The Status and Development of Biophysics

Comments and Communications

MOST physiologists must have been keenly interested in the thoughtful and provocative article by R. W. Stacy on "The Status and Development of Biophysics" (*Science*, 113, 169, [1951]). A thorough discussion of this frequently mentioned but rarely understood field of science has long been needed. Indeed, we feel that the very thoroughness of Stacy's presentation makes clear the weakness of his point of view.

Perhaps the most vulnerable statement in his article is the assertion that "Any physiologist will concur in the idea that his field embraces the physics and chemistry of living matter." This writer, as a physiologist himself, can testify to the inaccuracy of this statement. It has been many years since "physiological chemistry" started to sprout away from the parent physiology. The field of biochemistry has grown to its full maturity and most certainly deserves to stand now as an autonomous member in the broader field of the biological sciences. We believe that relatively few physiologists would continue to regard biochemistry as a subdivision of physiology. Those who, like Stacy, continue to place it in this category can be completely overbalanced by the vast majority of biochemists who, while in no sense denying their heritage, would refuse to recognize a continued allegiance and subordination to physiology. It must therefore be recognized that the "chemistry of living matter" is no longer encompassed within the scope of modern physiology.

There are certain phases of physiology that are not strictly physical. A good example is the physiology of the kidney, for renal physiologists are still actively engaged in the task of defining how much of kidney function is dependent upon physical processes of filtration and diffusion, and how much is based upon the strictly biochemical processes involved in active reabsorption and secretion. There is little doubt that, as soon as renal physiology has advanced to the point where its biochemical aspects have been clearly defined, these aspects will be dissected free and taken over by the biochemists. As another example, most physiologists tend to regard endocrinology as still being a subdivision of physiology, although this point of view would certainly be challenged by the biochemist.

Many chemical aspects of physiology are essential to a proper treatment of the physics of living matter. Thus the broader aspects of nutrition and total metabolism must be considered in an analysis of the energetics of living systems. The study of inorganic anions and cations is much more closely related to the physical side of physical chemistry than to chemical reaction systems. At present certain aspects of the chemistry of choline compounds appear essential to an understanding of the electrical phenomena occurring in the body. While recognizing these fringe areas and overlaps, we believe that the field of physiology is rapidly approaching the point where it can be adequately described as "the physics of living matter."

This is well illustrated in Stacy's article. In elaborating the scope of biophysics, he states that "The biophysicist should devote himself to physical measurement of the three basic phenomena of circulation: pressure, volume of flow, and velocity of flow." This would leave nothing in the circulation for the physiologist to worry about except such problems as the electrical changes associated with heart excitation, the sound vibrations associated with heart action, and the function of the circulation to the skin in determining the exchange of heat between the body and its environment. Yet certainly the latter aspects would also be encompassed in Stacy's concept of biophysics. Similarly, Stacy lists the "physics of gases" as of concern to the biophysicist interested in respiration. Again we find his concept synonymous with respiratory physiology. Stacy in studying the "biophysics" of respiration surely must devote just as much attention to the chemistry of hemoglobin and carbonic anhydrase as is now given in respiratory "physiology" to these areas of overlap. Similar reasoning is applicable to nerve physiology and its concentration on bioelectric problems, to muscle physiology and its focus on biomechanics, and to sensory physiology with its attention to physical stimuli derived from the environment. Up to this point, therefore, Stacy's argument would appear to be simply one for substituting a new term for the long-established term "physiology." Without debating the greater etymological accuracy of designating modern physiology as "biophysics," the necessity for rechristening such a well-established field is to our minds of doubtful value, especially when it is remembered that the name has already been usurped by many radiobiologists.

But Stacy makes it quite clear that his concept of biophysics goes far beyond modern physiology. He would extend its scope to encompass the "application of physical techniques to biological measurement." Here we find a point of view expressed which, to our minds, is shortsighted and lacking in any perspective as to the true nature of the problem. Indeed, Stacy makes it clear that he really does not mean "physical techniques" but rather is thinking in terms of physical gadgets of recent vintage and reasonable complexity. Thus he would specifically designate the biologist employing the electron microscope as a "biophysicist" and yet by inference he would exclude the vast array of biological scientists who employ the ordinary light microscope. Certainly the common light microscope is just as purely "physical" as is the electron microscope. Again, Stacy would identify the biochemist employing the infrared spectrophotometer as a biophysicist. But have the physicists ceased to claim the visual wavelengths of the spectrum? It would appear that the ordinary photoelectric colorimeter, or even the simple visual colorimeter, is every bit as physical as is the infrared spectrophotometer.

In the physiological field, the characterization of what is meant by "physical techniques" becomes even less tenable. By way of defining the scope of biophysics in this field, Stacy points out that "instruments like the ballistocardiograph, electrokymograph, capacitance cardiometer, and electromagnetic flowmeter are physical in nature." But may we also point out that instruments like the simple mercury manometer, the stethoscope, the ordinary mechanical kymograph, the sphygmograph, and the optical membrane manometer are equally physical in nature. The only consistent difference we can see between the "physical techniques" cited by Stacy and the vast majority of physiological techniques that Stacy ignores is that the latter techniques were in general use prior to the year 1930. Surely the designation "biophysics" does not validly distinguish between these two phases of physiological technology.

As a more extreme example, we may cite one of the oldest and most classical experiments in physiology. As routinely employed in elementary courses, the student removes a muscle from the leg of a frog, mounts it upon a stationary support, connects the free tendon to a simple lever commonly represented by a bamboo straw, which in turn writes upon a smoked paper surface moved by an old-fashioned clockwork type of spring motor. To establish time ordinates, the student makes use of either an ordinary tuning fork or a simple electromagnet driven by some form of mechanical interrupter. The lever is provided with a hook to which may be attached weights, and the muscle is commonly stimulated with a simple induction coil. Here, certainly, is a "physical analysis of biological behavior" employing strictly "physical techniques to biological measurement." Yet many "biophysicists" would be horrified or even insulted to have such pursuits identified with biophysics. Even from Stacy's account, in which muscle mechanics are recognized as being within the scope of biophysics, we get the impression that this experiment would not be representative of biophysics unless the recording were made with a piezoelectric crystal or a variable reluctance transducer operating through a carrier amplifier to drive a cathode-ray oscilloscope.

The development of physical instrumentation is one of the profoundest advances in science in the past two decades. It has had the greatest impact upon the biological scientist because, as Stacy correctly emphasizes, the biologist has been the least competent to make intelligent use of this new armamentarium of instrumentation. The practical import of Stacy's position seems to be that this present inadequacy should be corrected by setting aside a certain group of biological scientists to become competent with, and to train others in, the biological application of this new instrumentation.

Such an isolationist policy we feel does not meet the problem squarely or offer a sound solution for the future. Many physiologists are already disturbed by the increasing number of instances where skilled technologists apply complex physical instrumentation to physiological problems in which an inadequate comprehension of basic physiology tends to be masked behind the elegance of their instrumentation. In basic research, technology must always be strictly subservient to the biological scientist, and at no point should instrumentation rise above, or even be considered upon the same level as, the fundamental concepts and implications of the biological material. What is urgently needed is that *all* biological scientists and most certainly *all* biological scientists-in-training recognize the utmost importance of acquiring enough grounding in physics so that they can make intelligent use of physical instrumentation in the future advancement of the biological sciences.

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EVERY worker in the field of biophysics owes a debt of gratitude to Dr. Stacy for his timely article (*Science,* **113**, 169 [1951]). His remarks on the confusion that exists on the subject matter to be included in biophysics are very true, as anyone who has to teach the subject would testify. At the same time, I cannot help thinking that the source of the difficulties is to be found elsewhere.

To an experimentalist, biophysics must appear as an impenetrable jungle, but this does not dismay him for, in general, he is only interested in one particular kind of experimental problem. What is lacking in biophysics is a methodology, and this is a problem for the theoretical physicist.

In every textbook on physics one will find, sandwiched between mechanics and heat, a heterogeneous variety of topics such as surface phenomena, colloids, diffusion, viscosity, and others, which are generally included in "properties of matter," but which are not amenable to treatment by the same general laws that are so satisfying to the aesthetic soul of a physicist.

It is precisely in this field of open, irreversible heterogeneous systems that our present laws of physics are inadequate. Whether one follows Prigorgine in extending the second law of thermodynamics so as to free our concepts of entropy from the state restrictions of equilibrium and reversibility; whether one follows Wiener in denying the applicability of the second law to living systems and replaces it by a law of information based on ectropy or negative entropy; or whether, like Rashevsky, one abandons thermodynamics altogether, is not important. Whether a system of neural nets can be described in terms of Boolean algebra or by an electronic computing device, it is just as possible to understand the mechanism of the central nervous system, as Pitts and McCullough, who have had a foot in each camp, have shown.

As long as biophysics is a branch of physics, it should be taught on the lines traditional to physics. It will be as different from the biophysics of a medical school as thermodynamics ("physical chemistry") would be.

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I HAVE read with great interest Dr. Stacy's article about the status and development of biophysics in the United States. May I point out that in my own country (France) medical students have long since been given regular courses in bio- or medical physics, and this during the second semester of each of their first two years of study.

Their program includes Bioenergetics—first and second principles of thermodynamics as applied to human beings; Study of Body Constituents—solids (biomechanics), liquids (circulatory system), gases (respiratory system); Physical Chemistry of Cells and Tissues—pH, Rh, capillary effects, viscosity, membrane phenomena, etc.; Hearing; Speaking; Vision; Electrophysiology, Diagnosis and Therapy—electrocardiography, electroencephalography, diathermy, short waves, electric shock therapy, etc.; X-Rays—production and quick survey of their utilization; Radioactivity—natural and artificial; quick survey of utilization.

A current textbook has been written by André Strohl, head of the Medical Physics Department of the Paris Faculty of Medicine and is entitled *Physique médicale* (Masson et Cie, pub.). Teachers in the field are appointed by the French Ministry of Education after a special competitive examination held every third year and called the *Agrégation.* Candidates must all be M.D.s and usually have a Doctor's or Master's degree in physics plus, of course, a fair clinical training. Unnecessary to tell that it's not often that one gets such a position before he is thirty years old.

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THE breaking up of natural science into many fields of specialization has been forced upon us by the ever-increasing scope of knowledge. Such subdivisions develop traditional domains of interest and encourage research men to acquire special competence in particular modes of thought and methods of investigation.

Unfortunately, along with certain undeniable advantages in specialization, there are also very serious losses. Fields become separated by barriers of language and administrative convenience. Competition channels the research effort, discouraging collaboration and the interplay of ideas. Between these compartmented fields there remain almost untouched borderline problems. Virtual no man's lands are left behind in the precocious advance of science.

There can be no doubt that such a no man's land exists between physics and biology. Why? Chiefly because it is impossible in the conventional period of education to become adequately grounded in both physics and some fields of biological specialization. In order to bridge this gap the field of biophysics is being fostered by an increasing number of institutions. As yet there is no traditional domain, no well-developed audience for its publications, no established curriculum of prescribed education.

With understandable enthusiasm Dr. Stacy has attempted to call attention to this field and its problems. Unfortunately, he has failed to consider the latter from the standpoint of existing biological disciplines. Failure on the part of those who profess biophysics to exhibit a scholarly appreciation of the biological sciences will inevitably retard progress, because it encourages the attitude "Let the biophysicists do the instrumentation and the biologists do the thinking." No other concept of biophysics could be more fatal to the development of the field.

The driving motivation in any area of research must be curiosity and the desire to contribute to knowledge and understanding. If the brilliant minds needed in biophysics are to feel its challenge, it is the opportunity to exercise the imagination, to introduce new concepts and differing modes of analysis that will attract them.

Dr. Alexander has taken sharp issue with Dr. Stacy's definition of the biophysical field, and there is much merit in his views. No logical and well-defined demarcation can be offered that delineates biophysics from physiology. The difference is purely one of degree and emphasis. Every biophysicist must strive to be a good physiologist, as well as a good physicist. Within the scope of his research he must be well grounded in biology. Without biological perspective his work will betray the naïveté that has too often colored the work of physicists who have undertaken biological research. This is the reason so many of the capable biophysicists are those who obtained their biological training first.

For biophysics there must be adequate grounding in both biology and physics. It is of little moment which training precedes. Both are of equal importance. Few have the capacity and determination to encompass both fields. It is doubtful that a curriculum can be devised which will provide such training within conventional time limits. Probably it will always require additional years of study, as well as special abilities of intuition, analytical power, and judgment.

Biophysics overlaps not merely physiology, but also each of the other biological sciences. A borderline domain exists between physics and practically every field of biological specialization. A biophysicist can be guilty of poor cytology in electron microscopy, poor biochemistry in molecular investigations with infrared, or poor cell physiology in research on the biological action of radiation.

The staking out of claims has little merit. What we need is closer interchange of the *ideas* that develop so rapidly in each science. This can come only by comradeship and mutual respect. The fields that most intrigue me involve physical chemistry, as well as physics and biology. To obtain complete mastery of all three is hopeless. We must ask the tolerance of our fellow-specialists in other fields and not hesitate to admit our limitations. It is through our discussions with them, as well as through our reading, that we can avoid the pitfalls of naïveté. I don't see how one divorces scientific fields without retarding progress toward understanding.

Physicists have a somewhat different philosophy of instrumentation than do most biologists. Their fields of inquiry generally require the development of new instruments for particular investigations, and often this requires years of effort before the imaginative return can be garnered. Frequently biologists interpret this as a primary interest in instrumentation. For the good physicist this is just as fatal as in any other field of research. He has simply become accustomed to a greater demand on his patience and perseverance. He must command different fields of technology to accomplish his research. Gadgeteering as an objective spells the end of research. If biologists are to encourage physicists to take up biophysics, they must avoid demanding too much technological assistance and must help the physicist acquire biological familiarity and perspective. The physicist must be prepared to do a great amount of reading and laboratory work before he can claim to be a biophysicist.

Biophysics differs from the biological fields on which it may impinge simply in:

1. The more advanced physical concepts that may be brought into play.
2. The kinds of information on mechanism that may be sought.
3. The background of interpretation which can be drawn upon.
4. The kinds of analysis employed.
5. The development of new approaches derived from a different experience.

It requires just as much biological perspective, judgment, and factual knowledge.

To Dr. Alexander I would say that those of us who have entered biological research from physics need your help, encouragement, and guidance through our fledgling stage; we do have something besides instrumentation to offer biological research.

To Dr. Stacy I would suggest that we must not let enthusiasm be interpreted as presumptuousness. In whatever field of biology the biophysicist undertakes research, he must win his spurs. He cannot afford to be a physicist among physiologists and a physiologist among physicists.

Probably for certain purposes we have to be classified and put into pigeonholes, but let's not allow this zeal to prejudice our relationships, limit our interests, or cramp our thinking. The standards of good research are universal.

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Technical Papers

Source of Atmospheric Salts

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Evidence at the present time points to the importance of the sea as a primary source of hygroscopic salts in the atmospheric condensation process (*1–3*). These air-borne microscopic particles of salt are the universal condensation nuclei in the formation of rain, fog, and snow. Wind-borne salt spray has also been shown to be responsible for the zonation and spray forms of coastal vegetation (*4–6*). And the main source of soil iodine, absolutely essential in human nutrition, is wind-borne salt spray from the sea (*7*).

The exact source of these salts from the ocean has never been discovered, at least as far as the author was able to determine from literature reviews. Kohler (*1*) assumed that by some selective process salt particles or droplets of one particular size are driven from the sea. In his discussion of the composition of the atmosphere, Clark (*8*) states, "The figures for atmospheric chloride are even more surprising; but they represent in general salt raised by vapor from the ocean." Jacobs (*2*) suggested that the breaking of waves on the shore and the bursting of bubbles produced aerosols by the mechanical dispersion of the liquid. Stuhlman (*9*) has investigated the dispersion of tiny droplets in a gaseous atmosphere by the bursting of small bubbles. In water, bursting bubbles between 0.8 and 2.0 mm in diameter ejected more droplets to a greater height (14 cm) than bubbles either above or below this range. It was also shown that a smaller number of larger drops is projected to lesser heights as the size of the bursting bubble increases, and that the number and height of droplets projected plotted against the size of the bursting bubbles formed a Maxwellian-type curve.

During a study of the coastal vegetation of Brunswick County, N. C., the author had the opportunity to investigate this phenomenon. The first measurements of the landward movement of salts were made with cheesecloth salt traps (*6*). And, as previously shown, there was a decrease in salt concentration with distance from the ocean. However, it is significant that with a wind velocity of 4–6 km/hr, an average of 2.3 mg of salt/dm^2 of cheesecloth was measured in 8 hr