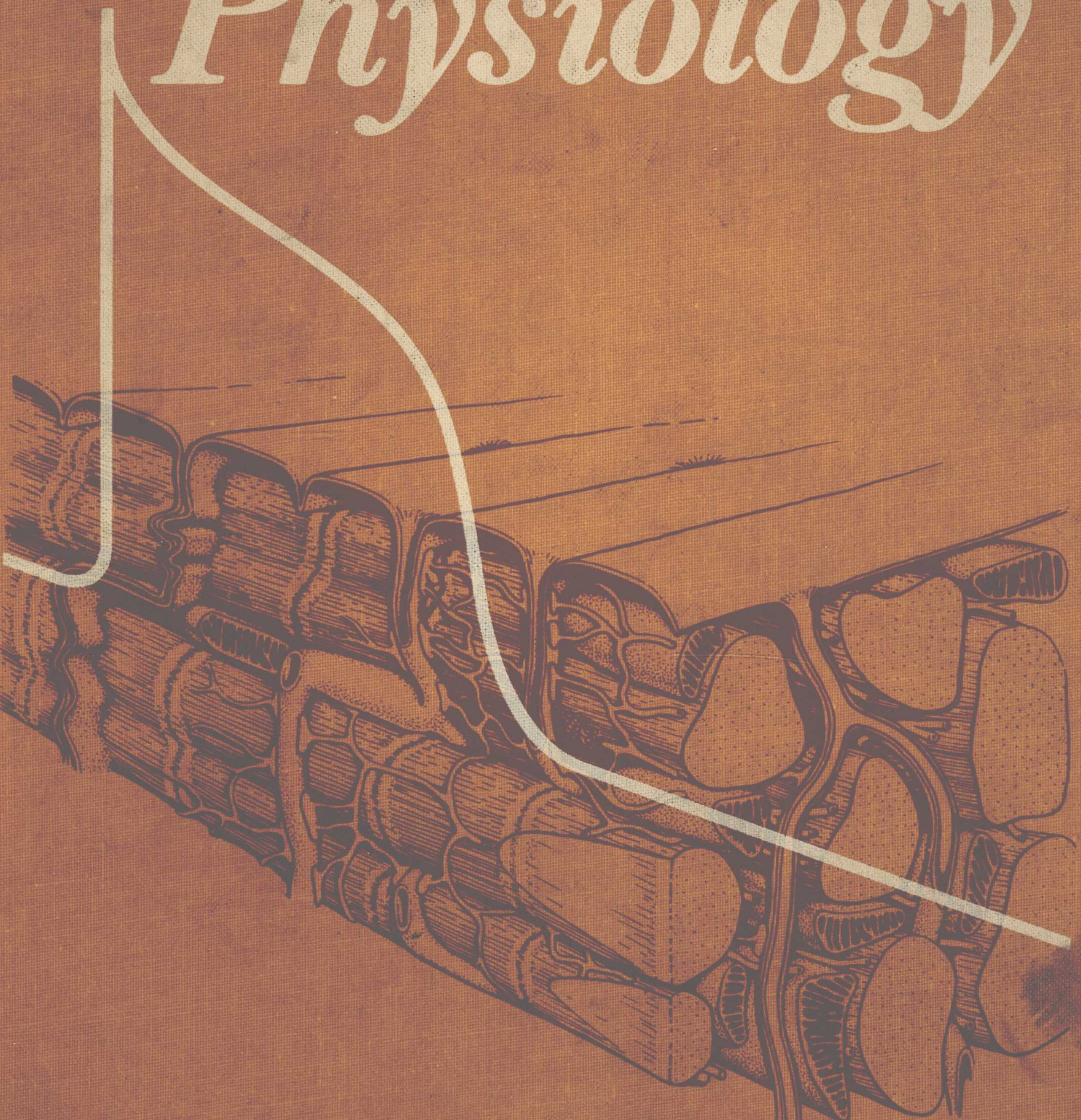
Animal Physiology

Eckert
&
Randall



Physiology

with Chapters 13 and 14 by
David Randall
THE UNIVERSITY OF BRITISH COLUMBIA

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Preface

The diversity and adaptations of the several million species that make up the Animal Kingdom provide endless fascination and delight to those that love nature. Not the least of this pleasure derives from a consideration of how the bodies of animals function. At first it might appear that with so many kinds of animals adapted to such a variety of life styles and environments, the task of even beginning to understand and appreciate the physiology of animals would be overwhelming. Fortunately (for scientist and student alike), the concepts and principles that provide a basis for understanding animal function are relatively few, for evolution has been conservative as well as inventive. The basic principles and mechanisms of animal physiology form the central theme of this book.

A beginning course in physiology is a challenge for both teacher and student because of the interdisciplinary nature of the subject. Not all students, even by their junior and senior years, have had exposure to all the chemical, physical, and biological subject matter required for an adequate background. On the other hand, most students are eager to come to grips with the subject and get on with the more exciting levels of modern scientific insight. For this reason, I decided several years ago to prepare a textbook in animal physiology that presents the essential background material in a way that allows the student to review it on his or her own. In that way it is hoped that the student is led gently but quickly to the ideas and principles of animal function and an understanding of their experimental elucidation.

Thus this book was written with the student's comprehension the major consideration.

This book attempts to develop the major ideas in a simple and direct manner, stressing principles and mechanisms over the compilation of information, and illustrating the functional strategies that have evolved within the bounds of chemical and physical possibility. This is done with examples selected from the broad spectrum of animal life, ranging from the protozoa at one end to our species and other vertebrates at the other end. It is the common principles that have been stressed, however, rather than the exceptions. Thus the more esoteric and peripheral phenomena have intentionally received only passing attention, if, indeed, any at all, so as not to distract from central ideas. Math is used where essential, but priority is given to the development of a qualitative and intuitive understanding rather than to quantitative derivations.

The ideas developed in the text are illuminated and augmented by liberal use of illustrations and parenthetical "boxes." Other pedagogical aids are a 1000-word glossary and various chapter end materials, including summaries, exercises, suggested readings, and lists of literature cited. References to the literature within the body of the text and in legends have been made unobtrusively, but hopefully with enough frequency so that the student becomes aware of the role of scientists and their literature in the development of the subject. The text often uses the device of a narrative describing actual, composite, or thought experiments to provide a feeling for methods of investigation while presenting information.

Originally I set out to write this book alone, but it became evident that this would take too long and spread my efforts too thin. I was fortunate, therefore, to have been able to enlist the collaboration of David Randall of The University of British Columbia to write the two chapters on respiratory and circulatory physiology.

The chapters of this book can be grouped into five sections. The first two chapters are intended primarily as introduction and for review of the essential physical and chemical background not covered in later chapters. Chapters 3 and 4 are devoted to a survey of cell energetics and regulation of the intracellular milieu. Chapters 5 through 8 deal with excitable membranes, nerve signals, sensory mechanisms, and the function of the nervous system. Chapters 9 and 10 consider the phenomena of contractility and motility, and Chapters 11 through 14 cover the systems (endocrine, osmoregulatory, respiratory, and circulatory) responsible for the homeostasis and supply of the internal environment. Certain special topics, such as temperature regulation, reproductive mechanisms, and adaptations to stressful environments, are considered along with those subjects to which they are most closely related, an approach that we feel is appropriate for an elementary book that stresses the general principles of animal function.

Finally, I would hope that our readers will not hesitate to help us with their suggestions for improvements and corrections for the next edition.

August 1977 ROGER ECKERT

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CHAPTER ONE

The Meaning of Physiology

Animal physiology can be defined as the study of animal function. The ultimate goal of this subject is to understand, in physical and chemical terms, the mechanisms that operate in living organisms at all levels, ranging from the subcellular to the integrated whole animal. This goal is indeed an ambitious one, for each living organism, even a single cell, is incredibly complex. For this reason it has proved convenient to divide the subject of physiology into a number of subspecialties. These include general and cell physiology; organ, organismic, and environmental physiology; respiratory, circulatory, digestive, endocrine, developmental, neuro-, behavioral, and sensory physiology; and others. In spite of these somewhat contrived divisions, it has become apparent that common principles recur throughout, providing a thread of continuity. It has also become apparent that these principles arise from the properties of matter and energy.

In an elementary textbook, it is necessary to introduce the specialties somewhat arbitrarily as separate chapters so as to avoid overwhelming the student with complexity. It is helpful to remind the reader, however, that the various body functions require the coordinated activity of a number of tissues and organs. The brain, for example, cannot function without a constant supply of blood, carrying oxygen and glucose, provided by the pumping of the heart. The heart cannot survive more than minutes without oxygen supplied to the blood by the lungs. The lungs cannot function without neural commands to the respiratory muscles from the brain. Similar examples abound also at subcellular levels of function. Thus many chemical reactions in the cell require the integrity and metabolic activity of biological membranes, whereas the latter depend on some of these same reactions for production of energy-donor molecules required for the regulatory functions of the membrane.

Why Animal Physiology?

From a biological standpoint, the human species is part of the Animal Kingdom, sharing a common evolutionary history, a common planet, and the same laws of physics and chemistry. The same principles and mechanisms of Mendelian and molecular genetics hold for us that operate for the creatures of the field, sea, and sky. Moreover, the fundamental biological processes that, in sum total, are termed "life," are shared in common by all animal species. Thus the processes that give rise to the beating of the heart in the human body are fundamentally no different from those that underlie cardiac functions in a fish, frog, snake, bird, or ape. Likewise, the molecular and electrical events that produce a nerve impulse in the human brain are fundamentally no different from those that produce an impulse in the nerve of a squid, crab, or rat. In fact, most of what we have learned about the function of human cells, tissues, and organs has first been learned on various species of both vertebrates and invertebrates.

The first step in physiological research is to ask a question—for example, "Which inorganic ion carries the current that initiates the nerve impulse?" The next steps include the choice of tissue in which to investigate the problem. In studying nerve cells, it is extremely helpful to use one that is large, so as to facilitate certain procedures. For that reason, the major findings on nerve function have been made in work done on the giant axons of the cuttlefish and squid (see Chapter 5). Subsequent experiments, done with newer methods and with the benefit of the groundwork laid by the work on the squid, have confirmed that the nerves of humans and all other animals function in basically the same way. Our purpose, in this book, is to emphasize those processes that are basic to all animal groups and to see how they have been investigated. In addition, we will note special adaptations that serve to illuminate the ways in which environmental challenges have been met during the course of evolution by selection of functional specializations.

Physiology and Medicine

The time is past when students unquestioningly accept a program of study simply because someone has decided that it is "good" for them. For that reason we will briefly consider why an understanding of body functions is relevant to the daily existence of modern man. First and most obvious is that physiology, especially as it applies to the human body, is the cornerstone of scientific medical practice. Throughout the ages, as in today's primitive societies, the approach to disease and malfunction has been almost entirely empirical—that is, by trial and error. Because this process has been applied over such long periods of time, human societies have found that certain ailments improve in response to certain treatments, be they herbs, hot water baths, acupuncture, or even the psychological treatments of witch doctors. In fact, the medicinal effects of many modern drugs—aspirin, for example—have been discovered by purely empirical means, and the primary actions of some important medicines remain unknown. As our understanding grows of function and malfunction of living tissue, it is becoming increasingly more feasible to develop effective, scientifically sound treatments for human ills. A physician who understands body function is better equipped to make intelligent and insightful diagnoses and decisions for effective treatment. Those who do not are, in effect, modern versions of the medicine man, dispensing drugs with little more understanding than that obtained from the advertising brochures of pharmaceutical firms.

Physiology and the Human Experience

Besides satisfying a natural curiosity as to how our bodies live, move, metabolize food, and procreate—basic physical manifestations of life—the study of physiology is of great philosophical interest in helping us understand the nervous and sensory systems—those biological substrata of the human spirit in which resides all subjective experience: consciousness, awareness, thought, memory, learning, language, perception, and intellect—the sum of what is most specially human.

All animals, including humans, depend entirely on their sense organs and nervous system for information about the environment and the internal status of their bodies. Sensory input, together with the genetically inherited organization and properties of the nervous system, is responsible for all "knowledge," and determines how each animal behaves. (Some have claimed that there are channels of sensory input that bypass the physiological senses, but evidence in support of extrasensory perception has been equivocal and totally unconvincing to the scientific community at large.) Our ultimate dependence on our sense organs and the very personal nature of sensory perception becomes profoundly evident when we contemplate the problem of communicating subjective experience. For example, how would you explain to an individual who has been totally blind since birth the visual sensations we term "red" or "green," or even "light" and "dark"?

It is difficult to say to what extent physiological and biochemical studies will explain higher mental experiences and answer such questions as "How does the brain 'remember' past experiences?" or "How is a mental image of a visual scene generated from past or present input to the eyes?" Questions about the origin of subjective experience may or may not be entirely answerable, but they are of such fundamental importance to human self-knowledge that the quest for answers must certainly equal or exceed in philosophical importance any other intellectual endeavor. The elucidation of the molecular basis of heredity and the exploration of the moon were the great scientific and technological adventures of the past 20 years. The elucidation of the mechanisms that give rise to human behavior and higher brain functions will undoubtedly be the great scientific adventure of the coming decades.

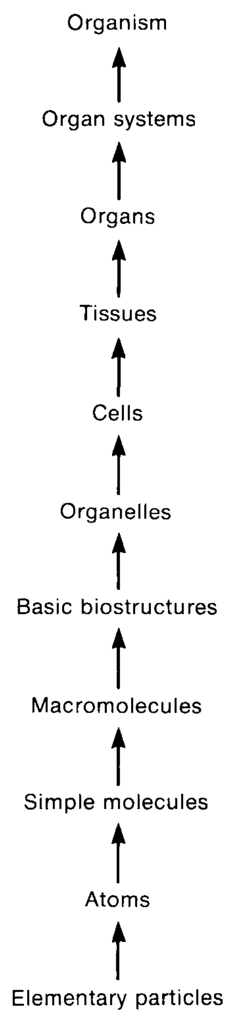
Central Themes in Physiology

As in all other fields, certain principles recur throughout the study of animal function. We will consider a few of these here. You will doubtless discover more as you go on to later chapters.

FUNCTION IS BASED ON STRUCTURE

The movement of an animal during locomotion depends on the structure of muscles and skeletal elements (e.g., bones). The movement produced by a contracting muscle depends on how it is attached to these elements and how they articulate with each other. In such a relatively familiar example, the relation between structure and function is obvious. The dependence of function on structure becomes more subtle, but no less real, as we direct our attention to the lower levels of organization—tissue, cell, organelle, etc. (Fig. 1-1). One of the most intensively studied examples of functional dependence on structure is the contractile machinery of skeletal muscle (Chapter 9). Our understanding of how a muscle contracts rests largely on an understanding of the ultrastructure of the contractile machinery as well as on its chemical properties.

The principle that structure is the basis of function applies to the biochemical events as well. The interaction of an enzyme with its substrates, for example, depends on the configurations and electron distributions of the interacting molecules. Changing the shape of an enzyme molecule (i.e., denaturing it) by heating it above 40°C is generally sufficient to render it inactive, since it no longer properly "fits" the substrate molecule.



1-1. Structural hierarchy in a metazoan animal. In a protozoan, the cell is also the organism. "Basic biostructures" include membranes, microtubules, and filaments. At each level, function depends on the structural organization of that level and those below.

GENETICS AND PHYSIOLOGY

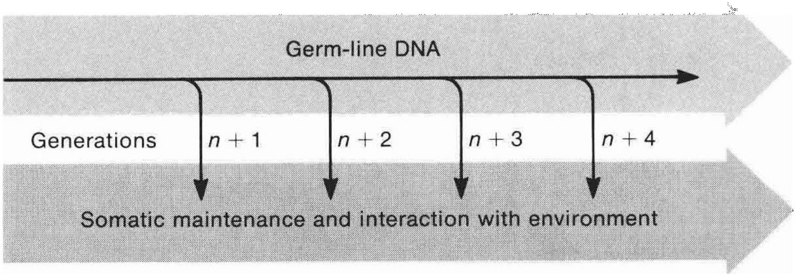
It is generally agreed among scientists that the information content of a deoxyribonucleic acid (DNA) molecule is the result of many generations of natural selection. Those spontaneous alterations (mutations) in the base sequence of the germ-line DNA that enhance the survival of the organism to reproduce are thereby statistically retained, and increase in frequency of occurrence in the population of organisms. Conversely, those alterations in the base sequence of the DNA that render the organisms less well adapted to their environment will lessen the chances of reproduction and thus will be statistically suppressed and perhaps eliminated. Though it is common knowledge that Darwinian evolution has determined the basic structural details of all living species, it should be evident that function (which is closely tied to structure, as noted above) has also evolved through Darwinian means. Nevertheless, since evolutionary pressure can work only within the confines of chemical and physical laws, the nature and function of living systems are ultimately limited by the fundamental chemical and physical properties of the constituent elements and molecules.

Toward the end of the nineteenth century, August Weismann elaborated a theory of heredity in which he postulated the *continuity of the germ plasm*—namely, that genetic material passed on from metazoan parents to their offspring is contained in a line of *germ cells* that, in each generation, is derived directly from parent germ cells, creating an uninterrupted lineage. This germ plasm is hereditarily independent of the somatic cells, which arise from the germ cells and die off at the end of each generation. DNA is the molecular equivalent of Weismann's germ plasm, and can be viewed as a continuous lineage of replicating strands that are passed from generation to generation within a species (Fig. 1-2).

The blind process of evolution is centered on the survival of the germ-line DNA, for it is the informational content of the DNA that encodes a species, and once the germ line is lost, that species becomes immediately and irreversibly extinct. Every somatic structure and function outside the continuous, generation-to-generation lineage of germ-line DNA is subservient to the survival of the germ line. Conversely, the soma owes its origin to the DNA.

There exists, then, a symbiotic relationship between the germ-line DNA and the rest of the organism. Neither can survive without the other. The soma owes its existence to the DNA, and the DNA cannot survive without the somatic functions concerned with the short-term survival of the organism. The philosophical loop is closed, so to speak, with the realization that the structure and function of a species, and even its behavior, have evolved through natural selection for one ultimate "purpose"—to enhance the probability of the survival of the germ-line DNA of the species. To this end, the somatic functions of an organism are all directly or indirectly concerned with the acquisition and conversion of energy and matter from the environment. All else is frosting on the biological cake.

1-2. Concept of germ-line continuity. The germ-line is preserved by the physiological activities of each succeeding generation. Natural selection favors those physiological processes that enhance the probability of reproduction, and thus the transfer of the DNA to the next somatic generation.

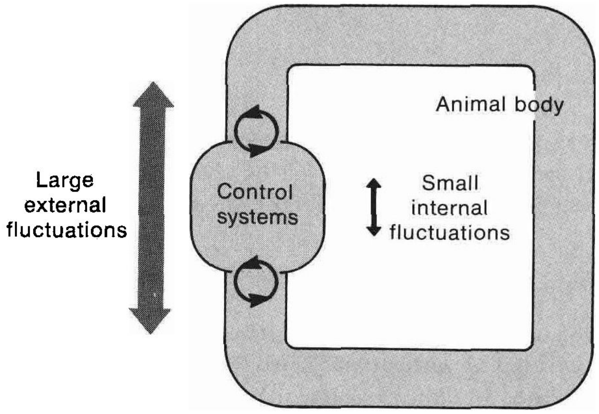


THE PRINCIPLE OF HOMEOSTASIS

The nineteenth century French pioneer of modern physiology, Claude Bernard, was the first to enunciate the importance of *homeostasis* in animal function when he noted the ability of mammals to regulate the condition of their internal environments within rather narrow limits. This is familiar to all of us from routine clinical measurements on human blood and measurements of our body temperatures. "Constancy of the internal milieu," as Bernard phrased it, has been found to be a nearly universal phenomenon in living systems, allowing animals and plants to survive in stressful and varying environments (Fig. 1-3). The evolution of homeostasis is believed to have been the single most important factor that has allowed animals to venture from physiologically friendly environments and to invade environments more hostile to life processes.

Regulation of the internal milieu applies to unicellular organisms as well as to the most complex vertebrates. In the latter and in other metazoans the composition of the fluid surrounding the cells of all tissues is subjected to constant regulation so that its composition (and even temperature in birds and mammals) is kept within a narrow range. Single-celled animals, the protozoa, have been able to invade fresh water and other osmotically stressful environments because the concentrations of salts, sugars, amino acids, and other solutes in the cytoplasm are regulated by membrane permeability, active transport, and other mechanisms that maintain these concentrations within limits favorable to the metabolic requirements of the cell, and quite different from the extracellular environment. The same is true for the individual cells of the metazoan organism, which also regulate their cytoplasmic milieu.

The regulatory processes of cells and multicellular organisms are based primarily on the principle of *feedback* (see Box 1-1). A man-made system can, in principle, be made so accurate that it will produce a predicted result under ideal, defined conditions. Living systems, however, do not function under ideal conditions; they must be able to function under the variable conditions to which they are subjected by the vagaries of nature. Control in the face of the finite accuracy of genetic and metabolic mechanisms—to say nothing of external perturbations—requires con-



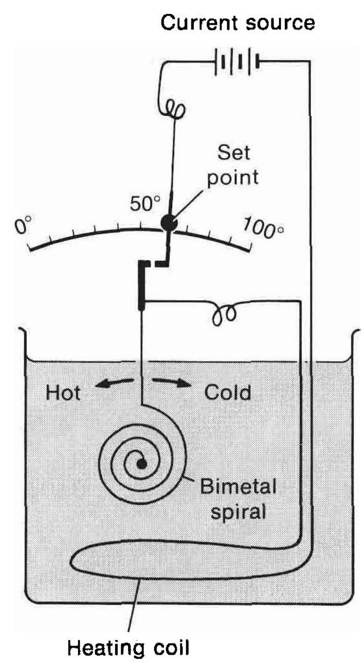
1–3. Physiological regulatory systems maintain internal conditions within a relatively small range of fluctuation in the face of large variations in the external environment.

tinuous regulation, which involves continuous sampling and correction. For example, suppose that an experienced driver is placed in a car on a straight, 10-mile long stretch of traffic-free highway, is allowed to position the car, is blindfolded, and is then required to drive the 10 miles without deviating from his lane. The slightest asymmetry in the neuromotor or sensory systems of the driver, or in the steering mechanism of the car—not to mention wind or unevenness of the road surface—makes this an impossible task. On the other hand, if the blindfold is removed, the driver will utilize feedback to stay in his lane. As he perceives a gradual drift to one side of the lane or the other, due to whatever internal or external perturbations, he will simply correct by a compensatory motor output applied to the steering wheel. This can be summarized in the terms used in Box 1-1. The visual system of the driver acts as the sensor in this case, while his neuromotor system, by causing a correctional movement in the direction opposite to the perceived error, acts as the inverting amplifier that corrects for deviations from the set point.

Another example of the regulation by negative feedback can be demonstrated with a thermostatic device that senses whether the temperature of a hot water bath is equal to or above or below the set point (Fig. 1-4). As long as the water temperature is below the set-point temperature, the sensor maintains the heater switch "on." As soon as the set-point temperature is achieved, the heater switch is opened, and further heating ceases until the temperature again drops below the set point. The "thermostat" that controls mammalian body temperature (situated in the brain) is set for about 37°C. Toxins produced by certain pathogens change the set point of this thermostat to a higher temperature, so that a fever develops.

Examples of physiological feedback systems occur in intermediary metabolism (Chapter 3), in neural control of muscle (Chapter 8), in circulatory control (Chapter 13), in respiration (Chapter 14), and in endocrine control (Chapter 11).

1–4. Example of a regulated system. A bimetal spiral, fixed at its center, unwinds slightly as the temperature of the water bath drops. The circuit is completed as the contacts touch, allowing electric current to flow through the heating coil. As the water warms, the contacts separate. The desired temperature set point is adjusted by positioning the contact of the thermostat.

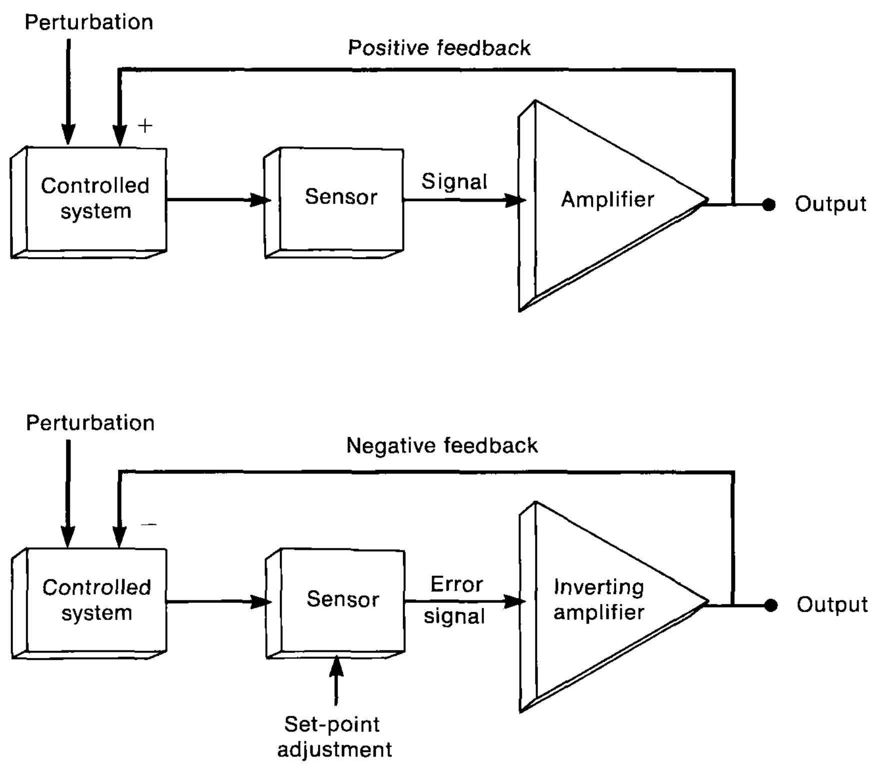


BOX 1-1 THE FEEDBACK PRINCIPLE

A servosystem uses *feedback* to maintain a given preselected state. Feedback is widely employed in biological systems, as well as in technology and engineering. Feedback can be either positive or negative, each producing profoundly different effects.

POSITIVE FEEDBACK

In the system shown in the upper diagram of the figure, an applied disturbance or perturbation acting on the *controlled system* is detected by a *sensor* and introduced at the *input* of an *amplifier*. Suppose the signal is amplified but that its sign (plus or minus) remains unchanged. In that case the *output* of the amplifier, when fed back to the controlled system, is reamplified and has the same effect as the original perturbation, reinforcing the perturbation of the controlled system. This configuration, which is called *positive feedback,* tends to be highly unstable, because the output becomes progressively stronger. A familiar example occurs in public address systems when the output of the loudspeaker is inadvertently picked up by the microphone and reamplified, generating a loud squeal. Although a tiny perturbation at the input can cause a much larger effect at the output, the output of the system is usually limited in some way. Thus, in the example of the public address system, the intensity of the output is limited by the power of the audio amplifier and speakers or by saturation of the microphone signal. In biological systems, the response may be limited by the amount of energy or substrate available. An important biological example of positive feedback occurs in the nerve impulse (Chapter 5). It should be noted that positive feedback is generally used to produce a regenerative, explosive, or autocatalytic effect.



Basic elements of feedback systems. Top. Positive feedback occurs when a perturbation acting on a system is amplified and the amplifier output is "fed back" to the system without sign inversion. Bottom. Negative feedback occurs if somewhere in the feedback loop there is a "sign" inversion. In that case, the inverted signal stabilizes the controlled system at the set point. A change in sensitivity of the sensor is one way in which the set point can be adjusted.

Imagine an amplifier in which the "sign" of the output is opposite to that of the input. Such signal inversion provides the basis for *negative feedback* (see lower diagram), which can be used to regulate a certain parameter (e.g., length, temperature, voltage, concentration) in the controlled system.

When the sensor detects a change in state (e.g., change in length, temperature, voltage, concentration) of the controlled system, it produces an *error signal* proportional to the difference between the *set point* to which the system is to be held and the actual state of the system. The error signal is introduced into an amplifier that both amplifies and inverts (i.e., changes sign). The inverted output of the amplifier, fed back to the system, counteracts the perturbation. The inversion of sign (i.e., *negative* feedback) is the most fundamental feature of feedback control. The inverted output of the amplifier, by counteracting the perturbation, reduces the error signal, and the system tends to stabilize near the set point. Thus negative feedback is used to regulate and stabilize. Since the sensor or the amplifier can generally be biased, any selected set point can be automatically maintained.

A hypothetical negative-feedback loop with infinite amplification would hold the system in precisely its set point state, because the slightest error signal would result in a massive output from the amplifier to counteract the perturbation. Since no amplifier—either electronic or biological—produces infinite amplification, negative feedback only approximates the set point during perturbation. The less amplification the system has, the less accurate is its control.

Finally, it should be noted that the elements of the physical example of feedback described here occur in a number of variations. For example, sensor and amplifier functions are, in some instances, carried out by a single element, and in others the inversion of sign may take place at the sensor. Nonetheless, the principles remain unchanged.

Summary

Animal physiology is concerned with the physical and chemical processes that take place in tissues and organs and form the bases of organismic function. The field is subdivided into many areas that are often interdependent and are interrelated by common genetic, physical, and chemical principles. Medicine, the practical application of physiology, is constantly evolving from a trial-and-error, empirical approach toward practice founded on a rational understanding of cell and tissue function.

Besides practical application, physiology has philosophical value for us. This is apparent, for example, in a consideration of subjective human experience. All that we experience in life depends on the properties of our sensory and nervous systems. An understanding of how living organisms function helps us understand "what we are," and enhances our appreciation of our place in this world.

Three major ideas in physiology are (1) that function is based on structure at all levels, beginning with atoms, molecules, and cell organelles; (2) that regulation of the intra- or extracellular environment (or both) provides the required constancy of conditions necessary for reliable and coordinated chemical and physical processes; and (3) that cell and tissue functions have arisen through Darwinian evolution and are genetically determined.