A Course in

BIOENGINEERING

E. F. LEONARD
Columbia University
New York, New York

IF BIOENGINEERING as an area of technical endeavor were to fulfill its many hopeful definitions; if the recognized problems of medical practice and biological research were to have all the help which it is now apparent that engineering could give them; if the human organism were to receive so much analysis relative to its complexity as it is now customary to assign to a new chemical process; if the delivery of health care were to be planned with so much care as is now used to optimize a distribution network for petroleum products; if, in short, there were to be demanded by the sprawling enterprise which man has built to study, strengthen and maintain himself only so much engineering effort as has been shown to be beneficial in more circumscribed endeavors, the requisite expansion of the profession of engineering would consume all its resources for many years to come. In fact, such a demand is unlikely.

Casting aside momentary concerns caused by retrenchments in the domestic budget of the United States, it is apparent even to the casual student of the sociology and history of science that there are more long-lived impediments. An intellectual divergence, began more than a century ago, has led to separate scientific conglomerates in the physical sciences (including engineering) and the biological sciences, the former based on presumptively determinate, precise, physical models usually as much formulated to suit the analytical tools available as to conform to the reality of interest, and the latter on necessarily indeterminate, qualitative, fractionally analyzable, biological systems, studied as found because they lost their nature when reduced in complexity. Admission to these circles has demanded commitment either to precision or to reality: in biology one might study a model but the ultimate test lay not in the consistency of the model's behavior but in its relevance to the living system it was made to represent; in physical science one might speculate about the utility of a model but peer judgment has largely centered about how completely it was analyzed and how internally consistent it was. The stunted growth of biophysics testified clearly to the difficulty of rejoining the goals of perfection in the abstract with relevance to life as lived.

THUS TWO MAJOR obstacles impede the introduction of engineering technology into medicine and biological science: the persistent complexity of analyzing living systems and the largely unreconciled standards of the peer groups in the biological and physical sciences. It is safe to predict that one or two generations of discovery and sociological accomodation will pass before engineering will, explicitly or implicitly, occupy an optimal role in the development and application of biological knowledge. Yet it is also safe to anticipate a happier future for bioengineering than for biophysics because the timeless role of engineering has been the reconciliation of abstract science with realities, those of nature and those created by the mind and hands of man.

Two steady trends create favorable circumstances for the development of bioengineering: pressure to use rapidly accumulating knowledge about parts of organisms which has not yet been fully exploited to predict the normal and disturbed performance of intact living systems, and the shift within all engineering to a stronger interplay between analysis and synthesis.

NOTWITHSTANDING such favorable omens, the challenge of passing optimally from the present flirtation to the future union is large. The interaction of engineering, including its many specialties, with the many biological disciplines is far too broad to serve as a focus of activity for the individual or a working group.

Classically, the specialties of engineering have proliferated by the interaction of an established discipline with an important, new area of application. A new discipline evolved when the interaction spawned concepts and techniques primarily useful in the area of application but of broad value in other areas of concern to engineers, when the transmission of these concepts to a new generation required new courses, when special subjects and the basic sciences on which they depended became central in the curriculum. How else was chemical engineering born but by the prolonged interaction of mechanical engineers with the chemical industry? Straightforward repetition of this pattern in the present instance appears impossible. The volume of information necessary to represent the field of application is enormous; the sciences and areas of engineering technology which are demonstrably useful encompass several curricula most of which are themselves near the bursting point. A 'bioengineer' educated to apply all parts of engineering to all parts of biology might be called upon to:

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- **make a kinematic analysis of the indeterminate structure represented by the bones and muscles of the skeleton.**
- **determine optimal positions and time schedules for administering drugs to specified target organs, minimizing dosage to other capillary beds.**
- **apply lubrication theory to the analysis of normal and diseased joints.**
- **design artificial organ systems based on membrane transport processes and enzyme reactions.**
- **determine if certain reactions occurring in the bloodstream were kinetically or diffusionally controlled.**
- **study damage to blood passed through artificial pumps, conduits, and exchange devices.**
- **evolve a systems model of all or part of the body's neuromuscular structures.**
- **find a quantitative relationship between electrical potentials on the skin surface and electromechanical events in cardiac muscle.**
- **determine the shape of normal and diseased erythrocytes passing through capillaries smaller than their major diameter.**
- **relate piezoelectric potentials to bone growth.**
- **study and model long-term effects of a weightless environment on gastrointestinal motility.**
- **devise radiotracer experiments to localize in space and on the reaction coordinate derangements of normal metabolic reactions.**

Consideration of the nature of these and many other tasks which have also been actually undertaken, as well as the scope of activity which they define, suggests that the interaction of engineering with the biological establishment can hardly avoid evolving as specializations between each of the major engineering disciplines now existing and appropriate clinical and scientific specialties in medicine and biology. No single discipline is broad enough to support bioengineering in the forms which have already developed and no single new discipline seems capable of encompassing the useful content of existing disciplines. Rather, at a time when the extant disciplines are becoming less clearly identified with a particular area of application and more clearly with concepts, sciences, and techniques, and in the absence of widely recognized, performed conceptual innovations in the area of application, bioengineering seems destined to develop as a collection of subspecializations, each potentially a major component of the parent discipline.

Bioengineering, as considered here, is primarily concerned with understanding, diagnosing, maintaining and augmenting the human organism. Chemical engineers have been and will be concerned with other biological endeavors: chemical processing with organisms and enzymes and processing of materials of plant and animal origin (often called 'biochemical engineering') and study of interactions among organisms and their surroundings (the analytical endeavor being called 'ecology' and the synthetic effort 'environmental engineering'). In each of these areas the biological information necessary for immediately (but not necessarily ultimately) effective action is more accessible and the activity is thus more technological and more closely related to classical engineering. In these areas control of the application of the engineering endeavor rests with the engineer and industrial managers. **In very large part the special educational and professional problem of the bioengineering considered here is the need for the engineer to become newly and deeply involved in biological science, even to the point of helping to restructure it, and deeply involved in applications**

As this manuscript was being completed, the author learned of the sudden death of Erwin H. Amick, professor and chemical engineering department chairman at Columbia. His encouragement was instrumental in some of the earliest as well as latest involvements of chemical engineering with bio-engineering at Columbia. His premature loss is mute testimony to what remains to be discovered that more of humanity might enjoy a full span of useful life. With sorrow and respect this article is dedicated to his memory.

Since 1969, Edward F. Leonard has been Professor of Chemical Engineering and director of the Artificial Organs Research Laboratory at Columbia University. He received his B.S. degree from Massachusetts Institute of Technology and his M.S. and Ph.D. degrees from the University of Pennsylvania. He has served as an organizer of the Bioengineering Division of AIChE, as Chairman of the AIChE subcommittee on Engineering Fundamentals in the Life Sciences, and as Vice-chairman of the United States National Committee on Engineering in Medicine and Biology. At Columbia, where he has been on the faculty since 1952, he has been chairman of the committee on Bioengineering. He has devoted a large part of his research to a study of transport processes, particularly as related to the artificial kidney for which he has designed test cells for the evaluation of membrane peremeabilities, studied blood flow, and worked on designs of artificial kidney devices. He is the author of numerous papers in this field and has presented several AIChE Today Series on this subject. He has served as consultant for St. Luke's Hospital and lecturer at the Mt. Sinai School of Medicine.

of his effort which have classically been reserved to another profession — medicine.

THAT CHEMICAL ENGINEERING should father such a subdiscipline seems indisputable. The analogy between inanimate chemical processes and metabolism is widely recognized. Prototype studies by chemical engineers show the roles of homogeneous and heterogeneous kinetics, the effects of convection and diffusion on rates and yields in living systems, and the utility of both elementary and complex analyses based on stoichiometry, thermodynamics, and momentum, energy and mass transport. Chemical engineers have collaborated with physiologists, anatomists and biochemists as well as those in such clinical disciplines as pathology, internal medicine, surgery, pediatrics, orthopedics, and urology. These collaborations have addressed problems in basic research where methods well-known to chemical engineers have defined innovations in clinical research, permitting new approaches to the analysis of data and to the design of subsequent experiments; in therepeutic medicine, where dosage schedules and programs for the use of mechanical respirators have been fixed by engineering analysis; in diagnostic medicine, where more sophisticated processing of data has yielded a sharper identification of pathological states; and in artificial organ therapy, where engineered devices, in part prescribed and controlled by engineering criteria, have replaced natural organs, first only in acute but now also in chronic situations. (No tone of triumph should emanate from such a citation. Few of these accomplishments were the first of their kind. Some attempts have led to scientific failure or, worse, to clinical disaster clearly attributable to wrong or incomplete engineering analysis. In several cases engineering studies have been more successful in clarifying or extending concepts of general utility in engineering than in solving the biological problem, the new insight being contributed as much by the biological collaborator.)

In essentially all such studies the chemical engineer has either collaborated with a biological scientist or has previously had several years of such collaborative experience. The experience of these studies is sufficient to indicate the important ways in which chemical engineers will practice bioengineering in the years immediately ahead and the extent and kind of training which they will need. The balance of this paper details such an interpretation.

Serious involvement in bioengineering requires a reasonably complete knowledge of the elements of certain biological sciences: biochemistry, anatomy, cell and mammalian physiology. For most courses in biochemistry and physiology, organic and physical chemistry are respective prerequisites and both prerequisites are helpful for either biological science. Thus the chemical engineer is uniquely well prepared among engineers for the assimilation of the biological sciences mandatory for bioengineering.

MANY BIOCHEMISTRY departments offer a broad but rigorous graduate course for non-biochemists with content, but not necessarily emphasis, equivalent to what is offered to medical students. Such courses are not more poorly organized for the use of bioengineers than are typical courses in organic chemistry for chemical engineers. At Columbia University most chemical engineers with a major interest in bioengineering take the first semester of a two-semester biochemistry sequence; many continue into the second semester which concentrates on intermediary metabolism.

Anatomy as taught to medical students is overly long and detailed and fails to emphasize principles. Nonetheless, bioengineers can profit greatly from the study of anatomy. Needed, if at all possible prior to the study of physiology, are one skill and one area of understanding. The skill is the ability to recognize and separate biological structures such as nerves, muscles, bone, cartilage, arteries and veins, and the principles (as well as the few principal exceptions) which determine how these elements are juxtaposed. To acquire this skill some non-vicarious manipulative experience is necessary. The understanding is of functional anatomy: the why of anatomical structure and the response of living tissue to mechanical stimulation. At Columbia a good course offering 3 points of credit in each of two semesters is available; different parts of the body are considered in each semester. Normally one semester is taken, preferably that dealing with the torso.

Cell physiology is often self-taught as bridging material between biochemistry and mammalian physiology. Both related subjects are much better appreciated, especially for the chemical engineer, if a course in cell physiology based on reasonable amounts of physical chemistry is taken after the study of biochemistry and before physiology.

At opposite ends of this recommended chronology of study in biological science are courses in basic biology and mammalian physiology. In many universities the former presume no knowledge of quantitative chemical and physical concepts and are thus highly descriptive, compendious, and low in conceptual content. What is needed is a course in which fundamental concepts of biology are succinctly introduced with concise, not exhaustive, illustration. The concepts should include the basic metabolism of plant and animal cells; the metabolism of the single-celled organism and its environmental interactions; the phyla of multicelled organisms, their metabolism, their evolutionary position, and their rationale in terms of environmental interactions; and an introduction to the study of genetics, growth and development. Ideally such a course should bridge between engineering and

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biological terminology wherever possible (example: showing explicitly the increase in importance of convective transport as one considers larger, more complex organisms). Practically, a clear, precise, noncompendious course in biological concepts would alone be a large enough innovation on most campuses not to be risked by insisting on a bioengineering flavor. An appropriate introductory course is a recent innovation at Columbia. Previously, decisions about how to begin a sequence of study in biological science were made individually. Students who felt sufficiently secure even if only on the basis of a high-school course in biology or some summer reading were encouraged to start with biochemistry accompanied or followed by cell physiology.

THE CLIMAX of a bioengineer's exposure to contemporary biological science should be a full course in human physiology such as that given to medical students, and including the laboratory. Physiology integrates all other biological sciences and as much physical science as has been made operational in biology into an integrated view of the normal human organism. It also deals cursorily with pathological states and pharmacological interventions. Even with the preparation indicated above, engineers can find such a course to be difficult. The usual, detailed treatment of neurophysiology uses the nomenclature of neuroanatomy. The fact-to-concept ratio of physiology is large, reflecting the general state of biological science. 'Logical' explanations of neurohumoral mechanisms consist, in fact, of one of several possible explanations. The system under consideration is so complex that rare indeed is the instructor who can discuss alternate explanations and the reasons for finding most favor with one. These difficulties notwithstanding, medical physiology courses are the major sources of organized facts about human function and are not far removed from the state of the art with respect to the consideration of the human organism as a system. At Columbia the course is most easily available in the summer session, five and one-half full days per week for six weeks, for which nine semester credits are given. In the laboratory classical experiments

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coverage of numerical methods in fluid mechanics in an intense way, biomedical topics and — if current research in several locations is successful —the use of fluid mechanics to control polymeric crystallization processes.

Thus, a Ph.D. candidate with a strong interest in fluid mechanics can move to the frontiers of 7-10 areas, in a painless way, during his tenure. Perhaps even more important than the factual material covered is the clear manner in which a substantial number of complimentary approximation techniques can be brought to bear on various aspects of the subject, and the role and limitations of each. Too, the greatest weaknesses — the simplistic empiricism of almost all constitutive approximations, both thermodynamic and rheological — emerge vividly and focus attention on areas of research in which the chemical engineer is peculiarly well qualified to play a role.

IN SUMMARY, we have attempted to describe the separate roles and goals of our first and second level courses in fluid mechanics. Similarly structured is the presentation of heat and mass transfer, chemical kinetics and reactor design, and for the first time this year, thermodynamics. We believe such multi-level instruction to be important and exciting.

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are done, mostly by the students in small groups, using modern equipment.

Participating in this much biological course work takes about one-half of a student's time for a calendar year. How he spends the balance of this time may importantly influence his professional attitude. So much biological course work is not intended to convert the engineer into a biological scientist. Contact with and progress within the engineering curriculum should be maintained during this period. However, challenging courses in engineering which do not relate to bioengineering create a disturbing intellectual bifurcation in students at this stage. At least two semester-courses which integrate engineering with biology should be available. Such courses are difficult to construct. At Columbia we have used a bioengineering seminar at which contemporary research problems are discussed, about 50% by guest speakers, 25% by students in research, and 15% by engineering faculty. The seminar is school-wide, but because of the particular composition of interests at Columbia, more than half of the subjects are of direct interest to those with chemical engineering backgrounds. So broadly based a seminar might not be effective in other circumstances. Frequently, students will be beginning a thesis or research paper while taking biological courses. This effort may provoke satisfactory integration of concepts, but at a high cost in faculty time.

AT WHAT STAGE of education should such studies be undertaken? At present it seems best to begin at the master's level. To satisfy minimum point requirements in engineering at many schools, the M.S. program may need to be extended in time and credits. However only psysiology need be taken at the graduate level, so that it is possible for the undergraduate to anticipate much of the biological science desideratum. It is, of course, also possible to commence biological studies at a later stage. In each of these suboptimal situations, however, it is substantially more difficult to achieve integration of engineering and biological concepts.

Artificial organs technology has been, for us, a valuable educational vehicle. These devices can be considered with only limited amounts of biological background although the treatment becomes more sophisticated and more satisfactory as the available background increases. We have given a one-semester course accessible to senior chemical engineers but designed to be challenging at the master's level. All possible emphasis is put on the integration of engineering concepts and biological fact. The behavior of blood in extracorporeal circuits is considered in terms of rheology, shear-susceptibility, undesired reactions with artificial surfaces, and problems of intraphase transport. Comparisons are made with intracorporeal circumstances and the problems, surgical and mechanical, of acute and chronic cannulation are considered. Primary and secondary specifications are established for cardiac replacement and assistance devices, comparing actual prostheses and their rationales with the heart and the characteristics and demands of the circulatory system. The artificial kidney and blood-gas exchangers are introduced as artificial capillary beds; specifications are established for transport capability, allowable volume, and pressure-flow characteristics, with recognition of how limitations imposed by contemporary technology prevent full reproduction of the performance of the natural counterpart.

Such a course meets several educational goals. Foremost, it provides an integrating experience the importance of which has already been stressed here. It also gives undergraduates an elective by which they can learn something of bioengineering. It demonstrates, as do other 'applications' courses in chemical engineering, the breadth of the field. It shows that the configuration of natural organs may lead to improvements in design of artificial devices even for industrial purposes. Finally such a course is often audited, seemingly profitably, by members of the biological science and medical communities and thus offers a chance to return an educational debt incurred through the many engineering students who enroll in courses in the biological sciences.

NO DISCUSSION of contemporary education for the chemical engineer interested in bioengineering should close without recognition of the extraordinary educational value of research in a field so new that much of contemporary knowledge and practice cannot yet be made available in course work. All chemical engineering M.S. students at Columbia must submit a master's thesis. For those interested in bioengineering this requirement always means exposure to a biological, usually medical, environment and frequent consultation with one or more biological scientists or academic physicians. These often serve as co-sponsors of the research.

What happens to chemical engineers who emphasize bioengineering in their graduate training? There is a small but growing artificial organs industry comprised with but a few exceptions of small companies. Perhaps a score of M.S. graduate could find employment in this industry each year. The extramural contract programs of the National Heart and Lung Institute and the National Institute of Arthritis and Metabolic Diseases put some tens of millions of dollars per year into private research organizations and thus provide employment opportunities for perhaps another twenty graduates at the master's or doctoral level. Paramedical industries have developed with little help from bioengineers (but not other engineers working on problems which could be divorced from their ultimate environment such as packaging, filtration of parenteral fluids, stress analysis of surgical instruments, design of disposable injection equipment and low-noise amplifiers for biological signals). Increasingly, these industries are seeing the need for engineers to solve problems which are much less easily separable from the biological environment, but it is difficult to say how rapidly such opportunities will become available. Perhaps, again, a score or more jobs, mostly at the M.S. level, is all that can be expected each year in the early '70's. Other openings are provided by the biological component of the United States' space effort. Both research and development are included, but the uncertain scope and composition of this effort over the next several years makes quantitative predictions most uncertain. Most uncertain of all are opportunities in the country's enormous biological research establishment where most holders of the bioengineering doctorate will seek careers. The establishment behaves insularly, even among the biological sciences; but the early successes of interdisciplinary projects, the favorable bias of the federal granting agencies toward bioengineering, the tendency of bioengineers to create a research establishment for themselves, and the persistent governmental emphasis on reduction of biological knowledge to deliver health care all indicate, albeit uncertainly, an increasing job market.

The compromise which is contemporary bioengineering education should not persist. The biological sciences are lumbering slowly toward a solid basis in physical science. As biological science courses become more quantitative and conceptual they will become more acceptable as intrinsic parts of an engineering curriculum Chemical engineering, already a discipline which is concerned with more than the chemical and petroleum industries, will offer a wider set of examples in its course offerings, ultimately including, as a matter of course, some from living systems. Unpredictable factors will determine whether most engineering schools ultimately offer curricula in bioengineering, but it appears certain that the stronger programs for the forseeable future will be less sweeping and more concentrated. A wise but enthusiastic espousal of bioengineering as an option in chemical engineering departments offers the profession an unparalleled opportunity to expand its scope meaningfully, to study new material with potential value for all applications of the profession, and to broaden its service to humanity.