

# 18. Physiology

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## 18.1 A Control Process in Cell Membrane

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In dealing with nerve membrane, Hodgkin and Huxley described three voltage-sensitive controls that played on the same switchable ion-specific pores which, in turn, governed the membrane voltage by the ionic currents that passed through them. The regenerative part of the action with respect to the  $\text{Na}^+$  pores makes the nerve membrane a blocking oscillator or pulse generator, while the degenerative action with respect to the  $\text{K}^+$  pores speeds the recovery. But although the switchable pores (two-state — patent or sheet) were directly inferable from the Hodgkin-Huxley data and abundantly studied since, the V-sensitive controls remained mysterious.

Two types of research done later seemed highly relevant to a mechanism of control. One type, done by Frankenhaeuser and Hodgkin originally, showed that the voltage-sensitive controls were systematically related to the concentration of the  $\text{Ca}^{++}$  in the medium bathing nerve membrane. The other, done by two groups, Armstrong and Bezanilla as well as Keynes and Rojas, showed a voltage-sensitive capacitance in nerve membrane. By measuring the change in amount of charge stored or released by membrane as a function of membrane voltage, they described an increment that, when plotted, was eminently Boltzmannian but had an inexplicable coefficient.

On considering such data, we concluded that  $\text{Ca}^{++}$  could be coordinately bound to or released from membrane surface by the field across the membrane. So much could have been inferred, in fact, from experiments on monolayers done ca. 1930, but the mechanism was not obvious.

Knowing the Hodgkin-Huxley model and the studies mentioned above, we postulated the existence in the membrane of a compound with certain specific properties. To our surprise the compound actually exists, and its chemical composition is completely known. Very little search served to identify it once the necessary properties were given. It makes a well-defined

electromechanical transducer for membrane voltage in the presence of  $\text{Ca}^{++}$ ,  $\text{Mg}^{++}$  and other divalent cations.

Our hypothesis was verified not only by the computed characteristics of the compound but by a space-filling model that, when assembled, showed the electromechanical action vividly. Such an action can be used to govern the opening or closing of pores, the activation or shutting off of enzymes and a host of other membrane processes, making of them charge-coupled devices. The control action is then not limited to the special case of nerve membrane.

Using the kinetics that led to our identification of the compound, we have fitted closely the data (not the analytic expressions) published by Hodgkin and Huxley. But we view such a control system as being ubiquitous and active in almost all cell membrane.

## 18.2 The Problem of Color Constancy

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It is well-known that under daylight conditions, the colors of objects remain unchanged, although the spectrum of daylight changes. It is equally well-known that shadows are often colored. The former is called "object color constancy", the latter "simultaneous contrast". Both have been brilliantly exhibited in the displays made by Dr. Edwin Land.

Given the chromatic information in the retinal image, it is obvious that one must pay for seeing object colors as constant by seeing more vivid color changes in the illuminants, so that color constancy and simultaneous contrast are obverse aspects of the same process.

The attitude of research workers in this field is influenced by Helmholtz' comment that we see the world as if discounting the illuminant. He supposed that this perception is a so-called "higher-order" operation, in that it seems to involve memory, will, expectation and the like. But Professor Land successfully challenged this view by his assemblies of mutually bounding polygons (which he called "Mondrians"), in which there was no experiential basis for supposing any polygon to be a particular color. Such displays show the conditions under which both color constancy and simultaneous contrast occur. His theory, couched finally in an algorithm, makes the color of any area in the visual field determined by three independent operations over the whole field, reflecting the three degrees of freedom given by the pigmentary actions of the three

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types of cones. Such operations are, while preconscious, necessarily of higher order and, so, must occur in the brain where it is possible to compare parts from the whole visual field. These operations comprise his "retinex" theory.

But it seemed to us that color, being the primitive quality by whose spatial and temporal change we perceive objects and motions, must be computed early, before form and texture are processed from the image in terms of color changes at boundaries. So we sought a mechanism whereby the necessary operations could be done by the cones themselves. These operations do not provide color directly, but couch the data in such terms as already embody both color constancy and simultaneous contrast.

Our experiments, some of which are to be published in *Scientific American* later this year, require color printing and so cannot be shown here. They do not contradict the observations of Land, and before him, Helmholtz, but rather put them in a new perspective.

The first thing to realize is that the daylit world imposes some remarkably limiting constraints on images. These constraints make color constancy possible if we want to make the seen colors of diffusely reflecting surfaces somehow represent the reflectances rather than the light reflected. Two of the constraints are simple, the third complex.

1. The dynamic range of reflectances seldom exceeds a single decade, e.g., new snow reflects above 95% of the incident light anywhere across the spectrum. Natural black surfaces, such as black loam or coal, seldom reflect less than 10% of the incident light anywhere across the spectrum. The blackest ink on whitest paper is rarely greater than a 1:9 range, and then only directly after printing. All natural reflectances are mostly diffuse, the specular component (highlight) being a small fraction of the incident light, and the surfaces are generally rough in the fine, so that the diffuse reflection from any part is more or less homogeneous over a solid angle that is almost a hemisphere. This confinement of all reflectance spectra in the natural world to a decade at most is important to the design of photoreceptors.

2. When the spectral composition of daylight (400  $m\mu$  to 70  $m\mu$ ) is plotted over the visible range, the function is remarkably smooth and, at most, only slightly curved. Most of daylight variation can be described as a tilting of that envelope, or a slight bowing of it. Thus the redness under a misty sunrise or sunset tilts upward the long wavelength end; the blue sky with the sun obscured tilts upward the short wavelength end; the light under a leafy bower bows upward the midpart of the envelope. All such variations compared to the spectrum of sunlight and plotted, normalized, against the content at 500  $m\mu$  produce a sheaf of spectral envelopes that lie completely within a 10:1 range all along the spectrum. Thus, while the dynamic range of daylight under which we see color can vary over four or five decades, the normalized spectral envelope lies within one decade.

3. Finally, the world being a kind of determined chaos, the distribution of reflectance spectra in

any portion of the scene is most likely to average out to some neutral spectrum approaching that of the normalized spectrum of the illuminant. Furthermore, in that objects are opaque and occlude each other by interposition according to distance, the boundaries between things are more commonly terminated by third-order vertices. Fourth-order vertices, where four independent reflectances are represented in the image by four areas meeting at a point, are of measure zero. So also are annuli — i.e. doubly bounded areas in an image.

These several constraints are consonant with the strategy of our photoreceptors. Without pursuing the mechanism in detail, our cones act as if the signal they generate is, as Norman and Werblin found physiologically,

$$S = \frac{A - B}{A + B} = \tanh \frac{1}{2} \ln \frac{A}{B}$$

where S is the signal value, A is the present value of light and B is a running history of past values. A can be called the stimulus, B the adaptation. Under any steady state,  $S = 0$ , and over the range of step changes in light,  $S \sim \ln \frac{A}{B}$  within a decade centered on 0 and begins saturating for larger steps. If A is the value of light on a single cone but B is the averaged value of the running history among all the neighboring cones of the same type within a fair area of retina, we have the function needed for attaining color constancy. Adolph Cohen showed that cones of the same type are connected by gap junctions between the inner segments, so that we know cones are laterally connected ohmically. William Rushton showed that the adaptation produced by a bright line flashed on the retina spread  $\frac{1}{2}$  degree to each side of the line. Thus, the empirics support the idea that while A can be locally defined in space and time, B is broadly defined in terms of area and history.

In short, the value of the response of a cone type depends on the current value of the light on the cone and the running value of the history of light on all like cones in the neighborhood, including the cone itself. The adaptation, B, is history-dependent and, so, is not limited to the area where A is being taken.

Since by the diversity constraint in the image the running history in the three types of cone will average to something very close to the illuminant over the region seen, there is automatically the basis for an approach to color constancy. The ratios of reflectances across boundaries and around vertices provide the information about reflectances. Since reflectances are limited in dynamic range to within a decade, the cone mechanism accommodates them. The higher the local diversity, the more specific does each chromatic triple of cone values (including adaptation as well as instantaneous light) become in relation to the reflectance that the triple represents. And the more comparisons in the local image, the more definite yet are those values.

It were idle to pursue this more extensively without recourse to the illustrations that show the

role local diversity plays for the seen color of a polygon in a plenum of polygons. A detailed account (of which this is a preliminary sketch) is to appear shortly — together with the simple mechanism that provides the basis of both color constancy and simultaneous contrast as functions of cone action. The mechanism can be inferred from the nature of  $S = \frac{A - B}{A + B}$ .

### 18.3 Peripheral Vision

*The Rowland Foundation, Inc.*

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Objects of about the same size and complexity but different in form mask the perception of one another when they are clustered. This is most apparent in peripheral vision. It is the basis of Julesz' theory of "Textons". We have discovered that the transient presentation of a form at the center of gaze transiently enhances the same form in a cluster eccentrically seen, demasking that form. We have established this action by a set of experiments and in doing so have discovered a startling point. Subjects who are now dyslexic, or have been so in the past, do not experience this lateral masking in a cluster anywhere as strongly as do normal subjects. It is as if the cone of attention that suppresses perception of the surround is somehow not operating as distinctly.

We are pursuing both the demasking and enhancement actions further, but with careful and extended study paid to the interesting subgroup of dyslexics.

### 18.4 Frog Vision

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In the receptive field of type II fibers from the optic nerve of frog, there is a complex computation made that needs further description than was given in the original paper (1958). Suppose we offer a black spot on a white background to the center of the receptive field. There is a vigorous response. The spot is not moved but is suddenly exposed against a previously all white background. If two spots lie in the center of the field, the response is less vigorous. If three or more spots are presented, there is little if any response. This does not depend on the configuration of the three spots or their size over a wide range, but only on the number. If the three black spots are connected by thin black lines so as to present a single black phase, the response returns.

The computation underlying phase counting, which is the simplest way to describe what we observe, is done entirely in the retina and depends critically on the sharpness of the image in the frog's eye and the physiological state of the animal. As the sharpness is lessened or the frog preparation is deteriorating, the clarity of the effect becomes compromised. This is the first fact for our argument.

The second fact does not seem much related *ab initio*. It was shown anatomically first by Dr. Edward Gruberg, working in this laboratory, and now is given in far more detailed form by Dr. H. Karten in a paper now in press. The four optic nerve maps that lie in registration at different depths in the thick plexiform layer of the tectum are interdigitated with maps of like character (in terms of receptive field function) that arise from the ipsilateral nucleus isthmi, the "slave nucleus" for the optic tectum. Where the optic nerve fibers are excitatory in function, the fibers from n. isthmi are inhibitory. This alternation of function can be seen by physiological recording. If n. isthmi is ablated, as Gruberg has done, the animal acts almost blind except for gross light and dark detection. This is fact two.

What seems to be the case in the tectum is that accurate vision depends on attenuative functions that have the same kind of information as the excitatory representations. In the retina we find a set of cells whose dendritic topologies mirror those described for ganglion cells. That set is the amacrine cells. We are now persuaded that if amacrine cells are inhibitory to ganglion cells in the retina, function by function, as are n. isthmi cells to tectal cells in the brain, it is possible to shape such operations as phase-counting in a receptive field.

This problem requires a model that is now being devised.

The basis for this venture is a major discovery in this laboratory. The nervous impulses recorded in tectum are not generated by entering fibers. They are local dendritic responses in the receiving cells. These dendritic responses are sharply limited to the region of synopsis — they do not propagate. What we have been able to show is that such transients occur only with excitatory synapses. As expected from the descriptions of currents flowing through open  $K^+$  pores or  $Cl^-$  pores (those implicated in inhibition by shunting), there are no recordable electrical transients from dendritic patches that receive inhibitory synapses. We are submitting this finding for publication soon. It brings a new technique to the analysis of signals recorded in neuropil.