INTRODUCTION TO
NERVOUS SYSTEMS

Bullock
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The illustration on the cover is an enlargement of the lower part of the dendritic arborization that appears on the right side of page 348. Reproduced from *The Postnatal Development of the Human Cerebral Cortex*, by J. L. Conel, Harvard University Press, Cambridge, 1959.

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To the students
who inspired this book
and the loyal associates
who made it possible

LIST OF BOXES

PREFACE

The goal of this book is to provide for advanced undergraduates, early graduate students, and medical students an introduction to the nervous system with emphasis on its systems aspects.

The nervous system, together with its close companion, the endocrine system, is unlike the other organ systems in that it is primarily concerned with signals, information processing, and control rather than the manipulation of substances and energy; it is a communication device. Its components, of course, do use substances and energy in the processes of signalling, recognizing, choosing, and commanding, as well as in developing and learning.

An insight that has slowly dawned, and is still not acknowledged in many expositions of neurobiology, is that the central questions about nervous systems, "How do they work? What's going on? What's the principle of operation?" have no single answers. Instead, the mechanisms, the constituents, and the principles are there to be uncovered, layer upon layer, from levels below the stereochemistry of membrane molecules to levels above the consolidation of engrams. The explosively expanding branch of knowledge called "neuroscience," still in its relative youth, already claims to embrace a wider spectrum of complexity, a greater range of levels of explanation, than any other science. None of the levels, submolecular to interhemispheric, is adequate by itself; none is the key level or the queen of the science. The span is too great even for an elementary text such as this, hence choices had to be made. The result is that this book deals with the first question, "How does it work?" It emphasizes the middle levels and says less about the molecular below and the psychological above.

The core problems we take up are relations and transactions between the cells and among the assemblages of cells in the nervous system. We deal with the encoding and decoding of neural signals, the evaluation and weighting of inputs, the formulating of outputs, and even the simpler elements of behavior. The book therefore embraces neuroanatomy and neurophysiology from the cellular level to that of subsystems of the brain. It cannot do justice to neurochemistry, neuropharmacology, energetic and nutritive metabolism, or to the mechanisms of learning.

The main reasons for offering this book are two. The first is to redress the relative neglect of the integrative aspects in current textbooks. The second reason is to present a major segment of the impossibly wide span of neuroscience in a logical series of levels, more or less comprehensively.

Following an introductory perspective (Chapter 1), the next four chapters deal with cellular componentry, first structurally (Chapters 2 and 3), and then functionally (Chapters 4 and 5), first within the cell (Chapters 2 and 4) and then between cells (Chapters 3 and 5). The next block of chapters (6, 7, and 8) considers integrative mechanisms at neuronal, intermediate, and behavioral levels. The last two chapters survey the development of the nervous system in the life of the individual (Chapter 9) and its evolution in the animal kingdom (Chapter 10).

A Glossary that is more than merely indicative is provided. We feel that familiar terms are often used in contemporary writing with insufficient care and that understanding is poor unless a definition can be given that is both inclusive and exclusive. The Glossary is intended to be used continually, not merely for reference in extremis.

We have tried to distill in order to keep the size of this volume compatible with the intention that it be used in parallel with others that deal more fully with the cellular mechanisms on the one hand and the details of the human brain on the other.

The treatment within the succession of chapters is not homogeneous. We hope the reader will benefit from, rather than be distracted by, the diversity of outlook among three authors who have quite different perspectives. As the title page and table of contents indicate, my collaborators have had an asymmetry of roles in the building of the book, hence they cannot be held responsible for the philosophy or treatment of chapters other than their own.

It is a major accompaniment of the growth and specialization of this field that neuroscientists today diverge widely in "slant" and emphasis. The brain as seen by one scientist may be hardly recognizable by another. The approach of one may be basically to explain observations in terms of understood mechanisms, whereas another may be more impressed by the gap between the few phenomena we can explain and the many we can presently only characterize. Some neuroscientists are primarily general physiologists, impressed by commonalities and attracted by the lure of broadly applicable principles; others are essentially comparative, impressed by the range within the most differentiated system nature has evolved.

It has been my credo that we must be eclectic if we are to do justice to nature's achievement and be ready for the changes that tomorrow may bring. This book, by example, advocates that each inquirer, whether student or investigator, sample widely even among the more subjective "slants" of authors, and rethink frequently even the settled dogmas.

This book is the combined effort of many more than the three of us. Each has been inspired by his students and aided incalculably by staff and colleagues, and it is to them that my collaborators join me in gratefully dedicating this book.

Theodore H. Bullock

December 1976

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THE SPECIAL NATURE OF NERVOUS SYSTEMS AND NEUROSCIENCE

I. INTRODUCTION

To study the wellsprings of human nature should be challenge enough, but it isn't. At no time in his history has *Homo sapiens*, the wise one, been quite satisfied with an egocentric vision. To achieve peace on earth, human justice, health and well being—first order though they be—will never suffice as the only human goals. Man has a need to know, to understand, to experience. He probes the stars, the atoms, the heights of esthetic and creative feeling; he paints, he composes, and he walks on the moon. Despite a tendency to accept simplistic or supernatural answers, he nevertheless exhibits a drive to probe beyond the limited understanding that such answers offer.

In the tradition of inquiry and the need to know, the nervous system is a proper study of mankind—the nervous system in all its manifestations, the mysteries behind a true understanding of behavior, the origins of humanity. What is the nervous system's relation to behavior? How does it govern thought? What is it like in its simplest forms? How has this behavior machine evolved, specialized, acquired new capacities and transformed the old in the course of evolution?

In addition to satisfying our desire to know, the discovery of answers to such questions (even though the answers may be far from definitive) is often of profound **humanistic significance.** The brain makes us err, makes us selfish, makes us altruistic and rational. The human brain, source of the world's most serious problems, is also the world's principal hope. Seeking a thorough understanding of ourselves—probing to uncover the intricacies of the brain—is certainly one of the most promising human activities. Such study has a long and dramatic history, but the accumulation of information about brain and behavior has accelerated enormously lately.

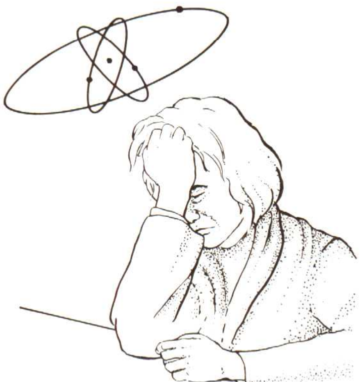
Building on the triumphs of the past few decades, life science is already well into the age of **neuroscience**—and still adjusting to an unprecedented kind of challenge. The familiar strategy of seeking the common denominators of life is unequal to this challenge. It is behavior and its neural substrate that has most evolved, that makes higher animals higher and the human species highest of all. It seems most unlikely that there is a *single* code to be broken to explain love and hate, the pianist and the perjurer. Nevertheless, single-gene, single-enzyme deficiencies can cause devastating brain disease, and simple lithium salts can dramatically relieve some subtle psychiatric disorders. The challenge is to integrate widely disparate levels of inquiry (Fig. 1.1) and disciplinary approaches. What are these approaches?

It has been said that "everything comes down to molecules," and the most basic of the approaches can be called molecular neurobiology. This is itself a combination of biochemistry and biophysics, and grades imperceptibly into the next higher level of cellular microstructure and function—the one that deals with membranes and organelles. Still higher levels of anatomy and physiology deal with the layers upon layers of ever more intricate organization that constitute the nervous system. Study at such levels grades into physiological psychology and neuroethology.

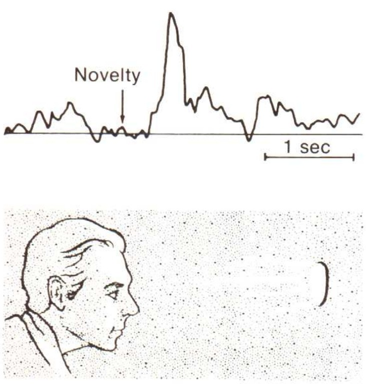
The outstanding feature of this **array of disciplines** is its breadth. We don't expect to understand speech by limiting our investigation to cells, let alone to molecules or atoms. Nor can we wait to deal scientifically with motivation, drive, and emotion until we have systematically discovered all the fundamentals of enzyme dynamics, and then of cell organelles, cellular differentiation, and tissue organization.

Practicality and scientific strategy both demand that biology **advance at the same time on many levels** and many fronts, always struggling toward the integration of approaches and disciplines. It is obvious from the intricacy of the common object of study, the brain, that the subject matters, vocabularies, and problems of such disparate approaches as the chemistry of subcellular particulates and the systems analysis of constellations of cells in the cortex will be far apart for many years, given the relative primitiveness of our essential understanding of the whole. Great effort is required to integrate even closely related approaches.

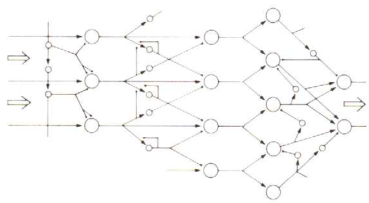
Figure 1.1
Levels of inquiry.

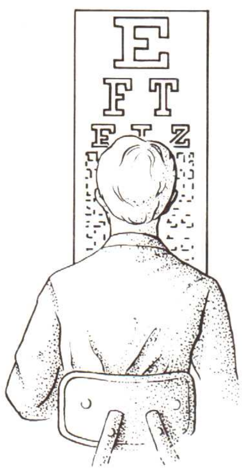


A specific cation may relieve severe depression.



A specific wave of synchrony in a population of cells may signal the experience "What's that?" in response to a novel stimulus in a boring series.





A specific array of active neurons may recognize **E**.

In this book we limit our scope primarily to the signalling and **systems aspects**—that is, to the intermediate levels, which depend particularly for their significance on the organization of the cells. We will not deal in detail with intracellular componentry. Nor will we attempt, at the other end of the possible array, a full treatment of the organization of the human brain. That is thoroughly treated in many other books. But the principles of organization and integration, encoding and decoding, line-labeling, recognition, command, and the use of pattern are not. To discuss those subjects is our central objective. But in defining our scope, we must make other choices in another dimension.

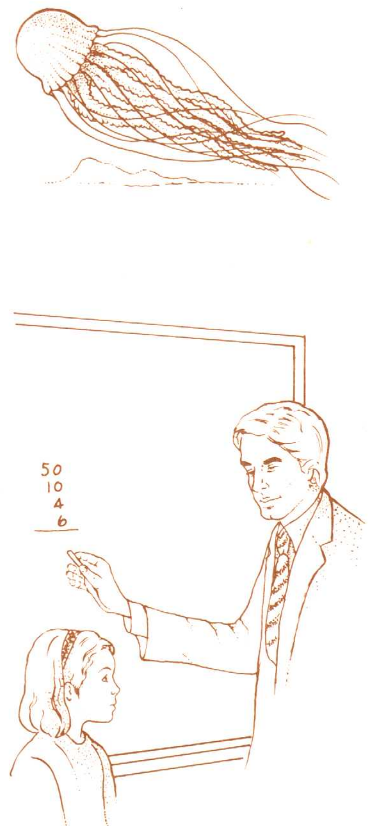
As **evolution** from humble origins to lofty achievement is a universal feature of life, the nervous system—from diffuse nets in jellyfish to the human brain—is the outstanding consequence of evolution. The nervous system truly represents a biological phenomenon, and it is our contention that it cannot be understood simply as a part of general physiology or of human biology without the evolutionary perspective. Far more than for other systems, we are dependent, for any claims to adequate appreciation, upon the comparative view. To make this real now, before we are immersed in details, it suffices to point to the accomplishments of nervous systems—that is, to behavior in all its repertoire, nuances, and malleability. Contemplate the gulf between jellyfish and human (Fig. 1.2). It is almost as great as that between synapse and thought. Once more the sweep of our subject is so wide that we must make a choice. But for this choice, instead of cutting off one end of the possible range, as in the previous choice, we shall select animal groups at various points on the phylogenetic tree, aiming for at least a modest introduction to the indispensable biological perspectives.

II. NERVOUS SYSTEMS

The subject and theme of our book is nervous systems as systems. What, then, is a nervous system? It may be defined as an **organized constellation of nerve cells** and associated nonnervous cells; it includes receptors, but not most effector cells. Nerve cells—which we shall hereafter synonymously call **neurons**—may be defined as cells specialized for the generation, integration, and conduction of excited states, including most sensory but not effector cells. A corollary of this definition of nerve cells is that they derive their excitation intrinsically or from the environment, from special sense cells, or from other neurons and deliver it to other excitable cells or to effectors, such as muscle cells. A corollary of the definition of nervous systems is that they differ both quantitatively and qualitatively from other organ systems, because they deal only incidentally with materials and energy. Their function and specialization is to process information, and their organizational complexity greatly exceeds that of any other system.

Besides the defining features, certain **common attributes, of neurons,** though not universal, are usually helpful in distinguishing them. Such attributes include a brief impulse and refractory state, a local form of response at junctions, called a postsynaptic potential (further defined in the Glossary and in Chapter

Figure 1.2
Lower and higher animals differ primarily in elaboration of the nervous system.



5), and some electron-microscopic and biochemical specializations associated with these junctions. An important general statement about nerve cells, however, is that compared to other types of cells they are outstanding in the degree of differentiation among themselves (Fig. 1.3). A major theme of Chapter 2 is the variety of types of nerve cells. Heterogeneity and specificity are the hallmarks of neurons—not only in their forms, branches, and connections but in their distinctive chemical, physiological, pharmacological, virological, and other properties, and in their reactions to injury, disease, and external agents. Neurons are the least interchangeable of cells.

Nervous systems are easy to recognize in higher animals, but the defining criteria are difficult to apply in the lowest groups. As is true for the neuron, it is helpful to know certain **common attributes of nervous systems.** A central nervous system can be distinguished from a peripheral nervous system more or less clearly in all but the simplest forms (i.e., from flatworms upward). The **central nervous system** (CNS) contains most of the motor and internuncial cell bodies —that is, the nucleated parts of the neurons that innervate muscles and other effectors and of the neurons that are between sensory and motor cells. The **peripheral nervous system** (PNS) contains all the sensory nerve cell bodies, with rare exceptions, plus local **plexuses** (diffuse tangles of nerve cells and fibers) concerned with the body wall or viscera, local **ganglia** (knots of nerve cells) of either sensory or motor-and-internuncial composition, plus the peripheral **axons** (long processes of neurons), which make up the **nerves** (bundles of axons). We believe there are no isolated peripheral plexuses or ganglia without connection to the rest of the nervous system. All receptor cells are nerve cells except those of a few special sense organs of vertebrates, including taste buds, one form of touch corpuscle, acousticolateralis systems, and, according to the usage of some, rods and cones of the eye. These receptors are connected to the axons of the first-order afferent (incoming) neurons. Most sensory axons go all the way into the central nervous system, but a small number of them relay in peripheral plexuses, the remainder of the connection with the central nervous system being made by second-order afferent (entering) fibers. Similarly, most effectors are innervated by motor axons originating in the central nervous system, though some central motor neurons relay with peripheral motor neurons.

As we observed for neurons, these simple rules give only a hint of the elaboration achieved in the systems of higher animals. We know all too little of the essential achievements that have occurred during the **evolution of organized systems** of neurons. But a great deal is known of the trends in gross anatomy and in microscopic differentiation of nervous tissue. Higher groups (see the Glossary for a definition of "higher") in general have more differentiated receptors, more kinds of neurons and textured masses of neurons. In the lower phyla the distinction between peripheral and central nervous systems is less distinct; the increased distinction in higher phyla is called **centralization.** With increase in the complexity of these higher groups, there is repeatedly and independently a tendency toward **cephalization**—the greater concentration of neural masses and functional responsibil-

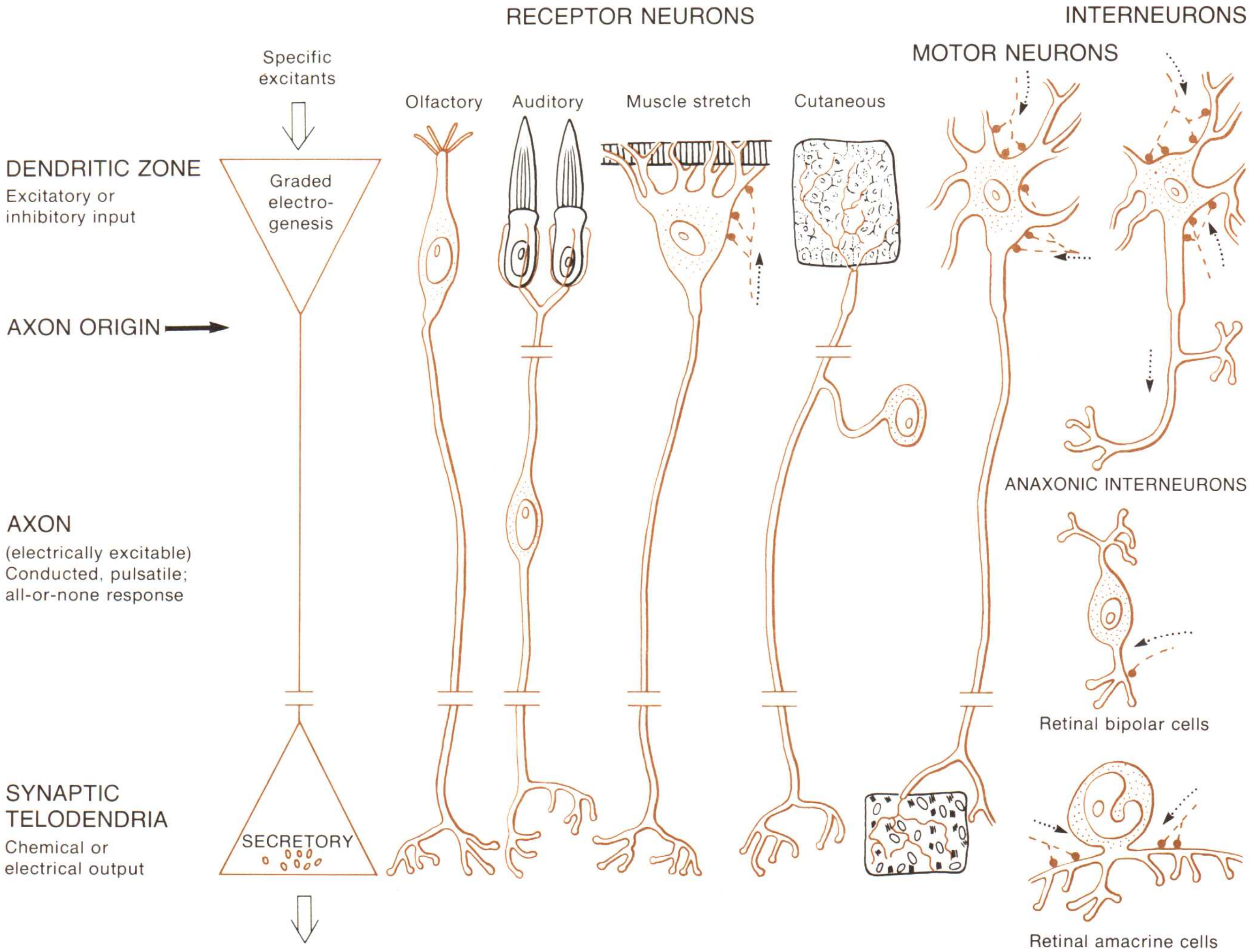
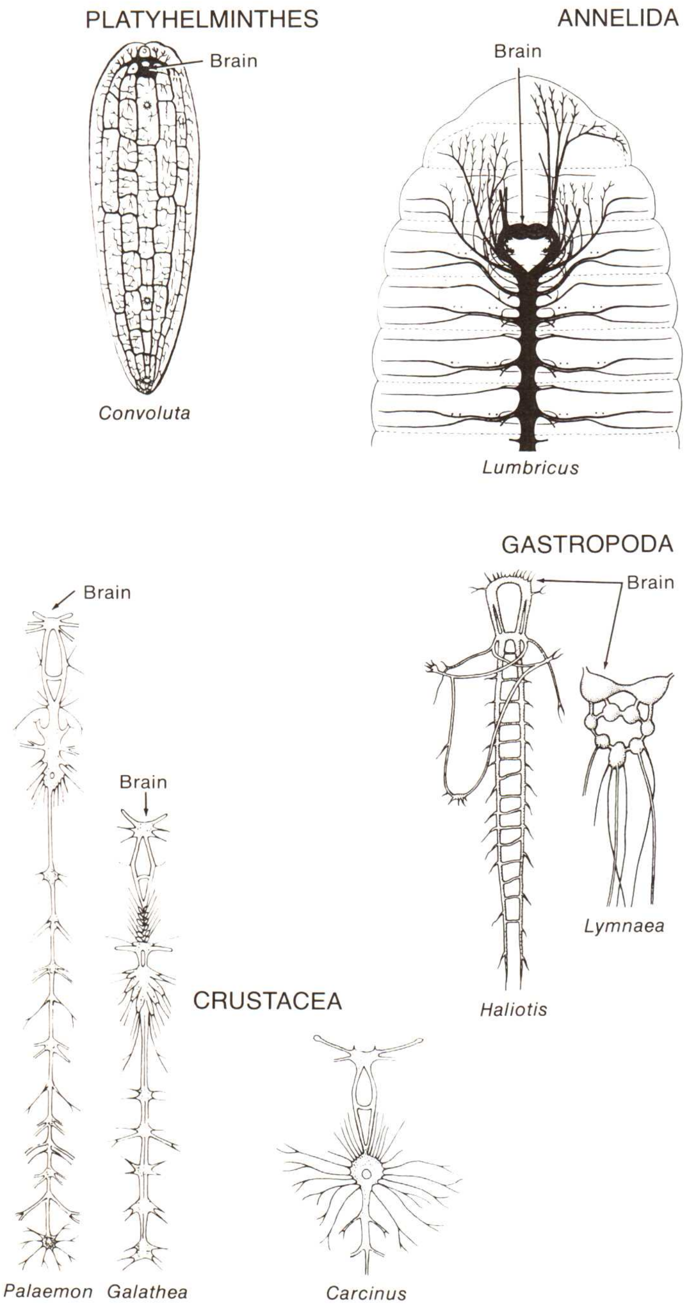


Figure 1.3
Diagram of a variety of afferent neurons, efferent neurons, and interneurons, arranged to bring out the basic agreements in functional and structural features. The position of the soma or nucleated mass of cytoplasm does not have a constant relation to the functional geometry in terms of impulse origin. In axon-bearing neurons, the four major zones of interest in terms of neural processing (dendritic zone, zone of axon origin, axon zone, transmitting or synaptic zone) conform approximately to the functional diagram of the generalized neuron proposed by Grundfest. But some axons do not conduct impulses, some dendrites transmit as well as receive, and some telodendria receive as well as transmit. Anaxonic neurons, in which the impulse-conducting region is absent, may be regarded as having processes similar in nature to dendrites and telodendria. [Bodian, 1967.]

Figure 1.4
Types of central nervous systems and peripheral nervous systems.



ity toward the head of the body (Fig. 1.4).

These trends are but superficial signs of the essential structural and functional aspects of evolution, which are much more difficult to specify. The **two major roles of the nervous system** are both discernible from the lowest to the highest groups. These roles are, in short, to counteract and to act (Fig. 1.5). In the first, the role of **regulation,** the nervous system acts homeostatically—that is, serves to preserve the status quo by making compensatory responses to stimuli that displace or perturb some condition of the organism. In the second, **initiation,** it acts to alter the status quo by replacing one mood or phase of behavior with another. Both roles show astonishing evolutionary development from the simpler invertebrates to the mammals; the initiating role has probably shown the most.

Learned behavior can be superimposed on either the regulating or the initiating category, but it pertains mainly to the second. For most animals, learning primarily promotes a more adaptive aiming, combining, and timing of species-characteristic acts that tend to occur anyway. Certainly there has been remarkable evolution in the degree and perfection of this form of plasticity.

Viewing the significance of the nervous system from a different standpoint, we may note that it performs in such a way as to extend the range of **speeds,** and therewith the **intricacy** of behavior: witness, for example, the capabilities of a pianist! Speed allows for an increase in the number of intervening steps between sensory input and motor output, the integrative transactions, and hence for numerous units of information