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to provide the means for employment of more scholars in careers of research.

Solutions to the cancer problem, to the still larger medical problem of heart disease, or to the many problems of pollution associated with a high standard of living are not going to be found by untrained individuals. The great advances in biology in recent years may be directly correlated with the support given by certain foundations and by the National Institutes of Health, support that made it possible for universities to maintain men committed in large part to research. It was this kind of support, for example, that resulted in a vaccine against polio and thereby saved millions of dollars that would otherwise have had to be spent for hospitalization and therapy of people crippled in youth by this disease. It is this kind of support that now permits some to contemplate a "final push" against cancer.

Rather than curtail training programs, we should work for future increases in job opportunities. One way to do this is to establish graduate universities and research institutions affiliated with them. The latter might be centered on practical problems but could approach these problems with a long-range view and in an interdisciplinary way. The Woods Hole Oceanographic Institution and its new graduate school of oceanography affiliated with the Massachusetts Institute of Technology provide an excellent working example.

It is already clear that such research and training centers are needed in diverse fields. They have to be staffed with scientists who have an equivalent of the Ph.D. A sharp curtailment in training of Ph.D.'s now will leave us short of the young people we will need.

WILLIAM TRAGER
Rockefeller University,
New York 10021

Breath Test Machines

In his letter (2 July) criticizing my report on alcohol breath tests (2 Apr., p. 57) Edwards raises three questions explicitly or implicitly. These are: (i) Are the data presented correct? (ii) Was the report really necessary in view of the fact that the defects described were "well known"? and (iii) Whose problem is alcoholism and whose problem is the correct calibration of an instrument used by traffic police?

Neither Edwards nor anyone else has questioned the accuracy of my data. I stated in my report that "There have been occasional warnings about the inaccuracy of Breathalyzer or other alveolar gas tests . . . but these are rare, generally nonquantitative, and inaccurate." To date, I have found no evidence to indicate that this statement was incorrect. Edwards does not cite any previous paper in which the Breathalyzer or any similar instrument was properly calibrated. In addition to the disputed time factor, still inaccurately stated by Edwards, other errors in usage of breath test machines needed to be corrected. For example, it has been assumed that "true reactions with alcohol in expired breath from other than alveolar air (eructation, regurgitation, vomiting) will, of course, vitiate the breath alcohol results, but can be detected by observation of the test subject, and [italics mine] prevented by having the subject rinse out his mouth with water" (1). This assumption, also, was demonstrated in my report to be false.

Alveolar gas tests are also used in scientific laboratories. It was for this purpose that a Breathalyzer, with its book of instructions (omitting mention of time factors), was sold to the NASA Langley Research Center for use in a study of alcohol effects upon human motor, sensory, and mental performance. Convinced that, in principle, this instrument could not perform as claimed by the manufacturers, I suggested to Mr. Maraman, of the Langley center, that we should test the accuracy of the instrument. As indicated in reference 7 of my report, I presented these data to a plenary session of the 16th International Symposium on the Prevention and Treatment of Alcoholism at Lausanne, Switzerland, in June 1970. None of the assembled (scientific, medical, and legal) experts hinted to me, in the lively discussion that followed, that they were old hat. Indeed, I was persuaded by my colleagues at this meeting to give wider circulation to these data. After my report was published in Science, M. V. Stack, of the Medical Research Council Dental Research Unit in Bristol, England, called to my attention that he had reported to a meeting in 1957 some of the difficulties with residual mouth alcohol in usage of the Breathalyzer. Unfortunately this information (apparently not published in a journal) was to be found neither in the instruction book issued with the Breathalyzer 11 years later, nor in recent reviews of this subject.

I had and have no interest in pro-
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Table 1. Expectation and occurrence of the number of games in the World Series from 1905 to 1971.*

<table>
<thead>
<tr>
<th>No. of games</th>
<th>Expectation</th>
<th>Actual occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>.125</td>
<td>6/37 = .162</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4/27 = .148</td>
</tr>
<tr>
<td>5</td>
<td>.250</td>
<td>14/37 = .378</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4/27 = .148</td>
</tr>
<tr>
<td>6</td>
<td>.313</td>
<td>9/37 = .243</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4/27 = .148</td>
</tr>
<tr>
<td>7</td>
<td>.312</td>
<td>8/37 = .216</td>
</tr>
<tr>
<td></td>
<td></td>
<td>15/27 = .555</td>
</tr>
</tbody>
</table>

*The years 1919, 1920, and 1921 are excluded because the series consisted of the best five out of nine games.

has won that game only four times! If the teams are matched, the probability of winning less than five times is

\[ \sum_{m=1}^{5} C_m \cdot (1/2)^m = 0.0096 \]

The phenomenon becomes even more unlikely when one realizes that the teams are not evenly matched and that the team that was ahead going into the sixth game was possibly the stronger team.

The theory has been advanced that there is a “back-to-the-wall” effect operating which tends to favor the trailing team in the sixth game. This explanation, however, is refuted by the fact that prior to the end of World War II the sixth game phenomenon is not detectable; the length of World Series agrees moderately well with theoretical prediction, although occurrence is biased toward slightly shorter series, probably due to team imbalance (Table 1).

Furthermore, analysis of other “back-to-the-wall” situations fails to indicate that this is a significant effect. The anomaly is clearly associated with the sixth game and with post-World War II baseball. Clearly some hitherto undetected behavioral influence is operating that warrants further investigation.

WILLIAM SIMON
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Na channels in the squid membrane (experimental estimates agree on ~50/μm²) and to a rather detailed description of the K channel and its gate. Both tetramethylammonium ion (TEA⁺) derivatives and Cs⁺ inside an axon inhibit K currents in a time-dependent manner. By testing for the recovery from inhibition it has been possible to work out the kinetics of channel blocking and of channel recovery after the membrane has been repolarized. The model that emerges is one with a voltage sensitive gate at the inside by the membrane. A region under the gate must supply ion selectivity both for blocking substances and for K⁺.

Two additional topics relating to voltage clamp currents were discussed in some detail: (i) single versus separate channels for the Na and K currents and (ii) the problem of gating (or carrier) currents. Although a poll was not taken, it is likely that most investigators are impressed by the pharmacological specificity of TTX and TEA for the Na and K channels. Most theorists started their work with a coupled Na-K channel but have now shifted to an emphasis on separate channel models. Some evidence was offered that the Na channel may be a coupled system in the sense that the Hodgkin-Huxley conductance parameters m and h are not independent. Experimental support for this depends on high precision measurements of h versus (Eₚ). Mainly such a shift of models has been occasioned by an appreciation of the difficulties posed by the results of the Cole-Moore experiments, that is, the continuous delay of K currents with increasing hyperpolarization. The Na currents are unaffected by values of membrane potential more negative than ~75 mV.

Gating current—that is current that should precede the start of ion conductance change—has never been observed experimentally. Yet most investigators thought that there must be such a current. Those who thought that it was possible to devise a model showing a voltage sensitivity of ion conductance but no gating current were challenged to come up with a model; no such model was offered during the conference. It was also suggested that gating currents could well be hidden in the capacitative transient. A further experimental attack on the problem seems possible by the use of signal averaging equipment.

One session was devoted to tracer

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methods of measuring ion fluxes (T. I. Shaw and R. E. Taylor) and optical methods for following Ca$^{2+}$ fluxes (A. L. Hodgkin). Recent measurements of $^{22}$Na flux in voltage clamped axons at a variety of potentials have shown that the transference number for Na (as early current) is very close to unity. Some of the difficulties in using perfused axons for active transport studies were discussed. It was noted that the use of dextran in the interior of the axon seems to stabilize the membrane against what appears to be some sort of an irreversible uncoupling of the Na pump. If aequorin, a compound that emits light in the presence of Ca$^{2+}$, is injected into squid axons, it is possible to follow changes in [Ca], (and therefore Ca entry) by measuring light emission from the fiber. An early Ca$^{2+}$ entry that is synchronous with Na entry has been observed as well as a late entry seen in TTX-treated fibers. This latter process is especially interesting as it may be related to transmitter release phenomena which ordinarily are observed only in nerve terminals.

L. J. MULLINS

Department of Biophysics,
University of Maryland
School of Medicine, Baltimore

Note

1. The organizers of the conference were D. E. Goldman, chairman, K. S. Cole, and L. J. Mullins. There were about 30 participants, but no formal lectures. The conference was held 5 to 9 April at Ann Jordon Farm, Alexander City, Alabama, a conference center of the University of Alabama. Participants were welcomed by Dr. R. Hill, vice president for health affairs of the University of Alabama in Birmingham and were entertained for dinner by President J. F. Volker. The local arrangements were handled by Dr. W. Rehm, Chairman, Department of Physiology and Biophysics University of Alabama, Birmingham. Financial support for the conference was provided by the Grass Foundation, Quincy, Massachusetts, International Business Machines Co., and the University of Alabama at Birmingham. Support for the expenses of NIH personnel was provided by the National Institute of Neurological Diseases and Stroke, Bethesda, Maryland. The organizing committee is grateful to the University of Alabama in Birmingham for providing for the needs of the conference and to the agencies whose financial support made the meeting possible.

Membrane Structure

The theme and perspective for the Conference on Membrane Structure and Its Biological Applications, which was sponsored by the New York Academy of Sciences and held 2 to 4 June 1971, was set by the first two presentations, given respectively by G. Vanderkooi and J. Singer. Vanderkooi presented de-
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SCIENCE, VOL. 174
tailed molecular structural models for the disk membrane of the rod outer segment and for the membrane formed by cytochrome oxidase. Singer followed this up with a general treatment of membrane structure in which he emphasized the thermodynamic or energetic determinants of structure. The general picture given by both of these workers was very similar, namely, that the lipid in membranes exists as lamellar bilayer, just as Danielli and Davson proposed in the 1930's, but that the proteins are globular and penetrate deeply into the bilayer lipid. The terminology of intrinsic and extrinsic membrane proteins was introduced by Vanderkooi; this terminology proved very useful in the ensuing discussions of the conference, as it served to differentiate between those proteins that are an integral part of the membrane continuum (intrinsic) and those that are attached to the surface in miscellaneous ways (extrinsic).

One of the reasons for the success of this conference was the organization of the discussion periods. Most sessions consisted of three or four major papers, followed by a few programmed discussants who gave prepared remarks or a brief paper, which in turn was followed by an extended period of open questions and discussion from the floor. In this way, a partial consensus of opinion was actually gained during the course of the meeting. Such a consensus was an especially useful development for this particular meeting since the field of membrane structure has not been noted for unanimity of opinion or even for discussion of conflicting opinions.

After the papers on membrane models were presented, a long series of papers, which covered several sessions (but with no concurrent sessions running), dealt with the experimental aspects of membrane structure. While most of these consisted of experimental methods and results, the underlying thought was, "How do the data obtained by this technique contribute to our knowledge of membrane structure, and how do the results fit the various models which have been proposed for membranes?"

As a result of the numerous discussions, a higher level of agreement on the essentials of membrane structure was achieved than we have seen heretofore. The point which won universal acceptance, on the basis of several kinds of experimental data, was that the lipids in membrane exist predominantly as lamellar bilayer. It was agreed that any

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model that does not assign this structure to bulk lipid can be rejected. The second point on which there seemed to be general agreement, although with a somewhat weaker experimental foundation than for the first point, was that membrane proteins are globular, just as the majority of soluble proteins are, rather than extended fibrous structures which were proposed in the old unit membrane model. Further, there seemed to be general consent to the idea that the globular proteins that are intrinsic to the membrane do penetrate into the lipid bilayer, and that they do not simply bind electrostatically to the bilayer surface.

As far as general membrane models are concerned, the conferees were loath to accept the concept that a single membrane model could be constructed that will account for the basic structure of all membranes. It was pointed out by D. E. Green, however, and seconded by others, that the state of membranology may be likened to the concepts concerning nucleic acids before Watson and Crick. Confusion reigned until it was shown that the principle of the double helix could organize a wealth of data into a sensible picture. Likewise, there ought to be some fundamental similarities of membrane structure, which, once they are discovered, will simplify the whole membrane field.

In spite of the reluctance of the group to adopt a particular membrane model—possibly a reflection of the anxiety to avoid replacing the dogma of the unit membrane with a new progress-inhibiting dogma—a model was tentatively adopted for the structure of one particular membrane, the retinal rod outer-segment disk membrane. M. H. F. Wilkins reported that a careful analysis of his x-ray diffraction data on the retinal rods, interpreted with the assistance of molecular model building, now appears to indicate that the globular proteins are in fact about half submerged in the lipid bilayer, as proposed in 1970 by G. Vanderkooi and M. Sundaralingam. In his summarizing talk at the end of the conference, O. Hechter stated that the general opinion seemed to him to be that this retinal rod membrane model is "probably correct."

One might think that a good molecular model for myelin would have emerged from this conference, but it did not. This situation exists in spite of extensive electron microscopy and high quality (for membranes) x-ray diffraction data now available on the
myelin system. In one of the lively discussion sessions, C. Tanford felt compelled to point out that electron microscopy and one-dimensional x-ray analysis by themselves are incapable of solving membrane structure. These techniques are useful and provide valuable information, but the results must be interpreted in terms of a model. The x-ray and microscopy results put definite constraints on any suggested model, but do not of themselves provide sufficient information to generate a model. Thus we are back once again to model building: propose a model on the basis of as much evidence from as many different sources as possible, and judge the result on the basis of self-consistency of explanation.

At least two of the six sessions of the conference were devoted to phenomena, the rationalization of which depends heavily on our knowledge of membrane structure—facilitated transport through membranes, membrane permeases, complement fixation, and plasma lipoproteins. It was noteworthy that in attempting to visualize the kind of membrane structure that would account for facilitated transport, both W. P. Stein and S. Roseman proposed models not unlike those proposed by Singer and Vanderkooi.

A glimpse into the future of electron microscopy was provided by H. Fernández-Morán and the conference proceedings were summarized by O. Hechter.


In all there were 40 participants on the program and about 700 in attendance.

D. E. GREEN

Institute for Enzyme Research,
University of Wisconsin, Madison

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