System Theory and Physiological Processes

Engineers and physiologists working together in experimental and theoretical studies predict that the application of system analysis to biological processes will increase understanding of these processes and broaden the base of system theory. Richard W. Jones, professor of electrical engineering at Northwestern University, Evanston, Illinois, and John S. Gray, professor of physiology at Northwestern's Medical School, discuss these developments. Their articles are adapted from addresses delivered in Chicago in November 1962 at the 15th Annual Conference on Engineering in Medicine and Biology.

An Engineer Looks at Physiology

Historically the engineer is a constructor, a builder of devices, of structures, of systems. His forte has been the assembly of ever more intricate machines and of complex systems of which these machines are but a part. The technological advances resulting from these conventional spheres of engineering activity have already benefited the life sciences in a multitude of ways. One has only to mention the contributions of electronics, the development of artificial organs, and a host of others. But here I examine a less conventional contribution—the possible roles of engineering analysis and system theory in the study of physiological processes. The engineer immediately recognizes these ongoing systems as having many similarities to those with which he is more familiar. He recognizes them as dynamic interrelationships between a host of physical quantities—interrelationships in which the performance of the entire system depends upon that of all its components but transcends that of any one portion. This fairly recent engineering development offers promise of making contributions to the life sciences that equal if they do not exceed in value those of a more conventional engineering nature.

The engineer stands in a different relation to these biological processes than to the technological systems of his experience. He is now faced with a collection of pink boxes (not black ones) whose individual functional significance is only partially known, and whose interconnections may be only imperfectly mapped. Their operating criteria may usually be inferred, but the precise means by which these ends are secured form the basic problems of the life sciences. From observations one finds not one controller but control loop within control loop, the hierarchy of systems being obviously designed to assure self-perpetuation of the individual and its kind. Thus, though the engineer notes many seemingly similar features between his technological systems and the systems of physiology, can it be expected that the similarities will be sufficient to outweigh the striking dissimilarities of subject matter and approach? This is the question I shall examine here.

In turning to the study of physiological systems one finds a large amount of anatomical evidence available, but the structural information contained therein may bear little relation to a description of dynamic processes. Thus, in seeking a detailed, dynamic, and quantitative description of a biological process, one must frequently start from experimental observations of both structure and function and attempt to order these into a theoretical framework that will permit deduction of the properties of the system from the properties of its components. In embarking upon a study of living systems one is thus forced to develop an interaction between experiment and theoretical constructs, the one aiding the other in the development of a comprehensive quantitative description of a life process. The present gaps in anatomical knowledge (and there are many) are of such a nature that simple visual examination will not provide the answers. A salient contribution of the engineer at this point may well be the formulation of testable hypotheses growing out of attempts at theory formation.

Such a procedure, though typical of the scientific method, exhibits some novelty in this context in that it brings together two seemingly different disciplines. Cooperative investigations in which engineers and physiologists work together in the experimental and theoretical study of life processes have given clear evidence that such a mode of attack can lead to important advances in understanding. The engineer who contributes to this effort must have not only competence in his own field but a solid understanding of the biological processes in addition, so that he can aid in the theoretical formulations that lead to hypotheses and testable assumptions.

Mathematical Models

The development of mathematical models for biological processes is a study of this type—one which the engineer is well equipped to pursue. Underlying such a study is the view that an increase in understanding is likely to follow an increase in the precision and completeness with which a physiological process is described. The language of mathematics is believed to offer the means of describing the relationships between physical variables in a manner that will increase our understanding of systems too complex to be described verbally. The quantitative and dynamic relations that are represented in mathematical models and the necessity of developing a system description in themselves raise questions that would not be raised otherwise, and invariably lead to further experiments designed to test a specific hypothesis.

The development of a mathematical model for a dynamic process is bound to be an approximation procedure, but it should involve something more than the empirical fitting of curves to experimental data. In any discussion of mathematical modeling it is well to consider certain similarities between the prototype and the model, and the introduction of some specific terminology can be helpful. The physiological system is described by certain observable quantities, and by the functional relations between these physical quantities. The mathematical model consists of equations (mathematical functions) and the variables contained therein. There is then a correspondence between the physical system and the model. The prototype can be mapped onto the model through identification of the variables and the functions (relations between the variables) in the two systems. A physiological system and a mathematical model are said to be isomorphic if the elements in the two can be shown to have certain similarities in form. More specifically, a pair of variables in the prototype and a pair of variables in the model are said to be isomorphic if the two pairs show similar behavior with time under properly specified conditions. If the two pairs of variables are isomorphic, then the functions relating them may be said to be isomorphic also.

The degree of correspondence, or isomorphism, may vary widely, depending upon the details built into the model. The simplest case is that in which only two variables are selected—say the input and the output quantities—and a model is developed that within specified limits reproduces their behavior. Such a model (an analog) and the prototype would have the lowest possible degree of isomorphism, and the function relating the two variables in the model might bear little relationship in its details to the function relating them in the prototype. For certain purposes such a model might be entirely adequate. This would be the case if one wished to study a larger system, of which this prototype forms only a part. The study of the larger system would not be impeded by the lack of detailed knowledge of one of its components, provided the study did not carry the components out of the region in which their models had been shown to be valid.

It is thus reasonable to ask, Can a mathematical model do more than this? Can it lead to a genuine increase in understanding of system behavior? The answer to questions of this character is yes, provided the modeling process is continued with the express purpose of increasing the degree of isomorphism. That is, as more variables and functional relations are mapped from prototype to model, one can say that understanding has increased. With this goal of increasing the isomorphism, one attempts to develop more detailed descriptions of the component processes, being guided on the one hand by considerations of anatomy and physiology and on the other by the observed dynamic properties of the complete system. Although the dynamic behavior may provide few direct and unique clues for adding details to the model, it does supply a wealth of indirect evidence. The observed dynamic properties of the system reveal some information regarding the kinds of elements that must be present, but possibly even more significant is the negative evidence supplied, which serves to exclude certain classes of process or function from further consideration. However, the essential point seems to be that any attempt to increase the degree of isomorphism immediately leads to new hypotheses and new experiments. It is thus the modeling process itself, the continued interaction between theory and experiment, that provides a mechanism leading to greater understanding.

In any attempt to increase the isomorphism of model and prototype it is necessary that the mathematical functions have their counterparts in physiological processes. Thus, one needs a "library" of mathematical functions whose physiological significance has been demonstrated in order that the mathematical models may have more than a purely formal value. For example, a pure integrating element, represented technologically by a servomotor, may be difficult to find in a neural network or a muscle "motor." On the other hand, one finds physiological processes whose mathematical description is quite different from anything found in a technological context. An example is the retinal neural network, which apparently must be described by some form of absolute derivative function. Thus, for model building, elementary functions known to exist in physiological processes should be used, not processes found in technological systems. A great deal more work is required at the single-unit level before an adequate picture of these functions will be available.

Selection of Variables

In the modeling process one must select the variables to be used in the system description. This is equivalent to selecting the elements or components into which the system is to be resolved. The observer (the model builder) has considerable freedom of choice in this matter, and the success of his final description may well turn upon the wisdom with which he makes these selections. One factor to be considered will be that of measurement. Can the variables selected be observed directly, or at least inferred from experimental findings? A second factor is that of the mathematical form which the resulting expressions take, inasmuch as these must be amenable to manipulation and analysis. It may well be that the choice of certain variables is dictated largely by the form of the resulting mathematical expressions.

As an example, one might consider the neural pulse trains that constitute a significant communication channel in many physiological processes. Let us assume here that the information carried by a nerve fiber is represented by the interval between pulses, so that the signal may be described as a signal having pulse-frequency modulation. Thus, pulse amplitude and pulse width are ruled out of this discussion, although conceivably they may prove to be significant in certain situations. The instantaneous pulse frequency is a staircase function—that is, it has a fixed value between two pulses that is a function of the previous pulse interval. Such a mathematical function is extremely difficult to handle, and thus the question is raised whether pulse interval (or pulse frequency) is the proper variable to use in describing a physiological control system, even though it is easily measured.

To pass from consideration of a single nerve fiber to consideration of a complete nerve trunk raises further questions. The multifiber trunk transmits a multiplicity of messages, and this transmission must be described by several terms: the pulse frequency and, in addition, the number of active fibers changing as they do with recruitment, and the relative phase of the pulses between the several fibers. Each of these quantities may be undescribable by a single variable, and some form of distribution function may be required. Not every neural channel will require as much detail as this for its description, because there will be many instances in which average values are quite adequate. On the other hand, the degree of complexity inherent in neural communication channels cannot be ignored. The extent to which the complete picture can be approximated or simplified will depend upon both the nature and the needs in each particular case.

In the light of such considerations, one may well ask whether an individual neural event is the best variable to choose. It may be that some quantity other than pulse interval would serve better. One that comes immediately to mind is the postsynaptic potential, which, though it fluctuates rapidly with neural events, is nevertheless a continuous variable whose magnitude bears a direct relationship to the signal. Choice of such a variable, while hard to justify on grounds of ease of measurement, might expedite the mathematical analysis.

Another aspect of this question deserves passing mention. A nerve trunk has many parallel fibers, each possibly carrying a slightly different signal, and thus a question is raised as to just what aspects of these signals are significant. The answer can be obtained only through observing what these signals do, not from the signals themselves. Thus, one must consider in detail the demodulation of the neural signal at the muscle or gland that the nerve innervates. It is the behavior of this final control element that will govern, in many instances, the choice of variable for neural signals.

Feedback Control

Many of the physical variables within the body are maintained within close limits despite wide deviations in the external conditions, and thus one suspects the occurrence of feedback control. This is implied in the term *homeostasis*. But can a feedback controller in fact be demonstrated? To establish the occurrence of regulatory feedback in the usual sense of that term, it is necessary to show that the prototype is described by a set of cyclic relations between variables, with a sign reversal somewhere in the set of mathematical functions. In technological regulators one usually finds a reference input, established by some constant physical quantity such as a battery or a Zener diode, whose function it is to establish and maintain a constant value for the output. It seems extremely unlikely that a physiological system contains the counterpart of such devices. But this function may be performed in other ways.

The construction of a model should be based on physiological considerations alone, and these will seldom conform to the simple textbook examples. Since most of these systems obviously are nonlinear, one is forced to base development of a model initially upon a set of differential equations from which block diagrams and linear approximations may be evolved.

As examples, let us consider some of the visual-system reflexes. There can be little doubt that optical fixation is mediated by a feedback mechanism, although the precise location and mode of operation of the error-sensing element is far from clear. The same thing is true of the accommodative reflex. On the other hand, the opticostatic reflex through the labyrinths probably does not involve feedback.

One of the distinguishing aspects of physiological systems is the fact that the describing variables are in part continuous functions of time (such as temperature, pressure, and chemical concentration) and in part discrete quantities (individual neural events). Within the organism as a whole there are many transformations between discrete and continuous quantities, as for example at muscles and at proprioceptors. Even within the neural network itself, one finds these transformations at each neuron, as incoming pulses result in postsynaptic potentials which in turn lead to membrane depolarization and the generation of a new pulse. Thus, the operations by which the input pulses from several axons are combined, take place by means of the continuous postsynaptic potential within the neuron soma and in general are not the logical combination of digital-type signals. The spatial and temporal summation properties of the neuron are inherently nonlinear and vary significantly from cell to cell.

Although von Neumann in *The Computer and the Brain* (*1*) speaks of the prima facie evidence for considering the nervous system digital in character, he is quick to point out that one can draw a different conclusion as soon as one considers all the properties of the neuron. Present evidence forces one to conclude that although the transmission of information is discrete, the actual operations performed upon the information are carried out by means of continuous variables. The frequently drawn comparison of the brain to a telephone switchboard or a digital computer is probably as misleading an analogy as can be imagined. On the basis of present neurological evidence, one cannot accept the statement that neurons act as relays or binary elements.

Behavior of Neural Networks

Examination of the behavior of neural networks (insofar as these are known) reveals that they are capable of a wide variety of signal processing. The transformation from discrete to continuous to discrete signal within each neuron may well prove to be a most significant process, and one which is of the greatest importance in endowing the nervous system with the broad spectrum of properties it quite obviously possesses.

Thus, one is led to ask whether it is possible to treat complex neural networks at the individual-unit level rather than resort to various statistical measures. There can be little doubt that the events associated with a single neuron do have functional significance for the organism, despite the fact that the loss of one or more units may not result in any impairment of gross behavior. On the other hand, even a single neuron may exhibit what appears to be highly random behavior that requires statistical measures for its description. The physiological significance of random behavior can be discussed only in terms of the effect such behavior is observed to have on the unit (neuron, gland, muscle) to which the neuron is connected. This effect becomes of paramount importance in the study of neural response to known stimuli, and the separation of random and determinate components in the response is by no means easy. The use of averaging techniques appears to be a promising development, provided, of course, one does not lose a significant portion of the signal in the process.

My purpose in describing neural events in some detail has been twofold. In the first place, only by examining such processes in detail can one obtain a sufficiently complete description of a physiological system for construction of a model. The evidence clearly suggests that it is at these levels that some of the principal physiological functions are performed, and that these neural events, expressed in suitable mathematical form, must be included in some manner in any description of the system. In the second place, there is every evidence that the continued study of life processes will ultimately result in the development of better technological systems. Inasmuch as mixed systems, discrete and continuous, are relatively new in engineering design, it may well be that physiological concepts will be incorporated with greater frequency in the future.

Finally, returning to our earlier question, I maintain that the application of system analysis to physiological processes can make significant contributions to our understanding of living systems. This development cannot take place through forcing physiological systems into conventional block diagrams. It can take place if we start from experimental studies and develop a description of the system to suit the observations. This approach promises to lead to an increase in our understanding of physiological processes and, in all likelihood, to a major broadening of the base of system theory.

—RICHARD W. JONES

Reference

1. J. von Neumann, *The Computer and the Brain* (Yale Univ. Press, New Haven, Conn., 1958).

A Physiologist Looks at Engineering

The collision of two dissimilar air masses generates a meteorological front, marked by turbulence, murkiness, and precipitation. The meeting of two different scientific disciplines creates a frontier likewise characterized by turbulence, murkiness, and precipitation. One who lacks the prudence to come in out of such weather is apt to get lost in the fog and to be buffeted by currents and dashed with cold water. He is also likely to experience a curious mixture of exhilaration and frustration. Eventually, however, a brilliant new pattern of ideas and outlook is likely to emerge.

I have been asked what happens to a physiologist when he ventures across the frontier into engineering. Judging from my own experience, I think the result can be expressed in two sentences. The physiologist is not apt to become an engineer, for, as the saying goes, you cannot make a silk purse out of a sow's ear. But the physiologist can learn from engineering an enormous amount of pure physiology that he cannot learn from any other source. This may sound like a paradox, but I will explain why it is not.

One hears a great deal today about the burgeoning field of biomedical engineering. No one seems to like the term, but it does encompass a bewildering variety and an impressive range of activities, from the most practical to the most abstract; from the design of electronic instruments to the exploration of living systems; from automatic data analysis in the laboratory to diagnosis-by-computer in the clinic; from mathematical modeling to the development of medical prostheses.

One of the most active of these areas has been the exploration of living systems. For this area, at least, there is an ancient and honorable name —physiology. For centuries it has been the avowed goal of physiology to understand how the living organism works, or functions. This was the goal when the only available tools were the naked eye and a scalpel. It remained the goal when the manometer of the physicist and the test tube of the chemist became available. It is still the goal today, when the engineer's instruments, techniques, and concepts are brought to bear on the age-old problem. There is one difference, however; this latest addition to the armamentarium promises to be more effective than its predecessors in helping physiology attain one of its goals.

Despite faithful and persistent efforts, physiology has found one of its goals to be exceedingly elusive. What this goal is may be illustrated by a parable. Imagine a race of brilliant but primitive jungle dwellers who have just captured a television set from our strange civilization. They organize a Manhattan Project to investigate this wondrous thing, with the goal of understanding how it works. With great enthusiasm they dissect it into its elementary components, which their expert taxonomists find they can neatly classify into conductors, resistors, capacitors, and inductors. Teams of researchers are then assigned to study each of these classes exhaustively. Eventually, having learned absolutely everything there is to know about these components, they declare a national holiday to celebrate the attainment of their goal of understanding how the television set works.

Laugh if you will at these poor aborigines who have so egregiously missed the boat. We know that they have learned nothing about the television *set*. We know it to be a *system* —an organized arrangement of interacting components—whose unique circuitry confers capabilities utterly lacking in any of its isolated components.

What is obvious in the case of the television set is no less obvious in the case of the living organism. The longest-recognized fact about the latter is that it is a self-maintaining, self-regulating, self-adapting, self-operating, self-reproducing system. It is the system to end all systems. In fact, we might say that the very secret of life is organization. Physiology must come to understand living systems as well as their isolated components.

The living organism is a hierarchy of control systems organized at a succession of levels. Each component is both a subsystem in itself and an element in a supersystem. At the highest level is the organism-as-a-whole; at successively lower levels come organ systems, organs, tissues, cells, organelles, macromolecules, and ultimately the particles of physics. At each of the living levels of this series the components are organized as control systems. If the organism is to survive, none of these systems can run rampant; each must operate in the interest of the whole.

Analysis and Synthesis

At each level of this hierarchy of control systems there is a physiology, involving both analytic and synthetic problems. Analysis strives to define the behavior of components isolated from their systems; synthesis strives to deduce the behavior of systems from a knowledge of their components and organization. Thus, analysis moves downward through the hierarchy while synthesis moves upward. But in order to understand a system, at whatever level of organization, one must synthesize as well as analyze. Both are necessary, yet neither is sufficient. Analysis properly comes first, but synthesis must follow.

Although impressive and truly exciting progress has been made in the analytic phase of physiology, we are only on the threshold of an effective synthetic phase. Further delay, however, invites calamity, for without the organization and assimilation which only synthesis can provide, the accelerating accumulation of analytic knowledge threatens physiology with the frightening fate of the sorcerer's apprentice. Guidelines for fruitful physiological synthesis have not come, and are not likely to come, from physics and chemistry, for synthesis in these disciplines is restricted to the subliving level of organization. It has not proved easy for physiology to develop its own guidelines when confronted with systems of baffling complexity. It is simply not the way of intellectual evolution to lick the toughest problem first.

Yet there is a field, traditionally unrelated to physiology, which has long concerned itself with systems—with their analysis and synthesis as well as with theory and principles. It had the good fortune to be able to evolve naturally from the simple to the complex as a growing body of theory and methodology provided the catalyst. That field, of course, is engineering. Its earlier successes, from designing wigwams to keep us warm to building giant machines to amplify our muscle power, shed little light on living systems. But the present century has witnessed an explosive evolution in engineering. The principle of the closed-loop system, through which information as well as power is transmitted, has been exploited in the design of devices exhibiting responsive, adaptive, and controlled behavior of a kind hitherto seen only in living things. In a sense, the engineers have unlocked some of the secrets of nature's design principles. The accompanying theory and methodology are precisely those that physiologists have long been seeking as guidelines to the synthetic phase of their own science. It is thus no paradox that engineering has much to offer that is meaningful to physiology.

Control Systems

The discovery that the principles of control systems so beautifully worked out by engineers can be fairly directly translated into fundamental principles of physiology was an exciting one. Knowledge of the principles of control systems sheds a penetrating light on the behavior of physiological systems, results in a more powerful approach, and reorients one's outlook to such a degree that all one's thoughts, experiments, and teachings in physiology are affected. Take, for example, the concept of homeostasis, fundamental in physiology. It recognizes that if an organism is to survive, certain critical factors in its internal environment must remain constant within tolerable limits in spite of threats from a host of disturbing factors. It emphasizes this constancy almost to the point of ignoring the nature of the mechanism essential to its achievement—a mechanism which must necessarily involve a system with an actively manipulated variability. The concept of homeostasis is an initial expression of a principle that has found powerful and illuminating expression in engineering control theory. A physiologist can learn more about it from a brief study of engineering sources than from an exhaustive study of classical physiological sources. At the same time he will discover that the concept has been generalized to include the more sophisticated following device, or servomechanism, counterparts of which are also to be found in nature.

Most physiological control systems, whether regulators or servomechanisms, are of the closed-loop variety, which may prove treacherous to one accustomed to think in terms of the simpler open-end system. When an open-end system is forced, responses occur only ahead of the point of forcing and the rest of the chain can be conveniently ignored. But the responses of the closed-loop system inevitably involve the entire circuit, no matter where the forcing is applied; hence, no part of the system can be ignored. It follows that any experimental interruption of the circuitry profoundly alters the behavior of a closed-loop system. This affords a most useful means of exploring the system, to be sure, but special pains must be taken to avoid mistaking the modified system for the original. The behavior of components is apt to be quite different in isolation than in circuit; the circuitry may suppress certain responses while exaggerating others. The isolated, piecemeal outlook so comfortable and appropriate for the open-end system can become a booby trap when unconsciously carried over to the closed-loop system.

I do not want to leave the impression that engineering literature is nicely designed for the casual perusal of the physiologist. On the contrary, it is presented in a fashion best suited to the specialized needs of the designer of systems to be synthesized from simple, known parts to meet predetermined specifications. The problem of the physiologist, however, is to explore unknown systems grown by nature from components often hard to delineate, rarely well understood, and seldom linear. Accordingly, the physiologist must pick and choose and digest the engineering material, seeking the most general, ferreting out the specialized restrictions, and translating constantly from the problem of design to that of exploration, and from hardware to flesh and blood.

In addition to translatable control principles, engineering has other things to offer, perhaps even more valuable in the long run—a methodology and an attitude. The methodology is the powerful one of systems analysis, which is simply analysis followed by synthesis as the means of exploring, representing, and understanding system behavior. Physiological systems are no different from engineering systems in one fundamental respect: both are mechanisms whose behavior is determined by the nature, number, and circuitry of their components. Each component has some input-output function which it is the goal of analysis to establish. Synthesis of these component functions according to their unique circuitry can yield the determinate behavior of the whole system.

Mathematical Modeling

A key feature of systems analysis is mathematical modeling. This is merely a new designation for the old practice of representing functional behavior in quantitative mathematical form. The ultimate goal is to achieve a final, valid model which faithfully describes the entire spectrum of system behavior. But this, of course, is an ideal, approachable only as a limit. In the earlier, more realizable stages, mathematical modeling plays two indispensable roles: it summarizes present understanding in a precise form, and it guides further inquiry. Experimentation without modeling may become random and sterile, for it is insight that makes experimentation fruitful and enables the experimenter to recognize the fruit. On the other hand, modeling without experimentation soon becomes unbridled speculation, a mere exercise in the abstract. It is the continual, intimate interaction of experiment on modeling and of model on experimenting that yields optimal progress. This does not mean that the experimenter and modeler must be one and the same person, but it does imply that each must be responsive to the other.

Physiological as well as engineering systems are dynamic in nature—that is, their behavior exhibits time factors that are of critical importance. This the engineer fully understands and turns to his advantage, for the dynamic approach permits a more penetrating analysis of the system. But the dynamic features of physiological systems have sometimes been ignored, with inevitable confusion resulting from failure even to differentiate transient and steady-state responses. Admittedly, the dynamics of nonlinear physiological systems pose a more formidable mathematical problem than those of linear engineering systems. This may well justify a decision to make the initial attack on the simpler, steady-state phenomena, but even then the experiment must be so designed as to yield proven steady-state responses. On the other hand, dynamic analysis, as developed by the engineer, offers a relatively unused but potentially powerful tool for exploring physiological systems.

The Rigorous Attitude

The engineer resembles the pure physicist and the pure chemist in an important characteristic for which there is no accepted word. All three strive to explore thoroughly and with painstaking logic all the implications of their concepts, to rely on mathematics to guarantee straight thinking in quantitative matters, and to make all assumptions and simplifications explicit in order to facilitate the observance of any restrictions they may impose on the applicability of the result. For lack of a better word, and at the risk of raising the hackles of mathematicians, I shall call this the rigorous attitude. The engineer learned it the hard way when his building collapsed, or his bridge oscillated to destruction in a wind, or his billion-dollar rocket fizzled. Physiology needs this attitude even more than most sciences, for the more complex the problem is, the more essential a rigorous treatment becomes. Rigorousness demands the application of mathematics, however painful the thought may be.

The successful use of mathematics often presupposes simplification, abstraction, and approximation in the initial attack. Although physiologists have never hesitated to borrow simplifications from the "exact" sciences (ideal-gas laws, for instance), they have traditionally insisted that simplification of the complexities that plague their own field must lead only to misleading inaccuracies. But "exact" scientists long ago discovered that it is nonrigorous deduction from confused complexity that is most surely misleading. By contrast, rigorous deduction from ingenious simplification is extraordinarily illuminating and has the further crucial advantage that it focuses attention on residual discrepancies that both prompt and guide further attempts to achieve a closer approximation. This is merely an example of the truth of the ancient maxim that progress emerges from error far more easily than from chaos. Simplification makes rigorous treatment possible. The mastery of the complex comes in steps, but sound, sequential steps are more effective than rickety, haphazard steps.

The engineer has developed one device for enforcing an elementary rigorousness that is refreshingly simple and general. This is the block diagram, a qualitative mathematical model which conveniently displays, without distracting detail, all the components and variables of a system together with their circuitry. For each component mechanism of the prototype one draws a box; for each input to the component (there are often several) one draws an entering arrow, and for each output, an exiting arrow. The box thus stands for whatever input-output function governs the component. Synthesis of the system is represented by joining the boxes through those arrows they have in common. We have found this mathematical device to be a boon, not only in our thinking and research but in our teaching.

On several occasions I have had the opportunity to watch a fellow physiologist attempt to represent in this simple form and at this elementary level the system on which he is expert. He is usually flabbergasted to discover that his ready knowledge is unequal to the task. He finds he is uncertain about numerous items suddenly revealed for the first time to be of key importance. The usual result is a period of cerebration more intense, novel, and cogent than any he had previously accorded the system, punctuated by trips to the library to find answers to questions never before asked. If a workable diagram is eventually formulated, the light it sheds may be truly exciting. One can suddenly see physiological flesh and blood as a coherent, determinate, functioning system instead of a collection of mnemonically ordered facts. This is what physiology has long been striving for.

Conclusions

Over the past centuries physiology has weathered a series of revolutions generated by the introduction of powerful tools and concepts from other disciplines, notably physics and chemistry. On each occasion such infusion of new ideas has enormously strengthened and enriched physiology. Today, the introduction of tools and concepts from engineering promises another revolution with another strengthening and enrichment. Among the things engineering has to offer are some that are close to the heart of physiology. These must be adapted and thoroughly integrated into the body of physiological concepts, attitudes, and operations. This goal presents a challenge which physiologists cannot afford to ignore. It calls for an "operation bootstrap" on the part of those of us long past our student days. It will entail a changing pattern of undergraduate preparation and graduate education for those who will become the physiologists of the coming generation. But a welcoming of the challenge and an encouragement of efforts to meet it will transform this opportunity, as others have been transformed, into another revolutionary advance in physiology.—JOHN S. GRAY