

## XXIV. NEUROPHYSIOLOGY\*

### Academic and Research Staff

Prof. J. E. Brown  
Prof. J. Y. Lettvin  
Dr. E. M. Ettienne

Dr. E. R. Gruberg  
Dr. S. A. Raymond

B. Howland  
Janet MacIver  
Rosalyn V. Stirling

### Graduate Students

R. E. Greenblatt  
I. D. Hentall  
C. D. Jones

J. E. Lisman  
M. Lurie  
K. J. Muller

J. F. Nolte  
R. S. Stephenson  
Susan B. Udin

## RESEARCH OBJECTIVES AND SUMMARY OF RESEARCH

### Part A

1. During the past year we constructed an analog model for nerve membrane that in an elegant way and with very few components matches, almost to an identity, the Hodgkin-Huxley equations. Basic to the model was the concept that the adsorption of  $\text{Ca}^{++}$  to the surface of the membrane could be varied by changing the field across the membrane. While the predictions by this model have turned out to be good, the basic experiment suggested by it remains to be done, i. e., to show that the adsorption of cations to a bimolecular leaflet of, say, phosphatidyl-serine can be changed by trans-leaflet voltages. We shall be working on this point during the coming year.

2. The hypothesis that culminated several years of work, namely, that the tele-dendron axon is a shaped filter in the time domain, and is capable of transforming purely temporal codes on the parent axon into temporo-spatial codes in the termini, now seems to have much supporting evidence. The theoretical problems posed by this idea, however, at least in our hands, are incurable. One of the questions that looked tractable was whether a simple set of rules for recursive operations could be defined so that an axon would grow into a branching system that in some vague way did a good job of separating the various statistical messages that could be shown in the pattern of firing of the parent axon. It appears now that there are, or might be, such simple rules; they have been arrived at not a priori, but with a certain amount of playing around on computer models. Our feeling has been that with such rules carried genetically, the fine structure of a nerve system need not be specified branch by branch. Further study on this problem is to be done this coming year.

3. In the late thirties and in the forties, Professor Paul Weiss advanced the hypothesis that neurons forced to a destination other than the normal would reconnect themselves to inputs appropriate to the new destination. There has been much argument over this hypothesis but surprisingly little discriminatory work. We are beginning a set of studies in amphibian colliculi to test whether reorganization of perverted brain tissue is due to reconnection or to neuronogenesis, using tritiated thymidine as marker.

4. Because of some questions concerning the nature of receptive fields in cat retina, one of the doctoral candidates is restudying these fields.

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5. The tissue culture studies on cockroach ganglia are still proceeding, but there are no clear-cut results yet.

6. A prolonged experimental series on the threshold of myelinated nerve fiber is almost concluded. The aftereffects on threshold of a single impulse can be tracked up to a minute, and aftereffects of a burst at physiological frequencies can be tracked up to 15 minutes. In the light of findings by Mullins<sup>1</sup> that the membrane pump is absolutely unaffected by membrane voltage, we must now engage in accounting for these long fluctuations without the use of the pump as a deus ex machina.

7. The coding of taste fibers, while studied grossly in terms of average frequencies, has not been studied carefully in terms of fine structure of pulse intervals. One of the doctoral candidates is engaged in this research, at present.

8. Several ancillary projects are going on. One has to do with the analysis of animal sounds. A preliminary publication by a student from Rockefeller University, who was associated with our laboratory during the past summer, will show our method of real-time analysis of whale sounds. The same technique is being applied to the study of other animal sounds.

Along with the projects listed above, we are doing a fair amount of instrumentation and some new devices have appeared. A few of them may be of clinical use, and we are now examining this possibility. The instrument used for the analysis of speech and animal sounds may be equally useful for diagnosis of chest and heart sounds.

J. Y. Lettvin

References

1. L. J. Mullins, Private communication, 1970. (This material is to be published soon.)

Part B

Our work on the generation of receptor potentials in photoreceptor cells is proceeding along the following lines.

1. In collaboration with John E. Lisman, we have voltage-clamped single photoreceptor cells in the ventral eye of Limulus. In dark-adapted cells, we recorded spontaneous discrete waves in the clamping current. These discrete events correspond to the "quantum bumps" seen in the records of membrane voltage reported by other workers. We can elicit one such "bump" in the clamping current (of average amplitude and latency) with a brief, dim flash. When we double the intensity of that flash, the amplitude of the induced clamping current doubles. That is, there is a linear relationship between light intensity and membrane current; this linear relationship extends over more than two log units. For brighter lights, the amplitude of the light-induced current begins to saturate, and the latency is decreased; however, the membrane current remains a linear function of intensity for early times on the rising phase of the response. We plan to continue the study of the "quantum bumps," using the voltage-clamp technique and statistical methods.

2. In collaboration with John F. Nolte, we plan to continue the study of the physiology of the median ocellus of Limulus. We have determined the spectral sensitivity of the depolarizing receptor potentials recorded from single photoreceptor cells. There are two populations, one speaking at 525 nm (Visible cells), the other at 365 nm (UV cells). We have now determined that the spectral sensitivity of the repolarization of the UV cells, when long wavelength light is superimposed on a steady UV stimulus, peaks at 480 nm. Thus, this hyperpolarizing component of the receptor potential (i. e., repolarization) cannot arise by synaptic interaction with the visible-cell population. To explain these data, we hypothesize that there are two states of the same photopigment

each coupled to the physiological membrane processes that generate receptor potentials. We plan to continue the study of the median ocellus to determine the physiological relationships between pairs of cells, each impaled with a microelectrode; the cells will be marked by intracellular iontophoresis of dye molecules.

3. In collaboration with Professor Charles E. Holt III, of the Department of Biology, M.I.T., we plan to continue the study of ion fluxes in the photoreceptors of the ventral eye of Limulus. We have found that there is a large light-induced increase in  $K^{42}$  efflux in the cold (at  $2^{\circ}C$ ), if the eye has been dark-adapted. This result was not expected, based on the proposed involvement of active transport (enzymatic) processes in the generation of the light response. The active transport might reasonably be assumed to be negligible at  $2^{\circ}C$ . We have also measured a large receptor potential at  $2^{\circ}C$ , recorded from dark-adapted photoreceptor cells by means of microelectrodes. These data indicate that perhaps active transport is not required directly for the generation of the light response. We plan to continue the study of potassium fluxes and to attempt to study the movement of sodium ions in the ventral eye photoreceptors by injecting labeled  $Na^{+}$  into cell bodies via diffusion down their axons.

J. E. Brown

