Biophysics

Topics dealing with past and current biophysical research were discussed at an international meeting of the Commission on Cell and Membrane Biophysics and the Commission of Communication and Control Processes in Biophysics of the International Organization for Pure and Applied Biophysics, held in Paris and Orsay, France, during the week of 22-27 June 1964. M. F. Perutz delivered the opening lecture. In the context of communication between heme groups and the control of hemoglobin's primary functions, the celebrated work of Perutz and Kendrew and their colleagues on the structure of myoglobin and hemoglobin was reviewed. Perutz presented new evidence showing that there are significant structural differences between the oxygenated and reduced hemoglobin molecule. Evidence is clear that in the transition from the oxygenated to the reduced state, the two β -chains move apart by about 7 Å. However, the structural change is dependent upon the presence of the α -chains because no such change is observed in hemoglobin H, a tetramer of β -chains. Undoubtedly, this structural change is associated with the cooperative heme-heme interaction.

B. Pullman discussed aspects of molecular orbital calculations bearing upon the electrical structure of nucleic acids. He drew particular attention to possible implications of charge transfer of different organic conjugated systems (in particular, the aromatic hydrocarbons, the amino acridines, and actinomycin). A. L. Hodgkin gave a general review of those experiments in which the axoplasm of the squid giant axon is replaced by a perfusate. When the perfusing fluid is made up with a 100-fold reduction in the salt concentration (osmotic replacement being made with nonelectrolytes), the relation between sodium permeability and membrane potential is shifted so that the membrane is still excitable in spite

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of a very low resting potential. It was also found that the duration of the action potential could be increased enormously by the use of potassiumfree perfusates at low ionic strength. Hodgkin expects that this giant nerve fiber may be as useful in biochemical studies as it has been in the past in physiological investigations.

In a session on membrane and phase boundary phenomena, T. E. Thompson spoke on some of his artificial lecithintetradecane bilayer membranes. He has determined that although the membranes are approximately 61 Å thick and are characterized by a high electrical resistance, they are relatively permeable to water. The relation of these membranes to natural membranes is a matter of considerable interest. In a report on the molecular biophysics of intercellular membrane systems, A. L. Lehninger discussed the polyfunctional nature of the mitochondrial enzyme systems. He considered their chemical transformations, mechano-chemical properties, and osmotic properties all interrelated, and he emphasized their role in the control of mitochondrial function.

F. M. Snell, with P. K. Chowdhury, presented some results on microelectrode penetration of frog skin and toad bladder. Their investigations suggest that the electrical potential is distributed across the sodium-transporting cells rather than discretely located in the cellular boundaries. The results further showed that the sodium- and potassium-sensitive functions, previously attributed to the bounding cell membranes, are distributed throughout the cell.

L. D. Peachy, A. F. Huxley, and R. H. Adrian reviewed the morphological and functional interpretation of the micro-tubular systems of muscle sarcomers. The evidence seems clear that these tubules are responsible for the inward spread of activation, that is, the coupling of excitation to contraction. Particular models have been put forth by Freygang and Adrian which account for many of the observations with respect to the negative afterpotentials in isolated muscle fibers.

Emphasis on cytoplasmic microtubules characterized a session on cellular contractility and protoplasmic movements. By some mechanism not entirely understood, these tubules appear to play a role in protoplasmic movements and spindle fiber formation. A number of impressive films were shown which provided dramatic demonstrations that the living cell is in continual dynamic motion.

In a discussion of ion transport, H. Passow described some of his experiments on passive ion flux across the erythrocyte membrane. His interpretation of the cation fluxes in terms of charged pores (3-molar fixed positive charge) and a Donnan distribution between the external solution and these channels appears to describe the results well in those experiments where the pH and ionic strength were variables.

P. Horowicz described the results of his recent research which indicated that the rate of strophanthidin-sensitive sodium efflux from frog semitendinosus muscle fibers was a function of membrane depolarization. The efflux increases with increasing depolarization by an increase in external K^+ or by addition of NaN₃ to the bathing solution.

In a discussion on transport of organic molecules, R. K. Crane, and S. G. Schultz with R. Zalusky, each presented some of their findings on the intestinal mucosa. They have worked out the relations between glucose and sodium transport and between amino acids and sodium transport. There is no doubt that these phenomena are coupled. Although the hypothesis, set forth by Crane, and supported by Schultz, explains many of the observed phenomena, it will have to stand the test of further critical experiments.

Sessions on biophysics of communication and control processes opened with a paper by G. von Békésy on the role of inhibition in sensory biophysics. In reviewing a large area of sensory psychophysics, which included many of his own pioneering discoveries in auditory and tactile perception, von Békésy emphasized the great similarities among various sensory modalities. Many of these subjective findings clearly involve inhibition at peripheral levels of sensory systems. Von Békésy suggested that the considerable body of quantitative psychophysical evidence now on hand for simultaneous, delayed, and frequency-sensitive inhibition could provide the basis for a revealing search for neurophysiological correlates. This concern with finding more extensive relationships between psychophysics and neurophysiology, as exemplified by an increasing emphasis on the role of inhibition in neural information processing, was reflected in many of the subsequent papers.

In the presentation of his and T. N. Wiesel's recent findings on "hypercomplex" cells in cat visual cortex, D. H. Hubel reviewed the work which has progressively revealed more and more Gestalt perception by single cells. Their earlier results had demonstrated "simple" units in the primary visual cortex. The units respond to a retinally presented edge, for example, but only for a fixed orientation and position. More centrally, "complex" cells had been found to be interested in orientation but indifferent to stimulus position over a region of the retina. Now, at neurons which are only seven or eight synapses removed from the retinal receptors, Hubel and Wiesel find "hypercomplex" responses which generalize lines of particular orientation and length.

Wiesel subsequently presented his and Hubel's findings on the interrelations of form and color response in rhesus monkeys. He described three classes of lateral geniculate units. Class 1 cells, represent both form and color; those of class 2 read color alone; and class 3 units respond only to form. In a report of color vision in the pigeon, H. R. Maturana described the responses of diencephalic cells to diffuse retinal stimulation. There are "red," "blue," and "yellow" units which respond to small regions of the spectrum and which are actively inhibited by retinal illumination containing remote spectral components. These remote components alone cannot excite the diencephalic units, in contrast to the responses found at retinal ganglion cells. It is intriguing to see how such studies are beginning to reveal for both form and color the successive transformations of information as one proceeds centrally from the sensory transducers.

Spectrally antagonistic excitatory-inhibitory interplay in fish retina has been known for several years. T. Tomita, curious to know at what level in the retina these opposed processes originate, developed an ingenious new

technique. (All prior attempts to record potentials with micropipettes at the receptor level had failed; recordings had been obtained only at the ganglion and bipolar-cell levels.) Instead of conventionally thrusting a microelectrode into the retina, Tomita tosses the retina repetitively at a slowly advancing pipette by means of a vibrating electromagnetic plate. Spectrally selective responses are found and are believed to be direct measurements of cone activity.

L. S. Frishkopf and R. R. Capranica have been able to demonstrate a close relationship between croaking behavior and auditory electrophysiology in the bullfrog. The mating call can be experimentally evoked by simultaneous presentation of acoustic energy in two regions of the spectrum. The call can be suppressed by adding energy in an intermediate frequency range. Correspondingly, the neural response of the inner ear is inhibited by introducing an acoustic stimulus whose frequency lies between two maximally excitatory ranges. Thus responses of first-order sensory units at least qualitatively resemble aspects of whole-animal behavior, and are similar to the results of recent studies with the frog's visual system.

Studies with electronic models of neurons to examine the roles of excitatory and inhibitory time courses in single-unit input-output functions were described by L. D. Harmon. Two reciprocally inhibitory units with common excitatory input produce firing patterns of surprising complexity which change in discrete steps as stimulus frequency is varied. Pattern change, however, depends on the direction of stimulus change (that is, there is hysteresis). Such action, if physiologically demonstrable, may have interesting implications for neuromuscular control systems.

Responses of *Limulus* eye to stationary patterns were used by K. Kirschfeld and W. Reichardt to develop the transfer characteristics of two visual subsystems. The dioptric apparatus, because of visual field overlap of adjacent receptors, reduces spatial frequency resolution. Conversely, the lateral inhibition system by enhancing spatial contrast tends to compensate for the dioptric smearing. Although in principle the compensation could be complete, actually the two systems are not perfectly matched.

It has become increasingly apparent that to examine the role of noise in

nervous system operation is profitable. A. A. Verveen and H. E. Derksen described a new approach to the analysis of fluctuations of excitability and membrane potential in axons. A series of noise measurements in both internodal segments and single nodes has revealed a complicated noisepower spectral function which is inversely proportional to frequency over a considerable range. The similarity to flicker noise, well known in electronic cathodal emission, and to conductivity fluctuations which produce semiconductor excess noise suggests several intriguing approaches to a fresh analysis of membrane ionic conduction mechanisms. W. M. Siebert examined the implications of the stochastic nature of first-order auditory neurons whose detailed responses to identical acoustic stimuli are unpredictably variable. A result of particular interest is that since spike interval histograms can be superimposed by linear scaling, the notion of absolute time becomes unimportant. That is, only relative time (or count) may be the essential measure for a large class of auditory information processing.

Problems of systemic coordination and control were examined from several different aspects. S. V. Fomin discussed studies, with I. M. Gelfand, V. S. Gurfinkel, M. L. Zetlin, and M. L. Shick, on motor control activity in man. Spectral analyses of limb tremor were shown to uniquely reflect the particular motor tasks intended. Distinctions between the tremor spectra of healthy and neurologically diseased humans has considerable analytical and clinical utility. R. A. Chase, reporting on work done in collaboration with J. K. Cullen, Jr., and S. A. Sullivan, described the effects of altering both motor output and sensory feedback to analyze input-output relationships in neuromuscular control systems. These studies indicate that feedback from muscle spindles may be implicated in several of the clinical syndromes that involve such abnormal voluntary movements as intention tremor. L. Stark summarized a revealing series of studies on human eyemovements, pupillary reflexes, and hand tracking. Motor systems are shown to be complex, multi-loop controllers; some are adaptive and intermittent, while others are nonpredicting and highly nonlinear. The applications of engineering control system theory to behavioral and neurophysiological data has proved to be extremely profitable to the analysis and understanding of both normal and pathological aspects of motor activity.

A general session on Education in Biophysics elicited considerable interest and delegates discussed the problems associated with the evolution of biophysics as a discipline in their respective countries.

As an experiment, the meeting was organized with invited speakers only; more than 100 papers were presented. Although this procedure evoked considerable criticism, the meeting was undeniably stimulating and provided some excellent discussions.

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Aquatic Pollution

The pollution of marine waters was the subject of a symposium held by the Aquatic Biology Group at the meeting of American Society for Microbiology in Washington, D.C., 5 May 1964. Robert Littleford (U.S. Public Health Service) severely criticized the increasing pollution of our waters and called for new approaches to the problem. He said that dumping waste into the marine environment and forgetting it as it floats away nullifies responsibility. Over the years the pollutants have increased 1000-fold, and the variety from almost every industrial organization has also increased. Pollution, an environmental problem, is also a biological problem, yet biologists have shirked pollution study. He called for studies by virologists of the shellfish hepatitis problem, and emphasized the need for a critical overhaul of microbiological techniques. The methodology for other ecosystems cannot simply be adapted for the marine environment. Littleford called for a coordinated approach to pollution study-one in which biologists, oceanographers, sanitary engineers, and other specialists would work as a team. There should be an end to projects that do not consider the whole environment, especially the life in these polluted waters. These studies should take into account the interaction of organisms and environment, the spread of infective agents arising from sewage and other manmade wastes, and the negative and positive effects of treated sewage on the

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