XX. NEUROPHYSIOLOGY[*]

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A. FORM-FUNCTION RELATIONS IN NEURONS

Nerve membrane communicates with itself by means of electric currents flowing from one part to another. The current is generated by a system of charge separation whereby the two major cations, K^+ and Na^+, can be gated differentially through the membrane. Since there is an energy storage across the membrane in the form of a concentration-difference cell, the differential gating can be used to produce current. The energy storage is achieved by an ion pump, driven by metabolism, which expels Na^+ from the inside of the cell. The Na^+ current generator runs continuously and is balanced by the passive diffusion of Na^+ across the membrane. This distributed current generator sets up an IR drop across the membrane through the passive diffusion path, and the potential thus obtained across the membrane drives the freely diffusible ions, not pumped, such as K^+ and Cl^-, to that equilibrium at which the potential between their concentration within the cell and without balances the potential generated by the pump system. Thus, the energy storage is in part in the Na^+ concentration difference, and in part in the concentration of the ions at equilibrium with the membrane potential. There are two possible effects from gating ions. If one gates an ion species at equilibrium with membrane potential, there is no change in potential and no current flow. (Under conditions of applied external current, the increase of K^+ conductance shows up as a shunt across the membrane.) If one gates the ion with which the pump sets the membrane potential, then the membrane potential alters violently, for it will tend to come to the concentration potential of that ion species and there will be a current of that ion. For example, Na^+ has been pumped out of the cell against a gradient, until its diffusion into the cell equals the rate at which it is extruded. If the rate at which it can diffuse into the cell is then increased, the membrane potential changes and also produces an Na^+ current. Thus, as far as one piece of membrane can affect another electrically, it does so either by gating Na^+ ions and thus serves as a current generator, or by gating K^+ (or Cl^-) and thus serves as a shunt (or both and serves as a partially shunted current source). Under these conditions, I suggest that subthreshold excitatory events tend to

add to each other in a receiving cell, whereas an inhibitory event tends to shunt, or divide, the excitation rather than subtract from it. This, in fact, seems to occur experimentally — in the well-known studies of Kuffler and Eccles on the character of inhibition.

If the very cursory discussion given above gives a true picture, then the placement of synapses on a dendrite is not permutable. For, suppose that a single dendrite leads to a cell body. Let an excitatory synapse occur at the tip. An inhibitory synapse anywhere between the tip and the cell body will attenuate the excitatory signal. But if the inhibitory synapse also occurs distally, then excitors closer to the cell body will not be shunted by that inhibition. Rather, the constellation of inhibitors and excitors in the distal portion of the dendrite, decoupled from the cell body by the resistive path down the dendrite, will act as a current source of variable strength. The signal from this current source will be additive with that from the more proximal excitors. We already have experimental evidence to show additive and divisive inhibitions in the same cell. One should then be able to determine the crude order of connectivity to a cell by exciting its inputs by pairs. With this hypothesis, the effect of the array of endings along an idealized single dendrite is expressible crudely in terms of a set of nested fractions, as in the familiar Euclidean algorithm. But as soon as one considers a dendritic tree, the complexity increases greatly, and it is obvious that the nest of nested functions so expressed is dictated by both the geometry of the tree and the order of its inputs. Thus, without any special appeal, or without requiring an exact statement of the character of synaptic transmission, but simply by virtue of the electrical effects that one piece of membrane can have on another, it is possible to show that the anatomy of a dendritic tree has a necessary relation to the function taken by that tree, and also that one can synthesize such complex functions by the arrangement of current sources and shunts in a resistive tree. But the implication is also that any function that can be expressed by a fractional expansion can be expressed by a dendritic tree and a particular order of inputs.

If every dendritic tree can be so considered — and this is the fundamental meaning of our work on frog vision — then the whole character of a nervous system becomes expressible in certain general terms.

Let us consider the simplest case — that of a sheet array of neurons, each with an arbor that extends in great overlap with those of its neighbors, and let all arbors be of the same sort, i.e., let each perform the same operation on the input. Let the synaptic input be an array of an arbitrary number of types of elements with the only stipulation being that each type be uniformly distributed, i.e., a particular kind of input ought to have the same density everywhere and end in the same relative order with respect to other inputs on the dendritic trees. If the input maps the distribution of qualities in an image of the external world, for example, as rods and cones map the distribution of light and color, then the output of the neuron sheet expresses two sorts of things. A

single neuron enciphers in its firing the presence of the sort of arrangement that its
dendritic tree perceives as a positive value of the function which it is built to calculate.
This response indicates that in the neighborhood of the center of the dendritic tree a
particular event occurs. Thus the arrangement of exciting events in the image of the
world is mapped into a distribution of excitements which preserves the order and dis-
tances of those events. But the meaning of a point in the space given by excitements
is not simple. For the nervous array, any point in the image has two meanings. First,
that it is or is not in the neighborhood of an exciting event and second, that it has a
particular position in space. The first meaning is embodied in the firing of neurons
that see this point in common. The second is embodied in the center of a single dendritic
tree. Thus, the local properties of a representation taken by a neuron are not to be
extended. No continuum need exist, and in general does not exist, between the local
function given by one dendritic tree and the distribution in space given by the order of
excited neurons.

This variety of what is called, I believe, the discrete manifold has spatial properties
that are different from those that can be obtained from a continuous manifold. Notably,
regions and operations can be connected arbitrarily without having to worry about
what to do with the in-between, which is a bother with a continuum. Thus one constructs
hierarchical layers of neurons.

This report is very short, but represents much of the substance of a longer paper
that is in preparation.

J. Y. Lettvin

B. OLFACTION

After R. C. Gesteland completed his thesis, we decided to plan the work on smell
for effortless recording over a long term, since with this sensory modality, more than
with any other, secular variations of the response to stimulus, early fatigue, and enduring
block from overstimulation cause difficulties in recording which, however convincing
the pictures may be to an experimenter, obscure the lucid and compelling details from
the casual observer. That problem, far from being confined to our work alone, is native
to the whole field of nervous physiology, and plagues alike those who penetrate the brain
and those who specialize in the peripheral nervous system. All find it troubling to sepa-
rate the signals from different nervous fibers that are seen commonly through the same
electrode, and some have even resorted to computer analysis. It is not unusual to find
that what might evade the eye is discovered readily by digital manipulation, given enough
words and time. But there is a simple pleasure in coupling immediately and discrimi-
natingly to raw events. It is also cheaper.

If several axons are being recorded at the same time through one electrode, their

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impulses may be distinguished not only by height but by shape. In unmyelinated fibers the impulse may be as long as 5-7 msec, may be monophasic, diphasic or triphasic (determined by the degree of blocking of the fibers by the electrode), and may be of either polarity or sequence of polarities (determined by the local boundary conditions). It is never hard to separate one fiber from another if the time base is fast enough to allow resolution of shape. But the rate of firing of the several units rarely exceeds 10 per second, and then only with a strong stimulus. Recording events so widely spaced on fast-moving paper or film is not only wasteful but also fatiguing to read later. Because all of the impulses lie within essentially the same frequency band, filtering to improve the signal-to-noise ratio leads to making the transients look more alike and washes out small differences that may be useful in separation. The best strategy that we have found is to record from the nerve broad bandwidth, and to trigger an electronic switch from signals of a particular polarity which exceed the peak-to-peak noise. The electronic switch couples the signal into the recording system for a prechosen interval, say, 3 msec, and then decouples the signal from the record. At the same time as this "window" filter is set off, the same trigger starts a ramp function of the same length as the window. The ramp is added to the time base, so that the record, going on as slow a time base as one wishes, exhibits transient dilatations of the time base to resolve the shape, as well as the height, of the transient. The results are very elegant. The circuit is a simple modification of a commercial instrument. This circuit makes possible meaningful recording from a mixed group of neurons.

<div style="text-align: right">J. Y. Lettvin, R. C. Gesteland</div>