory and visual saccades were collected in separate blocks. Typically 8-10 of each movement were collected. Not all eccentricities were investigated in each subject. Equivalent visual and memory saccades were compared.

**Investigation of orbital and head position effects**

We tested for orbital effects by displacing the fixation spot by 15 deg from straight ahead. Blocks of 15 deg memory and visual saccades in the eight directions were then collected.

We tested for head-on-body effects in monkey M88 by manually rotating the head by 15 deg down or up, and then locking the head in that position for the blocks of memory and visual saccades collected from that position. The monkey appeared to suffer no inconvenience with his head rotated by 15 deg.

In our analyses of orbital and head position effects, we carefully chose comparisons to avoid any possible errors that might have been introduced by the tangent screen.

**Investigation of non-target visual cue effects**

In all of the above manipulations, data were collected in a completely darkened chamber. However, for one human and one monkey subject we investigated the effects on non-target visual cues on the performance of 15 deg memory saccades from straight ahead. In one condition, the chamber was dimly illuminated ($6.5 \times 10^{-3}$ cd/m$^2$ average room illumination) so that visual contours from the apparatus

were available. In the other condition, a random dot pattern (0.5 cm black dots at 1.2 spots/$cm^2$) on a white background was backprojected onto the tangent screen (average illumination of the screen was 8.2 x $10^{-2}$ $cd/m^2$). Saccades in each of these conditions were compared with corresponding visual saccades.

**Investigation of accumulation of error**

In two humans we measured memory saccades in the eight directions in blocks of trials with either a standard 400 ms delay, or one of 1500 ms. In monkey M88 we varied the delay period over a wide range of values up to 2300 ms. Different delay periods we pseudorandomly interleaved for saccades in one direction, with saccades in another direction occasionally added. We analysed data for 15 deg right saccades collected on 9 days over a 10 week period.

## RESULTS

### Characteristics of memory saccades

In fig. 1 typical 15 deg memory (M) saccades (with a 400 ms delay) and visual (V) saccades are compared for one monkey and one human subject. These plots reveal several characteristics of memory saccades (when compared to visual saccades):

1. trajectories are often highly curved and variable.
2. velocities are lower (see also fig. 8).
3. there is considerable more inter-trial variability in end point. This is true of all our subjects (individual F tests, $p < 0.01$).
4. there are constant errors in the end points. For all the monkeys this constant error is an "upshift", such that saccades have a hypermetric upwards component, and a hypometric downwards component, regardless of their direction. Typically there is no constant error in the horizontal. The constant error was not as consistent across our human subjects, although three showed evidence of a similar upshift.

Fig. 2 shows representative M saccades made by monkey M88 to targets at 10, 15, 20 and 30 deg. eccentricity. Note that the saccades to different targets show similar spatial distortions. We have illustrated in summary form the distortions for our monkey (fig. 3) and human (fig. 4) subjects. The "head" of each "lollipop" represents the target location and the "stick" the amplitude and direction of the mean error for that location.

These errors (horizontal and/or vertical) were significant for all but one of our subjects (see Table 1). Inspection of figs. 3 and 4 and Table 1 reveal further details of the distortions:

1. It is not a uniform upwards shift for all end points. There were significant interactions of direction and target eccentricity on both horizontal and vertical error. Had the shift been uniform, all the "lollipops" would have been of the same size and orientation for a subject.
2. The amplitude of error was not a constant fraction of eccentricity of target ("Length/eccentricity", Table 1).
3. The amplitude of error was correlated with length of movement (M88, r=0.99; M13, r=0.75; H52, r=0.65; H54, r=0.55).

**Orbital position effects**

M13 was tested on 15 deg M saccades (in all eight directions) with the eye starting at nine different orbital positions (15 deg up and left, 15 deg up...straight ahead....15 deg down and right). M88 was tested for M saccades made from five orbital positions (15 deg up, left, right, down, and straight ahead). H54 was tested with three orbital positions (15 deg up, down, and straight ahead). As always, M saccade were compared with V saccades collected from the same starting eye position and to the same targets.

Representative M saccades from different orbital starting positions are shown in fig. 5. It is remarkable that the spatial distortions are quite similar, for a given subject, regardless of the starting eye position. This suggests that the distortions we observed from the straight ahead position are not due to our subjects tending to look to specific locations in space. In particular, that the upshift persists for different orbital positions suggests that it cannot simply be due to orbital mechanical factors. However, close inspection of fig. 5 and of Table 2 reveal that there are systematic effects of eye position on end point and trajectory of M saccades.

**Head position effects**

We studied the effects on 15 deg M saccades, to the eight target locations, of various combinations of head and eye position. Data analysis (Tables 3 and 4) was only performed on saccades for which any potential errors in depth due to the tangent screen were equivalent. Eye/head combinations were:

1. Eye and head both straight ahead (the standard condition used elsewhere in this study).

2. Head straight ahead, but eye position rotated 15 deg up. The central fixation spot and all targets were moved up 15 deg.

3. Head 15 deg up, eye straight ahead (with respect to the head). The central fixation spot and all targets were moved up 15 deg.

4. Head 15 deg up, eye 15 deg down (with respect to the head). Thus the eye was "straight ahead" with respect to gravity and the tangent screen. The central fixation spot and all targets were all presented in

their "normal locations".

Table 3 provides the mean targeting errors for these combinations. We investigated three issues:

1. Are the distortions of M saccades independent of orbital and head position?

Table 4 reveals that there is an interaction between target direction and head-eye condition. Thus the distortion is not independent of head and eye position. Note that we have already seen that eye position alone affects the spatial distortions. These results suggest that the sensorimotor transformations underlying the production of M saccades cannot be simply be oculocentric.

2. Are the distortions "craniotopic", i.e., are they the same for equivalent orbital positions but different head positions?

This was tested by comparing M saccades with head and eye both straight ahead with M saccades with targets and head rotated 15 deg up (thus the eyes were straight ahead with respect to the head). There was a significant interaction of head position with vertical but not horizontal error. These results suggest that the transformations underlying the production of M saccades cannot be purely craniotopic.

3. Do eye and head position effects add linearly to provide a "somatocentric" frame of reference?

This was tested by comparing M saccades made to the same locations on the screen (and thus with respect to the body), with the eye and head in different positions. In the first test, we compared "eye up 15 deg" with "head up 15 deg" (in both conditions the targets were rotated up 15 deg, of course). There were significant effects in this test. In a second test of this hypothesis we compared eye and head straight ahead with eye down 15 deg/head up 15 deg. In this case there was no significant interaction or main effect of the head-eye condition.

This contradictory pattern of results suggests that interactions between head and eye rotation are non-linear.

**Saccade dynamics**

A characteristic of M saccades is that they have a great variability in trajectory, compared with V saccades (e.g., see fig. 1 and 5; also

Carpenter 1988). In particular they frequently have curved trajectories, due to a mismatch in the timing of the horizontal and vertical velocity components.

V saccade velocities are related to amplitude of the movement, such that larger saccades have greater peak and mean velocities (see Carpenter 1988 for review). This has been referred to as the main sequence of saccades (Bahill et al. 1975; 1981). M saccades do not follow this main sequence; for any given amplitude, they are slower than the corresponding V saccade. This can be seen in fig. 8 and has been reported by others (e.g., Becker and Fuchs 1969; White and Sparks 1986; Rohrer et al. 1987; Smit et al. 1987). However, they appear to follow their own main sequence, for a given delay period (fig. 8).

**Accumulation of end point error**

We noted that the size of the constant error increased rapidly as the delay period was lengthened. Most of the error accumulated with the first 800 ms of the delay. Thereafter the rate of accumulation fell. We did not study delay periods beyond 2300 ms. Fig. 6 shows the vertical error in 15 deg M saccades made to the right by M88. Note that the variable error increased with a similar time course.

We also found a significant interaction of the delay period length and the direction of eye movement. Thus the distortions changed non-uniformly with time in the different directions. M13: horizontal, $F(7,652) = 40.39$, $p < 0.001$; vertical, $F(7,652) = 10.6$, $p < 0.001$. H52: horizontal, $F(7,143) = 75.3$, $p < 0.001$; vertical, $F(7,143) = 83$, $p < 0.001$. H53: horizontal, $F(7,66) = 2.1$, NS; vertical, $F(7,66) = 5.4$, $p < 0.001$.

**Effects of non-target visual cues**

We investigated the effects of non-target visual cues in two further conditions. In one the chamber lights were dimly lit, providing some visual contours to our subjects (M88 and H54). In the other, a random dot field was backprojected onto the tangent screen (see methods for details). In fig. 7 we see the performance of M88 in M saccades to 15 deg targets in the three conditions (dark, dim light, random dot) and his equivalent V saccades. The addition of non-target cues clearly improved his performance ($F(14,626 = 9.00$, $p < 0.001$), although non-

uniformly for each direction. Variability was greatest in the dark (horizontal, $F(207,215) = 9.11$, $p < 0.001$; vertical, $F(207,215) = 4.08$, $p < 0.001$). The degree of curvature decreases (fig. 7) and peak velocity improves as one goes from dark to dim light to random dot conditions (see fig. 8).

*Dim light:* although there is a clear improvement in performance, M saccades (compared to V saccades) are still inaccurate (multiple t tests, $p < 0.001$) and more variable (horizontal, $F(164, 193) = 10.84$, $p < 0.001$; vertical, $F(164,193) = 3.59$, $p < 0.001$). Main sequence plots (fig. 8) show that they are also slower. Inspection of fig. 7 reveals that these M saccades are still somewhat variable in trajectory.

*Random dot background:* there is a clear improvement in the saccade dynamics: velocities are almost equal to those of V saccades (fig. 8) and the trajectories are straighter and less variable (fig. 7). However, there were constant errors in the horizontal and/or vertical components of M saccades in all eight directions (multiple t tests, $P < 0.001$). In addition, variable errors remained greater than those in V saccades (horizontal, $F(150,276) = 1.89$, $p < 0.001$; vertical, $F(150,276) = 4.93$, $p < 0.001$).

*H54:* this human subject showed a similar pattern of improvement with additional non-target visual cues. The improvement in the vertical domain was nonuniform ($F(14,158) = 8.7$, $p < 0.001$) but significant and uniform in the horizontal ($F(2, 158) = 6.6$, $p < 0.01$).

# DISCUSSION

## Summary of results

For both monkey and human subjects, the imposition of a delay period of only a few hundred ms between the offset of a visual target and the "go" signal for the saccade (offset of the fixation spot) leads to a considerable decrement in performance. Compared to equivalent visual (V) saccades, these memory (M) saccades are slower, have more variable and curved trajectories, and show both constant and variable end point errors. The constant error that we have observed is most intriguing: for all monkey and some of our human subjects, it is an "upshift" of the end point, such that saccades end consistently above the location at which the target had been presented. Although the overall pattern is one of an upshift, the distortions are non-uniformly dependent on direction of saccade. Errors accumulate rapidly over the first 800 ms of delay, and then more slowly. Both eye and head position affect the distortion and other aspects of M saccades. Non-target visual cues markedly improve the performance of such saccades.

As M saccades are being increasingly used in neurophysiological (e.g., chapters 2 and 3; Funahashi et al. 1989, 1990), psychophysical (Smit et al. 87; Smit and van Gisbergen 1990) and even clinical (e.g., Pierrot-Deseilligny et al. 1991b) studies, we hope these studies will provide an important database. However, we believe they offer further insights on the workings of the saccadic system.

## Constant errors

Our finding that variable error increases with delay is perhaps not surprising. One can readily imagine synaptic or other neural noise adding to and degrading the target location signal. But why should this noise lead to a constant error? This would imply that noise was being added in a "directional" fashion. It is as if the memory for the target location "drifts up" with time. However, the significant interactions with target direction and eccentricity suggest that there is a non-retinotopic degradation of the representation of the target and/or intended movement too.

### Eye and head position effects

We have seen that the distortions are affected by both eye and head position. This suggests that the coordinate frame for programming saccades is not simply retinotopic. It is clear that the saccadic system must take into account orbital factors when programming eye movements. Different patterns of motor innervation are required to move the eyes equivalent distances from different locations in the orbit (see Carpenter, 1988, for review).

It is of interest that head position in addition to eye position affects the distortion: this implies that the system underlying the production of M saccades has access to information about head orientation (perhaps from neck proprioceptors or the otoliths). It is neither simply retinotopic nor craniotopic. Skavenski and Steinman (1970) have observed similar effects of body position on attempts to maintain steady fixation in the dark. Almost all psychophysical and physiological studies of the saccadic system have been made with the subjects' head fixed (e.g., Carpenter, 1988, for review). This is clearly an unnatural situation; usually primates make combined eye and head movements when making large shifts of gaze (e.g., Morasso et al. 1973; Tomlinson and Bahra 1986a, b). It is therefore perhaps not surprising that we have found evidence for head position influences on M saccades.

### Dark drift

The most striking result of this experiment is the upshift in saccade end point for M saccades made by all monkey and several human subjects. Is it related to the "dark drift" (Maldonado and Schlag-Rey, 1982) that monkeys tend to exhibit when attempting to maintain fixation in the dark? (It has also been termed "dark nystagmus" as upwards slow drifts are occasionally interrupted with down fast phases.) The drift is of a similar magnitude and time course to the upshift, but cannot be the explanation of the upshift for several reasons: (1) large saccades have a bigger upshift than smaller saccades, even when the delay periods are equal (and therefore presumably the amount of "dark drift" are the same); (2) the end point errors are directionally dependent, but again the delay period is held constant; (3)

the subjects had to maintain fixation of a continually present fixation spot throughout the delay period.

The possibility that the perceived location the target does indeed drift up during the delay period is amenable to psychophysical investigation (see below).

**Effects of non-target visual cues**

The addition of a visible background clearly improved the performance of our subjects, in both the dynamics and accuracy of the saccades. The dim contours of the room, or (better) the random dot field, clearly reliably aided performance. It is possible that our subjects were localising the target with respect to "permanent" visual cues, such as a local arrangement of dots. It is of interest that both accuracy and velocity measures improved. See below for a discussion of velocity.

Traditionally eye movements have been studied in the ascetic environment of the psychophysical laboratory, where the contents of the subject's field of view are tightly controlled and scarce. However, it is becoming increasing clear that non-target visual information affects eye movements (e.g., Kowler 1990).

**Effects of training**

M02 received trial-by-trial feedback and was our most accurate monkey, whereas the other two (M13 and M88), who received a permissive training schedule, were less accurate. We have subsequently trained other monkeys in the M saccade task, and have found that feedback can improve their performance somewhat, although a marked upshift persists. Hansen and Skavenski (1985) have shown that training improves that ability of humans to maintain fixation of a remembered location in the dark. However, error cannot be entirely eliminated (Skavenski and Steinman, 1970). In all, it appears that the process is somewhat plastic.

Are the constant errors a consequence of our training methods? Several factors argue against this possibility. First, all monkeys (including animals not reported here) and many humans have the upshift in M saccades, regardless of the amount of training they have received. Second, the upshift persists, regardless of the type of training

they receive. Third, our human subjects show constant errors, although none reported any specific strategy which might have produced such behaviour (they in fact reported that they only had a vague sense of their accuracy).

### Secondary saccades

It is a commonly held belief that humans make saccades in preprogrammed, "two saccade" packages, a primary saccade which covers approximately 90 % of the distance to the target, followed by a secondary or "corrective" saccade (SS) which brings the target onto the fovea (Becker and Fuchs 1969). Numerous experiments confirm that SS's are truly corrective in normal conditions (Becker and Fuchs, 1969; Becker 1972; Weber and Daroff 1972; Prablanc and Jeannerod 1975; Shebilske 1976; Hallett 1978; Prablanc et al. 1978; Deubel et al. 1982). In their pioneering study of M saccades, Becker and Fuchs (1969) reported that some of their (human) subjects made SS's (to an incorrect location) at the end of the primary saccade. However, Prablanc and Jeannerod (1975) showed that subjects only made corrective SS's when visual feedback was available at the end of the movement. Our results are largely in accord with those of Prablanc and Jeannerod (1975).

Our subjects occasionally made SS's. We found SS's with a latency of less than 200 ms to be rare (less than 1% of 15 deg M and V saccades in monkeys; up to 20 % for the V saccades of one human). In general, these movements did not appear to be "directed"; especially in the humans, the primary M saccade seemed to be followed by drifting or searching behaviour. Since the SS's were small (usually less than 1.5 deg) and infrequent, we decided to only include the primary saccade in our analyses. Primary M and V saccades were, of course, compared.

SS's of longer latency were not considered, as it is unlikely that they are part of a preprogrammed double movement (see, e.g., Becker 1989).

### Accumulation of error

We have found that error accumulates rapidly for about 800 ms and then then the accumulation slows down. Becker and Fuchs (1969) reported that the slowness of M saccades became apparent after 100-350 ms delay, but had nearly plateaued by 1100 ms. Skavenski and Steinman (1970) and Skavenski (1971) showed that error in fixation of a

remembered target location accumulated rapidly in the first few seconds, and remained quite stable for several minutes thereafter. It is possible that in the first few hundred ms of delay, the saccadic system goes from being visually based to one which relies on a spatial memory which is moderately stable in time.

**Possible neural substrata for M saccades**

Neurones carrying a signal related to the desired change in eye position in tasks requiring a certain "memory" have been reported in several areas of the brain including the superior colliculus (Mays and Sparks 1980b), the frontal eye fields (Bruce and Goldberg 1985), area LIP (chapter 2), and the dorsomedial prefrontal cortex (Funahashi et al. 1989; 1990). It is likely that these areas are involved in the production of M saccades (see chapter 9 for evidence of a neural analogue of the end-point upshift in area LIP). In LIP (unpublished observations) and SC (Rohrer et al. 1987), certain units fire for V but not M saccades. In all these areas, neurones are broadly tuned; it is likely that saccades are coded in a distributed fashion (see, e.g., Lee et al. 88). It is an attractive possibility that fewer units in such populations are active for M saccades, and thus the representation of the saccade is less precise. Thus M saccades might be more variable. If there were a bias as to which cells were and were not active, the upshift might also be partially explained.

If there were fewer active cortical cells driving the SC and other downstream saccade centres, and thus fewer active SC cells, this might also be an explanation for the slowness of M saccades. Indeed, Hikosaka and Wurtz (1985e) and Lee et al. (1988) have shown that reducing the number of active SC cells results in slower (and inaccurate) saccades.

There appears to be a relation between the firing rate of individual cells in SC and saccadic velocity (cat: Berthoz et al, 1986; Munoz and Guitton, 1987; monkey: Rohrer et al. 1987; van Opstal and van Gisbergen 1990). Thus it is also possible that a reduction in the number of active cortical cells might be manifest in lessened activity within single SC neurones.

Traditionally, the dynamics of saccades have been "consigned" to the brainstem, with the supranuclear centres issuing the kinematic

commands (e.g., Robinson 1975). The results discussed above suggest that we should perhaps take a more holistic view of the system. Given the spatio-temporal coding transformation that must occur within the saccadic system (for a review, see van Gisbergen and van Opstal, 1989), it is reasonable to expect alterations in spatial representations of saccade kinematics to affect the dynamics of movement.

### Controls

In theory the fact that we used a tangent screen might have affected our results, as it imposed slightly different vergence demands on our subjects at different screen locations. However, we believe this has not been a factor in our results for the following reasons. First, we took pains to compare data from movements for which the vergence demands were equivalent. Second, even for targets at 40 deg eccentricity, the required divergence is only about 0.5 deg, considerably smaller the the average errors made (about 3 deg for monkeys, 1.5 deg for humans).

We chose to compare the final end points of V and M saccades directly, rather than to the actual target locations. We found that V saccades were extremely accurate. We felt that this measure was appropriate as it might discount idiosyncrasies of particular subjects, and also because we were primarily interested in the differences in performance of V and M saccades.

### A possible future experiment

One plausible interpretation of the upshift in M saccades in that the perceptual memory of target location shifts upwards (with respect to the veridical positions) with time. In the present experiment, subjects have been localising targets actively (i.e., with saccades). One could investigate whether there is an analogous perceptual upshift. Subjects could be required to localise passively (i.e., in the absence of eye movements) the remembered location of peripheral visual targets. The experiment would be designed to be as similar as possible to the active localisation experiment described in this chapter:

Subjects would fixate a central fixation spot throughout the trial. After 800 ms, a peripheral target (0.5 deg) would be presented for 300 ms. 200-2000 ms after the offset of the target, a second spot would be

flashed at the same location, or slightly above or below it. Subjects would report where the spot appeared with respect to the first target. Psychophysical techniques would be used to determine whether, and if so by how much, the perceived location drifts. One would expect the second spot to appear lower than the first target is the memory of the first target drifts up. Any "perceptual drift" would be compared with the saccadic upshift.

**A related study of pointing to remembered visual targets**

Soechting and Flanders (1989a) have investigated the performance of humans subjects required to point to the remembered position of a previously presented visual target. There was usually a three to five second interval between target presentation and the end of the movement. Although the authors focus on the marked constant errors in distance that their subjects make, inspection of their data (figs. 1 - 3) reveals that subjects also show a consistent error in elevation: they point to above the location in which the target was presented.

Soechting and Flanders (1989a) have suggested that the errors they observed are due to "errors in the sensorimotor transformation from the visual representation of the target to the kinematic representation of the arm movement" (p. 582). These authors have shown (Soechting and Flanders 1989b) that subjects have a quite accurate visual representation of target location. They (Soechting and Flanders 1989b) have suggested that the errors are due to the subjects' performing a linear interpolation from extrinsic (visual) to intrinsic (shoulder-centred - Soechting et al. 1990) coordinate frames. In this chapter we have proposed that the upshift in memory saccade end points may also be a result of the sensorimotor transformations underlying the production of memory saccades.

## FIGURE LEGENDS

**Figure 1:**

Saccades made to visual targets (upper panels) and to remembered target location (lower panels) by monkey M13 (left panels) and human H53 (right panels). The same targets were used in each condition. Each dot represents an eye position sample (sampled at 500 Hz), therefore closely spaced dots indicate a slow saccade. Scale marks = 15 deg.

**Figure 2:**

Memory saccades made to targets of different eccentricities by M88. Scale marks = 15 deg.

**Figure 3:**

Summary diagram of the constant errors for each monkey. The "head" of each "lollipop" represents the target location, and the "stick" the direction and amplitude of the constant error of memory saccades made to that target location. The weighted average standard deviation for all of the targets is indicated by the horizontal and vertical error bars drawn on one constant error line for each monkey.

**Figure 4:**

Summary diagram of the constant errors for each human. Data presented as in fig. 3.

**Figure 5:**

Memory saccades made from different initial orbital positions by M88 (left panels) and H54 (right panels). Axes are centred on straight ahead. Scale marks = 15 deg.

**Figure 6:**

Accumulation of vertical constant error as a function of the delay

from offset of target and the beginning of the saccade. Data are from M88, for 15 deg memory saccades to the right. The inset at the top of the figure shows the same data (plus data for longer delay periods) on an expanded time scale.

**Figure 7:**

Effects of visual cues on saccade performance of M88. In each condition saccade targets were presented at 15 deg. Dark: standard memory saccades; no ambient light. Dim light: memory saccades; chamber dimly illuminated. Random dot: memory saccades; random dot pattern back-projected on screen. Target: saccades to visible targets. Scale marks = 15 deg.

**Figure 8:**

Effects of visual cues on peak tangential velocities of the saccades illustrated in Fig. 7. Open symbols = visual saccades. Closed symbols = memory saccades, made under the various conditions listed in the legend to fig. 7.

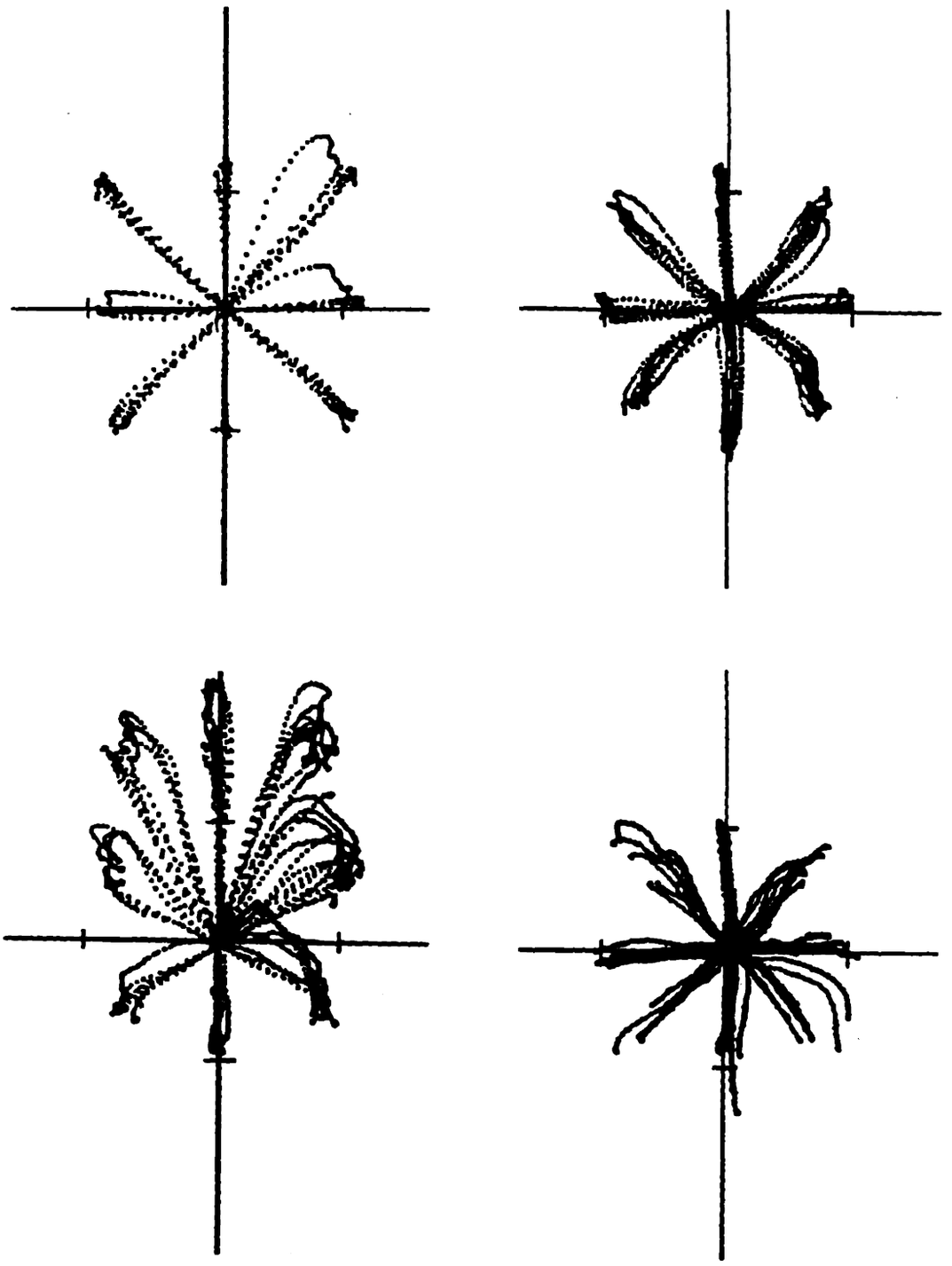


Figure 1

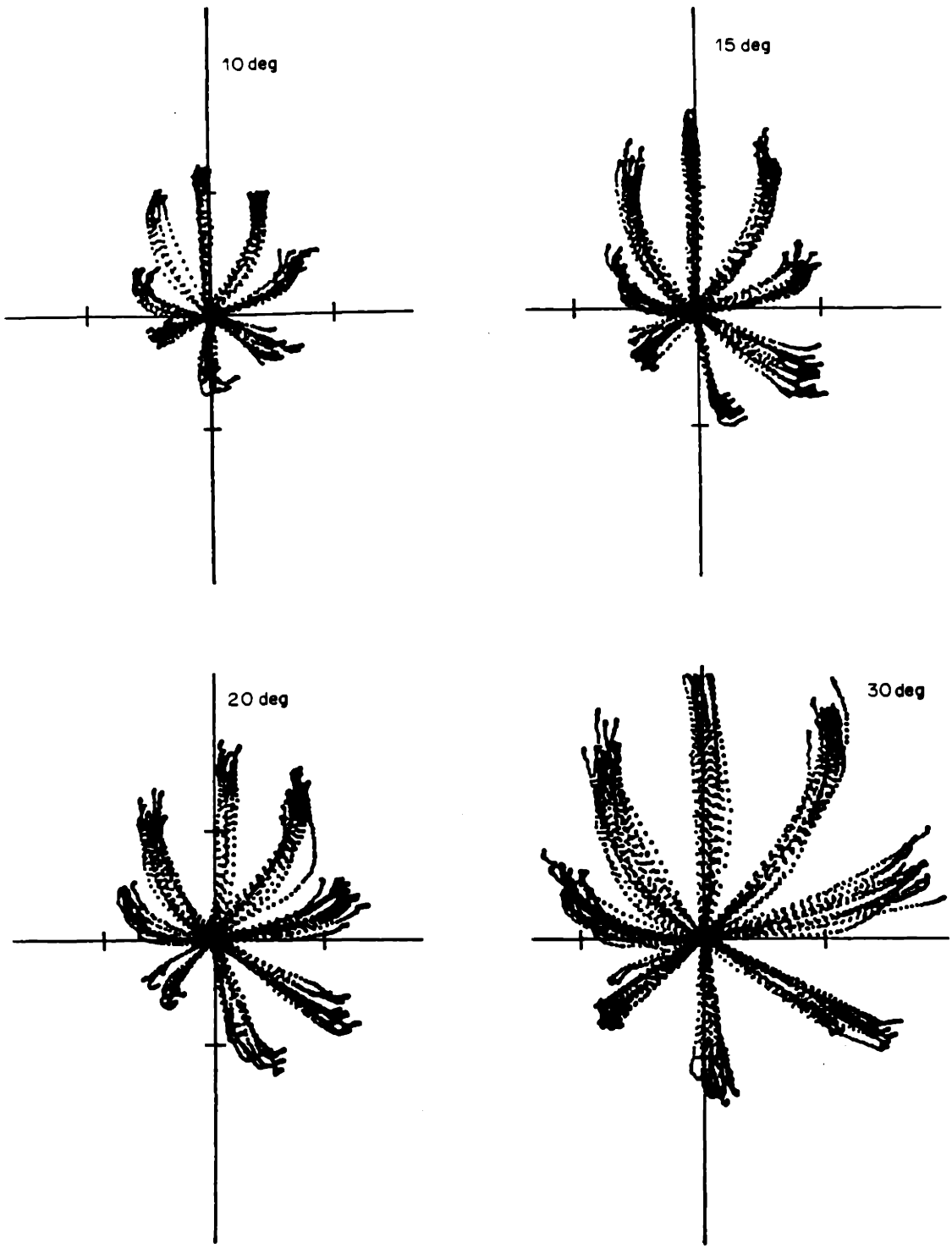



Figure 2

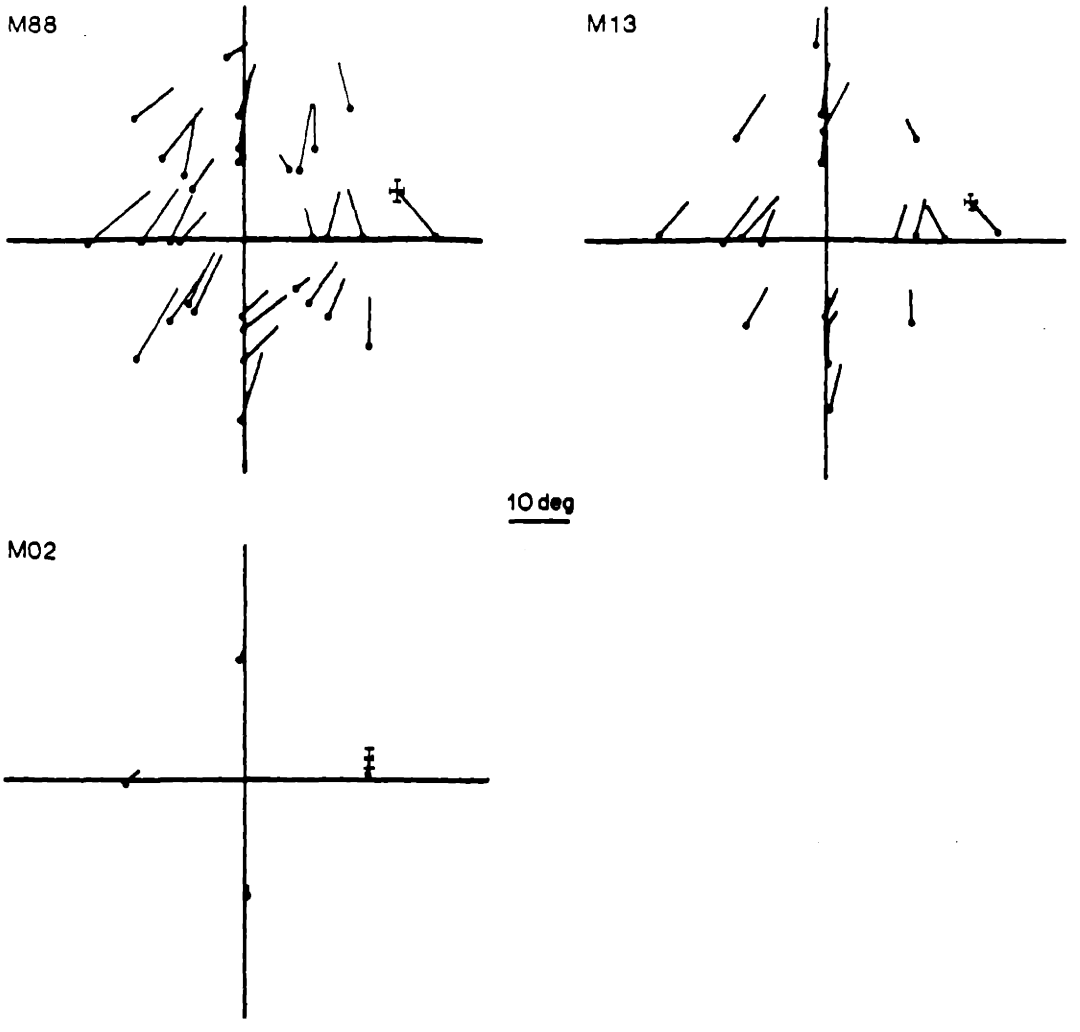



Figure 3

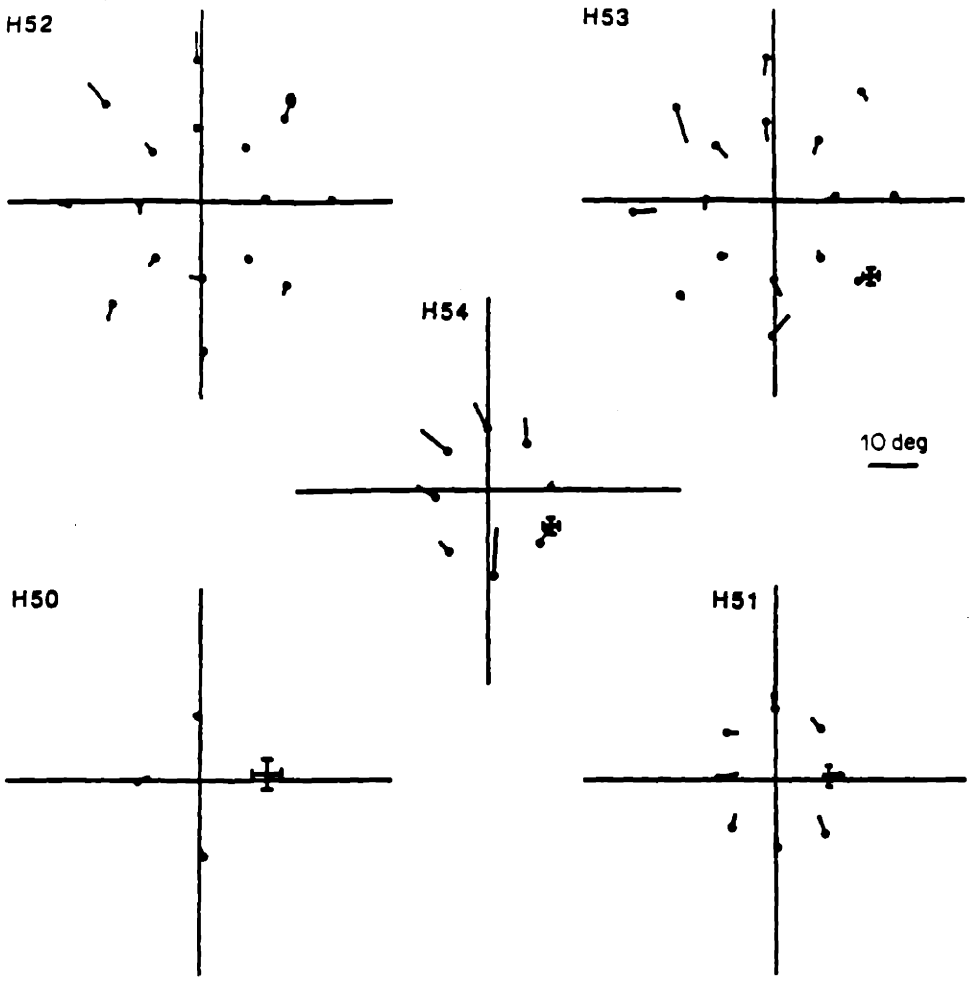



Figure 4

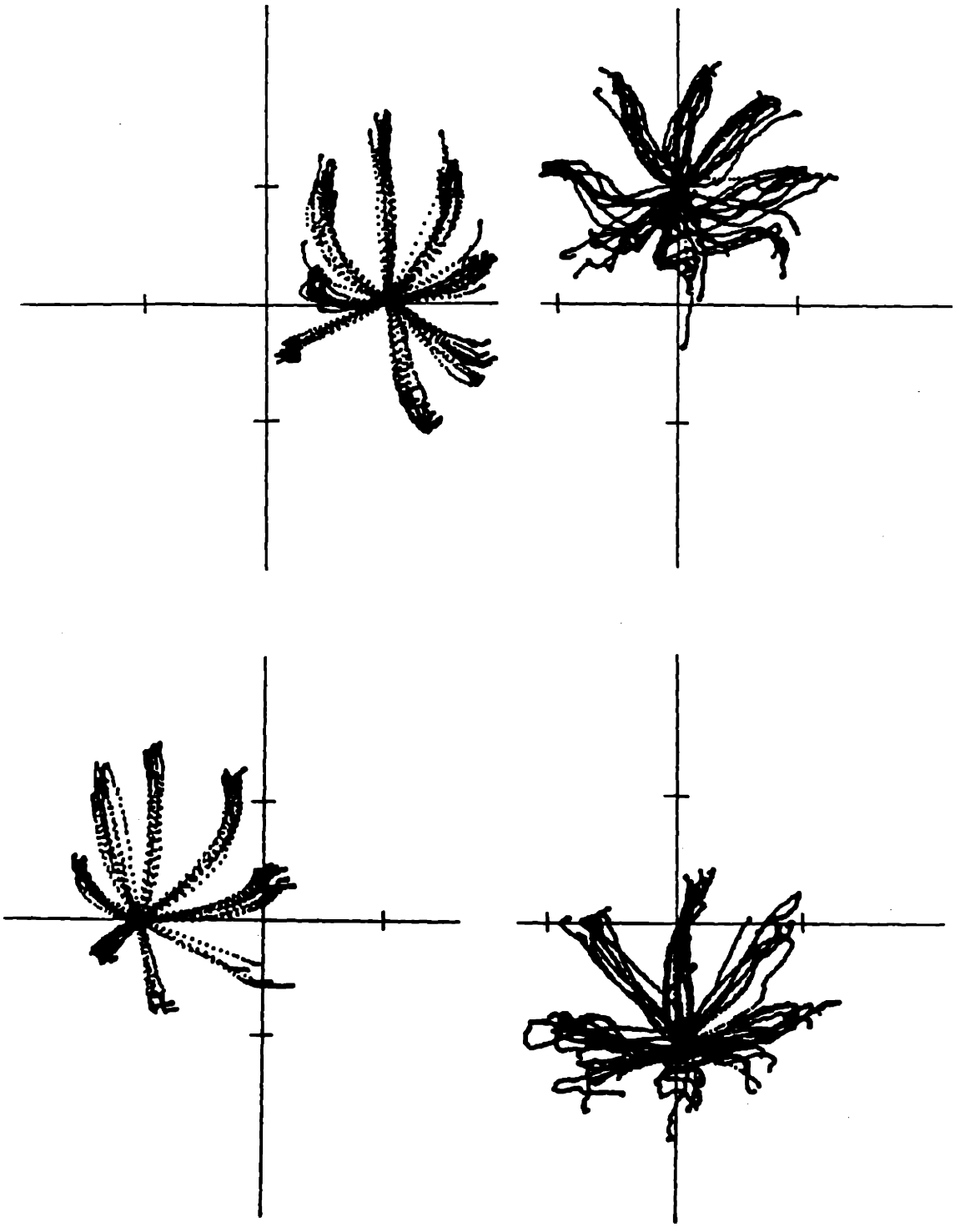


Figure 5

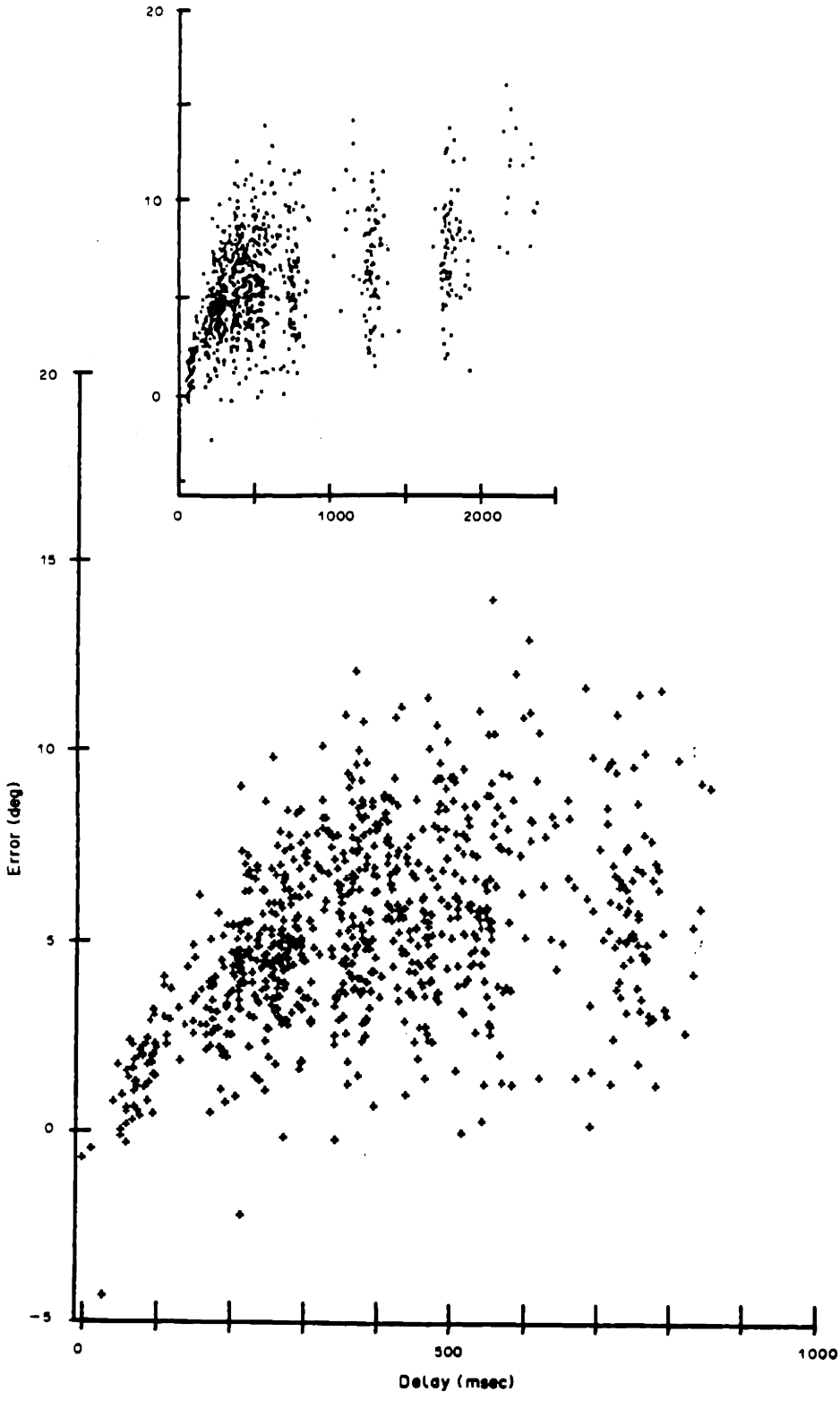



Figure 6

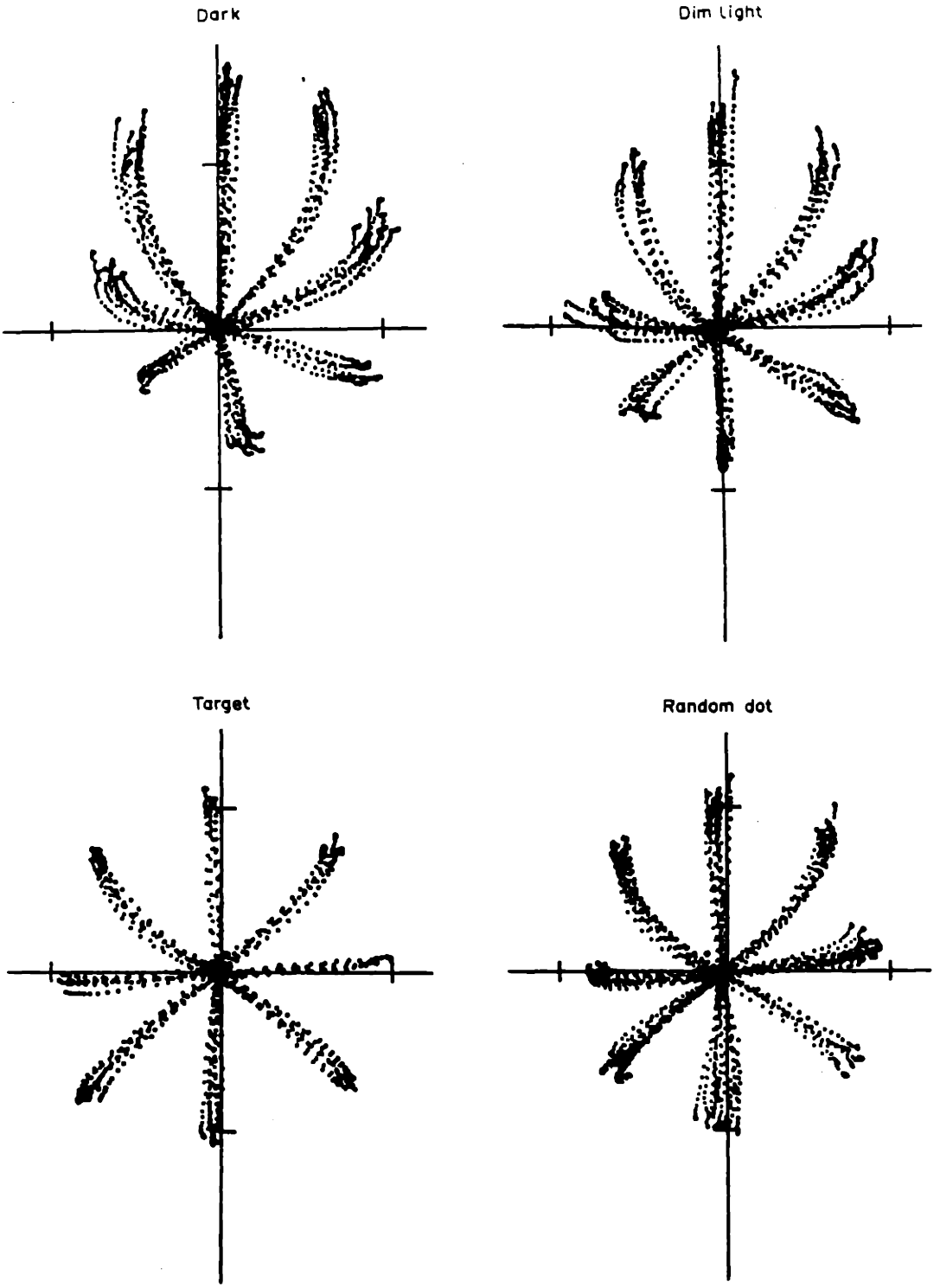



Figure 7

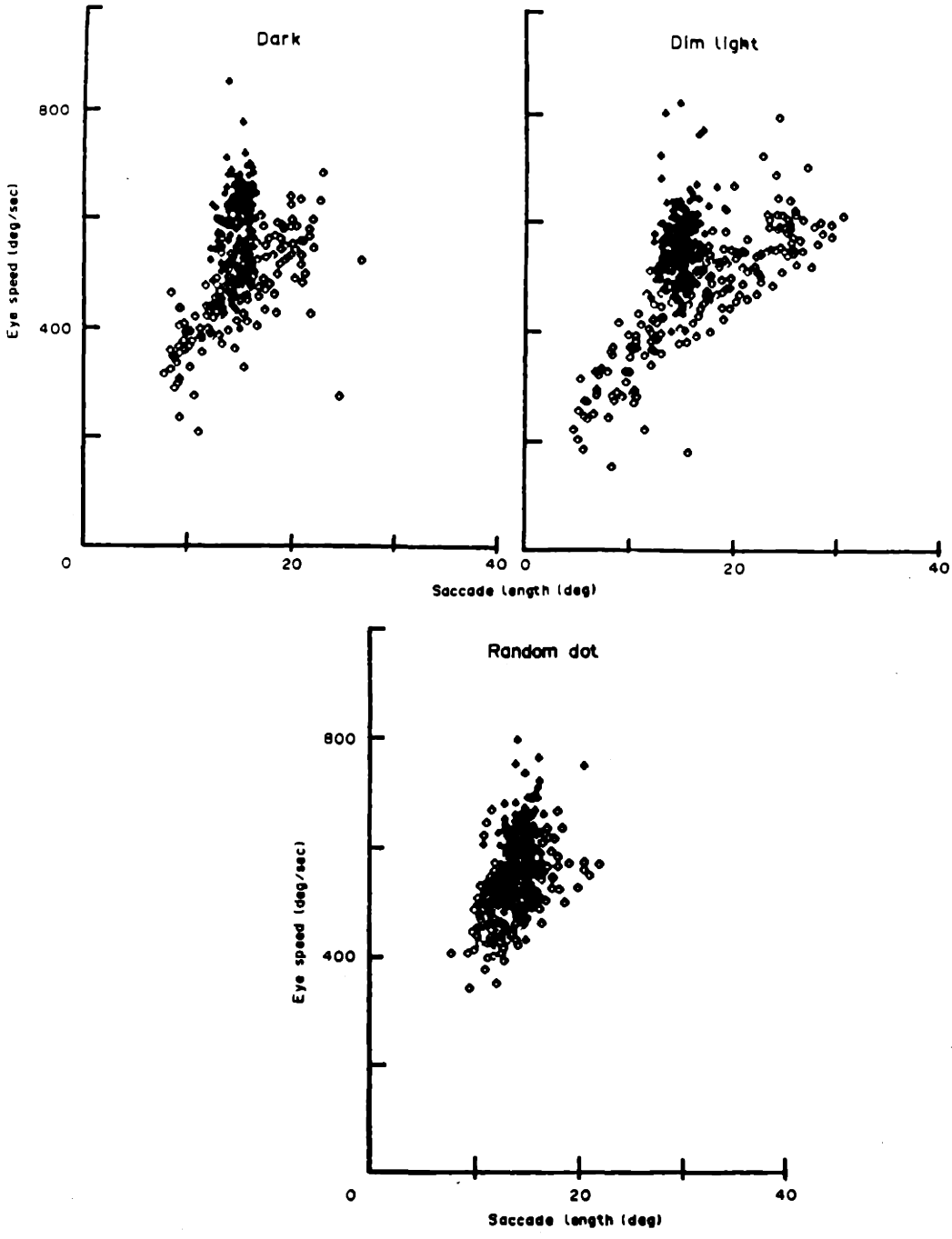

Dark
Dim light
Random dot
800
400
0
20
40
Eye speed (deg/sec)
Saccade length (deg)

Figure 8

| Subject | Dir. of error | Factor | F (d.f.) | Sig. level |
|---|---|---|---|---|
| M88 | Vertical | D*E | F(21,1320) = 26.10 | P < 0.001 |
| | Horizontal | D*E | F(21,1320) = 57.92 | P < 0.001 |
| | Length/ecc. | D*E | F(21,1320) = 24.58 | P < 0.001 |
| M13 | Vertical | D*E | F(9,298) = 39.81 | P < 0.001 |
| | Horizontal | D*E | F(9,298) = 87.21 | P < 0.001 |
| | Length/ecc. | D*E | F(9,298) = 135.89 | P < 0.001 |
| M02 | Vertical | D | F(3,53) = 0.81 | NS |
| | Horizontal | D | F(3,53) = 6.15 | P < 0.01 |
| H52 | Vertical | D*E | F(7,137) = 33.75 | P < 0.001 |
| | Horizontal | D*E | F(7,137) = 6.51 | P < 0.001 |
| | Length/ecc. | D*E | F(7,137) = 11.34 | P < 0.001 |
| H53 | Vertical | D*E | F(7,63) = 4.52 | P < 0.001 |
| | Horizontal | D*E | F(7,63) = 1.82 | NS |
| | Length/ecc. | D*E | F(7,63) =4.66 | P < 0.001 |
| H54 | Vertical | D | F(7,43) = 12.99 | P < 0.001 |
| | Horizontal | D | F(7,43) = 10.63 | P < 0.001 |
| H51 | Vertical | D | F(7,135) = 1.30 | NS |
| | Horizontal | D | F(7,135) = 14.15 | P < 0.001 |
| H50 | Vertical | D | F(3,47) = 0.86 | NS |
| | Vertical | D | F(3,47) = 0.19 | NS |

**Table 1:** ANOVA for target direction and eccentricity. Null hypothesis is that error is uniform for each target location. Significant results indicate non-uniform spatial errors. Dir., D = direction. Ecc., E = eccentricity. D.f. = degrees of freedom.

Mean error (standard deviation)

| T.P. | D.E. | Orbital position | | Sig. level |
|---|---|---|---|---|
| | | **M88** | | |
| | | Right 15 deg | Left 15 deg | |
| 15 deg up | H | 1.30 (0.89) | -7.63 (7.16) | P < 0.001 |
| | V | 7.73 (1.88) | 12.16 (4.44) | P < 0.001 |
| 15 deg down | H | 4.97 (1.78) | -7.73 (5.17) | P < 0.001 |
| | V | 2.57 (2.05) | -16.51 (9.46) | P < 0.001 |
| | | Up 15 deg | Down 15 deg | |
| 15 deg left | H | 4.64 (1.04) | 4.38 (1.49) | NS |
| | V | 5.19 (1.50) | 8.87 (1.78) | P < 0.001 |
| 15 deg right | H | 0.03 (1.42) | 2.42 (2.06) | P < 0.001 |
| | V | 4.97 (1.54) | 8.96 (1.38) | P < 0.001 |
| | | **M13** | | |
| | | Up/left 15 deg | Down/left 15 deg | |
| 15 deg right | H | 2.44 (1.44) | 0.97 (0.86) | P < 0.01 |
| | V | 5.22 (1.41) | 4.70 (0.67) | NS |
| | | Up 15 deg | Down 15 deg | |
| 15 deg right | H | -1.90 (5.12) | -0.62 (0.89) | NS |
| | V | 5.14 (2.15) | 5.10 (1.40) | NS |
| | | Up/right 15 deg | Down/right 15 deg | |
| 15 deg right | H | -4.90 (8.49) | -4.05 (0.71) | NS |
| | V | 2.40 (6.55) | 7.22 (4.90) | NS |
| | | Up/left 15 deg | Up/right 15 deg | |
| 15 deg up | H | 2.12 (0.45) | 0.35 (0.72) | P < 0.01 |
| | V | 10.63 (2.41) | 10.12 (1.31) | NS |
| | | Left 15 deg | Right 15 deg | |
| 15 deg up | H | 2.42 (0.56) | 0.47 (0.88) | 0.01 |
| | V | 7.12 (2.07) | 8.21 (1.78) | NS |
| | | Down/left 15 deg | Down/right 15 deg | |
| 15 deg up | H | 1.61 (0.60) | 1.50 (0.46) | NS |
| | V | 8.69 (1.98) | 7.86 (2.63) | NS |

**Table 2:** T tests, effects of orbital position. Continued on next page.

| | | Up 15 deg | Down 15 deg | |
|---|---|---|---|---|
| 15 deg left | H | -2.18 (3.94) | -3.90 (2.79) | NS |
| | V | 0.81 (3.51) | 2.87 (1.09) | NS |
| 15 deg right | H | 2.52 (2.06) | 2.65 (1.84) | NS |
| | V | 0.43 (1.06) | 2.09 (1.28) | $P < 0.01$ |

**Table 2** (continued from previous page): T tests, effect of eye position. Comparison of mean errors for different orbital positions at target positions where tangent screen effects were symmetrical. H = horizontal (+ = right, - = left). V = vertical (+ = up, - = down). For up movements, + = hypermetria and - = hypometria. The opposite is true for down movements. For right movements, + = hypermetria and - = hypometria. The opposite is true for left movements. T.P. = target position. D.E. = direction of error.

| T. P. | Dir. of error | Mean | Standard deviation |
|---|---|---|---|
| *Eye and head straight ahead:* | | | |
| 15 deg left | Horizontal | 3.90 | 1.10 |
| | Vertical | 10.49 | 1.28 |
| 15 deg right | Horizontal | 5.02 | 1.97 |
| | Vertical | 7.69 | 1.47 |
| *Eye up, head straight ahead:* | | | |
| 15 deg left | Horizontal | 4.81 | 0.67 |
| | Vertical | 10.15 | 1.79 |
| 15 deg right | Horizontal | 1.35 | 2.08 |
| | Vertical | 9.44 | 3.89 |
| *Head up, eye straight ahead:* | | | |
| 15 deg left | Horizontal | 4.42 | 1.24 |
| | Vertical | 9.41 | 1.70 |
| 15 deg right | Horizontal | 4.71 | 1.60 |
| | Vertical | 4.54 | 2.25 |
| *Head down, eye up:* | | | |
| 15 deg left | Horizontal | 3.21 | 0.94 |
| | Vertical | 10.19 | 0.95 |
| 15 deg right | Horizontal | 5.01 | 1.85 |
| | Vertical | 6.76 | 2.09 |

**Table 3:** Mean error, target direction and eye-head manipulations. Horizontal (+ = right, - = left). Vertical (+ = up, - = down). For right movements, + = hypermetria and - = hypometria. The opposite is true for left movements. T.P. = Target position.

| Dir. of error | Factor | F (d.f.) | Sig. level |
|---|---|---|---|
| *First null hypothesis: oculocentric organization - no effect of head or eye position (eye and head straight ahead; eye up, head down; eye down, head up):* | | | |
| Horizontal | Direction*Eye-head | F(3,155) = 30.42 | P < 0.001 |
| Vertical | Direction*Eye-head | F(3,155) = 8.69 | P < 0.001 |
| *Second null hypothesis: craniotopic organization - no effect of head position (head straight ahead; head up):* | | | |
| Horizontal | Direction*Head | F(1,80) = 2.00 | NS |
| Vertical | Direction*Head | F(1,80) = 9.71 | P < 0.01 |
| Horizontal | Head | F(1,80) = 0.71 | NS |
| *Third null hypothesis: somatocentric organization - linear addition of effects of eye and head position.* | | | |
| *(1) Eye and head manipulated equally (both up):* | | | |
| Horizontal | Direction*Eye-head | F(1,79) = 40.58 | P < 0.001 |
| Vertical | Direction*Eye-head | F(1,79) = 17.29 | P < 0.001 |
| *(2) Eye and head manipulated in opposite and equal fashion (eye down, head up):* | | | |
| Horizontal | Direction*Eye-head | F(1,80) = 1.14 | NS |
| Vertical | Direction*Eye-head | F(1,80) = 0.99 | NS |
| Horizontal | Eye-head | F(1,80) = 0.27 | NS |
| Vertical | Eye-head | F(1,80) = 3.93 | NS |

**Table 4:** ANOVA for target direction and eye-head factors. (Tests of the effects of head and eye positions where tangent screen effects were symmetrical.) D.f. = degrees of freedom.

# Chapter 9

## Evidence for a neural analogue in area LIP of the spatial distortions of memory saccades

## SUMMARY

Saccadic movements made in the dark to remembered targets typically end above target locations, suggesting that an up-shift occurs in some central representation of saccade target held in memory (see previous chapter). In chapters 2 and 3 we described a representation of both visual targets and saccades in the Lateral Intra-Parietal area (LIP). During memory-guided saccades, LIP neurones show separate light-sensitive (LS), memory/motor intention (M) and saccadic (S) activities. Each type of activity has its own preferred direction; in the same neurone these directions are usually similar to one another (chapter 3). By comparing the vertical components of the preferred directions we show here that there is a systematic change from LS to M to S of the vertical component, in the upward direction. This change is a neural correlate of the behavioural up-shift of the saccade end-points, described in the previous chapter. A similar analysis showed no analogous horizontal neural shift, in accord with the absence of a horizontal shift of saccade end-points. These results reinforce the contention that area LIP is involved in sensorimotor transformations underlying saccadic eye movements.

## INTRODUCTION

Most of the numerous paradigms used for studying saccadic eye movements (see Carpenter, 1988) have in common the following condition: the movement is made in the presence of a target light. The target is illuminated before the saccade begins, and remains on until well after the movement is completed. An important exception is the paradigm of memory saccades (Hikosaka and Wurtz, 1983c; M- or MO-saccades of Carpenter, 1988). Here a saccade is made to the position of a previously flashed target. Thus a "memory interval" exists in this paradigm, starting at the offset of the target, and continuing until the "go" signal. During the memory interval, a spatial representation of the remembered target location and/or a plan for the forthcoming movement must exist in memory.

Memory saccades are considerably less precise than visually-guided saccades. This has been noticed since the introduction of this paradigm (Hikosaka and Wurtz, 1983c). Only recently, however, have these imprecisions been studied in detail (previous chapter). We have found that memory saccades, when compared to visual saccades, are slower and more variable in trajectory. Moreover, they show both constant and variable end point errors First, the spread of the end-points of memory saccades is larger than the spread in visual saccades; they show greater variable error. This might be explained by a general, diffuse degradation of spatial representation in memory. The second type of imprecision is not as intuitively obvious: memory saccades end above target locations. This is a constant error (Granit, 1972), which may indicate a specific distortion of spatial representation in memory: an upward shift of remembered target location. The shift occurs between the beginning of the memory interval and the saccade. Our psychophysical results (see previous chapter) show that this upshift accumulates rapidly during the first several hundred ms of delay, and then more gradually as the delay period is extended out to two seconds. Thus the shift is a continuous, accumulating process. Examples of visual and memory saccades made by human and monkey subjects are given in figures 1 and 7 of the previous chapter, and in fig. 1 here.

We have suggested (see previous chapter) that the up-shift distortion originates in central processing, rather than in the orbital mechanics. The reason was that similar patterns of up-shift distortion

were observed regardless of the fixation position of the eye in the orbit. This raises the question of whether a neural analogue of this behavioural up-shift can indeed be observed in known central representations of memory-guided saccades.

We have made extensive use of the memory saccade paradigm in our physiological studies of area LIP (see elsewhere in this thesis). One advantage of the memory-guided saccade task is that it allows for the temporal separation of light-sensitive (LS) and saccadic-related (S) activity. In addition, a third type of activity revealed in this task is related to the memory (M) of the target or the plan to saccade to it. Further experiments suggest that memory activity reflects the monkey's intention to make a saccade (chapters 3 and 5). These three types of activity (LS, M and S) are separated in that they occur in different phases of the task.

Most LIP neurones are active in at least one (and usually more than one) of these phases. The activity is spatially tuned. Different activity phases of the same neurone are usually similarly tuned, that is, their preferred directions are aligned (see chapter 3). These findings, and others (see elsewhere in this thesis), indicate that area LIP holds spatial representations that may well be used in the sensorimotor transformations underlying the production of saccadic eye movements. Here we show that there is a neural analogue in these representations of the behavioural up-shift distortion observed in memory saccades.

# METHODS

## General methods

The general methods used in this experiment and analysis are described in great detail in chapter 2. Therefore, they are described here only in brief.

Two young adult *Macaca mulatta* monkeys were implanted with a head post and a scleral search coil for measuring eye position (Robinson 1963; Judge et al., 1980). In separate operations, recording chambers were mounted over the posterior parietal cortex. All surgical procedures were carried out under general anaesthesia (10 mg/kg Ketamine followed by 10 mg/kg Nembutal i.v.). Post-operative care included administration of analgesics. The general well being of the animals was observed according to NIH guidelines. Veterinarian monitoring was provided daily. During training and recording periods the animals were deprived of water in their home cages 4 or 5 days a week. We carefully monitored fluid intake in these periods, and water supplemented apple juice rewards if full daily ration was not reached during training or recording sessions.

Stimuli were 45 candela/$m^2$, 0.5 degree diameter circular spots, presented on a featureless tangent screen 57 cm in front of the animal, in total darkness. Galvanometer-mounted mirrors and electronic shutters controlled stimulus position and timing. Calibration procedures corrected for nonlinearities.

Eye position was sampled by a 12-bit A/D converter, usually at 500 Hz, sometimes at 100 Hz. Glass-coated platinum-iridium electrodes, 1-5 MΩ at 1 Khz, were used for neural recordings.

A trial of the memory-guided saccade task is illustrated in the bottom right corner of figure 2. A fixation spot appears directly in front of the monkey, at eye level. The trial begins when fixation of the spot is attained; the spot remains on for additional 1500 ms, during which its fixation has to be maintained. During this fixation period, 800 ms after the trial begins, a target is flashed on the screen for 300 ms. The target is located in one of 8 points spaced 15 deg apart on an imaginary grid centred on the fixation spot. Following fixation spot offset the monkey has to saccade to the location in which the target was previously flashed. Thus in the last 400 ms of fixation, subsequent to

target offset, the monkey has to remember target location.

The monkey made memory saccades in eight pseudorandomly varied directions. The outer panels of fig. 2 illustrate the spike rasters and histograms for memory saccades made in each of the eight directions. The up-and-left panel presents data from up-and-left M saccades, etc. (See chapter 2 for details.)

We calculated the firing rate in each phase of activity (LS, M, S; see Introduction), in each direction. Using these data we assigned a preferred direction to each type of activity, in each neurone (provided the neurone showed clear excitation in the given phase). This analysis is described in detail in chapter 3. In the central panel of fig. 2 we illustrate the preferred directions of the LS, M and S activity of this neurone.

**Calculation of the vertical and horizontal "shifts" of a neurone**

The analysis described in the last paragraph gave us three preferred directions, one for the LS activity, one for the M, and one for the S, for the neurone illustrated in fig. 2. We calculated preferred directions for each phase showing clear activity for each neurone. Our aim was to relate any change between these preferred directions with the behavioural phenomenon of saccade end-point up-shift.

A preferred direction may represented by a unit-length vector. We decomposed each vector into horizontal and vertical components. We compared the vertical (and horizontal) components of vectors representing the different preferred directions for each cell.

Figure 3 illustrates the procedure for calculating a neurone's vertical shift in preferred direction from LS to S. Figure 3a shows the neuron's LS and S preferred directions. (The directions used here are those of the neurone illustrated in figure 2.) Figure 3b illustrates the vertical components of these directions. A vertical component is rendered by the standard trigonometrical decomposition, that is, it is equal to the sine of the anticlockwise angle between rightward horizontal and the given preferred direction. Figure 1c illustrates the difference between the vertical components of the LS and S preferred directions. We define it as the neurone's "vertical shift" (from LS to S).

We can similarly calculate the difference between the vertical components of the LS and M, and M and S, vectors.

In a similar manner we calculated the neurone's horizontal shift from the horizontal components (given by the cosine function).

# RESULTS

## Database

We recorded 145 units from LIP in three hemispheres of two rhesus monkeys. The temporal and spatial properties of the activity of these units were studied extensively (see chapters 2 and 3). In the present analysis, we were concerned with the preferred directions of the LS, M and S activity of these units.

## Predictions

Our main prediction was that, in our population of cells, there should be bias towards positive values for the vertical shifts, i.e., that S preferred directions should tend to have a greater upwards component than M preferred directions, and M greater than LS. This would constitute a neural analogue of the behavioural upshift. We also predicted that there should be no comparable shift in the horizontal components, as there is no consistent dysmetria in the horizontal components of M saccades (see also chapter 8).

We also expected any effects to be subtle, as (1) the behavioural upshift is marked but not large, and (2) we had already determined that the preferred directions of different phases of activity in a given neurone are generally fairly well aligned (see chapter 3).

## The up-shift distortion in memory saccade end-points

We first corroborated our previous observation (see previous chapter) of the existence of upshift. Figure 1 illustrates typical trajectories of memory-guided saccades (actually the eye movements made during the recording of the single unit data shown in fig. 2). There is a marked up- shift in the saccade endpoints. There is no similar shift in the horizontal dimension, to either left or right. The clusters of end points in Figure 2 are vertically almost collinear with the targets.

In contrast, visual saccades have rather straight trajectories that end at the targets or very close to them (previous chapter; see Carpenter, 1988).

### Activity of LIP neurones during memory-guided saccades

Figure 2 illustrates typical activity evoked in an LIP neurone during performance of memory-guided saccades. Flashing a target in the neurone's receptive field evokes a burst of spikes. Since the monkey may not move his eye at this stage of the trial, nor for some time afterwards, this discharge is light-sensitive (LS). For targets to the left, the neurone remains active after the extinction of the target. This sustained discharge is called memory (M), reflecting the "behaviour" required of the monkey at this stage of the task. Fixation offset serves as the "go" signal; the saccadic movement follows it. At the time of the saccade the neurone becomes again active, typically starting before the saccade but outlasting it. Since this burst occurs in complete darkness, it is called saccadic (S). See chapter 2 for an extensive analysis of the temporal properties of area LIP activity during memory saccades.

The activity in each of these phases (LS, M, S) is tuned in direction. We have studied this direction tuning in detail (see chapter 3). For each neurone, we assigned to each phase a preferred direction, provided there was clear excitatory activity in that phase in at least one direction. We found that, in the same neurone, the LS, M, and S activity phases tend to be directed in similar directions. The general alignment of the LS, M, and S preferred directions suggests that neuronal activity in LIP may be involved in the sensorimotor transformation underlying the production of memory saccades.

### A neural vertical shift

In chapter 3, we did not study *signed* differences in preferred directions, only their absolute values. We found that the absolute values are usually small (that is, the preferred directions are similar). Do the signed differences, though small, vary significantly from zero? In other words, does a neurone's preferred direction change systematically from one phase to another? The importance of this question is, of course, that such changes might be related to the behavioural up-shift of saccade end points, described above. However, the differences of directions contain both horizontal and vertical components (see methods above). We focus here on the vertical

components of the LS and S activity. Our prediction is that as the trial progresses from the LS phase to the S phase, the vertical components will shift upwards. We have also looked for an analogous change in horizontal components, as a control: since there is no horizontal shift of saccade end points, we expected to find no horizontal neural shift.

Figure 4 shows the results. Figure 4a illustrates the distribution of vertical shifts for the 68 neurones having clear excitatory activity in both phases, LS and S (of our sample of 145 neurones). The distribution is biased towards positive (that is, upward) shifts in these neurones. The mean vertical shift is 0.256, significantly different from zero ($p < 0.0037$). (The range of possible values the vertical shift could take is from -2 to 2, as the shift is a difference of sines.)

Figure 4b illustrates the distribution of horizontal shifts in the same neurones. The distribution is symmetric, indicating the absence of a neural shift. The mean horizontal shift is -0.018, not significantly different than zero ($p > 0.4$).

The M activity takes intermediate directions between LS and S, close to LS. We calculated the vertical neural shifts in each case for neurones that had excitatory response in both phases in question. From LS to M, the mean vertical shift is 0.05, $p > 0.2$ (for 61 neurones). From M to S the mean vertical shift is 0.13, $p > 0.15$ (56 neurones).

In the analysis described above, we have assigned a uniform weight to all neurones, regardless of their rate of activity. Some investigators weight the preferred direction by the firing rate when computing a preferred direction (e.g., Georgopoulos et al., 1982). We repeated the analysis, scaling each neurone's vertical shift by its maximal rate. The results were the same - the vertical component was significantly different from zero (mean 21, $p < 0.0025$). The horizontal shift was not significantly different from 0 (mean -6.2, $p > 0.25$).

## DISCUSSION

In this chapter we have shown that there is a neural analogue in LIP activity of the behavioural up-shift observed in memory saccades. There is a shift upwards in preferred direction from the LS to M to S phases of activity. This result reinforces our notion of a linkage between activity in area LIP on the one hand, and sensorimotor transformations underlying saccades on the other.

What can we say about the time course of this "neural upshift"? Clearly the preferred direction shifts up gradually from the LS to M to S phases of memory saccades trials. Thus there is no sharp discontinuity in either the initial memory encoding nor in the saccade production. Our physiological results rather favour the notion that the shift occurs gradually during the memory-related sensorimotor transformations underlying the production of such saccades. That the up-shift accumulates gradually with time (see previous chapter) supports this suggestion. It would be of interest to measure the neural upshift at different time points during memory saccades with a longer delay period. One could for example record neuronal activity during memory saccades with a two second delay period. The preferred direction of the neurone could be calculated for successive 400 or 500 ms time periods during the delay period. We would predict a gradual increase in the size of the neural upshift, paralleling the increase in the behavioural upshift seen in memory saccades of increasingly longer delay periods.

This correlation between the behaviour and the physiology supports our notion that LIP is involved in the sensorimotor transformations underlying the production of memory saccades.

## FIGURE LEGENDS

**Figure 1:**

Trajectories of memory-guided saccades made in the dark to the remembered locations of eight targets. Target locations, marked with + signs, were spaced 15 deg apart on an imaginary grid.

**Figure 2:**

Activity of an area LIP neurone recorded while the monkey performed the memory-guided saccades illustrated in figure 1. The up-and-left panel shows all trials directed to the up-and-left target, the up panel shows all trials directed to the up target, etc. Panels show a spike raster for each trial, and a histogram of all trials in the panel. The dotted lines mark, from the left, stimulus onset and offset, and fixation offset. Fixation offset is the "go" signal for the saccade. The timing is further illustrated below the bottom right panel. The center panel shows the neuron's preferred directions in each of the LS, M, and S activities.

**Figure 3:**

Calculation of a neurone's vertical shift. (A) illustrates the preferred directions in the LS and S phases of the area LIP neurone illustrated in fig. 2. (B) illustrates the vertical components of the preferred directions. (C) illustrates the neurone's "vertical shift". See text for details.

**Figure 4:**

(A) The distribution of vertical shifts from LS to S phases of activity for the 68 area LIP units having clear excitatory LS and S responses. The distribution is biased towards positive values.

(B) The distribution of horizontal shifts from LS to S phases of activity for the same 68 area LIP units. The distribution is essentially symmetrical.

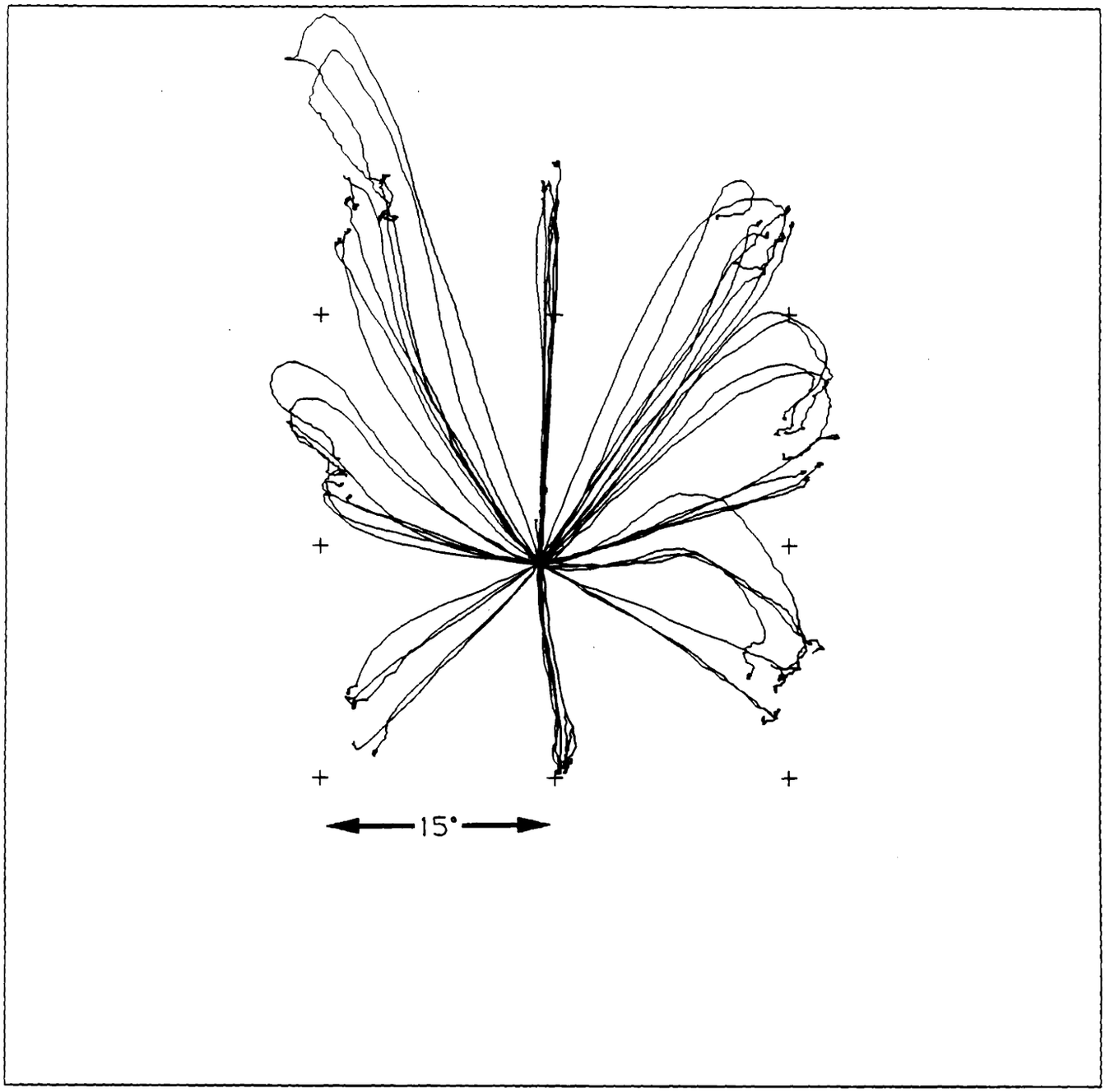



Figure 1

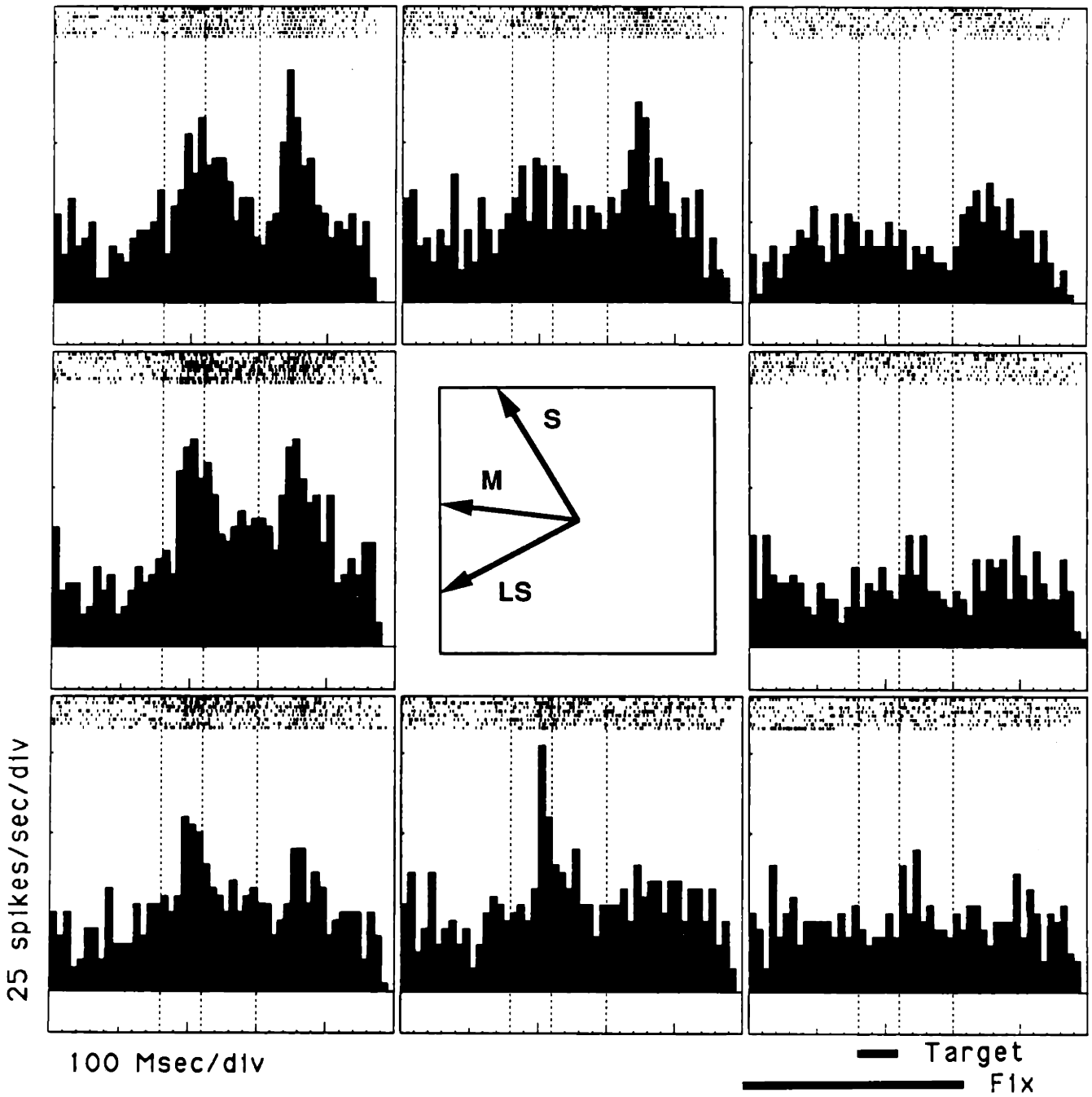
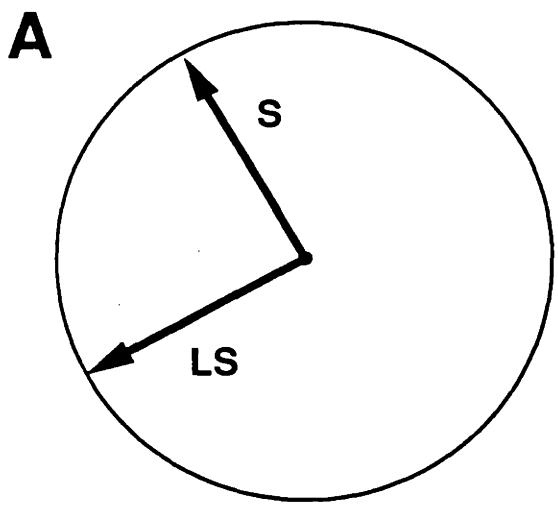
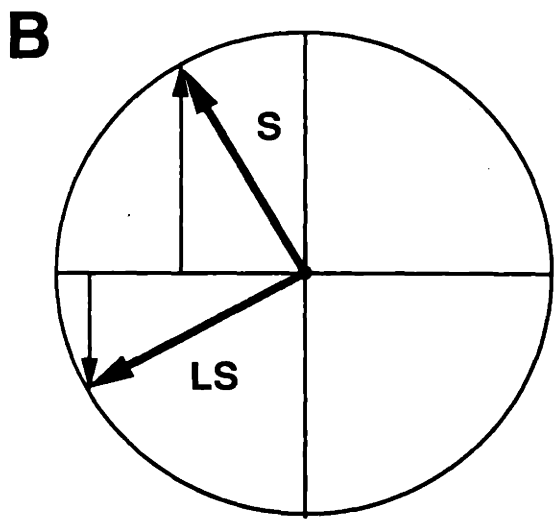



Figure 2



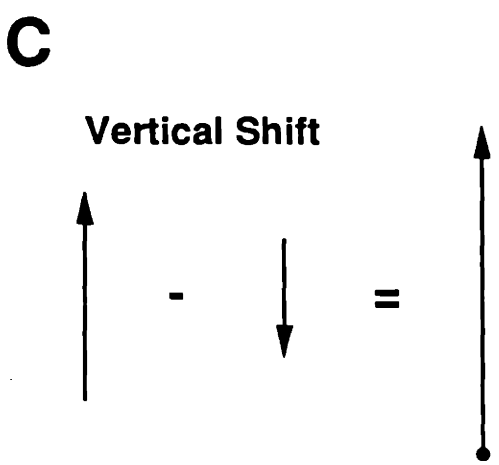
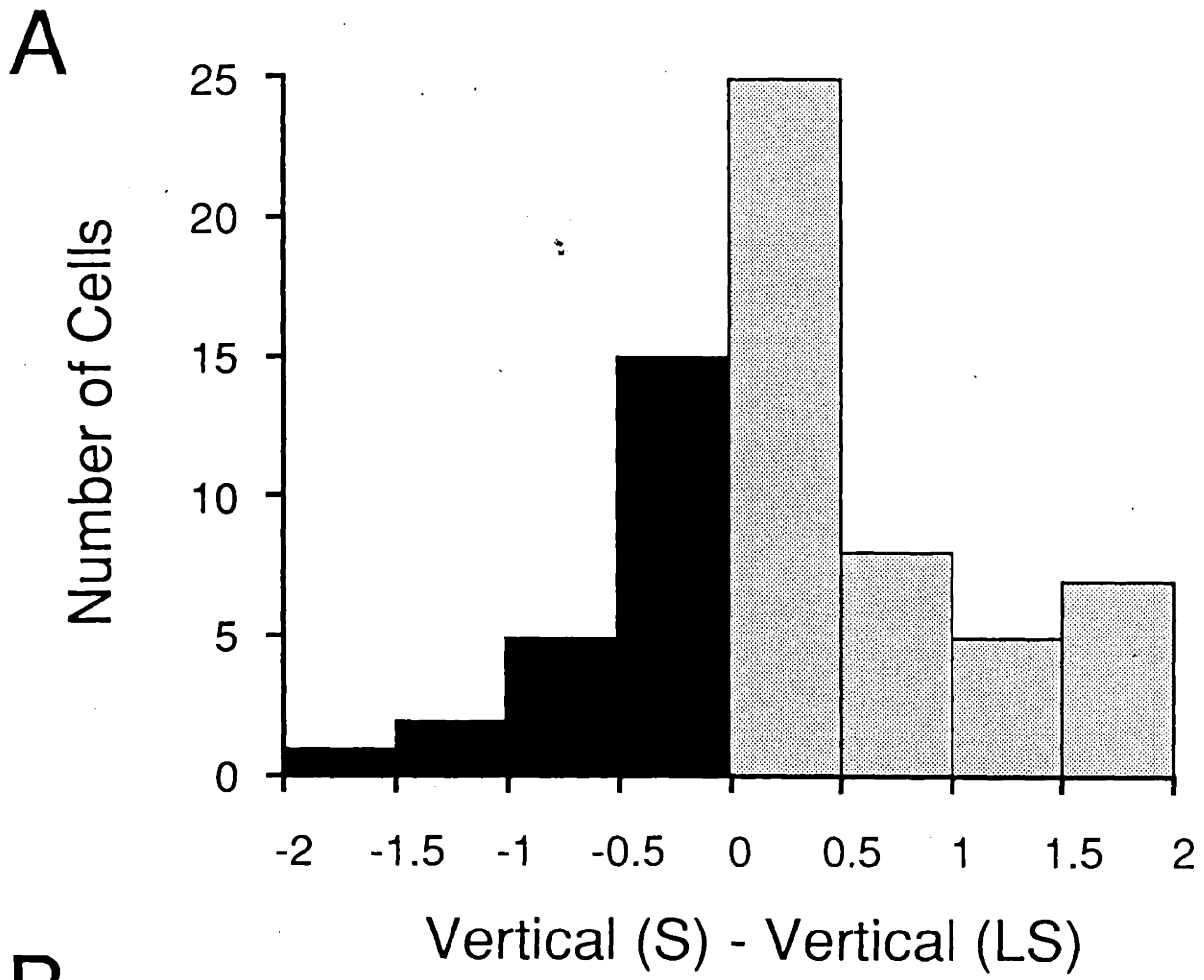




Figure 3


A
Number of Cells
25
20
15
10
5
0
-2
-1.5
-1
-0.5
0
0.5
1
1.5
2
Vertical (S) - Vertical (LS)

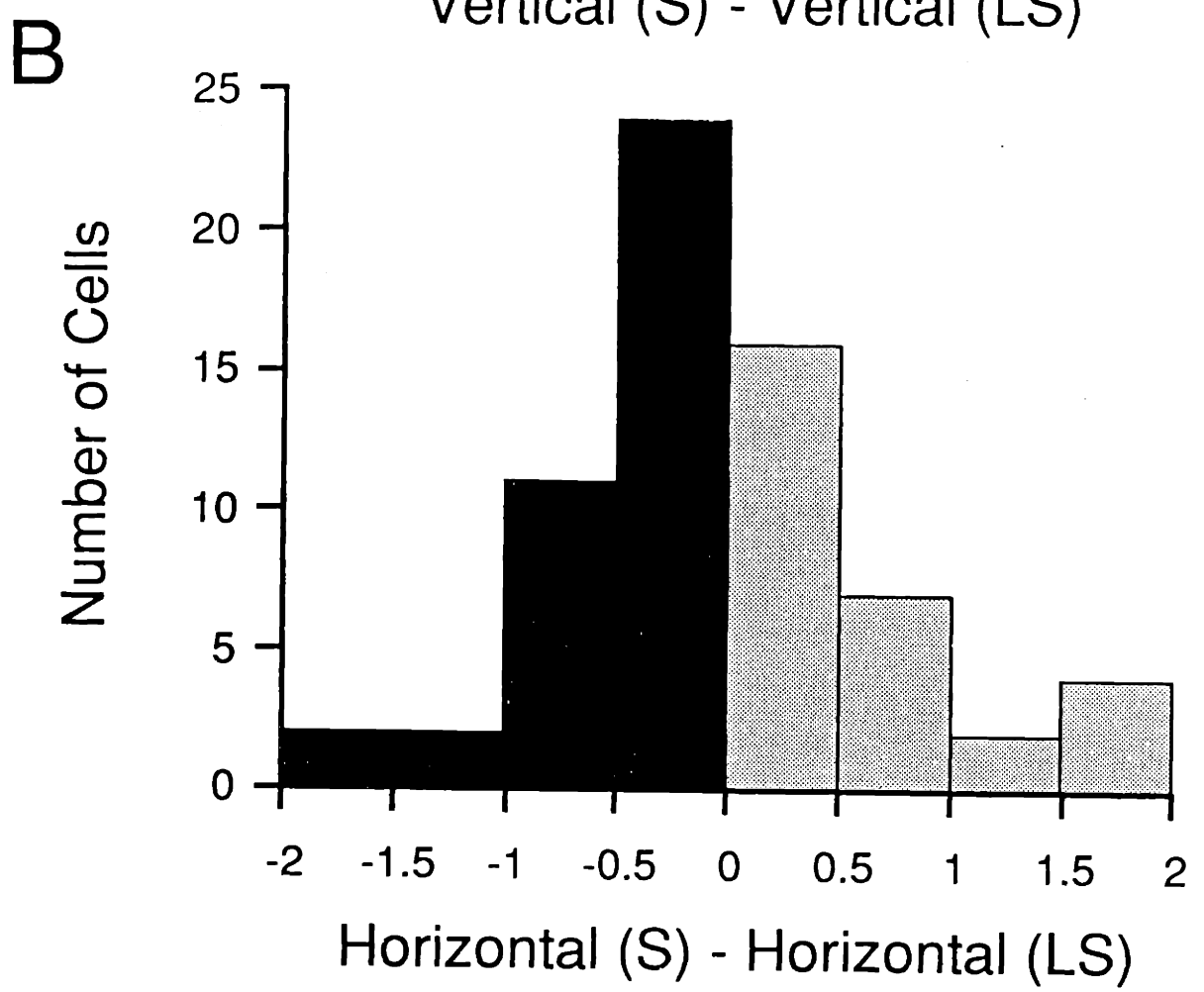

B
Number of Cells
25
20
15
10
5
0
-2
-1.5
-1
-0.5
0
0.5
1
1.5
2
Horizontal (S) - Horizontal (LS)

Figure 4

# Chapter 10

## General discussion

## SUMMARY

In this dissertation, I have reported the results of a series of studies designed to investigate the role of the posterior parietal cortex of primates in the control of saccadic eye movements. Most of the work involved single neurone recordings from awake, behaving macaques, trained to perform a variety of visual and oculomotor tasks.

In chapter 1 I reviewed the relevant clinical, anatomical and physiological literature. Here I introduced the lateral intraparietal area (LIP), a recently described subdivision of the macaque posterior parietal cortex. It is the focus of most of the work reported in this dissertation.

In chapters 2 and 3, I reported the results of a detailed, quantitative study of the properties of visual and saccade-related neurones in areas LIP and 7a. Many neurones are found to have both visual (LS) and motor (S) fields. Moreover, many also manifest activity during the delay period of a memory saccade task. This memory (M) activity is shown to be in motor coordinates and to reflect the monkey's intention to make a saccade into the neurone's motor field. Area LIP is found to be physiologically distinguishable from neighbouring area 7a, in particular by its high proportion of pre-saccadic neurones.

In chapter 4, I reported that the LS, M and S activity of neurones in areas LIP and 7a is modulated by eye position, and suggest that this modulation may play an important role in the visuo-motor coordinate transformations underlying the programming of saccades, and the representation of visual space.

In chapter 5, I introduced a novel experimental paradigm, the "delayed double saccade". I showed that M activity in area LIP generally reflects the monkey's intention to make the next in a sequence of saccades.

In chapter 6, I provided further evidence that M activity in area LIP reflects the monkey's plan to make the next saccade: alterations in the monkey's intentions, even in the absence of overt behaviour, are manifested in alterations in neuronal activity in LIP.

In chapter 7, memory saccades to auditory targets were used to investigate the generality of the intention activity in area LIP.

In chapter 8, a detailed, behavioural study of memory saccades in monkey and man was presented. The most striking finding here is that memory saccades tend to show an "upshift": they consistently end

above the target location. In chapter 9 I presented evidence for an analogue of this behavioural upshift in neuronal activity in area LIP.

Much discussion of the details and implications of specific experiments is to be found in the relevant chapters elsewhere in this thesis. In this chapter, I discuss some issues of more general interest related to the work reported in this dissertation, and suggest some possible future experiments.

## CORTICAL SACCADE AREAS

Currently four cortical regions have been reasonably well established as "saccade areas". They are the frontal eye fields (FEF) (Bruce and Goldberg 1985), the supplementary eye fields (SEF) of the supplementary motor area (SMA) (Schlag and Schlag-Rey 1987), the dorsolateral prefrontal cortex (PFC) (Boch and Goldberg 1989, Funahashi et al. 1989, 1990) and the posterior parietal cortex (PPC), especially LIP. Why are there so many areas? Do they play different roles in the control of saccades?

### Posterior Parietal Cortex (PPC)

The latencies of reflexive visually-guided saccades (i.e., those made to the sudden appearance of a target in the periphery) increase from 200 to over 300 ms after PPC lesions in man (Pierrot-Deseilligny et al. 1987, 1991). Similar increases are seen in monkey (Lynch and McLaren 1989). In contrast, lesions to the three frontal areas are reported to cause only small increases in, or have no effect on, latency (man: Pierrot-Deseilligny et al. 1991; monkey: Deng et al. 1986). This difference between the parietal and frontal lobes has been used to argue that the PPC is the most important cortical area for the initiation of reflexive visually-guided saccades (Pierrot-Deseilligny et al. 1991a). Isolated biparietal lesions affect mainly the triggering of visually-guided reflexive saccades (Pierrot-Deseilligny et al. 1986), whereas bilateral frontoparietal lesions affect the initiation of intentional and reflexive saccades (Pierrot-Deseilligny et al. 1988).

Keating et al. (1983) have shown that after superior colliculus (SC) ablation, saccades may no longer be evoked by PPC stimulation. As

discussed in chapter 1, LIP projects onto the deeper layers of the SC.

Together, these findings suggest that the PPC may be involved in the triggering of reflexive visually-guided saccades via its direct projection to the deeper layers of the SC.

Lesions to the PPC have been shown to cause deficits in both "intentional" (more purposive, less reflexive) and memory saccades (reviewed in chapter 1). It may be more involved in the production of "intentional" and memory saccades via its projections to the frontal oculomotor areas.

**The dorsolateral prefrontal cortex (PFC)**

This area corresponds to area 46 of Walker in the monkey (Joseph and Barone 1987, Boch and Goldberg 1989, Funahashi et al. 1990), and probably to area 46 of Brodmann in man (Goldman-Rakic 1987).

Guitton et al. (1985) showed that frontal patients were especially poor at inhibiting saccades to the visual target when requested to make antisaccades (i.e., to saccade in the opposite direction to the target). Pierrot-Deseilligny et al. (1991a) have replicated this finding, and narrowed down the cortical locus for this effect to area 46; FEF and SMA patients were not significantly worse than controls.

The physiological findings of Boch and Goldberg (1989) and Funahashi et al. (1989, 1990) also support the contention that PFC is involved in inhibiting unwanted reflexive visual saccades. It is likely that this inhibition is exerted directly on subcortical structures, rather than via FEF or SEF, since damage to those areas did not result in such poor behaviour in antisaccades. PFC seems to have the requisite connexions for such a role: it projects directly onto the SC (Goldman and Nauta 1977; Leichnetz et al. 1981; Fries 1985), and probably onto the basal ganglia (Goldman and Nauta 1977), and to the region of the brainstem in which omnipause neurones are located (Leichnetz et al. 1987).

PFC neurones also show directionally specific activity during memory saccades (Funahashi et al. 1989, 1990). Dorsolateral PFC lesions in man result in inaccurate memory saccades with increased latencies. Pierrot-Deseilligny et al. (1991b). It has been claimed that PFC activity follows PPC activity in memory saccades (Chaffee et al. 1989). It is thus possible that PFC is part of a distributed network (presumably including LIP) that encodes memory saccades.

**Frontal eye fields (FEF)**

The frontal eye fields are the most venerable of the cortical eye fields (Ferrier 1876), and perhaps the most widely studied. Since Ferrier (1876), other groups have redefined the FEF on the grounds of electrical stimulation (e.g., Robinson and Fuchs 1969; reviewed in Goldberg and Segraves 1989). With the passing of time (and the use of smaller currents and awake animals!), the FEF have shrunk. Bruce and Goldberg (1985) have restricted FEF to a small region mainly on the rostral bank of the arcuate sulcus (parts of Walker's areas 8a and 45). (See also the cytoarchitectonic study of Stanton et al. 1989). Electrical stimulation of this region still evokes saccades after lesions of the SC (Keating et al. 1983).

Bizzi (1968) reported that FEF cells became active only after the initiation of saccades. However, in his study monkeys were making spontaneous saccades in the dark, which probably explains the apparent conflict with more recent results which show that many FEF neurones have presaccadic activity before purposive saccades (Bruce and Goldberg 1985). Mohler et al. (1973) showed that FEF cells have visual receptive fields. Wurtz and Mohler (1976) showed that the visual responses are enhanced when the animal saccades to the target in the field. This enhancement is specific to saccade targets (Goldberg and Bushnell 1981). Bruce and Goldberg (1985) showed that 54 % of FEF cells fire before purposive saccades in the dark. "Visual" cells only had visual responses, not firing before learned saccades in the dark. "Movement" cells in contrast had little or no visual response and did fire before learned saccades in the dark. "Visuomovement" cells had both visual and movement activity. 17 % of Bruce and Goldberg's sample of FEF neurones were postsaccadic. Some cells are fixation-related (Bizzi 1968; Bizzi and Schiller 1970). The activity in some of these cells may be explained by foveal responses (Suzuki and Azuma 1977; Suzuki et al. 1979). Some fire when fixation is released.

Segraves and Goldberg (1987) showed that the saccade-related and fixation-related cells are relatively enhanced in the population of layer 5 FEF cells projecting directly to the SC.

As noted above, FEF lesions only at most slightly lengthen the latency of visually-guided reflexive saccades in man (Pierrot-

Deseilligny et al. 1987, 1991a) and monkey (Deng et al. 1986; Schiller et al. 1987). This suggests that it is not normally involved in initiating such saccades. However, when combined with an SC lesion, all saccades are abolished (Schiller et al. 1980). FEF lesions result in longer latency and more inaccurate memory saccades in man (Pierrot-Deseilligny et al. 1991b) and monkey (Deng et al. 1986). Bruce and Borden (1986) have reported that FEF is essential for predictive saccades.

FEF has three major oculomotor outputs (reviewed in Leichnetz and Goldberg 1988): First, it projects onto the oculomotor layers of the SC. Second, it projects to the caudate, which in turn projects to the substantia nigra, and thence to the SC. Third, it projects directly to the oculomotor brainstem. It is an attractive possibility that the first pathway relays both details of saccade metrics (from the movement cells) and "decisions" to make saccades (from the fixation cells). The FEF may relieve the SC of its tonic inhibition from the substantia nigra (Hikosaka and Wurtz 1983a-d, 1985a, b) via its projection to the caudate (which inhibits the nigra, which in turn inhibits the SC). It is presumably via the third pathway that FEF can compensate for SC lesions. This pathway normally may play a role in the passing to the brainstem "decision" (and perhaps "metrics") signals - it presumably does not lie dormant waiting to compensate for SC lesions!

FEF cells are active during memory saccades (Funahashi et al. 1989). Hikosaka and Wurtz (1983c) reported responses specifically related to memory saccades in the substantia nigra. It is possible that (part of) the influence of FEF on the programming of memory saccades is via the frontal cortex-caudate-nigra-SC pathway.

**Supplementary eye fields (SEF)**

Both human (Fox et al. 1985; Melamed and Larsen 1979) and monkey (Mann et al. 1987; Schlag and Schlag-Rey 1987; Tehovnik and Lee, pers. com.) experiments suggest that SMA is involved in saccades of various kinds (review in Schall 1991c).

It is of interest that SEF lesions in man do not affect reflexive, visually-guided saccades, antisaccades or *single* memory saccades (Pierrot-Deseilligny et al. 1991a, b; Gaymard et al. 1990), but they do impair the production of *sequences* of two or three memory saccades (Gaymard et al. 1990). Analogous findings have been reported for arm

movements (Dick et al, 1986). It is an attractive possibility that SEF is involved in controlling the sequencing of memory saccades (see chapter 5). This role is in accord with the rather high position in motor control that the SMA is thought to occupy (see, e.g, Goldberg 1985).

**A note on the superior colliculus**

Although this section is primarily devoted to the cerebral cortex, even the most chauvinistic of cortical investigators cannot ignore the superior colliculus (SC) in any discussion of brain areas involved in programming saccades. A great deal of evidence has accumulated to suggest that it plays a major role in the production of saccades (for reviews, see Schiller 1984; Sparks 1986). However, ablations of SC in primates cause small deficits (decreased frequency of spontaneous saccades, increased latencies, decreased velocities and slightly impaired accuracy) (Albano and Wurtz 1982; Butter et al. 1982; Schiller et al. 1980). The only major permanent deficit appears to be a loss of express saccades (Schiller et al. 1987). SC lesions abolish saccades evoked by electrical stimulation of the striate, extrastriate and parietal areas, but not the FEF (Keating et al. 1983; Schiller 1977). However, combined SC and FEF lesions have devastating, long-lasting effects on saccadic performance (Schiller et al. 1980). This, and other, evidence leads one to the notion that there are two pathways for the generation of saccades: one from the SC and one from the FEF. Local injection of muscimol (a GABA agonist) into the SC leads to dramatic deficits in contralateral saccades (Hikosaka and Wurtz, 1985e; Schiller et al. 1987). This suggests that SC is normally the "main controller" of saccades. It takes a while for FEF to compensate for loss of SC function.

Butter (1983) has shown that FEF lesions compromise visual search and the temporal sequencing of eye movements. FEF is also the recipient of more highly processed visual information than the SC (Schiller 1985). These data support Schiller's (1985) suggestion that SC is mainly involved in making saccades to easily discriminable targets (reflexive, visually-guided saccades), whereas FEF may make use of more extensively processed visual (and other) input to programme (more "intentional") saccades in visual search tasks, for instance. The increased saccadic latencies which follow IPL lesions suggest that the tectal projections of IPL (mainly from LIP) play an important role in

collicular programming of saccades.

## HIERARCHIES AND DISTRIBUTED PROCESSING

It is natural to ask where in the pathway from the retina to the extraocular muscles area LIP lies. Neurophysiologists have traditionally thought in terms of a fairly simple step-by-step information processing system. As information moves centrally from the periphery, it is gradually refined for the purposes of the organism. Hubel and Wiesel's (1962) explanations for the construction of simple cell receptive fields in cat striate cortex from "lines" of geniculate cells, and of complex cells from simple cells, is perhaps the most celebrated example of such "linear" thinking. Whilst there is indubitably some step-by-step elaboration of sensory input, it now seems clear that much information processing is distributed across widely separated but interconnected areas of the cortex (see, e.g., Goldman-Rakic 1988; Andersen et al. 1990; Felleman and van Essen 1991).

There is a related conceptual problem: neurophysiologists have a tendency to divide complex information processing tasks into "functions", and assign each function to a separate area of the brain. For instance, a fairly strict segregation of function in visual processing has been proposed by Zeki (e.g., 1978) and Livingstone and Hubel (e.g., 1988). However, recent work has suggested that there is actually extensive cross-talk between areas supposedly in different processing streams. Moreover, it is unlikely that certain functions are carried out uniquely by certain areas (see, e.g., Schiller and Logothetis, 1990).

In the "motor" system, an illustrative example is the recent, extensive study by Alexander and Crutcher of responses in the SMA, area 4 and the putamen. Alexander and Crutcher (1990a) reported directionally-selective preparatory activity in these three regions of monkeys performing a visuomotor step-tracking task. This activity was relatively immune to the effects of loading the limb, suggesting that the preparatory activity "may be coding for the intended direction of movement" (p 133) rather than lower level motor variables such as torque. Crutcher and Alexander (1990) went on the study two classes of neurones in these three areas. One class had "muscle like" firing, related to muscle load. Units in the other class were directional, firing for movements in a certain direction, but not exhibiting firing dependent on muscle force. Finally, Alexander and Crutcher (1990b)

used two versions of a delayed visuomotor tracking task, one in which the visual stimulus and limb moved in the same direction and one in which the relationship was inverted. Using these tasks, they were able to show neurones in all three areas that fired during the preparatory or execution periods, either in relation to the direction of limb or target movement. (There was, however, relatively more target-dependent activity during the preparatory period, and more limb-dependent activity during the execution period.) Therefore, even in these "motor" areas sensory information is extensively represented. It is clear from such studies that constructing simple linear "black box" models is inadequate.

These considerations should caution us to be wary before assigning separate functions to various regions: not only is there extensive "cross talk" between anatomically separate regions, but similar signals may be present in several areas, suggesting that many computations are being executed in parallel within distributed networks.

## COARSE CODING

It seems clear that if IPL is to be involved in the coding of visual space and the programming of saccadic eye movements, it must use a strategy of distributed coding. Individual neurones are generally broadly tuned (chapter 3), and may thus seem inappropriate for subserving our exquisite spatial abilities (e.g., see Previc 1990). However, a population of broadly tuned units may represent a value with a resolution far beyond that of the individual units (e.g., see Bracewell 1990 in his commentary on Previc 1990). This has been termed "coarse coding" in the computer literature (Hinton et al. 1986) and the notion that neural representations may employ coarse coding has gained increased prominence in recent years (e.g., Lee et al. 1988; Heiligenberg 1990; Georgopoulos et al. 1982, 1983, 1986, 1988; Caminiti 1990, 1991).

The motor cortex (area 4) has traditionally (in single unit recording experiments) been studied in monkeys trained to make simple single joint movements. Experimenters have attempted to relate simple parameters of the movement (such as torque) with single unit responses (see Evarts, 1981, 1986, for reviews). However, Georgopoulos

and colleagues (e.g., 1982, 1983, 1988; Schwartz et al, 1988) have studied shoulder-related cells in area 4 during a wide range of reaching movements. In general, cells exhibited broad, approximately radially symmetric tuning curves centred on a given preferred direction. In the population, all possible directions were uniformly distributed. These findings have two important consequences. First, a given cell fires for movements over a wide range of directions, albeit with differing levels of intensity. Second, cells with many different preferred directions are active for a movement in any given direction. Therefore, it is likely that coarse coding is used in area 4 to control reaching movements.

Georgopoulos et al. (1984, 1988) used a vector notation to demonstrate that movement direction could only be specified on a population level. They assumed was that each neurone's contribution to the command could be considered as a vector oriented along its preferred direction, but weighted according to the level of discharge observed for that movement. The population vector was the sum of all such single cell vectors. A similar coding scheme was proposed for area 5 (Kalaska et al. 1983).

Saccade-related neurones in the superior colliculus are also broadly tuned, and this has lead to the suggestion that it too employs coarse coding in its representations (e.g., van Gisbergen et al. 1987; McIlwain 1991). Direct experimental evidence in support of this hypothesis has been provided by Lee et al. (1988). They inactivated small regions of the oculomotor layers with lidocaine, and observed alterations to saccades consistent with the notion that direction, amplitude and velocity of saccades depended on the weighted average of the vector contributions of all the active neurones.

## COORDINATE FRAMES AND THE REPRESENTATION OF EXTRAPERSONAL SPACE

Although visual information is initially encoded in the retina, and is represented retinotopically in many early stations of the visual pathways (e.g., Felleman and van Essen 1991), our perceptions and actions are not tied to this coordinate frame. When we move our eyes and heads in a stationary environment, the pattern of retinal stimulation must vary widely. However, we perceive the world as

stable. We can make accurate eye and limb movements to targets that had been seen when the eye or head was in a different location. These commonplace observations argue for representations of extrapersonal space in head- and/or body-centred coordinates. Such coordinate frames may also be useful for integrating information from different modalities, such as hearing. It is likely that such non-retinotopic representations underlie both our perceptual and motor abilities.

Clinical evidence suggest strongly that the PPC in man in plays an important role in such representations. Visuospatial deficits are frequently reported after PPC lesions (see chapter 1; Critchley 1953; Andersen 1987; Stein 1989; Husain 1991). Recent evidence suggests that hemineglect following unilateral parietal lesions may be manifest in head- or body-centred space, rather than a retinotopic one (Karnath et al. 1991; Ladavas 1990). However, the issue of what space is neglected is somewhat complex (see, e.g., Marshall and Halligan 1989; Ishiai et al. 1990) and beyond the scope of the present discussion.

Physiological, lesion and anatomical studies have also implicated the PPC in monkey in spatial functions (see chapter 1; Andersen 1987; Stein 1989; Husain 1991). Andersen et al. (1985b) demonstrated that visual receptive fields in area 7a are retinotopic, but that the response of a neurone to a given retinal stimulus depends on the eye's position in the orbit. This modulation seems to be, for the majority of cells, a linear function of both horizontal and vertical eye position, giving "planar gain fields". Computer simulations (Zipser and Andersen 1988; Mazzoni et al. 1991a, b) have shown that a population of such units could subserve a craniotopic representation of visual stimuli, as discussed above. We (chapter 4) have replicated the findings of Andersen et al. (1985b) in area 7a, and extended the analysis to area LIP. Moreover, we have studied the modulation of memory/motor intention activity (M) and saccade-related (S) responses in these areas. Again we found that the direction tuning of the visual (LS), M and S responses did not change with eye position, but that the *magnitude* of the responses did. This modulation was again well fit by planar gain fields. Recently, Galletti and Battaglini (1989) have demonstrated similar "gain fields" in area V3A (which projects into IPL). It is an attractive possibility that modulation of basically oculocentric signals by eye position may represent a common algorithm used in coordinate transformations of the sort discussed above.

## COORDINATE FRAMES FOR ARM MOVEMENTS

Soechting and colleagues (Soechting and Ross 1984; Soechting and Flanders, 1989a, b; Soechting et al. 1990; Flanders and Soechting 1991; Helms Tillery et al. 1991) have studied psychophysically the coordinate frames in which arm movements are encoded. They suggest that, for whole arm pointing movements at least, there is a shoulder-centric coordinate framework. Moreover, they have provided evidence that the remembered visual target for a pointing movement is represented in the same shoulder-centric frame of reference. This transformation of visual information would allow it to be readily compared with kinaesthetic information about the initial position of the arm. Thus the computation of the desired arm movement kinematics would be facilitated. Jeannerod (1991) has also stressed the importance of the commensurability of the representations of visual target and arm position.

Caminiti et al. (1990, 1991) have recorded from single neurones in motor and premotor cortex, and have shown that the population seems to encode for arm kinematics in a shoulder-centric frame of reference. Arm trajectory information is apparently combined in these areas with arm position information to yield an "automatic" updating of the frame of reference in shoulder-centred space. This has similarities with the combination of visual, motor intention and saccade-related activities (which are oculocentric) with eye position information to potentially yield head-centred representations in areas 7a and LIP (Andersen et al. 1985b; chapter 4).

## HEAD POSITION EFFECTS AND GAZE ENCODING

As discussed above, it is likely that we have body- in addition to head-centred representations of our extracorporeal space. An important extension of this work would be to investigate the role of head position on the responses of IPL neurones. Modulation of visual responses by head position would suggest that there does indeed exist such a representation. Preliminary data from Brotchie (pers. com.) suggest that there exist two populations of neurones within the IPL, one whose responses are modulated by eye position alone, and one in which the modulation is gaze-dependent (i.e., on a combination of eye and head position). It is thus likely that some of the units reported in chapter 4 as eye position dependent are actually gaze-angle dependent.

Another important issue is whether the "saccade" responses that we have reported are perhaps related to gaze shifts. Of course, since we conducted our experiments with the monkeys' heads fixed, gaze shifts and saccades were equivalent. When monkeys are allowed to move their heads ("head free" condition), they usually accomplish small (< 20 deg) gaze shifts almost exclusively with a saccade; larger gaze shifts are largely (about 80 %) accomplished with head movements (Tomlinson and Bahra 1986a, b).

Bizzi and colleagues proposed that eye and head movements were programmed independently (Morasso et al. 1973). An identical saccade command was thought to be issued regardless of whether the head moved or not. Were the head to move, vestibularly-induced compensatory eye movements were thought to be added linearly to the saccade signal.

However, behavioural and physiological evidence accumulated since the Bizzi "linear summation" hypothesis was proposed suggests that the situation is more complicated. Stimulation of the rostral deep superior colliculus (SC) in cat evokes "fixed vector" saccades, regardless of the initial eye position (Roucoux and Crommelinck, 1976). In head free cats, such stimulation only evokes eye movements, which are subject to modification by the vestibular ocular reflex (VOR) (Harris 1980; Roucoux et al. 1980). In contrast, stimulation of the caudal deep SC brings the eye to a fixed orbital location, regardless of initial eye position (Roucoux and Crommelinck, 1976). In head free animals,

stimulation there evoke combined eye and head movements that shift gaze by a certain vector. These saccades are not VOR-modifiable (Harris 1980; Roucoux et al. 1980).

In monkey, small gaze shifts (< 10 deg) are accomplished by saccades, which are VOR-modifiable. Large shifts (> 40 deg) are accomplished by combined eye and head movements during which the VOR is "switched off". The gain of the VOR appears to decrease as gaze shift amplitude increases from 10 to 40 deg (Tomlinson and Bahra 1986a, b). Lauritis and Robinson (1986) reported the related finding that during gaze shifts of > 40 deg, mechanical perturbations of the head were not compensated for. Tomlinson and Bahra also noted that as head velocity increased, eye velocity decreased (even when the VOR was inoperative), suggesting that the eye and head movements are not programmed independently. The human studies of Guitton and Volle (1987) support the notion that large gaze shifts are achieved by head and eye movements that are conjointly planned.

Whittington et al. (1984) have reported that some brainstem burst neurones fire seem to encode saccade metrics, whilst others encode gaze shift metrics.

In sum, there is a growing body of evidence to suggest that large gaze shifts are achieved by head and eye movements that are conjointly planned. It would be of great interest therefore to study the role of "saccade" cells in IPL (especially LIP) in gaze shifts. This could be achieved by training head free monkeys to make eye, head and eye/head movements to visual and remembered targets. It would be of interest were LIP neurones to burst for gaze shifts of a given amplitude, regardless of how they are accomplished. This would be consonant with the preliminary results reported above that some IPL cells are modulated with gaze angle, rather than just eye position. It would also suggest that LIP lies quite high in the hierarchy, issuing somewhat general commands to lower premotor areas. As we have seen elsewhere, LIP does not appear to be "concerned" with the precise details of movement execution.

It should be determined whether stimulation of LIP can evoke head as well as eye movements. Furthermore, it would be would of interest to compare the effects of stimulation of the same site in head-fixed and head-free animals: if the same gaze position were achieved, it might suggest that IPL is involved in issuing somewhat general commands to

foveate targets of interest.

## INTERSENSORY INTERACTIONS

It is an attractive hypothesis that we have a single underlying representation of extracorporeal space. Kant, for instance, believed that space is an innate organizing principle of the mind - a way of perceiving (see O'Keefe and Nadel 1978). It would, for example, facilitate our ability to associate that rustle of leaves over there with the glimpse of a predator. Not only would it be useful in our construction of our model of the world (Craik, 1943), but it would facilitate direction of movements within the world.

In chapter 7 we present evidence that some neurones in area LIP may represent auditory and visual targets in the same part of extracorporeal space equivalently. Multimodal neurones in the deep SC of many species also in general have similar excitatory receptive fields for the different modalities (e.g., Knudsen 1982; Stein and Meredith 1990). Similar results are found in the more exotic case of the infrared and visual bimodal neurones of rattlesnakes (Hartline et al. 1978). Maps of the different modalities in the deep SC are generally aligned, at least when the head is facing straight ahead (reviewed in Sparks 1986).

There is a rich body of psychophysical literature on localisation in different sensory modalities (e.g., Blauert 1983 for a recent review of spatial hearing) and on intersensory interactions (see Welch and Warren 1986 for a recent review). There is a consensus that vision provides the most accurate spatial information (e.g., Fisher 1960). Auerbach and Sperling (1974) have provided strong evidence that there is a common frame of reference for both auditory and visual localisation. It is of interest that several studies (e.g., Warren 1970) have shown that subjects localise (unseen) sound sources better when a textured visual field is present than in the dark. Platt and Warren (1972) went on to demonstrate that this facilitation was due to target-directed eye movements against the textured background (neither the background alone, nor target-directed eye movements in the dark provided facilitation). It would be of interest to compare the activity of IPL neurones in comparable conditions: one might predict more robust auditory responses when a textured visual background was visible than

in the dark (and concomitant improved localisation accuracy).

Vision appears to be the predominant sense in the setting up of maps in the tecta of various species. For instance, Knudsen (1988) has shown that the auditory map in the barn owl tectum is degraded in birds raised with both eyelids sutured, suggesting that early visual experience is vital for the development of the auditory map. This would seem consistent with the greater spatial acuity of the visual system.

## MOTOR SET AND THE INSTRUCTIONAL STIMULUS

Many authors have used variations of the delayed response task to study various aspects of the "cognitive processes" underlying higher motor control (see Evarts et al. 1984 for a review). Typically in such studies a sensory stimulus serves as a cue (the "instructional stimulus" or IS), informing the monkey of the action he is to perform, *after* a delay period. Clearly there are formal similarities with the delayed saccade task we and others (e.g., Funahashi et al. 1989, 1990) have used extensively. It is important to distinguish between transient activity related to the IS, and sustained activity during the delay period.

Transient activity related to the IS has been reported in the prefrontal cortex (e.g., Kubota 1985; Vaadia et al, unpublished, cited in Evarts et al. 1984), area 4 (e.g., Evarts and Tanji, 1974; Poranen and Hyvarinen 1982), supplementary motor area, SMA (e.g., Tanji and Kurata, 1982), area 5 (e.g., Seal et al. 1983) and the dentate nucleus (Strick 1983). We too have observed IS-related activity in areas 7a and LIP. What is intriguing about this activity is that it is usually motor-contingent, i.e., the stimulus only evokes a response when it is behaviourally relevant for the animal.

Sustained delay period activity has also been reported in many areas of the brain, e.g., the prefrontal cortex (Fuster 1973; Watanabe 1981; Joseph and Barone 1987), the nucleus dorsalis (Fuster and Alexander 1973), the inferotemporal cortex (Fuster and Jervey 1982), the hippocampus (Watanabe and Niki 1985), the auditory cortex (Vaadia et al. 1982; Sakurai 1990), the premotor cortex (e.g., Wise and Mauritz 1985), area 4 (e.g., Evarts and Tanji, 1976), SMA (Tanji et al, 1980), area 5 (Crammond and Kalaska 1989), the putamen (Alexander 1987), the

substantia nigra pars reticularis (Hikosaka and Wurtz 1983c), the caudate nucleus (Hikosaka et al. 1989), and the frontal eye fields (Funahashi et al. 1989, 1990). In some studies the authors have attempted to distinguish between sustained activity related to the IS and sustained activity related to the forthcoming motor response, e.g., Niki and Watanabe 1976a reported that about 75% of prefrontal cells exhibiting directionally-specific delay period activity were related to the IS (i.e., they were active after a given IS regardless of the movement it indicated) and about 25% were related to the forthcoming movement (i.e., they became active after whichever IS indicated a movement in a specific direction).

Wise and colleagues have performed extensive studies of motor set in the PMC (for review, see Wise 1985). Their most important finding is that, for most PMC neurones, the delay period activity is related to the direction of the forthcoming arm movement, and not to the IS: (1) Activity was related to movement direction and not IS location (Weinrich et al. 1984). (2) If the IS indicated that the monkey should withhold his movement, there was little or no activity; however, if an identical IS was a cue to move, it did evoke delay period activity (Wise et al. 1983; Weinrich et al. 1984). (3) Delay period activity does not depend on the continued presence of the IS (Wise and Mauritz 1985). (4) Wise and Kurata (1989) reported that "set-related activity ... can be directionally specific when trigger stimuli do not indicate the target and when a trigger stimulus is absent" (*p* 455). (5) In a study in which the IS was changed during the delay period, directionally-specific motor set units showed concomitant changes in activity (Wise and Mauritz 1985). This study is similar to our "change of plan" study, although we did not present our targets (ISs) for the whole duration of the delay period. However, result (3) suggests that continual presence of the ISs in Wise and Mauritz' experiment does *not* account for the change in activity with change in motor plan which they observed.

Alexander and Crutcher (1990a, b; Crutcher and Alexander 1990) reported directionally-selective preparatory activity in the SMA, area 4 and the putamen of monkeys performing visuomotor step-tracking tasks. Both movement- and cue-related activity were found. These three studies are discussed in "Hierarchies and distributed coding" (above).

Funahashi and Goldman-Rakic (1990) have used a delayed antisaccade task to distinguish between delay period activity related to

the visuo-spatial cue (about 75% of prefrontal cells tested) and activity related to the forthcoming saccade (about 25%). Kalaska and Crammond (1990) have used a similar task (except that the response is an arm movement rather than a saccade) in areas 5 and 6. They report that neurones show a transient cue-related response, but that the sustained activity is related to the direction of the forthcoming movement.

We propose to record from LIP whilst monkeys perform a delayed antisaccade task. We predict, on the basis of our hypothesis that neuronal activity in LIP reflects the next intended saccade, that a sizeable proportion of LIP cells will show activity related to the forthcoming saccade direction, and not to the cue location. The results of our back saccade (see chapter 3) and double saccade (see chapters 3 and 5) experiments suggest that this will be the case, since they show that LIP units become active before saccades into their motor fields, even in the absence of a stimulus falling in their receptive fields.

Thus in many higher motor areas, neurones may fire in relation to the IS and also during the delay period of various delayed response tasks. In many areas, the "sensory response" to the IS is often motor-contingent: the response only occurs if the stimulus is a cue to movement. Delay period activity has also been shown frequently to reflect the animal's motor intention. We have observed similar results in LIP. (1) Units there may show sensory responses to auditory cues for saccades. (2) Sometimes, the visual response of LIP cells is contingent on the forthcoming behaviour of the animal. (3) The M activity of LIP cells reflects the monkey's intention to make the next saccade.

Lesion, anatomical, stimulation, and physiological studies have suggested that LIP plays an important role in the sensorimotor transformations underlying the production of saccades to visual targets. Individual LIP units carry both visual signals related to target location, and motor signals related to the saccade to that location. Eye position strongly modulates the responses of LIP units. LIP connects with other saccade centres such as the FEF and SC. The visual responses in LIP may well reflect its role in the visual-to-motor transformations that programming a saccade entails. Auditory responses, on the other hand, are perhaps more likely to reflect IS or cue-like activity. The spatial attributes of the auditory stimulus are

likely to be calculated elsewhere in the brain, and this preprocessed information sent to LIP (and other areas) involved in saccade planning.

## A NOTE ON ATTENTION

It seems clear from the human lesion literature that the PPC plays a vital role in visuospatial attention (see chapter 1; Andersen 1987; Critchley 1953; Husain 1991; Hyvarinen 1982a, b; Stein 1989). It has also been demonstrated that attention does modulate the responses of PPC neurones (e.g., Robinson et al. 1978). A major criticism that has been leveled at the work from this laboratory and that of Mountcastle is that what we consider to be "motor" activity is in fact "sensory" or "attentional". This view is perhaps most clearly articulated by Goldberg and Robinson (1980). In part this view rested on the belief that "all cells associated with saccadic and smooth-pursuit eye movements could be driven by stimuli in the absence of movement" (*ibid*, p. 505). This sweeping statement now seems untenable (see, e.g., Mountcastle et al. 1980). We have shown that the visual and saccade responses of LIP units may be distinguished (see chapters 2-4) and that some units may also exhibit memory or motor intention activity in the absence of a sensory stimulus falling in the receptive field (see chapters 3 and 5).

However, it is worth considering whether the activity (especially the "memory" activity) that we have studied is more related to the shifting of attention than to the planning of saccadic eye movements (or *intention*) *per se*. The term "attention" has been used to refer to a number of different phenomena (see, e.g., Parasuraman and Davies, 1984). In the context of IPL function it is typically used to refer to the selective allotment of attention to a given position in space. The analogy of the "spotlight" beam has been frequently used (e.g., Crick 1984; reviewed in Umilta 1988). The question of the linkage of overt (gaze) and covert shifts of attention has received considerable experimental attention of late. Initial studies seemed to support the notion that humans can deploy visual attention covertly to one location and their gaze to another (Posner 1980; Klein 1980), but these experiments are somewhat flawed and the conclusions drawn from them have been called into question (see Umilta 1988 for a review). The current consensus seems to be that the relationship between

saccades and attention shifts is asymmetric: attention may be shifted in the absence of eye movements, but not *vice versa* (Shephard et al. 1986). Thus we indeed may be observing neural correlates of shifts in attention in LIP, but that may be, in a deep sense, inescapable. It is of interest that Posner et al. (1982) showed that patients with progressive supranuclear palsy are deficient in shifting attention both covertly and overtly (with saccades).

Recently, much interest has been generated by the phenomenon of express saccades. Both monkeys (Fischer and Boch 1983) and humans (Fischer and Ramsperger 1984) can generate saccades with very short latencies, given the correct training and conditions. It appears that the disengagement of attention *prior to the appearance of the target* is crucial for these short latencies to be observed. These and related observations have led to the hypothesis that the disengagement of attention is an *essential* step in the production of a saccade (Fischer 1987, Becker 1989). This is true even if attention has already been deployed to the target location (Mayfrank et al. 1985, Fisher and Breitmeyer 1987, Braun and Breitmeyer 1988). Therefore one might expect a neuronal "attention" signal to be attenuated prior to a saccade. The signals we observe in LIP typically show the opposite behaviour: there is a saccade-related burst of spikes at a frequency clearly above that maintained during the memory period in our several paradigms.

The results of our various double saccade experiments (chapters 3 and 5) may also pose some difficulties for an attentional account: presumably a monkey attends to both targets in double saccade tasks, and yet we observe, by and large, activity related only to the forthcoming saccade.

We have shown that the M activity tends to be directed further upward than the LS activity in LIP neurones (chapter 9). This neural upshift is in accord with the behavioural upshift we have observed (chapter 8). It seems to reflect the animal's *intention* (to make a certain saccade) better than his attention (which is presumably to the target location).

# POSSIBLE FUTURE EXPERIMENTS

## Vergence and saccades

It was commonly held that saccades and vergence eye movements are controlled by separate systems. When a subject was required to look from one target to another at a different distance and angle from him, it was thought that the necessary vergence and saccadic (version) movements were programmed separately and executed in parallel. However, it is now clear from the work of Enright (1984, 1986) and Erkelens et al. (1989) that a substantial proportion of the required vergence change is actually effected by programming saccades of different amplitude for the two eyes (see also Bracewell et al. 1991). Lesion and physiological studies have shown that IPL plays a role in depth perception (see chapter 1), and the control of vergence (Sakata et al. 1980; Gnadt and Mays 1989) and of saccades. It would therefore be of great interest to record from IPL and monitor the positions of both eyes whilst the monkey was making saccades between targets at different distances from him. If IPL is indeed involved in the coding of 3 D visual space, as both lesion and physiological data suggest, then it would seem a likely place for combined vergence-saccade movements to be planned.

## Learning and area LIP

We and others have shown that neurones in PPC will respond to sensory cues to which they are normally unresponsive if they serve as cues to movement. If it proves practical to train monkeys quickly to associate arbitrary cues with given movements, one could record from LIP neurones whilst training a monkey on such a task. For instance, once a neurone with strong memory activity for upwards memory saccades had been isolated, one could then train the monkey that the fixation light turning colour to red indicated an upwards saccade. As the monkey learned the task, one might predict that the neurone should start to respond to the change of colour of the fixation light.

### Saccadic adaption

Humans (e.g., McLaughlin 1967) and monkeys (e.g., Fitzgibbon et al. 1986; Albano and King 1989) can rapidly (within a few hundred trials) adapt their saccadic gain when a consistent intrasaccadic target displacement occurs that causes a saccade to short of, or beyond, the final location of the target. Fitzgibbon et al. (1986) stimulated the superior colliculus before, during and after the adaption. They found that electrically-evoked saccades were unaffected by the adaption process. This suggests that higher centres are involved in the adaption process whereby a 20 deg target leads to, say, an 18 deg saccade. It would be of interest to record from and stimulate LIP before, during and after the adaption process, to see whether it might show the appropriate plasticity to underlie such adaptive behaviour. We have seen that it is an attractive possibility that LIP is involved in the visuo-oculomotor transformations that underlie the production of saccades to visual targets. It might therefore be a good candidate for plasticity in the adaption paradigm. Weinberger et al. (1990) have demonstrated that it is feasible to record rapid changes in receptive field properties in the auditory system during associative learning.

### Attention and intention experiments

We have suggested that "memory" (M) activity in area LIP is a reflection of the motor intention of the monkey to make the saccade into its motor field. We have noted ("A note on attention") that there is an alternative interpretation of the role of memory activity: it might be due to the monkey's deploying his attention to the location in which the target was presented. In the discussion of chapter 8, we suggested a psychophysical experiment designed to investigate the possibility of a "perceptual" upshift. In this experiment, a peripheral target would be presented briefly. After a memory period, a second target would be presented at the same location (or slightly above or below it) and the monkey would be asked to judge where the second target had appeared with respect to the first. Throughout the trial the monkey would be required to maintain fixation on the central fixation spot. Presumably, the monkey would deploy his attention to the peripheral location in which the first target was presented. If the

memory activity is indeed a neural correlate of attention, then one would expect to see memory activity during such trials. If, however, the memory activity is related to the intention to make a saccade, then there should be no memory activity.

**Functional properties of corticotectal neurones in LIP**

We have noted that there is strong projection from LIP to the motor layers of the superior colliculus (SC) (Andersen et al. 1985a; Lynch et al. 1985). It would be of great interest to study the physiological responses of identified tectal-projecting cells. Such cells could be identified by antidromic stimulation from the SC. A similar experiment has been conducted in the frontal eye fields by Segraves and Goldberg (1987). They demonstrated that there is a selective enrichment (relative to the total population of FEF cells) of movement-related cells in the tectal-projecting group.

**Auditory coding in PPC**

We have observed auditory responses in area LIP during auditory memory saccades (chapter 7). However, in these experiments we did not investigate the coordinate frame in which this activity was coded. Leinonen et al. (1980) reported auditory responses in area Tpt (see chapter 7). They suggested that these responses were in head-centred coordinates, but failed to control for eye position. It would be of value to investigate in what coordinate frames auditory information is coded in the PPC. It is an attractive possibility that it is essentially "retinotopic" but modulated by eye position, as visual responses are, in areas 7a and LIP (see chapter 4). Such a representation might at first glance seem unlikely (as sounds are initially encoded with respect to the head). However it would be compatible with the representation of visual targets in these areas, and thus might facilitate the programming of saccades (and other movements), since the same algorithm for sensorimotor transformations could be used for targets of both modalities.

Other examples of the remapping of auditory information into a different coordinate frame include the deeper layers of the monkey SC (Jay and Sparks 1984, 1987a, b).

In contrast, one might speculate that area Tpt does indeed encode sound location in a craniotopic frame. It lies closer to the auditory cortex (review in chapter 7) and may have more purely "sensory" responses than area LIP

**Comparison of memory activity during reaching and saccade tasks**

In the experiments detailed in this thesis, the motor response has always been an eye movement. We have proposed that the memory activity which is manifest by many LIP neurones in our tasks reflects the monkey's intention to make a saccade. How specific is this motor intention activity? Does it reflect a general intent to "acquire" a target of interest, whether by a saccade or an arm movement? (Such neurones have been reported in the prefrontal cortex by Mann et al. 1988). Or is it specific to eye movements?

A monkey could be trained to make either saccades or reaching movements to the remembered location of a stimulus presented on a monitor with a touch pad on the surface. The appropriate response could be indicated by the colour of the fixation spot. During reaching trials, the monkey would have to maintain stringent central fixation. The levels of memory activity during reaching and saccade trials could be compared. If these responses are similar, it would suggest that the neurone was involved in formulating a somewhat general motor plan. If the responses were specific, it would suggest that the plan is response-specific.

Lamarre et al. (1985) reported cells in area 7 that responded to stimuli if they were the target of an eye movement, but not if a reaching movement was made.

Batuev et al. (1985) reported that a small proportion of cells in area 7a that had "spacioselective" delay period and cue responses in delayed-response tasks. Also, Alexander (1982) reported delay period activity from rostral area 7a during delayed response tasks. This area connects with the principal sulcus (reviewed in Goldman-Rakic 1988), where neurones with spatially selective delay period activity in arm movement tasks have been found (e.g., Niki and Watanabe 1976; Kojima and Goldman-Rakic 1982).

It is thus possible that area 7a plays an analogous role to area LIP, but in the domain of arm movements.

If response-specific memory activity was observed, it would also

argue against an "attentional" explanation of memory period activity (see "A note on attention", this chapter).

## A CLOSING WORD

I hope to have conveyed some of the excitement of working in this fascinating area of the association cortex. I foresee the "present wide interest" in posterior parietal function continuing and, indeed, growing.

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