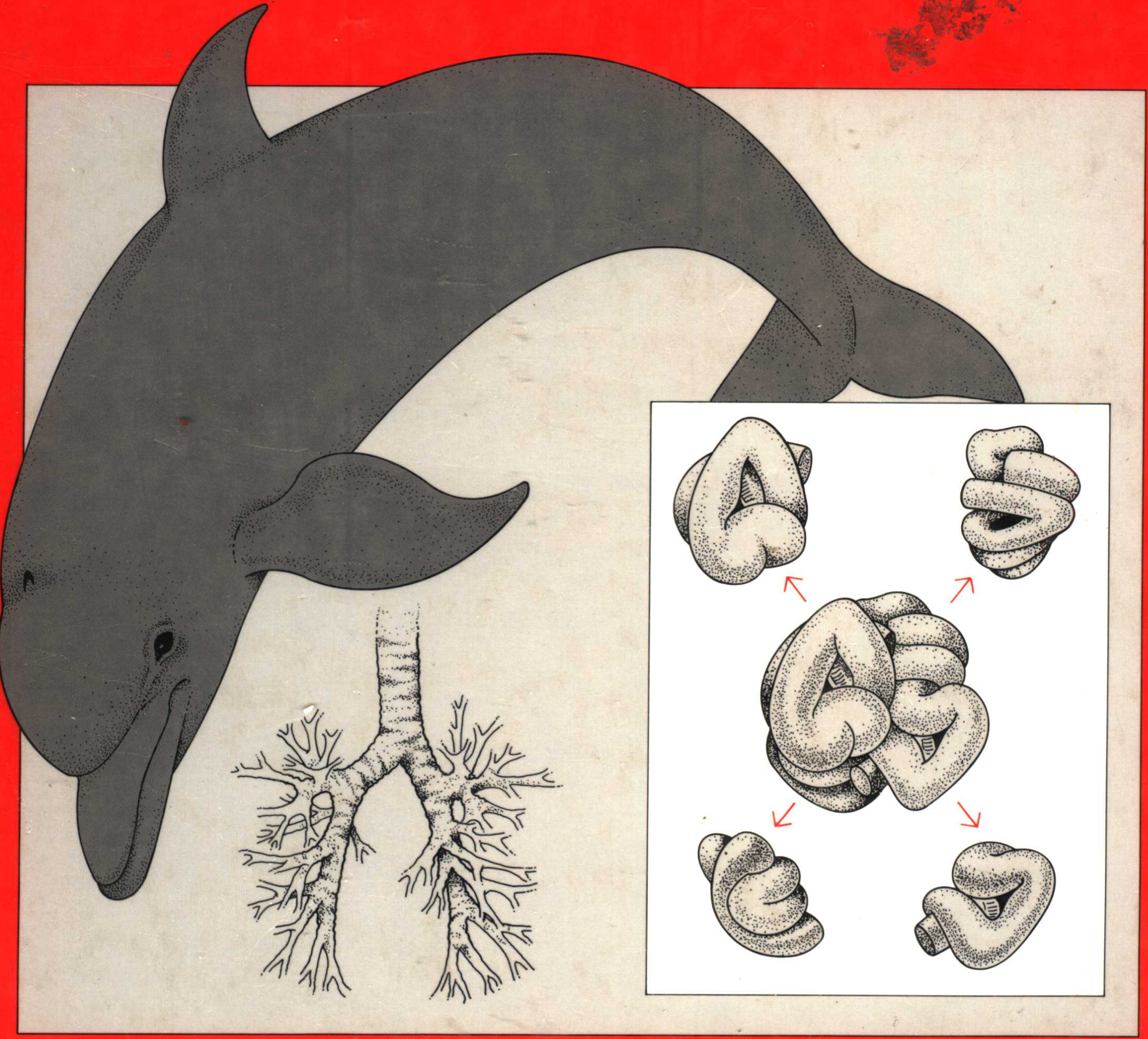
THIRD EDITION

ANIMAL PHYSIOLOGY

MECHANISMS AND ADAPTATIONS



ROGER ECKERT

DAVID RANDALL

GEORGE AUGUSTINE

THIRD EDITION

ANIMAL PHYSIOLOGY

MECHANISMS AND ADAPTATIONS

Roger Eckert

University of California, Los Angeles

With Chapters 13 and 14 by

David Randall

University of British Columbia

Revised in part by

George Augustine

University of Southern California

W. H. Freeman and Company

New York

To our loved ones

Library of Congress Cataloging-in-Publication Data

Eckert, Roger.
Animal physiology.

Bibliography: p.
Includes index.
1. Physiology. I. Randall, David J., 1938–
II. Title.
QP31.2.E24 1988 591.1 87-21085
ISBN 0-716-71828-6
ISBN 0-716-71937-1 (pbk.)

Printed in the United States of America

4 5 6 7 8 9 HL 9 9 8 7 6 5 4 3 2 1

Preface

The diversity and adaptations of the several million species that make up the animal kingdom provide endless fascination and delight to those who 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, this book has been organized to present the essential background material in a way that allows students to review it on their own and go on quickly to the substance of animal function and to an understanding of its experimental elucidation.

Animal Physiology develops 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. Examples are selected from the broad spectrum of animal life, ranging from protozoa at one end to our species and other vertebrates at the other end. Common principles, rather than exceptions, are emphasized. Thus, the more esoteric and peripheral details receive only passing attention, or none at all, so as not to distract from central ideas. Math is used only where essential, but priority is given to the development of a qualitative and intuitive understanding.

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

The chapters can be grouped into several sections. The first two chapters are intended primarily as an introduction and for review of the essential physical and chemical principles invoked 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 largely concern nervous systems, covering excitable membranes, nerve signals, sensory mechanisms, neural integration, and behavior, among other subjects. Chapter 9 deals with endocrine systems, including a general treatment of intracellular signaling mechanisms. Chapters 10 and 11 cover muscle contractility and other forms of cell motility, and Chapters 12 through 16 describe the systems responsible for the homeostasis and supply of the internal environment.

Although *Animal Physiology* has been through two well-received editions, a great deal of effort has gone into revising the text for this third edition. All 16 chapters have been extensively reworked and reorganized to stay abreast of new developments. These efforts have been aided by many helpful suggestions from colleagues who have used the previous editions. Chapter 9 has received special attention, reflecting recent advances in understanding intracellular signaling mechanisms. In this edition we have further extended the coverage of organismic physiology, to complement the extensive treatment of cellular and molecular aspects of physiology that has become a hallmark of this book.

From the start, *Animal Physiology* has been the product of the fertile mind of Roger Eckert. It therefore was a great blow when Roger died on June 13, 1986, while revising the third edition. *Animal Physiology* is only one of the many important contributions that Roger has made to physiology. He published numerous, seminal papers on a variety of problems in cellular physiology. Roger is best known for his investigations into the roles of calcium in regulating ciliary activity in *Paramecium* and in modulating calcium and potassium ion channels in molluscan neurons. His death is a tragic loss to the field and to his numerous colleagues and other friends.

Roger Eckert is primarily responsible for the revisions of the text for this edition of *Animal Physiology*. David Randall once again revised the chapters on respiratory and circulatory physiology and helped with proofreading of several chapters, while George Augustine completed revisions on the remaining chapters. For the material not contributed by Roger, we have attempted to retain the spirit and rigor that characterized Roger's efforts on *Animal Physiology* and have closely adhered to his plans for this edition.

Our goal has been to produce a balanced, up-to-date treatment of animal function. As in previous editions, we have striven for clarity of exposition to help the reader grasp basic concepts and have emphasized writing in a style that students can comprehend. We hope that readers will find *Animal Physiology* valuable, and remain grateful for constructive criticism and suggestions.

David Randall

October 1987 *George Augustine*

Acknowledgments

Numerous persons helped us in important ways in preparing the third edition of *Animal Physiology*. Thanks are due to Deanne Kuper and Bonnie Phan for typing the first draft of the manuscript, and Diane Conly for preparing revised versions. Diane, Stephen Hess, and particularly Christina Webb deserve special thanks for their assistance with proofreading. We also thank Donal Manahan (University of Southern California) for helping with revisions on Chapters 12, 15, and 16 after the death of Roger Eckert.

This edition of *Animal Physiology* has benefitted from detailed reviews by James N. Cameron (University of Texas, Austin), Ingrith Deyrup-Olsen (University of Washington), Martin Feder (University of Chicago), Russell D. Fernald (University of Oregon), David R. Jones (University of British Columbia), Harvey Lillywhite (University of Florida), Robert A. Linsenmeier (Northwestern University), Duncan MacKenzie (Texas A&M University), Axel Michelsen (Odense University), Malcolm Taylor (University of Delaware), and Chris M. Wood (McMaster University).

We also appreciate advice provided by R. Barlow (Syracuse University), M. Berridge (University of Cambridge), S. Bottjer (University of Southern California), H. Gainer (National Institutes of Health), G. Miljanich (University of Southern California), W. Sawyer (Columbia University), and P. Tyack (Woods Hole Oceanographic Institution). We apologize for being unable to acknowledge the specific contributions of many others who provided advice to Roger.

Our associates at our home institutions exercised commendable patience and provided many valuable comments while we were preoccupied with this project. Our families, too, have been understanding during the many hours that have gone into this edition. Commendations should be awarded to the Eckert family, for putting aside their personal anguish to help make this edition a reality. Finally, thanks are due for the high standards applied by the staff at W. H. Freeman and Company, especially to Gary Carlson for editorial guidance, to Julia DeRosa for production coordination, and to Helene De Lorenzo and Georgia Lee Hadler for their conscientious work as manuscript editor and project editor, respectively.

David Randall

October 1987 *George Augustine*

Contents

CHAPTER 1

The Meaning of Physiology

Animal physiology can be defined as the study of the function of animals and their constituent parts. 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. Among these are general and cell physiology; organ, organismic, and environmental physiology; respiratory, circulatory, digestive, endocrine, developmental, neuro-behavioral, sensory, and reproductive physiology. In spite of these somewhat contrived divisions, there are innumerable areas of overlap and common principles that recur throughout, providing a thread of continuity. It has also become apparent that these principles arise from the properties of matter and energy.

To facilitate comprehension, it is necessary in an elementary textbook to introduce the specialties somewhat arbitrarily as separate chapters. You should find it helpful, however, to remember 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 via the circulating 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 membranes depend on some of these same reactions for production of energy-donor molecules.

Why *Animal* Physiology?

From a biological standpoint, the human species is part of the animal kingdom, sharing with all other species 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 that hold for us operate for all creatures. Moreover, the fundamental biological processes that, in 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 vertebrate and invertebrate animals.

The first step in physiological research is to ask a question—for example, "Which ion carries the current that terminates 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, 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. Subsequent experiments, done with newer methods and with the benefit of the groundwork laid by the research 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 elucidated. In addition, we will note special evolutionary adaptations that serve to illuminate the ways in which environmental challenges have been met by the selection of functional specializations.

Physiology and Medicine

There are several reasons why an understanding of body functions is relevant to our daily existence. 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 of function and malfunction of living tissue grows, it is becoming more feasible to develop effective, scientifically sound treatment for human ills. A physician who understands body function is better equipped to make intelligent and insightful diagnoses and decisions for effective treatment, and is less likely to embark on a course of treatment that is disruptive of the body's physiological balance. Physicians who are unfamiliar with physiological principles 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 respire, 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 become profoundly evident when we contemplate the problem of communicating subjective experience. For example, how would you explain to a person 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 eventually be able to 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 30 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 discover more as you go on to later chapters.

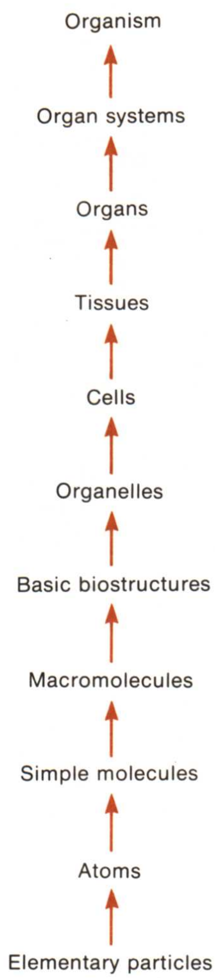
Function Is Based on Structure

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, and so on (Figure 1-1). One of the most intensively studied examples of functional dependence on structure is the contractile machinery of skeletal muscle. 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 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 biologically nonfunctional.

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



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.

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, as we have noted, is closely tied to structure) also has evolved through natural selection. 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.

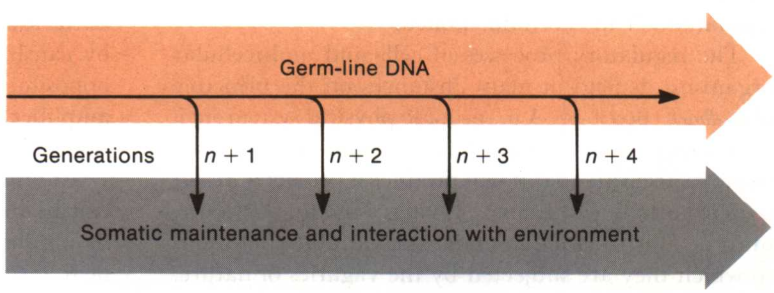
Toward the end of the nineteenth century, August Weismann elaborated a theory of heredity in which he postulated the *continuity of the germ plasm*—namely, that genetic material passed on from metazoan parents to their offspring is contained in a line of germ cells that, in each generation, are derived 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 (Figure 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 that is lost, the 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.

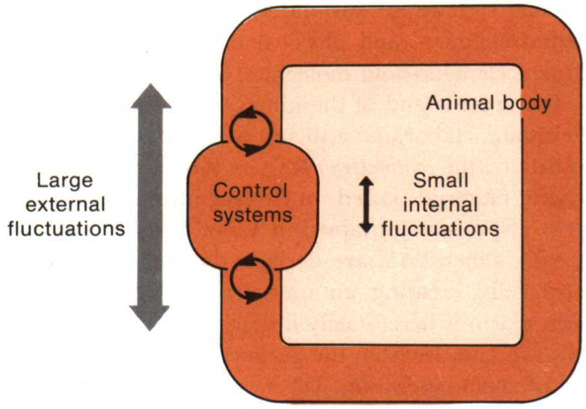
There exists, then, a symbiotic relationship between the germ-line DNA and the rest of the organism. Neither can survive without the other. The soma owes its existence to the DNA, and the DNA cannot survive without the somatic functions concerned with the short-term survival of the organism. The philosophical 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.

The Principle of Homeostasis

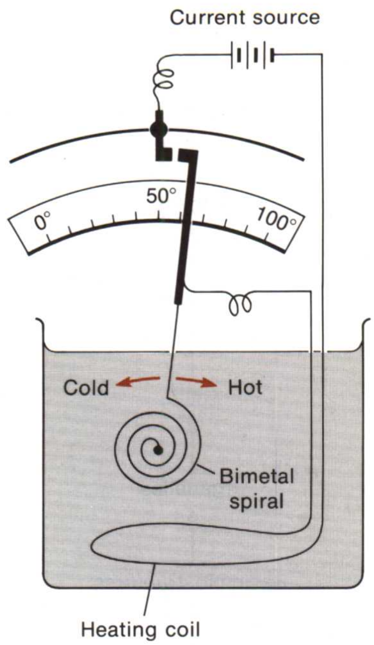
The nineteenth-century French pioneer of modern physiology, Claude Bernard, was the first to enunciate the importance of *homeostasis* in animal function when he noted the ability of mammals to regulate the condition of their internal environment within rather



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.



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.



1-4 Example of a regulated system. A bimetal spiral, fixed at its center, winds 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 coil unwinds slightly and the contacts separate. The desired temperature set point is adjusted by positioning the contact of the thermostat.

narrow limits. This ability 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 (Figure 1-3). The evolution of homeostasis is believed to have been the essential factor that allowed animals to venture from physiologically friendly environments and invade environments hostile to life processes. One fascination of physiology is discovering how different groups of animals have dealt, in the evolutionary sense, with given environmental challenges.

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 selective membrane permeability, active transport, and other mechanisms that maintain these concentrations within limits both 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 intracellular milieu.

The regulatory processes of cells and multicellular organisms depend in many instances on the principle of *feedback* (Box 1-1). A man-made physical system such as a computer or a ballistic guidance system can be made so accurate that it will produce a predicted result under normal conditions. Living systems, however, must be able to function under the variable conditions to which they are subjected by the vagaries of nature. In the face of the finite accuracy of genetic and metabolic mechanisms—to say nothing of external perturbations—regulation requires continuous sampling and correction. For example, suppose that an experienced driver is placed in a car on an absolutely 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 employ visual information with negative-feedback principles 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* (i.e., the center of the lane in this case).

Another example of regulation by negative feedback can be demonstrated with a thermostatic device that maintains the temperature of a hot water bath at or near the set point (Figure 1-4). As long as the water

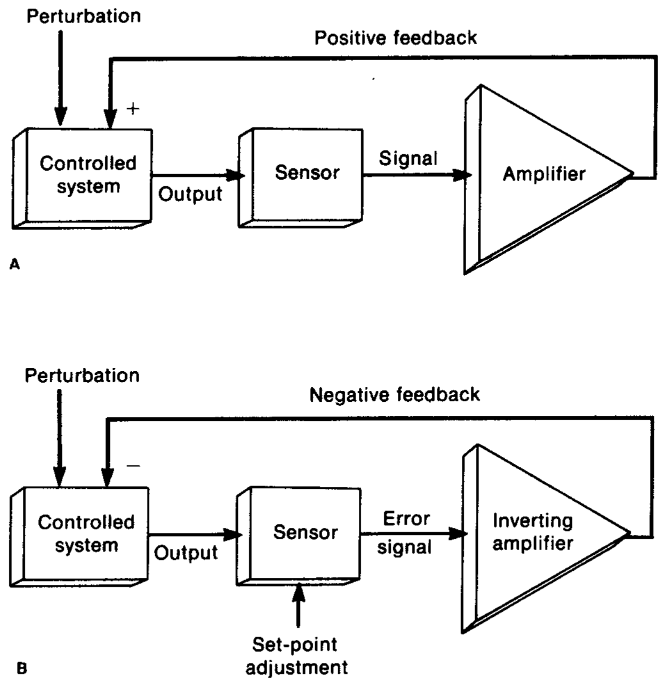
Box 1-1 The Concept of Feedback

Feedback is widely employed in biological systems, as well as in engineering, to maintain a preselected state. Feedback can be either positive or negative, each producing profoundly different effects.

Positive Feedback

In the model system shown in part A of the figure, an applied disturbance, or perturbation, is acting on the *controlled system.* The output of this system is detected by a sensor, which sends a signal to an amplifier. Suppose the signal input is amplified but that its sign (plus or minus) remains unchanged. In this case the output of the amplifier, when fed back to the controlled system, has the same effect as the original perturbation, reinforcing the perturbation of the controlled system. This configuration, which is called positive feedback, is highly unstable, because the output becomes progressively stronger as it is fed back and reamplified. A familiar example involves public address systems: When the output of the loudspeaker is picked up and reamplified by the microphone, a loud squeal is generated. Thus, 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; for example, in 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.

Positive feedback is generally used to produce a regenerative, explosive, or autocatalytic effect. In biological systems it is often used to generate the rising phase of a cyclic event, an important example of which is the upstroke of the nerve action potential.



Basic elements of feedback systems. (**A**) Positive feedback occurs when a perturbation acting on a system is amplified and is "fed back" to the system without sign inversion. (**B**) Negative feedback occurs if somewhere in the feedback loop there is a sign inversion. In this case the inverted signal stabilizes the controlled system near the set point.

Negative Feedback

Imagine an amplifier in which the "sign" of the output is opposite to that of the input (e.g., plus changed to minus, or vice versa). Such signal inversion provides the basis for negative feedback (see part B of the figure), which can be used to regulate a given parameter (e.g., length, temperature, voltage, concentration) of 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 then both amplified and inverted (i.e., changes in sign). The inverted output of the amplifier, fed back to the system, counteracts the perturbation. The inversion of sign is the most fundamental feature of negative-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.

A hypothetical negative-feedback loop with infinite amplification would hold the system precisely at the set point, because the slightest error signal would result in a massive output from the amplifier to counteract the perturbation. Since no amplifier—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, note 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 the same.

temperature is below the set point, the sensor maintains the heater switch "on." As soon as the set-point temperature is achieved, the heater switch opens, 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, and a fever develops.

Examples of physiological feedback systems occur in intermediary metabolism (Chapter 3), neural control of muscle (Chapter 8), endocrine control (Chapter 9),