BIOPHYSICS

Concepts and Mechanisms

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CONSULTING EDITOR'S STATEMENT

It is unfortunate that many students of biology regard biophysics as an esoteric and "difficult" subject. The introduction of Professor Casey's "Biophysics: Concepts and Mechanisms" to the REINHOLD BOOKS IN THE BIOLOGICAL SCIENCES should do much to dispel this view. Certainly, if every premedical student had a course in biophysics—and certainly no better book than Casey's exists for that purpose today—he would find his subsequent struggles with physiology enormously simplified. This is not to suggest that Professor Casey either dilutes or oversimplifies his subject. The simplicity of this book lies in the transcendent clarity and utter logic of the presentation. A brief introduction to the necessary mathematics starts the book. This leads to a discussion of the physical forces exemplified in man, of matter waves, electromagnetic radiations, and radioactivity as they apply to biological research. The author then passes to big molecules, and through them to an introduction to bioenergetics and the speed of biological processes. The chapter on biophysical studies on nerve and muscle that follows draws point to all that has come before. The chapters on ionizing radiations and biophysical control excellently round out the broad scope of the book. All this, it must again be emphasized, is couched in language intelligible to any interested science major. I feel confident that the physicist, clinician, and biologist will find this book an ideal synthesis of an exciting interdisciplinary science.

PETER GRAY

Pittsburgh, Pennsylvania
October, 1962

Preface

This book is primarily intended to provide the student of biological sciences or of medicine with a substantial introduction into Biophysics. The subject matter, discussed in the Introduction, has been carefully chosen during ten years of teaching the subject. During this time the author has watched, in the literature, the subject begin to crystallize out from a rather nebulous mass of ideas and practices; and at the same time he has been able to observe what the students of this discipline require. Therefore, the book has been written with the needs of both student and teacher in mind, with the hope that this presentation of the choice of subject matter and the method of presenting it will be useful to others.

Three objectives have been kept in mind in the presentation: (1) to build up from the easy to the difficult; (2) to make the presentation interesting; and (3) to unify it. Accordingly, the book generally increases in difficulty from an oriented review with pertinent examples in the first part, through more difficult material in the middle and later parts. Occasional relaxations, which reduce the information rate and afford occasions for exemplification with biological material, are included. A rather vigorous insistence on dimensional analysis has been hidden in the presentation, in the attempt to make the concepts and definitions precise. Following early definition, different units and methods of expressing them are used, so that the reader will not be awed by them when he studies further elsewhere. Wherever possible, recent work is introduced.

Since the name "Biophysics" means so many different things to so many different people, the big difficulty has been to decide what *not* to write. In the interests of a unified presentation within a two-semester book, the limits chosen were concepts and mechanisms, with a minimizing of the methodology which has already been treated in elegant fashion by others.

There are some novel features about this book. The author has found them useful in his classes and would be pleased to receive the reader's opinions. Although bioenergetics in the broad sense of the term permeates the major part of the book from Chapter 2 through Chapter 9, it reaches its peak of interest in Chapter 7 in a conceptual presentation where the rigor of thermodynamics is sacrificed in favor of the development of a useful impression containing the necessary relationships: and these are illustrated. The electromagnetic spectrum (Chapter 4) and the matter wave spectrum (Chapter 3) are both surveyed, and stress is placed on those fractions which interact with (exchange energy with) biological material. The treatment of the effects of ionizing radiations (Chapter 9) surveys the hierarchy of structures, from effects on simple molecules right up the scale to man. The unified treatment of speeds (Chapter 8) attempts to show similarities and differences of mechanisms among all rate processes: chemical reactions (catalyzed), fluid flow, diffusions, and electrical and heat conductance. The apparatus of physical control is described in Chapter 10; and in Chapter 11 the bases of control biophysics are introduced in terms which attempt to span the bridge between computer technology and brain mechanisms. The author has not hesitated to introduce a difficult concept if it would later serve a useful purpose, but has tried to get the reader through it in a simple manner.

Because the scope is so broad, depth in every part of the subject could not be achieved in a book of this size. However, the bibliography is substantial, and further reading is explicitly suggested in those cases where the proper direction is not obvious.

The chief inspiration for this work was the late Dr. Jean Ettori, Associate Professor at the Sorbonne and Professor of Biochemistry at the University of Ottawa. Known to his students as "the man who always had time," he died a hapless victim of cancer in 1961, at the age of 56. This man, who had gifts of vision in the biosciences as well as deep humility and love for his students, introduced the author to this subject and emphasized the need for what he called a "psychological presentation."

The following colleagues, all specialists in their own right—in chemistry, physics, or the biosciences—read parts of early drafts of the manuscript and made many helpful suggestions: Dr. C. E. Hubley, Prof. A. W. Lawson, Prof. L. L. Langley, Dr. J. F. Scaife, Prof. M. F. Ryan, Dr. S. T. Bayley, Mr. G. D. Kaye, Mr. G. T. Lake, and Dr. G. W. Mainwood. Several other close colleagues helped by catching flaws in the proof.

Mrs. Lydia (Mion) Labelle and Miss Nadine Sears struggled through the typing of a hand-written manuscript, Miss Sears in the important middle and late stages, and produced something which Mrs. Dorothy Donath of Reinhold could further mold into a finished text. The perceptive Miss Rosemary Maxwell turned out the best of the line drawings, and these in turn illustrate her talent.

The author has had the encouragement of Dr. J. J. Lussier, Dean of the Faculty of Medicine, University of Ottawa, and of Dr. H. Sheffer, Chief

Superintendent of the Defence Research Chemical Laboratories, Ottawa, where the author carries on a research program in the interests of National Defence.

E. J. CASEY

Ottawa, Canada
October, 1962

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Introduction

SCOPE

Biophysics is today the youngest daughter of General Physiology, a sister to Biochemistry and Pharmacology. The subject matter is not yet very well defined, as the introduction to almost any of the recent essays on the subject quickly attests. Although the basic skeleton is clear enough—it being the engineering physicist's concept of a "system" suitably molded to describe the living thing—it may be many years before the dust has settled on discussions of what appendages are proper to the skeletal framework of the subject.

Consider some of the pertinent disciplines in terms of Table 1. Biochemistry and biophysics attempt to describe and interpret the chemical and physical processes of biological materials in terms of the principles of organic chemistry, physical chemistry, and physics. Biophysics is concerned with questions about the physics of biological systems. It has the advantages of less complexity and more certainty than the biological subjects, but has the disadvantage of being limited to only specific aspects of the whole living system. For the human being, biophysics can be thought of as providing a description of his whole physical system from the particular view of physics. For medical research, for the highest forms of medical specialization, and for the general medical practitioner of the years to come, the requirement seems inevitably to be a strong background and experience in the medical arts, coupled with a thorough grounding in the scientific knowledge of medicine and the scientific approach to it. The same is true of the biosciences.

The scope of biophysics today is rather broad, if judged by the attitudes of authors of papers in several of the current journals, and in various essays. Yet the master, A. V. Hill, a Nobel prize winner who published his first paper in 1910 and is still active in research and physiology, has cautioned that the use of physical techniques or ideas alone for investigation of biological problems does not of itself make biophysics. He defines the subject as: "the study of biological function, organization, and structure by physical and physiochemical ideas and methods," and then hastens to emphasize that he has put *ideas* first. He further expands* and drives home the key point as follows:

*From "Lectures on the Scientific Basis of Medicine," Vol 4, Athlone Press, London, 1954-1955; reprinted in *Science*, **124**, 1233 (1956).

> There are people to whom physical intuitions come naturally, who can state a problem in physical terms, who can recognize physical relations when they turn up, who can express results in physical terms. These intellectual qualities more than any special facility with physical instruments and methods, are essential.... Equally essential, however, are the corresponding qualities, intuitions and experience of the biologist.... The chief concern in the development of biophysics is that those [experimental] skills should be acquired by people who start with the right intellectual approach, both physical and biological.

On the question of *scope* of medical biophysics, Hill says:

> ...If biophysics is to make its contribution to medicine, it is necessary that *most* physicians should have some idea at least of what it is about, while *some* physicians should have a pretty good idea. The ideas and methods of physics and physical chemistry are being applied today and will increasingly be applied, not only directly to physical medicine and radiology, but to neurology, to the study of circulation, of respiration and excretion, and of the adjustment of the body to abnormal conditions of life and work. At longer range, moreover, they will be aimed at the fundamental problems of minute structure and organization, of the physical basis of growth and inheritance, of the ordered and organized sequence of chemical reactions in vital processes, of the means by which energy is supplied and directed to vital ends.

TABLE 1. Disciplines Surrounding Biophysics

Increasingly descriptive approach; Increased Complexity ↑	Disciplines	↓ Increased use of scientific method; Increased definition
	Clinical Studies	
	General Biology, Bacteriology, Immunology	
	Anatomy	
	Histology, Pathology	
	Pharmacology, Physiology	
	Biochemistry, Biophysics	
	Physical Chemistry, Physics	
	Mathematics, Philosophy	

Today, by the very nature of its origin, biophysics reaches into general physiology to some extent. Today, what subject matter is proper to biophysics, and even more so to medical biophysics, is not unequivocally defined. Further, just as did biochemistry, it will probably take 25 to 50 years for the scope of biophysics to evolve into general acceptance.

SUBJECT MATTER

From recent and current literature, and within the scope discussed, it has been possible to arrive at a fair idea of the topics which are termed "Biophysics."

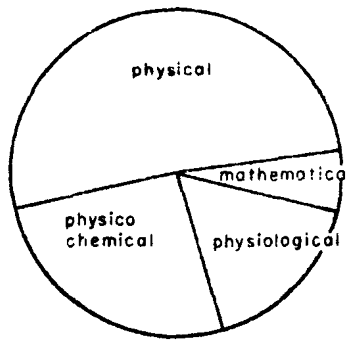
Table 2, aided by Figure 1, is an attempt to classify the subject matter in a form which lends itself to an integrated presentation. One must realize, of course, that clear-cut distinctions cannot be made, and that each of these subjects must overlap the other to a greater or lesser extent—for all are parts of a system; and these parts interact.

TABLE 2. A Classification of Biophysics

	Chapter
I. Physical Biophysics ("True" Biophysics)	
(*a*) Classical:	
Mechanics, hydrostatics and hydrodynamics, optics and sound in man	2, 3
(*b*) Modern:	
Radiological physics, both electromagnetic and matter waves; absorption; scatter; radioactive tracers	4, 5, 9
II. Physicochemical Biophysics (Biophysical Chemistry)	
(*a*) Structure of large molecules, colloids, and gels	6
(*b*) Energetics or thermodynamics:	
Energy balance and energy transfer; temperature; food values; electrochemical control of and by redox systems	7
(*c*) Kinetics and mechanisms of physical biological processes:	
Osmotic flow and water balance; incompressible flow in circulatory systems; membrane differentiation	8
III. Physiological Biophysics (Physical Physiology)	
(*a*) Classical:	
Bioelectricity; brain and heart measurements; volume conduction; membrane potentials	7, 8, 10
(*b*) Modern:	
Effects of high energy radiations; effect of physical and thermal shocks (radiation therapy, modern space medicine); system control; bioenergetics	9, 7
IV. Mathematical Biophysics	
Biostatistics; computers; cybernetics; growth rates and cycles; the systems concept	11

METHOD OF PRESENTATION

After a review of useful and necessary mathematics, which the author has found to be a pragmatic need and a valuable teaching aid, two chapters have been devoted to Topic I (a) (see Table 2). These are followed by two chapters which introduce Topic I (b). Then after one chapter on Topic II (a), three chapters deal with Topics II (*b*), II (*c*), and III (*a*), in an attempt to carry the important basic concepts through to useful applications. Systematic organization, so necessary in this era of specialization, demands a proper appreciation of the rather simple concepts which exist under the rather terrifying names!



The subject matter of biophysics (expressed as an "Area" of biological science).

Figure 1

Then the ninth chapter deals with biological effects of ionizing radiations, Topic III(*b*), and the tenth with more complicated biophysical subjects which have arisen out of physiology and for which the biophysical approach provides a useful method of organization and investigation.

Of special interest may be Chapter 11, on concepts and mechanisms of control, in which an introduction is given to some of the important consequences of the use of the systems concept, principles of control, and information theory.

Although the purpose of the book is to give physicians, medical students, and students of the biosciences a readable introduction to the concepts of biophysics rather than to make biophysicists out of them, students and practitioners of pure science and engineering may relish the zest of a human biological flavor in the presentation.

Some simple, pertinent problems or exercises have been given at the end of each chapter.

References to introductory and time-proven texts, and to some late reviews, have been carefully selected with emphasis on clarity and imagination in presentation; others have been selected for factual content only.

If the principles to follow are pondered at length, and reillustrated by the reader in other examples of his choice, the clarity of thought, and the true power and scope of the basic principle will become evident.

Conversely, it seems axiomatic, but it is often forgotten, that the serious reader should seek and expect to find in a book such as this a continuous thread of purpose in all the material contained between its covers.

CHAPTER 1

The Systems Concept, and Ten Useful Pillars of Mathematical Expression

In scientific thought we adopt the simplest theory which will explain all the facts under consideration and enable us to explain new facts of the same kind.

The catch in this criterion lies in the word "simplest." It is really an aesthetic canon such as we find implicit in our criticisms of poetry or painting.

The layman finds such a law as

$$\partial x/\partial t = k\partial^2 x/\partial y^2$$

much less simple than "It oozes," (or "It diffuses," or "It flows"), of which it is the mathematical statement.

The physicist reverses this judgement, and his statement is certainly the more fruitful of the two so far as prediction is concerned.

(J. B. S. Haldane.)

THE "SYSTEMS" CONCEPT

In modern science and engineering an almost unbelievably broad and comprehensive use is made of the term "systems" and its various connotations. Chemists have long used the term to indicate the collection of chemicals—the chemical system—on which an experimenter was working. Biologists have long used the term to indicate the group of materials and events