OPPORTUNITIES IN BIOPHYSICS

By Harold J. Morowitz

IN 1940, John R. Loofbourow wrote an article entitled, "Borderland Problems in Biology and Physics", which was published in the *Reviews of Modern Physics*. Since that time physicists have been puzzled by the "aberrant" behavior of some of their colleagues. Why does a theoretician like Max Delbruck start talking about mutations of bacterial viruses? How does it happen that an experimental nuclear physicist like Ernest Pollard begins worrying about bacterial replication? What is Schrödinger's concern with the problem of "What is Life?" Why does an astrophysicist like Gamow begin worrying about coding in biological systems? This straying from the orthodox fields of physics by these and many others represents an interesting modern trend of thought and poses both problems and challenges to the field of physics.

In a sense, the whole universe has been grist for the physicist's mill, so that it is somewhat strange that biophysics does not have the same age and venerability as astrophysics or geophysics. Somehow in the nineteenth and early twentieth centuries biology never looked enough like physics to tempt many physicists to face the smells of an anatomy or an organic chemistry laboratory. Descriptive biology with its elaborate vocabulary did not seem to offer laws of nature, while physiology, the science of biological process, was much more concerned with a rapidly developing chemistry.

A whole series of developments of the last fifty years has been encouraging physicists to look at biology. If I were to pick one to stress, it would be the development of chemical physics brought about by the development of quantum mechanics. For the concepts of chemical physics, incomplete as they may be, enable us to come to grips with the problems of molecular

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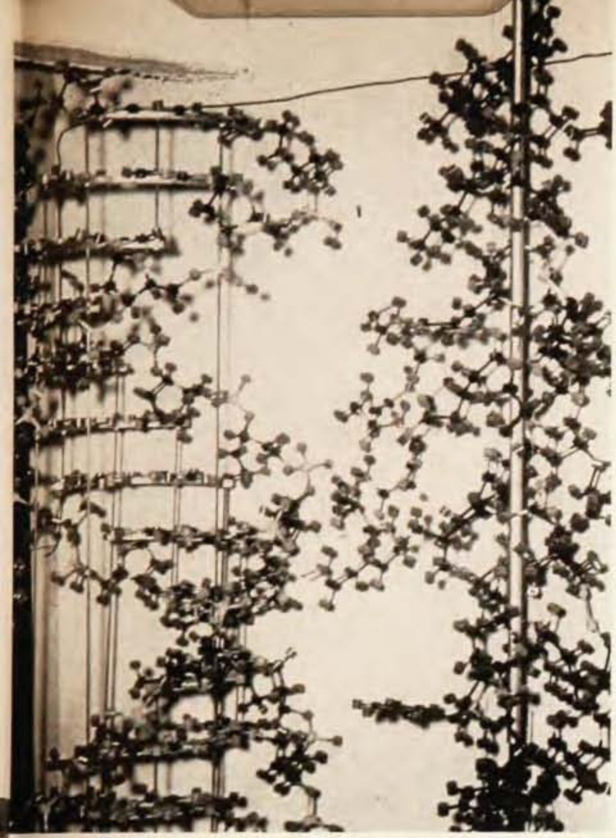
Erwin Schrödinger

John R. Loofbourow



Atomic models of two important biological macromolecules, deoxyribose-nucleic acid (left) and protein (right). X-ray diffraction studies have been instrumental in establishing the structure of these macromolecules.

biology. Biological structures may be resolved into molecular structures and molecular structures into relations between nuclei and electrons. The relation between structure and function becomes on a molecular scale a problem of force fields, a type of problem long familiar to physics.

What is then emerging as the modern science of biophysics and what relation does it bear to physics both in an intellectual and in a practical sense? In the aforementioned article by Loofbourow, he divided the borderland in biology and physics into three categories: application of physical methods to the investigation of biological and biochemical problems, study of the effects of external physical agents on living organisms and biochemical substances, and physical phenomena occurring in living organisms. These still seem like valid categories and we will employ them in briefly describing contemporary biophysics.

I. *Applications of physical methods to the investigations of biological and biochemical problems.*

The special skills of the physicist in precise measurement may often be useful in studying biological systems. The physicist's training in instrumentation is also valuable in this field. Perhaps even more striking is the development of new tools such as the electron microscope which extend the experimentalist's domain to new measurements.

One feature of this general area should be noted. As a new method develops, it becomes less the exclusive province of the physicist and becomes a generally accepted technique. An example of this is the use of radioactive tracers. Originally radioactive isotopes were the domain of the nuclear physicist. As biological applications began to increase and good commercial apparatus became available, radioactive isotopes became a generally accepted tool of biochemists and physiologists and now are no longer regarded as the physicist's exclusive domain. Many biological laboratories now employ radioactive isotopes without the assistance of a consulting physicist. Thus it is arbitrary to classify the optical microscope as the biologist's and the x-ray microscope as the physicist's. There may be historical reasons for this division, but it is not a well-defined classification.

In this brief article we will not attempt to catalogue the physical methods used in modern biology and biophysics. They range from mass determination to nuclear magnetic resonance spectroscopy. To the physicist interested in this field it is well to remember that any biological system is also a physical system and the measurement of any parameter of the system may be useful in elucidating its nature. Certain measurements are more interesting than others depending on current fads, but all of these "physical measurements" have a place in biology.

II. *Study of the effects of external physical agents on living organisms and biochemical substances.*

One may begin by posing the question, "what are the effects of magnetic fields, ionizing radiation, gravitational fields, etc., on various biological systems?" This may be asked as a phenomenological question or may be extended so that we may ask what can the effects of various physical agents on biological materials tell us about the nature of these materials. Since the external physical agent that has been most often used in this type of study is ionizing radiation, we will briefly discuss this topic as an example of the general approach.

A good deal of radiobiology is devoted to the practical question of determining and controlling the effects of radiation on living systems. Somewhat more akin to the viewpoint of the physicist is the attempt to develop radiation into a tool capable of yielding information on the nature of biological processes such as replication and enzyme action. Such studies operate conceptually in the following way. Samples of some biological material are subjected to a series of doses of radiation and one or more specific responses or effects are measured. From the knowledge of the physical action of the radiation and the responses observed, one tries to postulate something about the nature of the system that reacted in the observed way to the known perturbation. The method is somewhat akin to the technique of the nuclear physicist who irradiates atomic nuclei, observes responses (scattering, radiation, transmutation, etc.), and tries to deduce something about the nature of the nuclei. Such studies in biology have yielded information on the size, shape, location, and organization of functional units.

III. *Physical phenomena occurring in living organisms.*

This third classification is in many ways the most exciting and least explored branch of biophysics. Included under this heading is the attempt to understand the living organism as a physical system. In the limiting case this might involve predicting the properties of living systems from a solution of Schrödinger's equation. Needless to say, modern biophysics is far from this goal. However, significant information has been obtained.

Detailed atomic structures of proteins and nucleic acids are being obtained by x-ray diffraction and chemical methods of study. Numerous approaches are being made to the detailed physical mechanisms of enzyme action, energy transfer, and energy storage in living cells.

A new branch of formal or theoretical biophysics is emerging which deals with the systems properties of living organisms. Various approaches such as information theory and network analysis have been applied to these problems. In this connection a good deal is being done in applying computers, both analog and digital, to the study of biophysical problems.

Forces between large molecules play a very important role in biology. In addition very highly specific forces between molecules seem to be operative. This is a field where physics can be expected to play a large part.

WITH this very sketchy summary of biophysics today we can turn to two problems of immediate practical importance to college and university physics departments:

1. Should biophysics courses be offered by physics departments?

2. Should biophysics research be carried out in physics departments? The two questions are very closely linked and a yes answer to one almost automatically implies a yes answer to the other.

With respect to teaching biophysics courses in physics departments we might look at what has been done. Universities currently teaching biophysics do so in biophysics, physics, physiology, radiology, chemistry, and engineering departments. I think that there is little question that biophysics is a legitimate field of physics, although teaching a course with a "bio" title in a physics department might involve stepping on administrative toes. Some physicists might think that a biophysics course is an organic stain on the purity of their department.

The purely practical argument runs like this. An increasing number of people with undergraduate and graduate training in physics are going into biophysics. It would be a useful thing for these people to be able to obtain some formal course work in biophysics during their training period. That is to say, since biophysics is a professional category for people trained in physics, it would seem wise to offer some additional training in this specialty.

The question of biophysical research in physics departments is of more immediate concern. It serves to introduce the third section of this article which is a report on a summer conference on biophysics held at Yale and designed primarily for college physics teachers.

ABOUT a year ago the American Institute of Physics consulted with Ernest Pollard of Yale on the desirability of conducting a summer conference on biophysics. The AIP wanted to investigate the possibilities for biophysical research in physics departments, particularly those of small colleges. One of the motivating factors behind this move has been the rising cost in research in many branches of physics. Much of contemporary research in fields such as nuclear physics requires large machines, large installations, and very extensive budgets. This trend toward bigness tends to narrow the range of research available to smaller physics departments. Now a feature of biophysical research is that excellent work can be done by an individual working with restricted space and restricted budget. In this sense biophysical research is well suited to smaller departments with limited resources.

As a result of the discussions betwen the AIP and the Yale Biophysics Department a one-week summer conference was planned under the sponsorship of the National Science Foundation. The conference was entitled, "Summer Conference for College Teachers of Science to Present the Field of Biophysics as Offering Opportunity for Physics Research". The stated purpose of the conference was as follows:

> To provide opportunities and stimulation to physicists situated in physics departments in small colleges to carry on small-scale but significant research. Most new PhD's in physics come from research environments in at least graduate school and are careful to avoid jobs which do not provide some time, facilities, and incentive for research over and above straight teaching assignments. Colleges, and especially small colleges, will never compete successfully with industry and government, even on equal salary scales, unless such opportunities are provided.
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> The subject of biophysics, which is the investigation of living systems by physical means, does offer a great many opportunities for physical research with relatively small equipment. The problems of understanding biological systems are by no means insuperable and examples of work, either conceived and performed by physicists alone or done collaboratively, are abundant.

The conference was arranged as a series of morning and afternoon lectures and discussions. The first session of the conference was devoted to an introductory talk by Professor Pollard outlining the field of biophysics. The second session was given by Francis Carlson of Johns Hopkins University and dealt with the mechanics of living systems or, more specifically, the problem of motion, motility of cells, and muscular contraction. Professor Carlson discussed the phenomenological features of motion and then proceeded to a discussion of the molecular events underlying muscular contraction.

The second day began with a session by Professor Morowitz of Yale on the physics of living cells. This session reviewed the current status of the molecular view of cellular structure and function. The afternoon of the second day was presided over by Dean Cowie of the Carnegie Institute of Terrestrial Magnetism who discussed the application of radioactive tracers to the study of cellular processes. Dr. Cowie reviewed the basic features of the use of radioactive tracers and presented some of his own very elegant work to illustrate how tracers are used and how useful biophysical information can be obtained from their use.

The third day of the conference was devoted to a discussion of the biological applications of ionizing radiation. Lectures were presented by Professors Pollard, Franklin Hutchinson, and Walter Guild of Yale. All aspects of the subject were reviewed, including the effects of radiation on mammalian organisms, the basic mechanisms of radiation action, and the use of radiation as a tool in the study of cells and macromolecules. Consideration was also given to the types of experimental programs which could be set up in this field.

Henry Quastler of the Brookhaven National Laboratory, along with Professors Pollard and Morowitz, conducted the fourth day's sessions on theoretical biophysics. Among the topics covered were information theory, problems of biological coding, a review of the literature of theoretical biology, applications of thermodynamics to biology, and theoretical analysis of the data of radiobiology.

The lecturers in the morning session of the fifth day were Charles Thomas of Johns Hopkins and Frederick Forro of Yale. They discussed nucleic acids and viruses. Both lecturers used their own work to demonstrate the application of techniques such as radioautography to the problem of understanding the biological replication of nucleic acids. The final session was conducted by Paul Kaesberg of the University of Wisconsin. Professor Kaesberg discussed the general principles involved in the application of x-ray scattering and diffraction to biological materials. He then discussed some of the interesting work on viruses that he and his co-workers are carrying out at Wisconsin.

The conference was attended by forty teachers from nineteen states.

The program of the summer conference indicates many of the general topics included under the heading of biophysics. In the concluding section we should like to discuss in a rather abbreviated fashion some of the lines of biophysical research open to smaller physics departments. To provide concrete cases we shall choose examples from the *Proceedings of the First National Biophysics Conference* (Yale Press, 1959). At this point we might also note another general reference, Numbers 2 and 3 of Volume 31 of the *Reviews of Modern Physics,* which contain the papers delivered at a recent symposium on Biophysical Sciences.

First, it should be hardly necessary in an article written to physicists to note that there is an open field of theoretical biophysics requiring only pencil and paper in the hands of someone with knowledge and ingenuity. As examples of theoretical efforts in biophysics we might note Francis Carlson's paper on the Motile Power of Swimming Spermatozoon (p. 443) and Henry Quastler's essay on Quality of Radiation and Selectivity of Biological Effects (p. 704).

Experimental research is of necessity more limited by considerations such as equipment and funds. None the less much can be done with a limited budget and ingenuity. A good example of advanced instrumentation in biophysics may be seen in the article by Alexander Kohn entitled "Sorting of Macromolecules and Micro-organisms by Means of Electrokinetic and Electromagnetic Effects" (p. 125).

A good example of the application of tracer techniques to biological problems is found in the section on "Metabolic Pools and the Synthesis of Macromolecules" by Dean Cowie and Frank McClure (p. 400). An analysis of a more physiological problem is given by Robert Haynes and Alan Burton in "Axial Accumulation of Cells and the Rheology of Blood" (p. 452).

These papers plus a general perusal of the two references noted should serve to suggest to the physicist the types of biophysical problems that might reasonably be tackled.

We can conclude this article with the thought that biophysics as a discipline is here to stay. The relation between physics and biophysics is something that must be solved by the people concerned, which is after all the proper place for it to be solved.

An example of a development in physics which has had a major impact on biology, the electron microscope is now one of the chief tools in the study of biological structure. (*Norelco photo*)