2 Neuroscience Overview

1 INTRODUCTION

If we are to understand how the brain sees, learns, and is aware, we must understand the architecture of the brain itself. The brain's computational style and the principles governing its function are not manifest to a casual inspection. Nor can they be just inferred from behavior, detailed though the behavioral descriptions may be, for the behavior is compatible with a huge number of very different computational hypotheses, only one of which may be true of the brain. Moreover, trying to guess the governing principles by drawing on existing engineering ideas has resulted in surprisingly little progress in understanding the brain, and the unavoidable conclusion is that there is no substitute for conjuring the ideas in the context of observations about real nervous systems: from the properties of neurons and the way neurons are interconnected.

This chapter focuses on the "neuroscience" component of the "computational neuroscience" synergy. Ideally, computer modelers should know as much neuroscience as practising neuroscientists. In fact, however, there is too much neuroscience to be thoroughly mastered even by a single neuroscientist. An anatomist may know a lot about his designated region of the visual cortex, rather less about other cortical areas and subcortical brain structures, less again about central pattern generation in the spinal cord, and even less about plasticity of the vestibulo-ocular reflex. Our aim is to prepare the reader, from whatever constituency, for the general conceptual framework we deploy and the specific neurobiological examples discussed within that framework. Consequently, the material in this chapter is organized to cohere with a computational approach to exploring certain aspects of nervous system function. Because levels turn out to be pivotal in our grand scheme of things, characterizing levels in neurobiology is a matter of the first importance. The presentation in this chapter is therefore keyed to illustrating anatomical and physiological properties seen at different levels. Although understanding the techniques whereby neurobiological data are gathered is also essential, to keep the wagons moving we elected to provide this in the appendix at the end. Although this chapter is meant to provide some basic neuroscience background,

Substantial portions of this chapter are taken from Sejnowski and Churchland (1989).

in the context of specific neurocomputational models, relevant neuroscience will be introduced.

2 LEVELS IN NERVOUS SYSTEMS

Discussions concerning the nature of psychological phenomena and their neurobiological bases invariably make reference to the notion of "levels." In trying to be a bit more precise about what is meant by "level," we found three different ideas about levels in the literature: *levels of analysis, levels of organization, and levels of processing*. Roughly speaking, the distinctions are drawn along the following lines: levels of organization are essentially anatomical, and refer to a hierarchy of components and to structures comprising these components. Levels of processing are physiological, and refer to the location of a process relative to the transducers and muscles. Levels of analysis are conceptual, and refer to different kinds of questions asked about how the brain performs a task: into what subtasks does the brain divide the tasks, what processing steps execute a subtask, and what physical structures carry out the steps? In what follows, we elaborate on these distinctions.

Levels of Analysis

A framework for a theory of levels, articulated by Marr (1982), provided an important and influential background for thinking about levels in the context of computation by nervous structures.[1] This framework drew upon the conception of levels in computer science, and accordingly Marr characterized three levels: (1) the computational level of abstract problem analysis, decomposing the task (e.g., determining the 3-D depth of objects from the 2-D pattern on the retina) into its main constituents; (2) the level of the algorithm, specifying a formal procedure to perform the task so that for a given input, the correct output results; and (3) the level of physical implementation, constructing a working device using a particular technology. This division really corresponds to three different sorts of questions that can be raised about a phenomenon: (1) how does the problem decompose into parts?, (2) what principles govern how the parts interact to solve the problem?, and (3) what is the stuff whose causal interactions implement the principles?

An important element in Marr's view was that a higher-level question was largely independent of the levels below it, and hence computational problems of the highest level could be analyzed independently of understanding the algorithm which performs the computation. Similarly, the algorithmic problem of the second level was thought to be solvable independently of understanding its physical implementation. Thus his preferred strategy was top-down rather than bottom-up. At least this was the official doctrine though, in practice, downward glances figured significantly in Marr's attempts to find problem analyses and algorithmic solutions. Ironically, given his advocacy of the top-down strategy, Marr's work was itself highly influenced by neurobiological considerations, and implementation facts constrained his choice of problem

and nurtured his computational and algorithmic insights. Publicly, the advocacy of the top-down strategy did carry the implication, dismaying for some and comforting for others, that neurobiological facts could be more or less ignored, since they were, after all, just at the implementation level.

Unfortunately, two very different issues were confused in the doctrine of independence. One concerns whether, as a *matter of discovery*, one can figure out the relevant algorithm and the problem analysis independently of facts about implementation. The other concerns whether, as a *matter of formal theory*, a given algorithm which is already known to perform a task in a given machine (e.g., the brain) can be implemented in some other machine which has a different architecture. So far as the latter is concerned, what computational theory tells us is that an algorithm can be run on different machines, and in that sense and that sense alone, the algorithm is independent of the implementation. The formal point is straightforward: since an algorithm is formal, no specific physical parameters (e.g., vacuum tubes, Ca^{2+}) are part of the algorithm.

That said, it is important to see that the purely formal point cannot speak to the issue of how best to discover the algorithm in fact used by a given machine, nor how best to arrive at the neurobiologically adequate task analysis. Certainly it cannot tell us that the discovery of the algorithms relevant to cognitive functions will be independent of a detailed understanding of the nervous system. Moreover, it does not tell us that any implementation is as good as any other. And it had better not, since different implementations display enormous differences in speed, size, efficiency, elegance, etc. The formal independence of algorithm from architecture is something we can exploit to build computationally equivalent machines once we know how the brain works, but it is no guide to discovery if we do not know how the brain works.

The issue of independence of levels marks a major conceptual difference between Marr (1982) and the current generation of researchers studying neural and connectionist models. In contrast to the doctrine of independence, current research suggests that considerations of implementation play a vital role in the kinds of algorithms that are devised and the kind of computational insights available to the scientist. Knowledge of brain architecture, far from being irrelevant to the project, can be the essential basis and invaluable catalyst for devising likely and powerful algorithms—algorithms that have a reasonable shot at explaining how in fact the neurons do the job.

Levels of Organization

Marr's three-level division treats computation monolithically, as a single kind of level of analysis. Implementation and task-description are likewise each considered as a single level of analysis. Yet when we measure Marr's three levels of analysis against levels of organization in the nervous system, the fit is poor and confusing at best.[2] To begin with, there is organized structure at different scales: molecules, synapses, neurons, networks, layers, maps, and systems (figure 2.1). At each structurally specified stratum we can raise the computational question: what does that organization of elements do? What does it

contribute to the wider, computational organization of the brain? In addition, there are physiological levels: ion movement, channel configurations, EPSPs (excitatory postsynaptic potentials), IPSPs (inhibitory postsynaptic potentials), action potentials, evoked response potentials, and probably other intervening levels that we have yet to learn about and that involve effects at higher anatomical levels such as networks or systems.

The range of structural organization implies, therefore, that there are many levels of implementation and that each has its companion task description. But if there are as many types of task descriptions as there are levels of structural organization, this diversity could be reflected in a multiplicity of algorithms

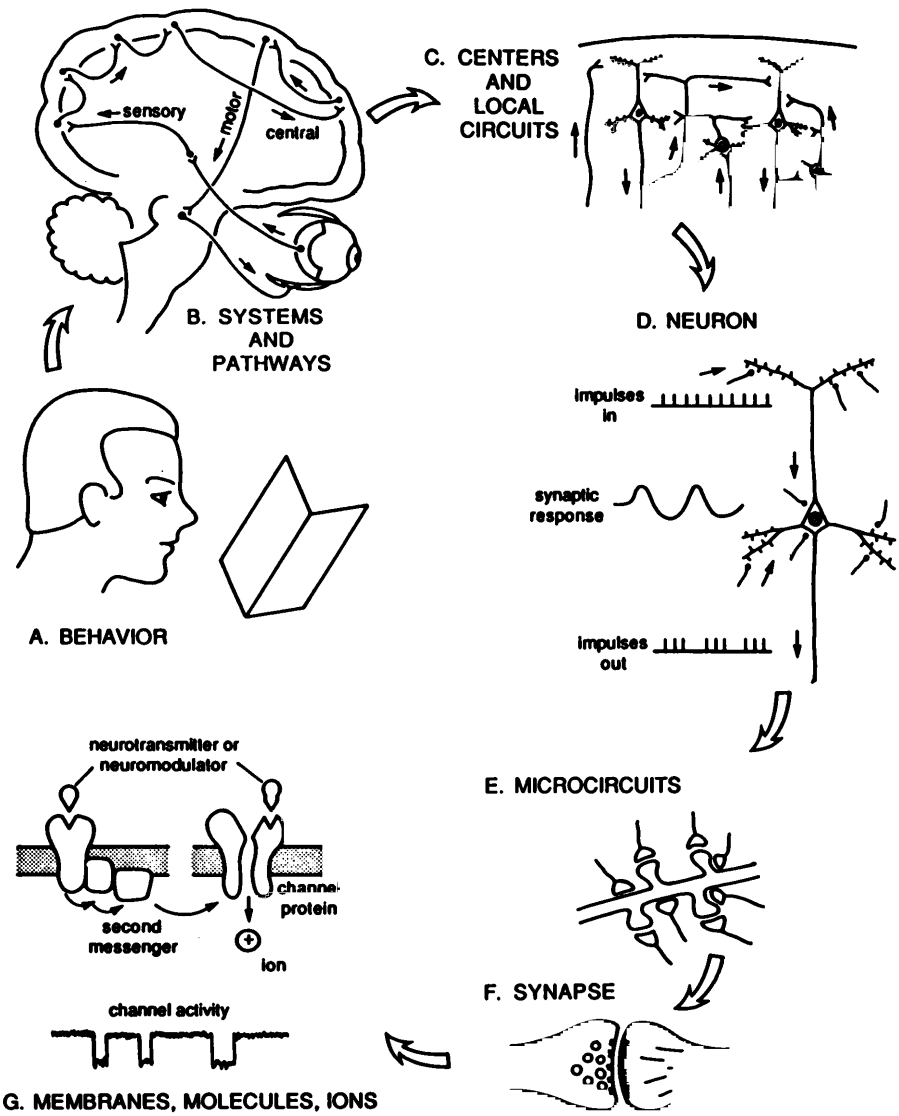

Figure 2.1 Levels of organization in the nervous system, as characterized by Gordon Shepherd (1988a).

that characterize how the tasks are accomplished. This in turn means that the notion of *the* algorithmic level is as over-simplified as the notion of *the* implementation level.

Note also that the very same level of organization can be viewed computationally (in terms of functional role) or implementationally (in terms of the substrate for the function), depending on what questions you ask. For example, the details of how an action potential is propagated might, from the point of view of communication between distant areas, be considered an implementation, since it is an all-or-none event and only its timing carries information. However, from a lower structural level—the point of view of ionic distributions—the propagating action potential is a computational construct whose regenerative and repetitive nature is a consequence of several types of nonlinear voltage-dependent ionic channels spatially distributed along an axon.

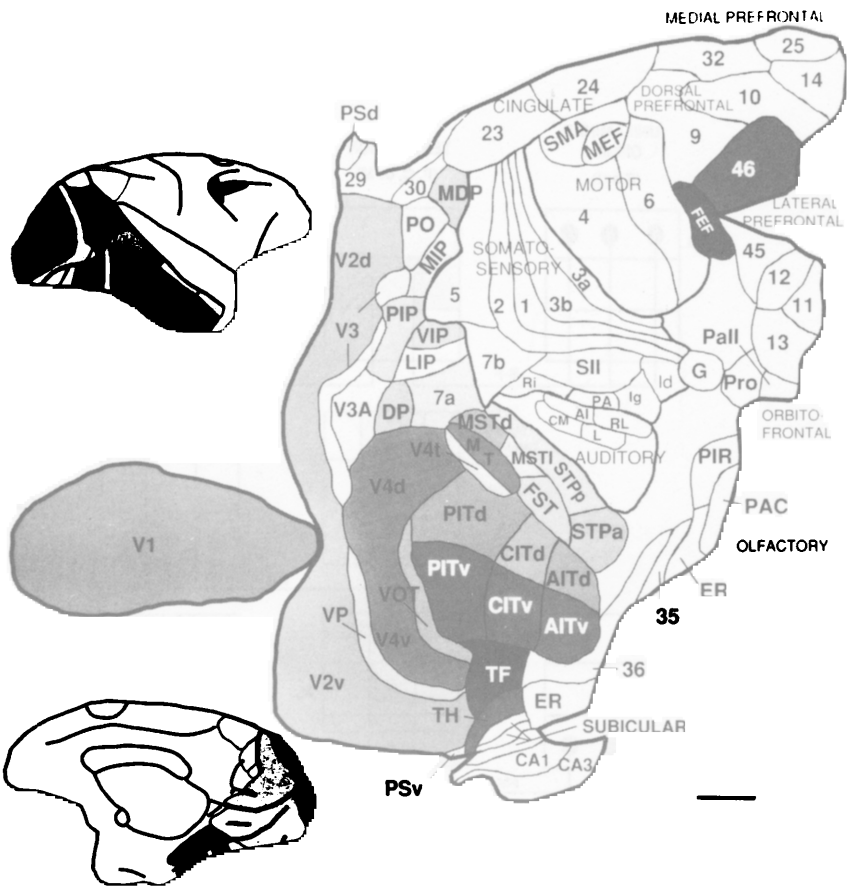

Figure 2.2 A flattened projection of the cerebral cortex in the right hemisphere of the macaque monkey. Stippling indicates cortical areas implicated in visual processing. (Upper left) Lateral view of macaque brain, showing visual areas. (Lower left) Medial view of macaque brain. (Reprinted with permission from van Essen and Anderson 1990.)

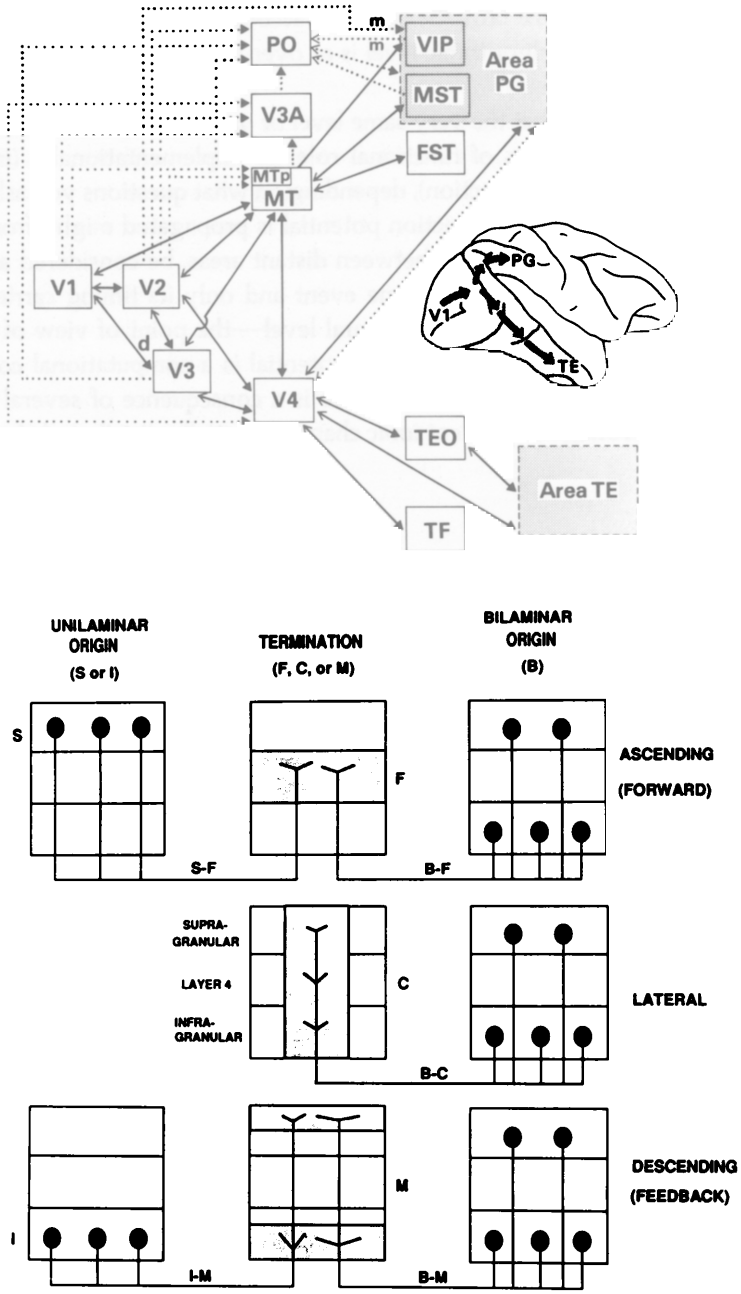

Figure 2.3 (Top) Schematic diagram of some of the cortical visual areas and their connections in the macaque monkey. Solid lines indicate projections involving all portions of the visual field representation in an area; dotted lines indicate projections limited to the representation of the peripheral visual field. Heavy arrowheads indicate forward projections; light arrowheads indicate backward projections. (From Desimone and Ungerleider 1989.) (Bottom) Laminar patterns of cortical connectivity used for making hierarchical assignments. Three characteristic patterns of termination are indicated in the central column. These include preferential termination in layer 4 (the F pattern), a columnar (C) pattern involving approximately equal density of termination in all layers, and a multilaminar (M) pattern that preferentially avoids layer 4. There are also three

The focus for this levels concept is the link between anatomy and what is represented in the anatomy. As a first pass, it assumes that the greater the distance from cells responding to sensory input, the higher is the degree of information processing. Thus the level-rank assigned is a function of synaptic distance from the periphery. On this measure, cells in the primary visual area of the neocortex that respond to oriented bars of light are at a higher level than cells in the lateral geniculate nucleus (LGN), which in turn are at a higher level than retinal ganglion cells. Because the nature of the representations and the transformations on the representations are still poorly understood, only the relative level—x is higher or lower than y—rather than the ordinal level—first, second, etc.—is referred to.

Once the sensory information reaches the cerebral cortex, it fans out through cortico-cortical projections into a multitude of parallel streams of processing. In the primate visual system, 25 areas that are predominantly or exclusively visual have been identified (van Essen et al. 1991; figure 2.2). Many (perhaps all) forward projections are matched by a backward projection, and there are even massive feedback projections from primary visual cortex to the LGN. Given these reciprocal projections, the processing hierarchy is anything but a one-way ladder. Even so, by examining the cortical layer into which fibers project, it is possible to find some order in the information flow. Forward projections generally terminate in the middle layers of cortex, and feedback projections usually terminate in the upper and lower layers.[3] So far, however, the function of these feedback pathways is not established, though the idea that they have a role in learning, attention, and perceptual recognition is not unreasonable. If higher areas can affect the flow of information through lower areas, then strictly sequential processing cannot be taken for granted (figure 2.3).

The organization typical of earlier sensory areas is only approximately, roughly, and incompletely hierarchical.[4] Beyond the sensory areas, moreover, not even that much hierarchy is manifest. The anatomy of frontal cortex and other areas beyond the primary sensory areas suggests an information organization more like an Athenian democracy than a Ford assembly line. Hierarchies typically have an apex, and following the analogy, one might expect to find a

characteristic patterns for the cells of origin of different pathways. Bilaminar (B) patterns, shown on the right, include approximately equal numbers of cells from superficial and deep layers (no more than a 70%–30% split) and are found to occur with all three types of termination pattern. Unilaminar patterns, shown on the left, include predominantly superficial-layer inputs (S pattern) which correlate with F-type terminations, and predominantly infragranular-layer (I pattern) inputs which correlate with M-type terminations. Within this general framework, a number of variations on a theme can be encountered. Some pathways terminate primarily in superficial layers, but they are grouped with the M pattern because they avoid layer 4. Other pathways are quasi-columnar, but do not include all layers; they are classified as a C pattern if the labeling in layer 4 is neither heavier nor sparser than in adjoining layers. Filled ovals, cell bodies; angles, axon terminals. (From Felleman and van Essen 1991.)

brain region where all sensory information converges and from which motor commands emerge. It is a striking fact that this is false of the brain. Although there are convergent pathways, the convergence is partial and occurs in many places many times over, and motor control appears to be distributed rather than vested in a command center (Arbib 1989, Altman and Kien 1989; figure 2.4).

The assumption that there is a sensory-processing hierarchy, if only to a first approximation, affords the possibility of probing the processing stages by linking various behavioral measures, such as task-relative reaction time (RT), to events taking place in the processing hierarchy at different times as measured by cellular response. To put it more crudely, temporal ordering helps determine what is cause and what is effect. Accuracy of response under varying conditions can be measured, and both humans and animals may be subjects. This is an important method for triangulating the brain areas involved in executing a certain task and for determining something about the processing stages of the task. For example, on the physiological side, one may measure the

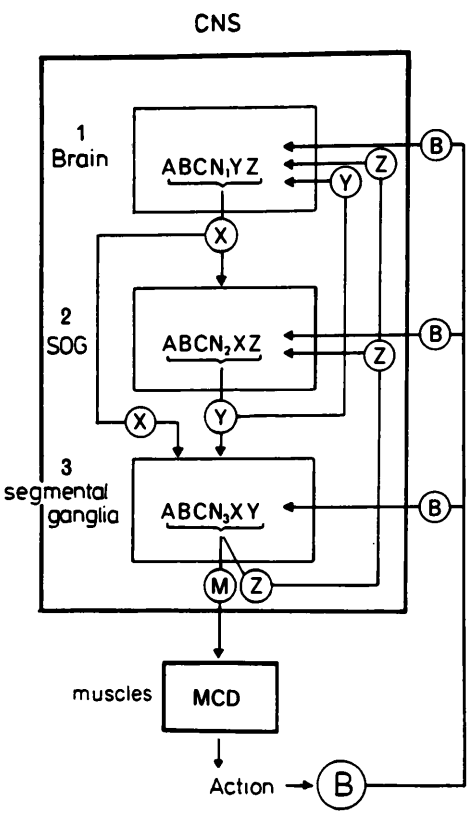

Figure 2.4 Model for decision-making in the insect nervous system. In the CNS, stations 1, 2, 3 contain local networks 1, 2, 3. These stations approximate the brain, the subesophageal (SOG), and segmental ganglia of the locust. The output of each station results from a consensus between the activity of the inputs and the local networks in that station, so the output of each station is different. The stations are thus linked in several parallel loops, and the output of the whole system is the consensus of the activity in all the loops. (From Altman and Kien 1989.)

delay between the presentation of a moving target and the first response by motion-sensitive cells in visual area MT, and on the behavioral side one may measure the response latency relative to degrees of noise in the stimulus. One surprise is that the latencies for signals reaching the visual areas in the cortex are so long, relative to the behavioral RT. The latency for MT is about 50–60 msec, and about 100 msec in inferotemporal cortex. Since human RT to a complex object is on the order of 150–200 msec including assembling the motor response, sending the signal down the spinal cord, and activating the muscles, this suggests that surprisingly few processing steps intervene between detection in MT and preparing the response in the motor cortex, striatum, cerebellum, and spinal cord. Such data help constrain theories about the nature of the processing.

By way of illustration, consider a set of experiments by William Newsome and colleagues (1989) in which they show a correlation between the accuracy of the behavioral response to motion detection and the spiking frequency of single neurons responding to motion stimuli in MT. (Newsome et al. 1989) In the task, tiny dots move randomly on a TV screen. The monkey is trained to respond as soon as it detects coherent motion, to either the right or the left. Across trials, what varies is the number of dots moving coherently and their direction of motion. The monkey detects direction of motion with as few as four dots moving coherently, and his accuracy improves as the number of dots moving together increases. What about the cells in MT? Suppose one records from a cell that prefers right-going motion. The visual display is set up so that it is matched to the cell's receptive field, with the result that the experimenter has control of the minimum stimulus needed to produce the maximum response. So long as fewer than four dots move coherently, the cell does not respond. With increasing numbers of dots moving coherently in the cell's preferred direction, the cell responds more vigorously. Indeed, the accuracy curve displayed in the monkey's behavior and the spiking-frequency curve displayed by the single cell are, to a first approximation, congruent (figure 2.5). This implies, to put it crudely, that the information contained in the cellular responses of single sensory neurons and the information contained in the behavioral response are roughly on par. It should, however, be kept in mind that the monkeys were very highly trained on this task and that the sensory stimulus was chosen to match the optimal response of each neuron. In a naive monkey, there may not be such close correspondence between the response of the single cell and the overt behavior.

The next phase of the experiment tests whether the information carried by directionally selective cells found in MT is really used in generating the response. To do this, Newsome and colleagues presented *left*-going visual stimuli, and at the proper latency they electrically stimulated the column containing cells preferring *right*-going visual stimuli. How did the animal behave? Would the electrical stimuli demonstrate its effectiveness by overriding, at least sometimes, the visual stimuli? The monkey behaved as though he saw right-going stimuli; more exactly, the electrical stimulus decreased the probability that the animal would respond to the visual stimulus and increased the

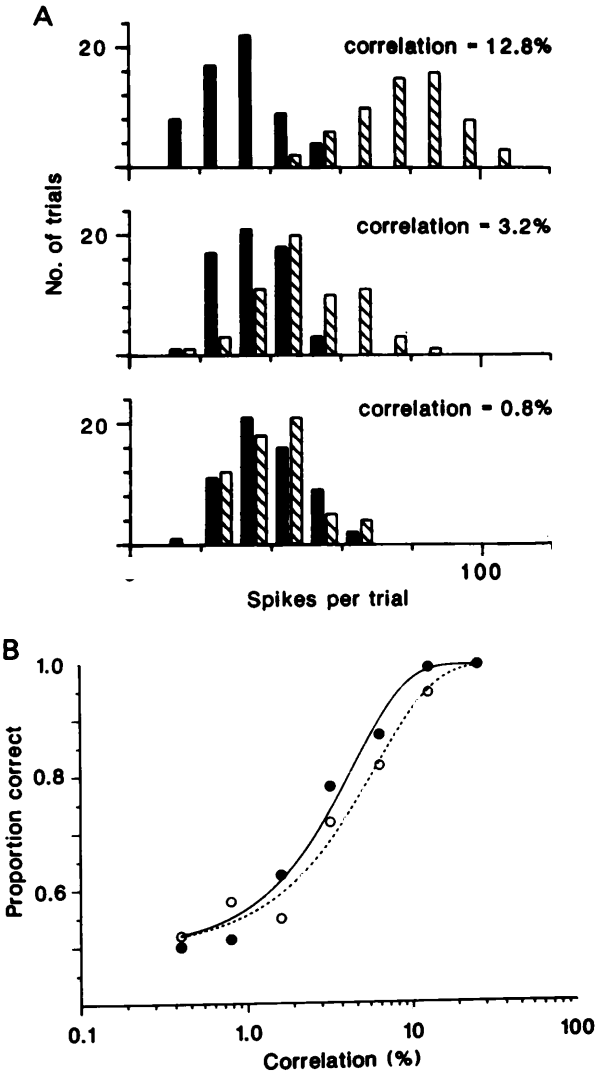

Figure 2.5 (a) Responses of a directionally selective neuron (in visual area MT) at three different motion correlations spanning physiological threshold. Hatched bars represent responses to motion in the neuron's preferred direction; solid bars indicate responses to motion 180° opposite to the preferred direction. Sixty trials were performed in each direction for each of the three correlation levels. Response distributions for a range of correlation levels were used to compute a "neurometric" function that characterized the neuron's sensitivity to the motion signal, and could be compared with the psychometric function computed from the monkey's behavioral response. (b) Comparison of simultaneously recorded psychometric and neurometric functions. Opens circles, psychophysical performance of the monkey; filled circles, performance of the neuron. Psychophysical performance at each correlation is given by the proportion of trials on which the monkey correctly identified the direction of motion. Neuronal performance is calculated from distributions of responses of the directionally sensitive MT neuron. The physiological and psychophysical data form similar curves, but the data for the neuron lie to the left of the data for the monkey, meaning that the neuron was somewhat more sensitive than the monkey. (From Newsome, Britten, and Movshon [1989]. Reprinted by permission from *Nature* 341: 52–54. Copyright © 1989 Macmillan Magazines Ltd.)

probability that it would respond as though presented with a stimulus in the opposite direction. This result implies that the cells' responses—and hence the information carried in those responses—are behaviorally significant (figure 2.6).

During the past hundred years, experimental psychologists have assembled an impressive body of RT information, and it is a valuable data base upon which neuroscientists may draw. Thus consider also a set of studies by Requin and colleagues (Requin et al. 1988, Riehle and Requin 1989). In the first stage, they measured the monkey's RT where the task was to make a wrist flexion in a certain direction and by a certain amount as indicated by a signal. There were basically three conditions: the monkeys were precued or not, and if they were precued, the cue indicated either the direction or the extent of the movement. Precuing was found to have a large effect on the RT but only a slight effect on the movement time, showing that precuing has its major effect on programming and preparing for the movement, rather than on the speed of execution of the movement. Additionally, if the advance cue specified where but not how much, the RT was shortened more than if the cue specified how much but not where. This suggests that information about extent of movement cannot be efficiently incorporated until the system knows the direction of the movement.

In the second stage, Riehle and Requin investigated the electrophysiological properties of cells in the primary motor cortex (MI) and the premotor cortex (PM). They found execution-related neurons, which were more common in MI, and preparation-related, directionally selective neurons, which were more common in PM. This coheres with other physiological data, and implies that PM probably involves an earlier stage of processing than does MI, since PM has more to do with preparing for the movement than with executing it. Moreover, within the class of preparation-related cells in PM, they found two subclasses: those related to programming the muscle movements, and those related to preprocessing the general components of the movement program. This is another instance of research that narrows down hypotheses about relative order of processing and the structures involved in a distinct aspect of processing by establishing behavioral reaction times and by correlating those data with specific responses of cells.[5]

3 STRUCTURE AT VARIOUS LEVELS OF ORGANIZATION

Identification of functionally significant structure at various spatial scales in nervous systems proceeds in partnership with hypotheses about a given structure's role in the nervous system's performance and the manner in which that structure's own subcomponents are organized to constitute the mechanisms to carry out that role. To be sure, functional architecture at various spatial scales is all part of one integrated, unified biological machine. That is, the function of a neuron depends on the synapses that bring it information, and, in turn, the neuron processes information by virtue of its interaction with other neurons in local networks, which themselves play a particular role by virtue of their place in the overall geometry of the brain.

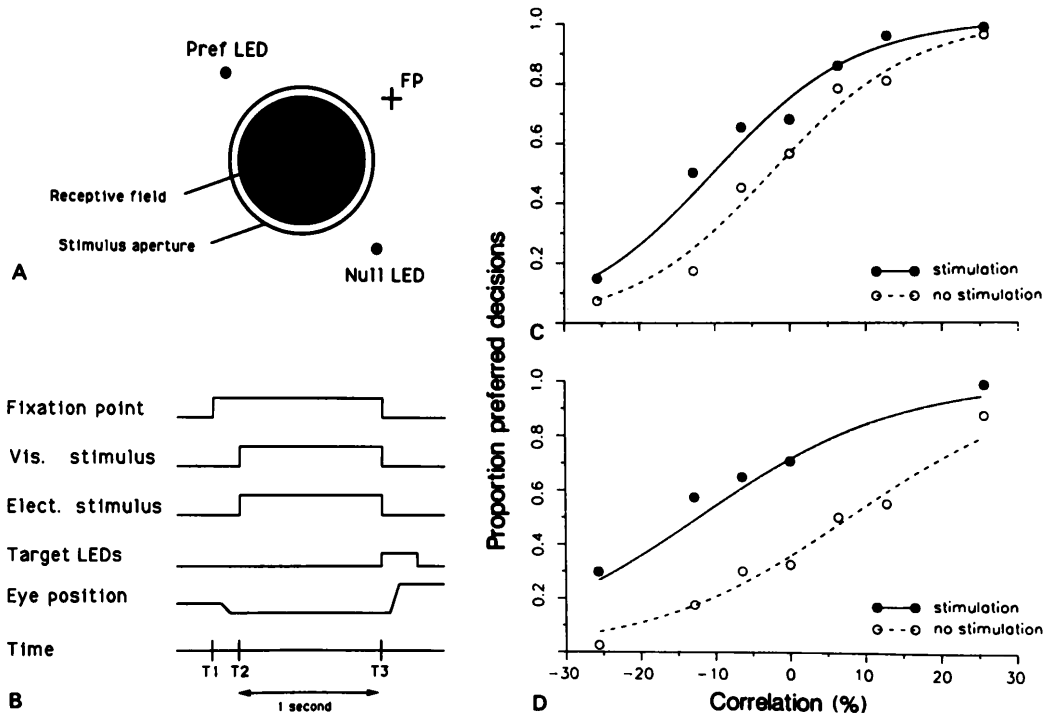

Figure 2.6 Microstimulation in cortical area MT biases perceptual judgments of motion. (A) Schematic diagram of the experimental protocol showing the spatial arrangement of the fixation point (FP), receptive field (shaded), stimulus aperture (thick circle), and response light emitting diodes (LEDs). (B) Schematic drawing illustrating the temporal sequence of events during a microstimulation trial. At time T_1 the fixation point appeared, and the monkey transferred its gaze to the fixation point, as indicated by the deflection in the eye position trace. At time T_2 the visual stimulus appeared, and the train of electrical stimulation pulses began. The monkey was required to maintain fixation for 1 sec until time T_3. The fixation point, the visual stimulus, and the microstimulation pulses were turned off at time T_3, and the target LED turned on. The monkey then indicated its judgment of motion direction by making a saccadic eye movement to one of the two response LEDs. (Right) The effect of microstimulation on performance for two stimulation sites in area MT (C and D). The proportion of decisions in the preferred direction is plotted as a function of the percent correlation in the moving dots during the stimulus presentation (positive correlation values indicate motion in the neuron's preferred direction). In half the trials (closed circles), microstimulation was applied simultaneously with the visual stimulus; the other trials (open circles) contained no microstimulation. The shift in the curves caused by the microstimulation is equivalent to adding 7.7% correlated dots (C) and 20.1% (D). (From Salzman, Britten, and Newsome 1990. Reprinted by permission from *Nature* 346: 174–177. Copyright © 1989 Macmillan Magazines Ltd.)

Accordingly, which structures really constitute a level of organization in the nervous system is an empirical, not an *a priori* matter. We cannot tell, in advance of studying the nervous system, how many levels there are, nor what is the nature of the structural and functional features of any given level. Some techniques used to study various levels will be surveyed in the appendix. In this section, seven general categories of structural organization will be discussed. In fact, however, the count is imprecise, for several reasons. Further research may lead to the subdivision of some categories, such as systems, into finer-grained categories, and some categories may be profoundly misdrawn and may need to be completely reconfigured. As we come to understand more about the brain and how it works, new levels of organization may be postulated. This is especially likely at higher levels where much less is known than at the lower levels.

Systems

To standardize references to brain locations, prominent landmarks, including major gyri, fissures, and the major lobes have been labeled (figures 2.7, 2.8). Using tract-tracing techniques, neuroanatomists have identified many systems in the brain. Some correspond to sensory modalities, such as the visual system; others, for example, the autonomic system, respect general functional characteristics. Yet others, such as the limbic system, are difficult to define, and may turn out not to be one system with an integrated or cohesive function. The components of these systems are not neatly compartmentalized but are distributed widely in the brain and are connected by long fiber tracts. For example, a particular brain system for long-term memory may involve such diverse structures as the hippocampus, the thalamus, the frontal cortex, and basal forebrain nuclei (Mishkin 1982). In this respect brain systems contrast quite vividly, and perhaps discouragingly, with systems designed by an engineer, where components are discrete and functions are compartmentalized.

One of the earliest systems concepts was that of a reflex arc, such as the monosynaptic reflex in the knee-jerk response (Sherrington 1906; figure 2.9). The pathways of some reflexes have now been traced in great detail; examples are the vestibulo-ocular reflex, which stabilizes images on the retina when the head is moving (Robinson 1981), and the gill withdrawal reflex in *Aplysia*, which has been a focus for research into the molecular mechanisms of plasticity (Kandel et al. 1987). The reflex arc is not a useful prototype for brain systems in general—or even, it appears, for most reflexes, such as the stepping reflex in the cat, or the nociceptive reflex (withdrawal of limb from a painful stimulus). Take, for example, the smooth pursuit system for visually tracking moving targets, where one pathway originates in the retina, leads to the lateral geniculate nucleus (LGN), to the cortex and through distinct visual topographic areas, down to the pons, and eventually to the oculomotor nuclei (Lisberger et al. 1987). (See chapter 6.) Despite the machine-like quality of smooth pursuit, it is to some extent under voluntary control and depends on expectation as well

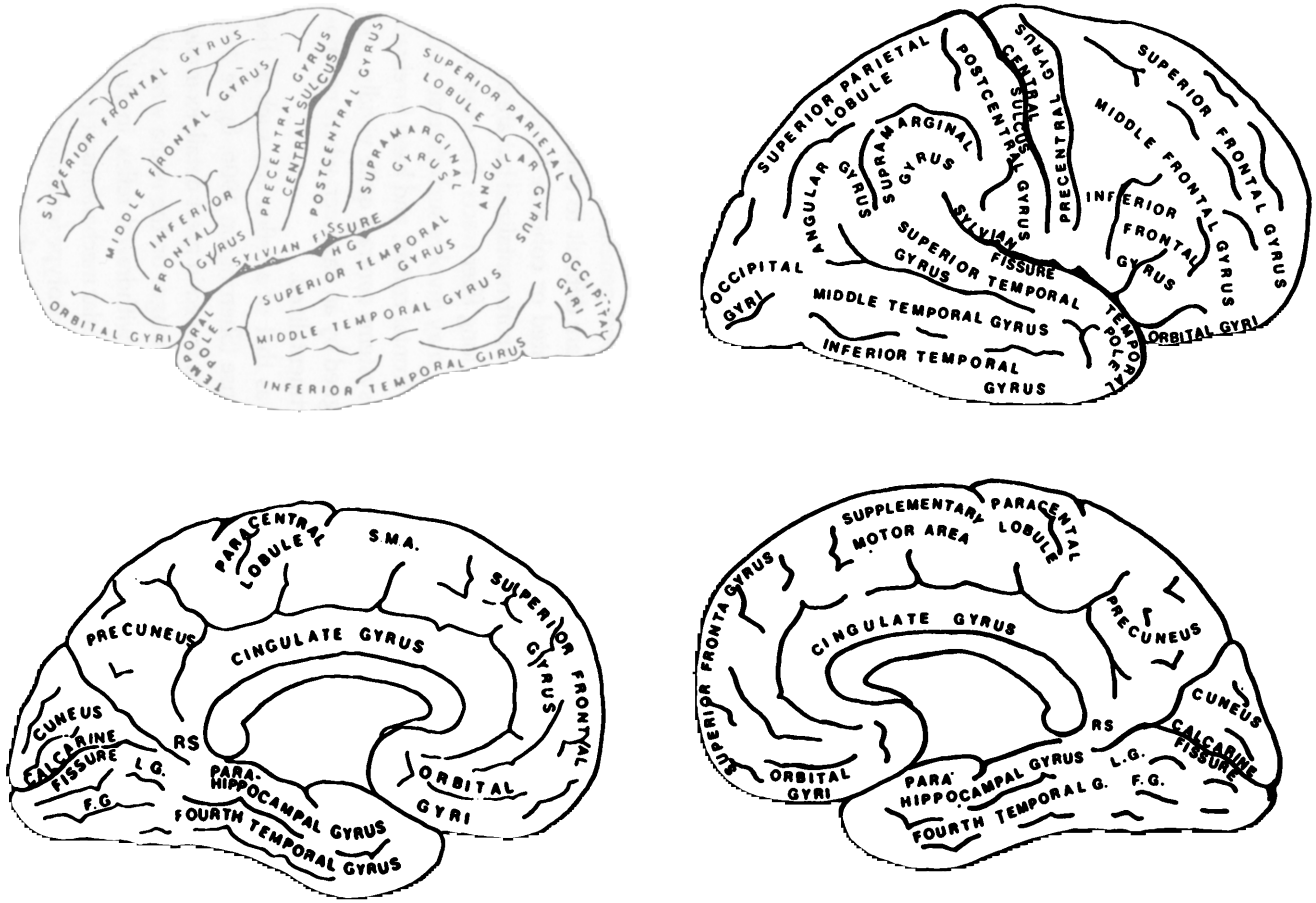

Figure 2.7 Major gyri and fissures of the human cerebral cortex. (Top) View from the outside or lateral aspect, showing left and right hemispheres. (Bottom) View of the inside, or medial, aspect of right and left hemispheres. Note that the hemispheres are not exact mirror images of each other. The precise location of gyri and fissures as well as the degree of asymmetry varies from brain to brain. (Courtesy Hanna Damasio.)

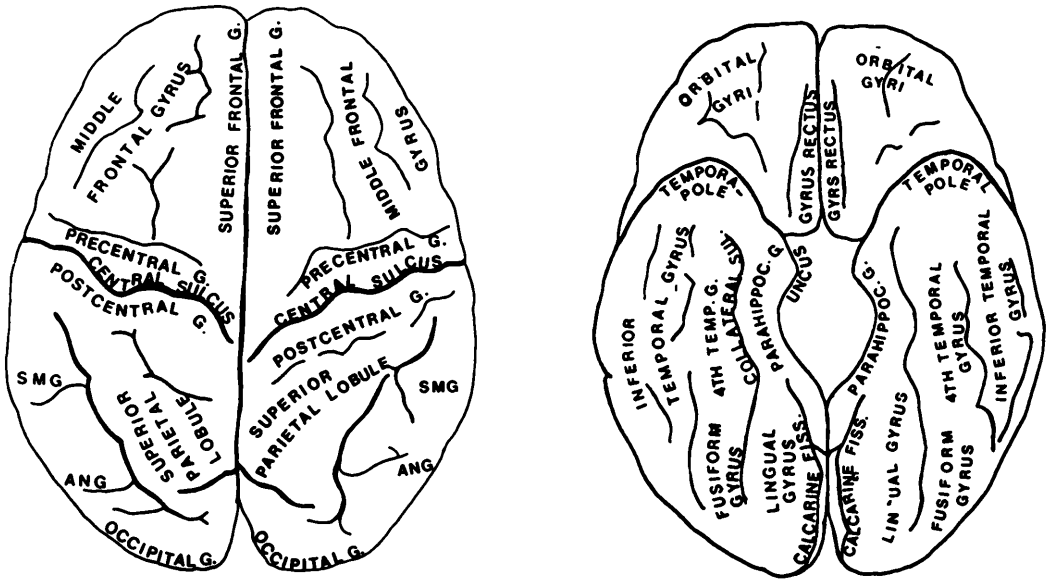

Figure 2.8 Major gyri and fissures of the human cerebral cortex. (Left) View from above (dorsal aspect). (Right) View from below (ventral, or inferior, aspect). (Courtesy Hanna Damasio.)

as the visual stimulus. Behaviors more sophisticated than simple reflexes probably exploit more complex computational principles.

In this regard, two important features of brain systems should be mentioned. First, there are almost always reciprocal (feedback) connections between brain areas, at least as rich in number as the feedforward connections. For example, the recurrent projections from the visual cortical area V1 back to the LGN are about ten times as numerous as those from the LGN to the V1. Second, although the simple models of reflex arcs suggest that a single neuron may be sufficient to activate the neuron on which it synapses, in fact a large number of neurons are almost always involved, and the effect of any single neuron on the next is typically quite small. For example, an important feature in the visual system is that input from a specific neuron in the LGN generally makes relatively weak synaptic contacts on a large population of cortical cells rather than a strong synaptic effect on just one or a few neurons (Martin 1984). This implies that cortical neurons rely on a convergence of many afferents, and correlations between pairs of neurons tends to be relatively weak.[6] There may be interesting exceptions to this; for example, chandelier cells in cortex make inhibitory connections on the axon hillocks of their targets, and they may, as single cells, have a strong, decisive effect on their target cells. Another exception is the strong influence that single climbing fibers have on single Purkinje cells in the cerebellum.

Topographic Maps

A major principle of organization within many sensory and motor systems is the topographic map. For example, neurons in visual areas of cortex, such as

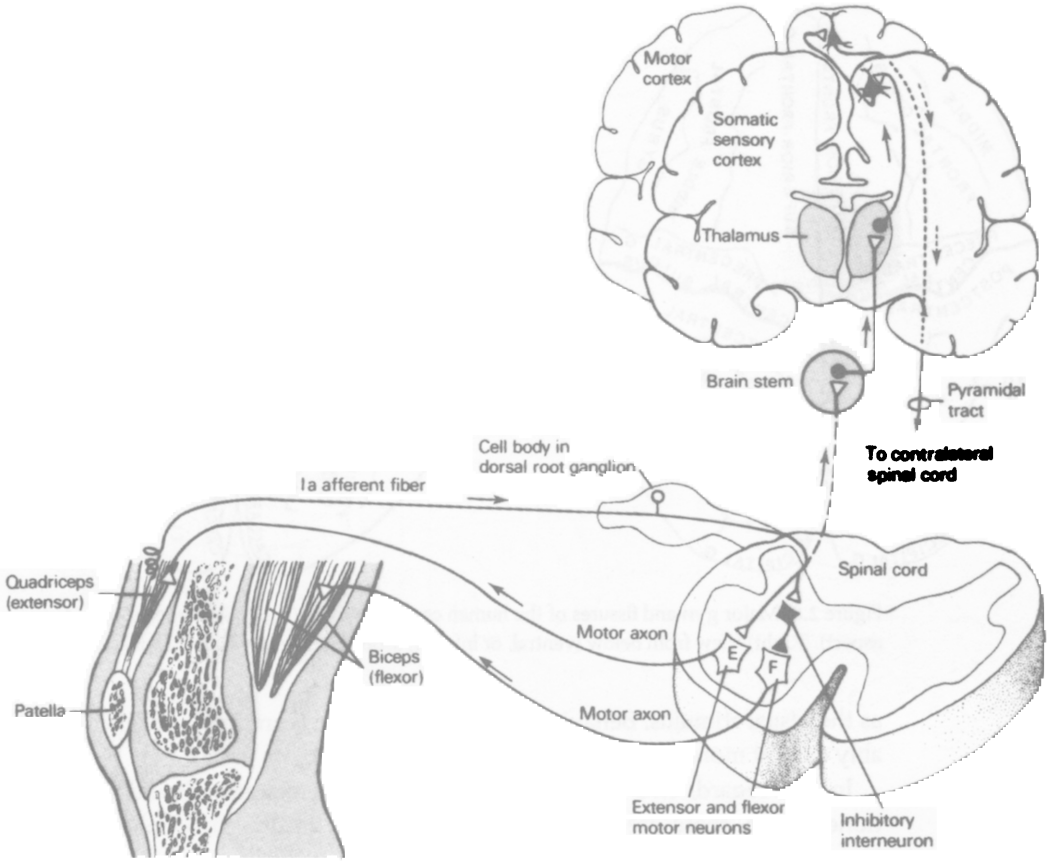

Figure 2.9 Schematic diagram of the pathways for the stretch reflex. Stretch receptors in musde spindles react to changes in length of the muscle, and afferent fibers carry this information along the dorsal roots to the spinal cord where they synapse on extensor motoneurons, which extend the knee, and inhibitory interneurons, which reduce activity in motor neurons that produce contractions of the antagonistic flexor muscles. Both of these actions combine to produce a coordinated expression of the knee-jerk reflex. This information is also conveyed to higher brain centers, which in turn can modify the reflex behavior through descending pathways to the spinal cord. (From Kandel 1985.)

V1, are arranged topographically, in the sense that adjacent neurons have adjacent visual receptive fields and collectively they constitute a map of the retina. Because neighboring processing units (cell bodies and dendrites) are concerned with similar representations, topographic mapping is an important means whereby the brain manages to save on wire and also to share wire (Mead 1989). It is significant that the maps are distorted, in the sense that some regions of the body surface occupy larger regions of cortex than others. The fovea, for example, occupies a relatively large part of V1, and the hands occupy a relatively large area of the somatosensory cortex. In visual area MT of the macaque, which contains many neurons selective for direction of motion, the lower half of the visual field has greater representation than the

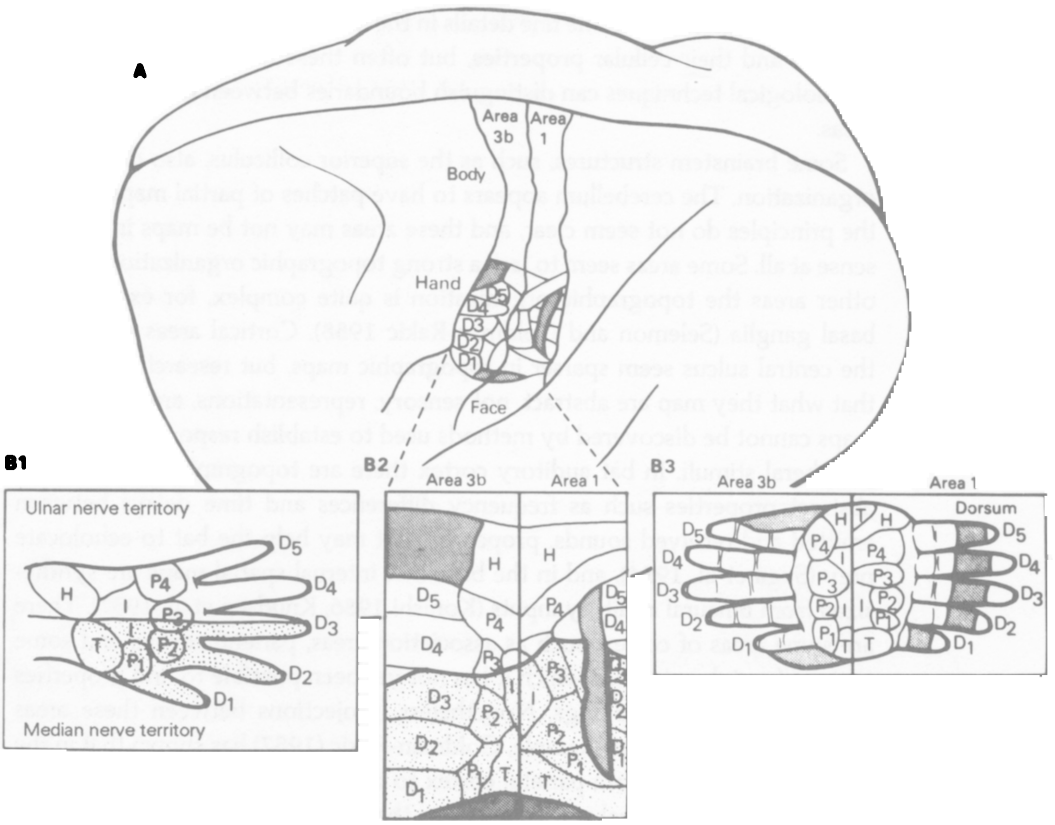

Figure 2.10 Schematic drawing of the multiple representations of the body surface in the primary somatic sensory cortex of the owl monkey. Because the cortex of the owl monkey is relatively flat, most of the body representation is located on the surface rather than in the convolutions found in the species of most other primates. (A) Two representations of the hand are shown in areas 3b and 1. (B) The hand of the owl monkey is innervated by the median and ulnar nerves, which have different territory on the ventral surface (B1) and are represented in adjacent areas of cortex in each of the two maps (B2). The topographical organization of the cortical map for the ventral surface of the hand is highly ordered (B3) in both areas. Cortex devoted to the ventral surface is indicated in white; that devoted to the dorsal surface, in dark shading. D_1 to D_5, digits; P_1 to P_4, palmar pads; I, insular pad; H, hypothenar pads; T, thenar pads. (From Kandel and Schwartz 1985).

upper half. This makes sense because it is the lower half of the visual field where hand skills—searching for termites, picking up lice, and so forth—require the greatest acuity (Maunsell and van Essen 1987.)[7]

In the visual systems of monkeys, physiologists have found about 25 distinct areas, most of which are topographically mapped.[8] A similar hierarchy of multiple topographic maps is found for body location in the somatosensory system (Kaas et al. 1979; figure 2.10), for frequency in the auditory system (Merzenich and Brugge 1973), and for muscle groups in the motor system (Ferrier 1876, Asanuma 1973). One possible exception is the olfactory system, but even odors may be spatially organized at the level of the olfactory bulb (Stewart et al. 1979). To some extent the different sensory maps can be distin-

guished by differences in the fine details in the laminations of neurons (see next section) and their cellular properties, but often these are so subtle that only physiological techniques can distinguish boundaries between different cortical areas.

Some brainstem structures, such as the superior colliculus, also display this organization. The cerebellum appears to have patches of partial maps, though the principles do not seem clear, and these areas may not be maps in any real sense at all. Some areas seem to lack a strong topographic organization, and for other areas the topographic organization is quite complex, for example the basal ganglia (Selemon and Goldman-Rakic 1988). Cortical areas anterior to the central sulcus seem sparser in topographic maps, but research may show that what they map are abstract, not sensory, representations, and hence such maps cannot be discovered by methods used to establish response patterns to peripheral stimuli. In bat auditory cortex there are topographic mappings of abstract properties such as frequency differences and time delays between emitted and received sounds, properties that may help the bat to echolocate prey (Suga et al. 1984), and in the barn owl internal spatial maps are synthesized from binaural auditory inputs (Konishi 1986, Knudsen et al. 1987). There are some areas of cortex, such as association areas, parietal cortex, and some parts of frontal cortex, for which it has not yet been possible to find properties that form orderly mappings. Nonetheless, projections between these areas remain topographic. For example, Goldman-Rakic (1987) has shown that in the monkey projections from parietal cortex to target areas in the prefrontal cortex, such as the principal sulcus, preserve the topographic order of the source neurons.

Maps of the surface of the body in the brain are formed during development by projections that become ordered, in part, through competitive interactions between adjacent fibers in the target maps (see chapter 5). Some of the neurons undergo cell death during this period, and with the possible exception of olfactory receptors, no new neurons are formed in the mature mammal (Cowan et al. 1984). However, competitive interactions between neurons continue, to some extent, even in adulthood, since the territory in cortex devoted to a particular part of the body surface can shift as much as 1–2 cm, but not much farther, weeks after injury to sensory nerves or after excessive sensory stimulation (Pons et al. 1991). Thus, regions in somatosensory cortex that are silenced following denervation of a sensory nerve will eventually become responsive to nearby regions of the body. It is not yet known how much of this rearrangement is due to plasticity in cerebral cortex, or perhaps in subcortical structures that project to cortical maps. Auditory maps, particularly in the superior colliculus, are also modifiable both in development, and in the adult following partial deafness (King and Moore, 1991). Nonetheless, this evidence, and further evidence for synaptic plasticity summarized below, make it difficult to think of the machinery in the adult brain as "hardwired," or static. Rather, the brain has a remarkable ability to adapt to changes in the environment, at many different structural levels and over a wide range of time scales.

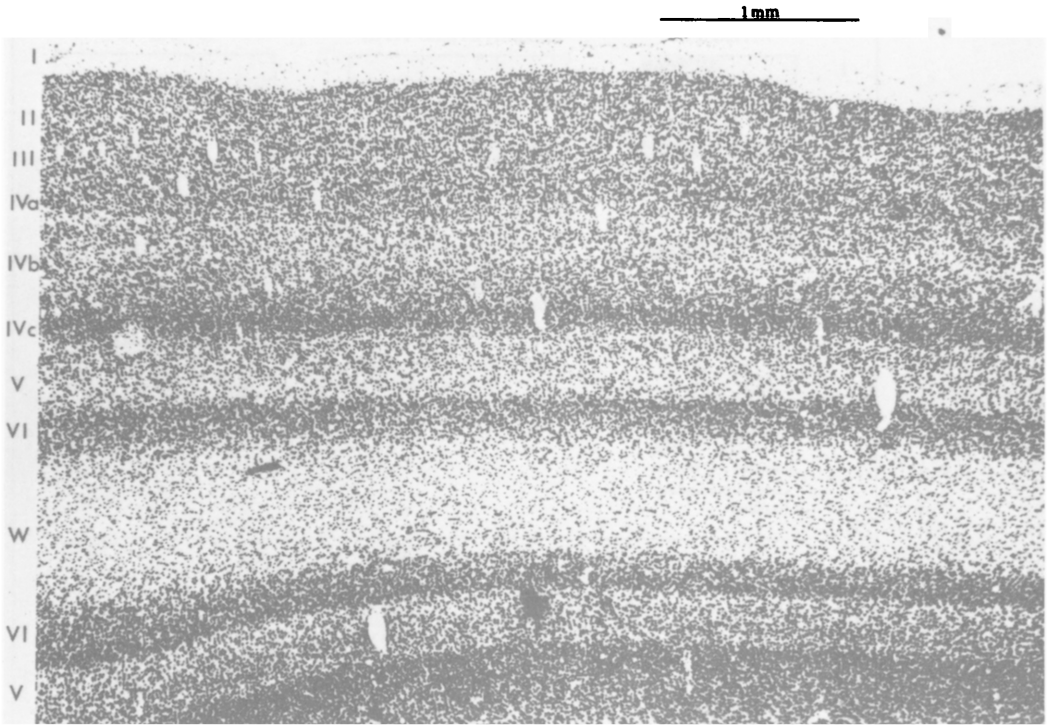

Figure 2.11 Cross-section through monkey striate cortex using cresyl violet to stain cell bodies. Laminations are clearly visible; the layers are numbered at the left. W, white matter. Deeper layers of the buried fold of cortex are shown in the lower part of the figure. (From Hubel and Wiesel 1977.)

Layers and Columns

Many brain areas display not only topographic organization, but also laminar organization (figures 2.11, 2.12). Laminae are layers (sheets) of neurons in register with other layers, and a given lamina conforms to a highly regular pattern of where it projects to and from where it receives projections. For example, the superior colliculus receives visual input in superficial layers, and in deeper layers it receives tactile and auditory input. Neurons in an intermediate layer of the superior colliculus represent information about eye movements. In the cerebral cortex, specific sensory input from the thalamus typically projects to layer 4, the middle layer, while output to subcortical motor structures issues from layer 5, and intracortical projections originate chiefly in (superficial) layers 2 and 3. Layer 6 mainly projects back to the thalamus (see figure 2.3). The basal ganglia do not have a laminar organization, but rather a patchwork of islands which can be distinguished by developmental and chemical markers (Graybiel and Hickey 1982).

As well as the horizontal organization seen in laminae, cortical structures also display vertical organization. This organization consists in a high degree of commonality between cells in vertical columns, crossing laminae, and is

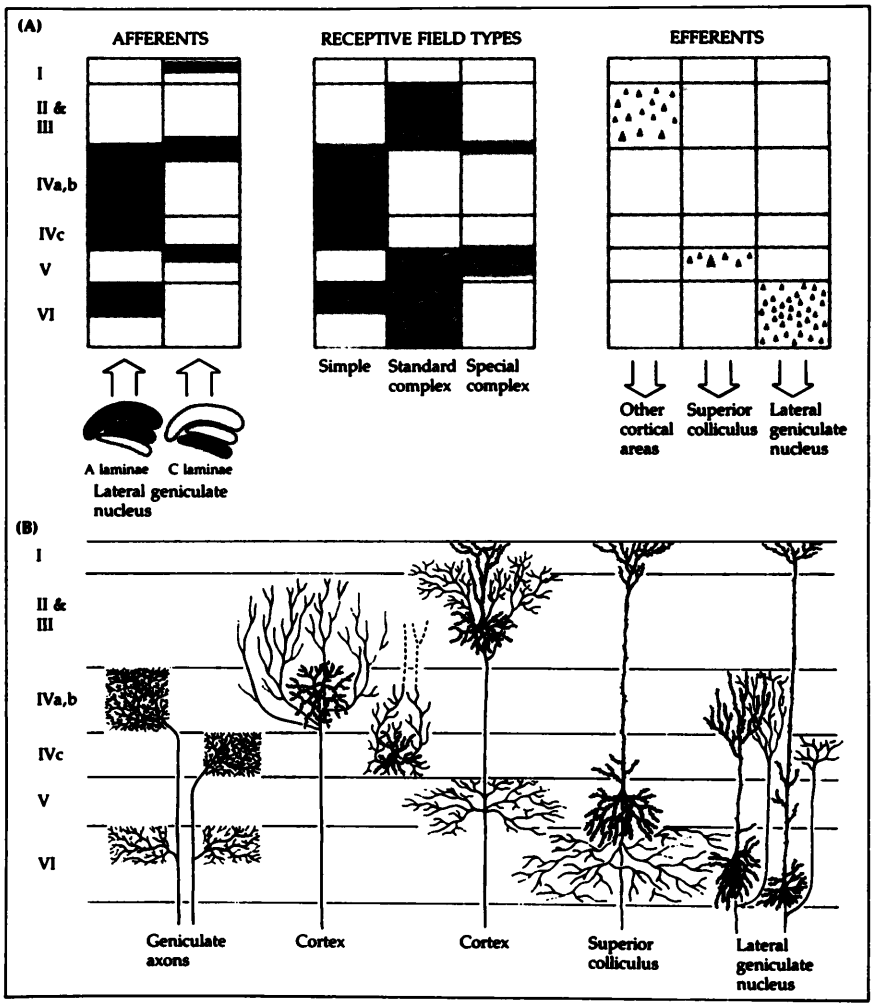

Figure 2.12 Schematic diagram of cortical connections in the cat. (A) Distribution of inputs from layers of the lateral geniculate, showing that geniculate axons project to different cortical laminae as a function of layer of origin in the geniculate. Cortical neurons with similar receptive field properties cluster together in particular lamina. The origin of fibers leaving a region of cortex varies as a function of target. (B) Schematic arborization patterns of the main cell types in laminae I–VI. (After Gilbert and Wiesel 1981.)

reflected both anatomically in terms of local connections between neurons (Martin 1984, Lund 1987) and physiologically in terms of similar response properties (Hubel and Wiesel 1962). For example, a vertical penetration of an electrode in visual cortex reveals cells which share a preference for stimuli with the same orientation (e.g., a bar of light oriented at about 20° from the horizontal). Another vertical penetration nearby will show cells which prefer a different orientation. Inputs and outputs are also organized in columns, such as the ocular dominance columns in V1, and inputs into the principal sulcus which alternate between parietal projections from the same side and projections from the principal sulcus in the opposite hemisphere (Goldman-Rakic 1987).

Typically, the vertically organized connectivity patterns do not result in columns with sharp boundaries, and the response properties tend to vary continuously across the cortex. Hence the expression "vertical column" may be slightly misleading. Thus for cells in visual area V1, orientation varies over the cortex smoothly, save for some fractures and singularities (Blasdel and Salama 1986), and a similar organization can be found in area V2 (Swindale et al. 1987), which receives a topographically mapped projection from V1. There are, however, places where vertical, cross-laminar columns with quite sharp boundaries are seen, for example the ocular dominance columns in layer 4 of area V1 and the "barrels" in the rodent somatosensory cortex, where each barrel contains cells preferentially sensitive to stimulation of a particular whisker (Woolsey and van der Loos 1970) (figure 2.13). Sharp anatomical boundaries are, however, the exception rather than the rule. Also, the spatial scale of columnar organization can vary from about 0.3 mm for ocular dominance columns to 25 μm for orientation columns in monkey visual cortex.

Topographic mapping, columnar organization, and laminae are special cases of a more general principle: the exploitation of geometric properties in information processing design. Spatial proximity may be an efficient way for biological systems to assemble in one place information needed to solve a problem. To consider a simple case, suppose it is necessary to compare differences between stimuli at neighboring locations, where comparison requires signals be brought together. Then topographic organization may achieve this efficiently while minimizing the total length of the connections. This is desirable since most of the volume of the brain is filled with axonal processes, and there are limitations on how big the brain can be as well as temporal tolerances that must be met. Lateral inhibitory interactions within the spatial maps are used to make comparisons, enhance contrast at borders, and perform automatic gain control. Mutual inhibition within a population of neurons can be used to identify the neuron with the maximum activity, a type of winner-take-all circuit (Feldman and Ballard 1982). (See also chapter 5, last section.)

Local Networks

Within a cubic millimeter of cortical tissue, there are approximately 10^5 neurons and about 10^9 synapses, with the vast majority of these synapses arising from cells located within cortex (Douglas and Martin 1991) (figure 2.14). These

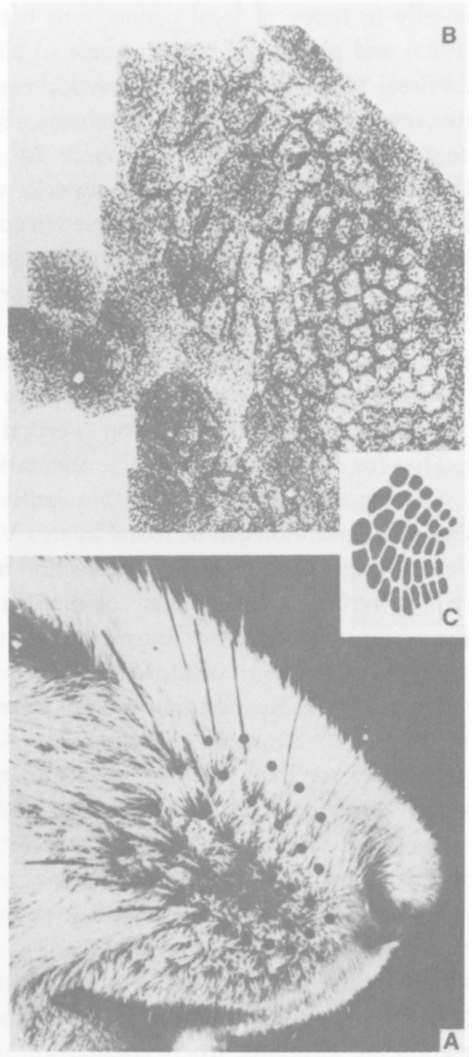

Figure 2.13 (A) Snout of a mouse; the vibrissae (whiskers) are marked by dots. (B) Sections across the somatosensory cortex that receive input from the snout. Each of the rings or "barrels" corresponds to an individual vibrissa, and are spatially organized to preserve the neighborhood relations of the vibrissae (C). (Reprinted with permission from Woolsey and van der Loos 1970.)

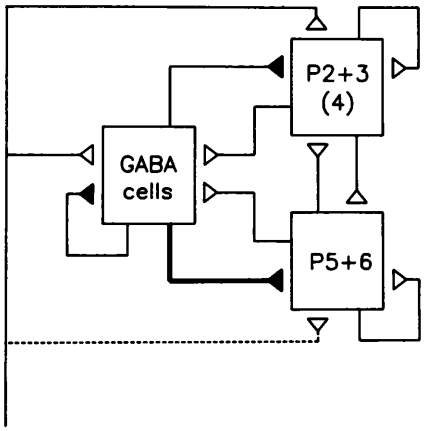

Figure 2.14 Schematic diagram of a microcircuit in the cerebral cortex that may be repeated again and again. Three populations of neurons interact with each other: inhibitory (GABA) cells, shown with solid synapses; and excitatory cells (open synapses) representing (i) superficial (*P*2 + 3) and (ii) deep (*P*5 + 6) layer pyramidal cells. Each population receives excitatory input from the thalamus, which is weaker (dashed line) to deep pyramidal cells. (Reprinted with permission from Douglas et al. 1989.)

local networks have been very difficult to study owing to the complexity of the tangled mass of axons, synapses, and dendrites called the neuropil. Nevertheless, some general features of local networks are beginning to emerge. For example, the orientation tuning of cells in V1 must emerge from nonoriented inputs and activity in local networks in ways that we are just beginning to understand (Ferster and Koch 1987).

Most of the data available on local networks are based on single-unit recordings, and to achieve a deeper understanding of the principles governing networks, it will be necessary to monitor a large population of neurons (see Appendix for recording techniques). Even a local network involves many cells, but only small populations can be studied by exhaustive sequential recordings from single cells. Consequently, we run the risk of generalizing from an atypical sample, and of missing circuit properties that can be inferred only from a richer profile. Therefore, to understand the principles of local networks, much more work must be done to determine the dynamical traffic within a larger population of cells over an extended period of time (figure 2.15).

Computer simulations may help to interpret single-unit data by showing how a population of cells could represent properties of objects and perform coordinate transformations. For example, network models of spatial representations have been constructed that help to explain the response properties of single cells in parietal cortex (Andersen and Mountcastle 1983, Zipser and Andersen 1988; figure 2.16). Another network model has been used to explain how the responses of single neurons in visual cortex area V4 could compute color constancy (Zeki 1983, Hurlbert and Poggio 1988). Network simulations can also suggest alternative interpretations for known response properties. For

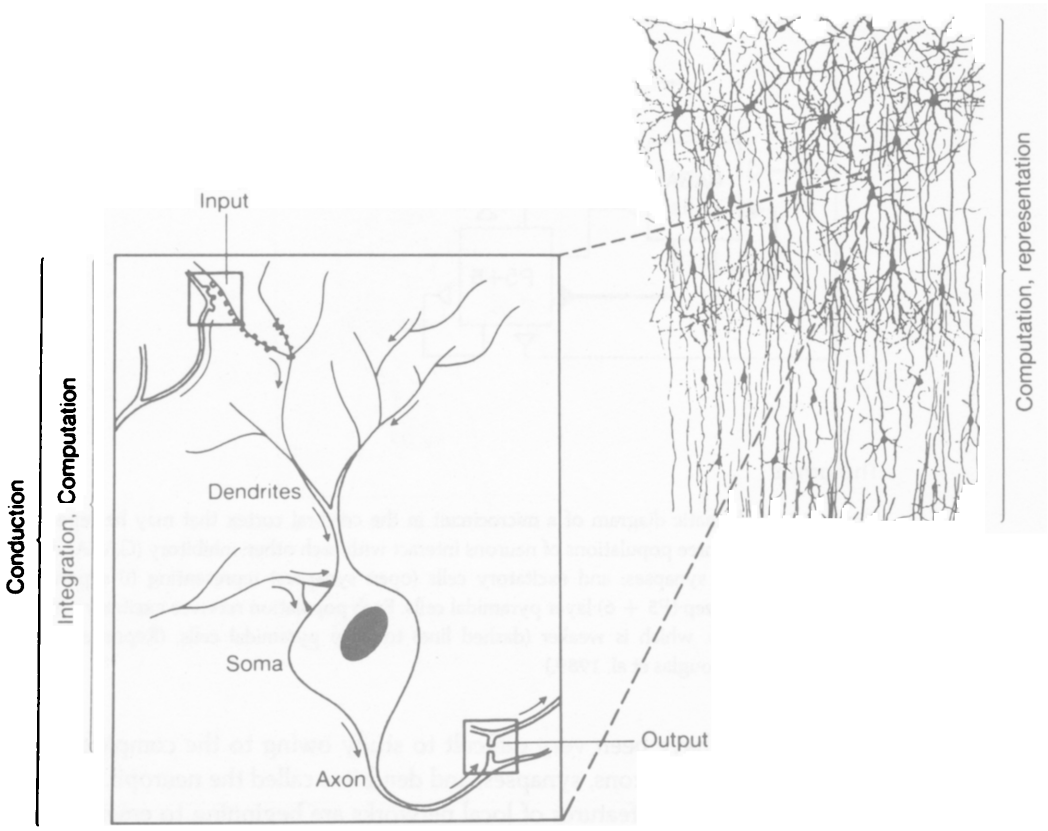

Figure 2.15 (Upper right) Network of pyramidal neurons in mouse cortex, stained by the Golgi method, which stains only about 10% of the population. (Lower left) Schematic of a generalized neuron showing one of its inputs to a dendrite, one to the cell body, and one of its axonal contacts. (Reprinted with permission from Dudai *The Neurobiology of Memory: Concepts, Findings, and Trends* [1989]. Copyright © Oxford University Press.)

example, there are certain oriented cells in V1 whose response summates with the length of the slit or edge of light up to the borders of the receptive field, but then the response diminishes as the length increases. This property, called "end-stopping," has recently been related to the extraction of the 1-D curvature of contours (Dobbins et al. 1987) and the 2-D curvature of shapes in shaded images (Lehky and Sejnowski 1988). An example of this approach is given in chapter 4 on visual processing.

Neurons

Ever since Cajal's work in the late nineteenth century, the neuron has been taken as an elementary unit of processing in the nervous system (figure 2.17). In contrast to Golgi, who believed neurons formed a continuous "reticulum," or feltwork, Cajal argued that neurons were distinct, individual cells, separated from each other by a spatial gap, and that mechanisms additional to those operating intracellularly would have to be found to explain how the signal

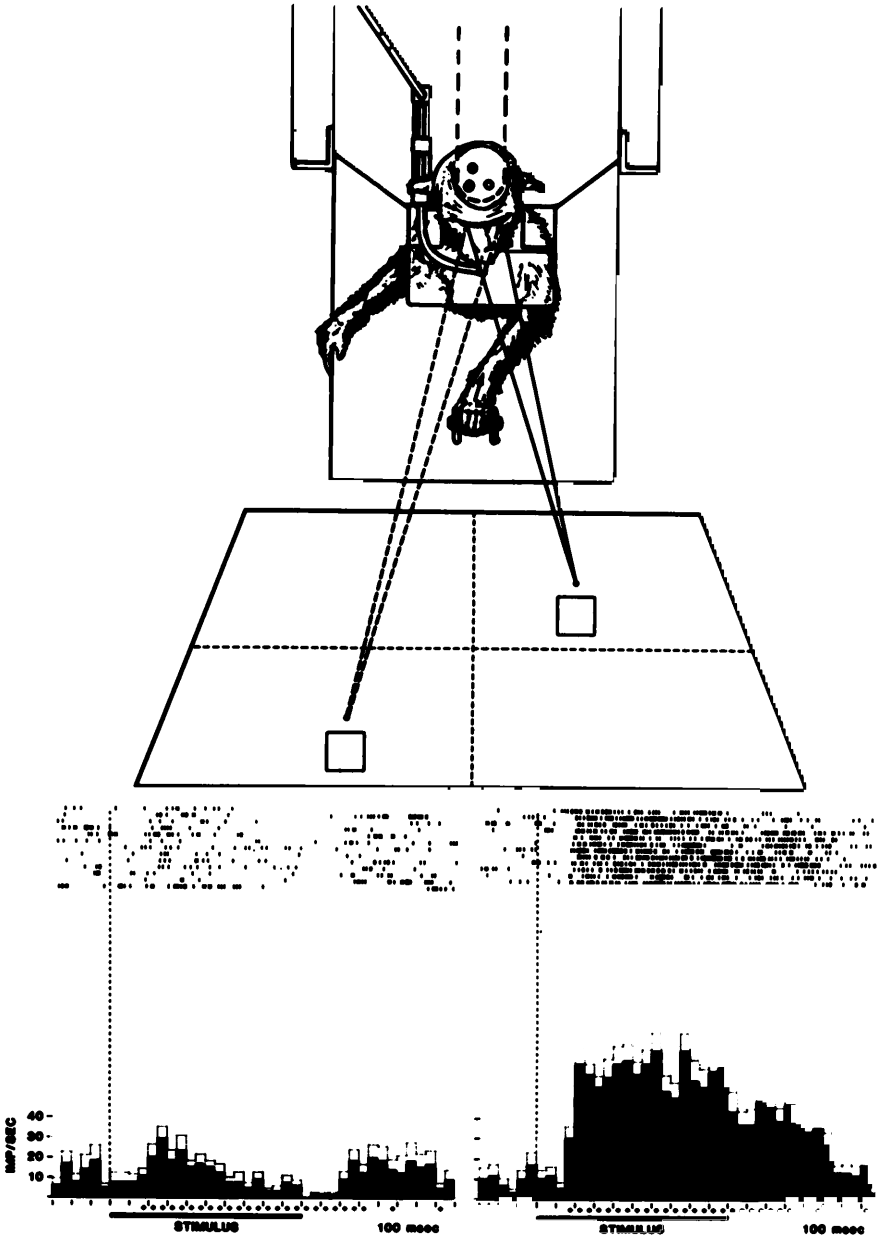

Figure 2.16 Illustration of the single-unit technique used to study the response of neurons in the parietal cortex of an awake, behaving monkey. The animal fixated a small target light placed at a series of positions on the screen, with its head fixed. The results obtained at two positions are shown here. At each fixation position a square was flashed for 1 sec at 10° above the point of fixation. Recordings from a single neuron are shown below the screen. Each line represents a single trial, and each small nick made on the line represents the discharge of an impulse by the neuron. The impulses were summed in the histograms on the bottom panel. The right side of the figure shows the responses for fixation to the left and down, and the left side shows the responses for fixation to the right and up. This and other experiments show that this class of neurons in parietal cortex has receptive fields that are specific to a retinal location, but the degree of activation of the neuron to a visual stimulus within the receptive field is modulated by the position of the eye. (See also chapter 4, section 10.) (From Andersen and Mountcastle 1983.)

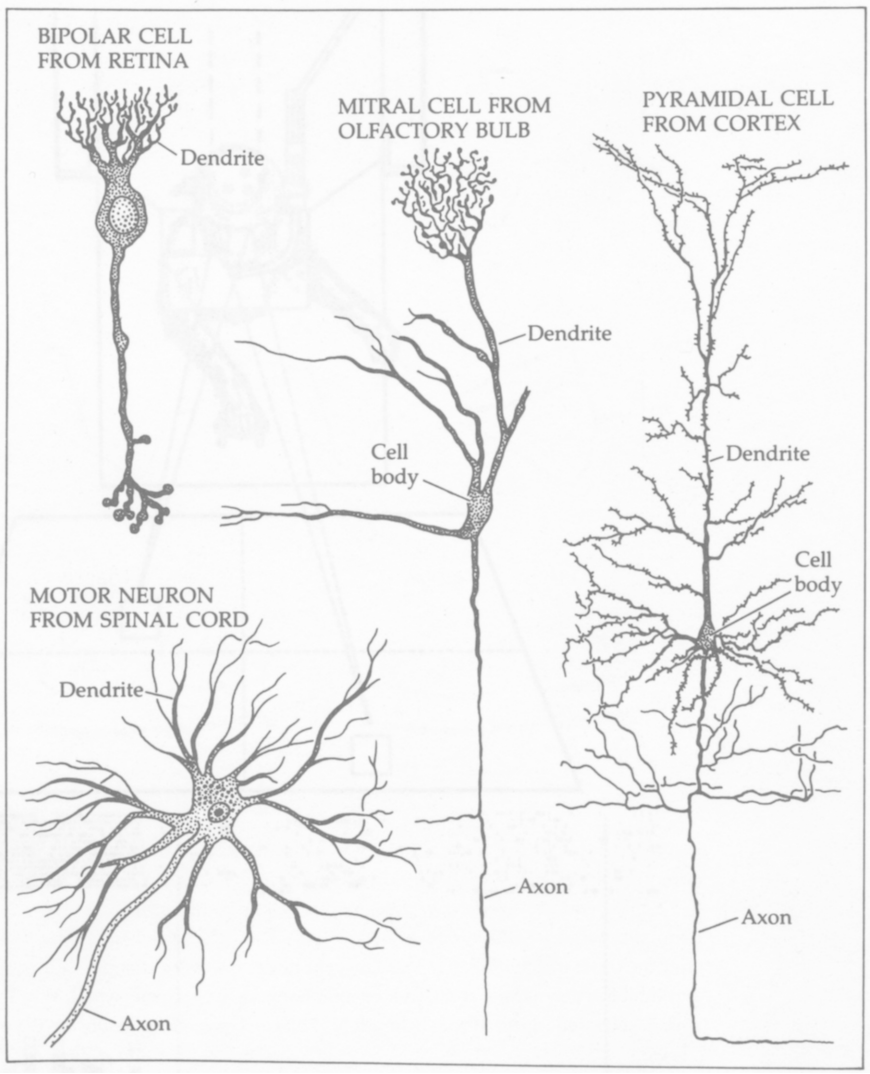

Figure 2.17 Examples of neurons illustrating the variety of shapes in different areas of the brain. (With permission from Kuffler, Nicholls and Martin [1984]. *From Neuron to Brain*. Sunderland MA: Sinauer Associates.)

passed from neuron to neuron. Physiological studies have borne out Cajal's judgment, though in some areas such as the retina, syncytia of cells that are electrically coupled have been found (Dowling 1987). As it turns out, these are rather more like the structures Golgi predicted because the cells are physically joined by conducting "gap junctions." These electrical synapses are faster and more reliable than chemical transmission, but are more limited in flexibility.

There are many different types of neurons, and different parts of the nervous system have evolved neurons with specialized properties. There are five general types of neurons in the retina, for example, each with a highly distinctive morphology, connectivity pattern, physiological properties, and embryological origin. In recent years, moreover, physiological and chemical differences

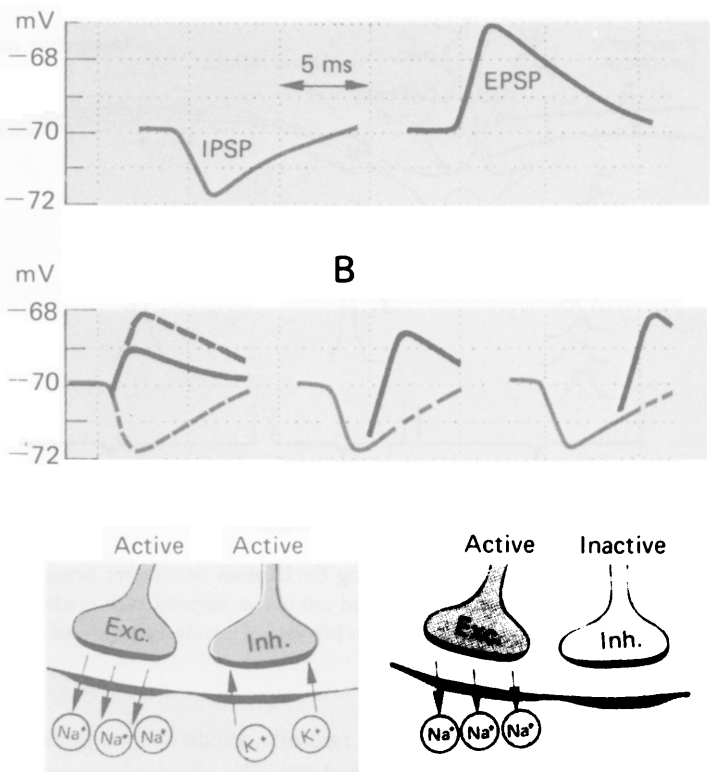

Figure 2.18 Inhibitory and excitatory synapses on a neuron. (A) The inhibitory postsynaptic potential (IPSP) means that the postsynaptic cell hyperpolarizes (dropping from −70 mV to −72 mV), and the excitatory postsynaptic potential (EPSP) means that the postsynaptic cell depolarizes (from −70 mV to −67 mV). (B) The EPSP was triggered about 1, 3, and 5 msec after the onset of the IPSP. (C) The subsynaptic conductance changes occurring when excitatory and inhibitory synapses are activated simultaneously (left) and when only the excitatory synapse is activated (right). (From Schmidt [1978]. *Fundamentals of Neurophysiology*. Berlin: Springer-Verlag.)

have been found within classes. For example, 23 different types of ganglion cells (whose axons project to the brain through the optic nerve) and 22 different types of amacrine cells (which provide lateral interactions and temporal differentiation) have been identified (Sterling et al. 1983). There are seven general types of neurons in the cerebellum and about 12 general types in the neocortex, with many subtypes distinguishable by their chemical properties such as the neurotransmitters they contain. The definition of a neuronal type is somewhat arbitrary, since judgments are often made on the basis of subtle morphological differences, which can be graded rather than categorical. As more chemical markers are found, however, it is becoming clear that the diversity of neurons within cerebral cortex has been vastly underestimated. On anatomical and immunocytochemical criteria, therefore, the number of subtypes of cortical neurons is probably between 50 and 500 (Sereno 1988).

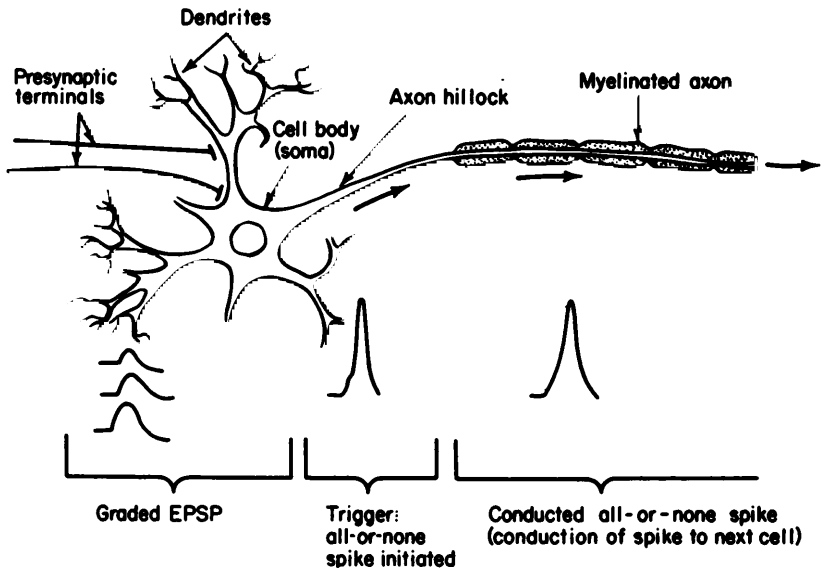

Figure 2.19 Summary diagram showing the location on a motor neuron of various electrical events. In many neurons, dendrites and cell bodies respond with graded EPSPs or IPSPs; the action potential is triggered in the axon hillock and travels undiminished down the axon. (From Thompson 1967.)

On the basis of their effects, neurons divide in two general classes: excitatory and inhibitory (figures 2.18, 2.19). The effect of an excitatory signal is to increase the probability that the postsynaptic cell fires, and the effect of an inhibitory signal is to decrease that probability (figure 2.19). Some neurons also have modulatory effects on other neurons, principally by releasing peptides or monoamines (see section 4). Another useful classification concerns projections: some cells ramify only within a confined area such as a column, for example stellate cells in cortex; other neurons, such as pyramidal cells, have long-range projections out of an area, where the route goes via the white matter rather than directly through the cortex itself. Research on the properties of neurons shows that they are much more complex processing devices than previously imagined (table 2.1). For example, dendrites of neurons are themselves highly specialized, and some parts can probably act as independent processing units (Shepherd et al. 1985, Koch and Poggio 1987).

Synapses

Chemical synapses are found in nervous systems throughout phylogeny, and they are a basic unit of structure that has been highly conserved during evolution. A synaptic bouton has a surface area of a few square micrometers and forms a highly stereotyped apposition with the postsynaptic membrane, which itself is highly specialized (figure 2.20). Synapses are the primary gateways by which neurons communicate with one another, and they consist of specialized

Table 2.1 Selected biophysical mechanisms, possible neural operations they could implement, and computations they might help perform

Biophysical Mechanism	Neural Operation	Example of Computation
Action potential initiation	Analog OR/AND one-bit analog-to-digital converter	
Repetitive spiking activity	Current-to-frequency transducer	
Action potential conduction	Impulse transmission	Long-distance communication in axons
Conduction failure at axonal branch points	Temporal/spatial filtering of impulses	Opener muscle in crayfish
Chemically mediated synaptic transduction	Nonreciprocal two-port "negative" resistance Sigmoid "threshold"	
Electrically mediated synaptic transduction	Reciprocal one-port resistance	Coupling of rod photoreceptors to enhance detection of signals
Distributed excitatory synapses in dendritic tree	Linear addition	α, β cat retinal ganglion cells Bipolar cells
Interaction between excitatory and (silent) inhibitory conductance inputs	Analog AND-NOT, veto operation	Directional-selective retinal ganglion cells Disparity-selective cortical cells
Excitatory synapse on dendritic spine with calcium channels	Postsynaptic modification in functional connectivity	Short- and long-term information storage
Excitatory and inhibitory synapses on dendritric spine	Local AND-NOT "presynaptic inhibition"	Enabling/disabling retinal input to geniculate X-cells
Quasi-active membranes	Electrical resonant filter analog Differentiation delay	Hair cells in lower vertebrates
Transmitter regulation of voltage-dependent channels (M-current inhibition)	Gain control	Midbrain sites controlling gain of retinogeniculate transmission
Calcium sensitivity of cAMP-dependent phosphorylation of potassium channel protein	Functional connectivity	Adaptation and associative storage of information in *Aplysia*
Long-distance action of neurotransmitter	Modulating and routing transmission of information	

From Koch and Poggio (1987).

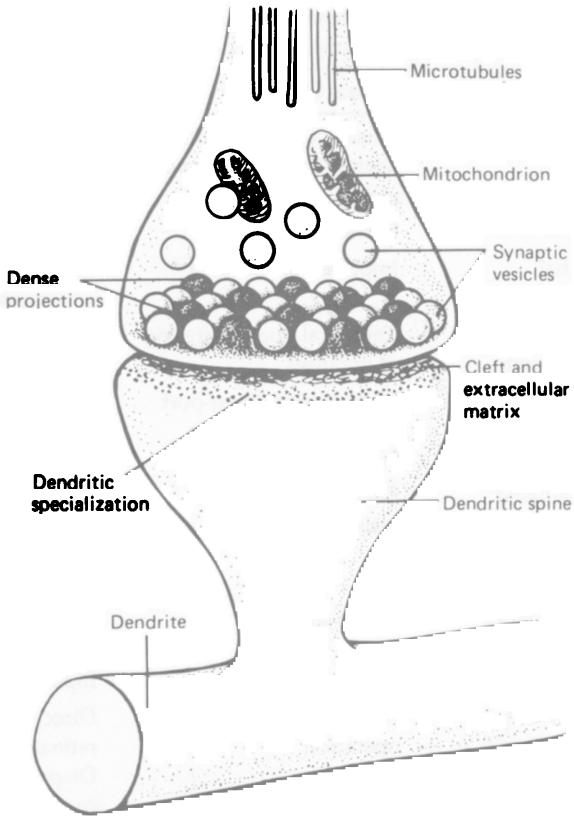

Figure 2.20 Schematic diagram of a synapse on a dendritic spine. Dense projections in the presynaptic membrane are surrounded by vesicles that presumably contain neurotransmitter molecules. This morphology characterizes a type I synapse, which is excitatory. Type II synapses (not shown) have flattened vesicles as viewed in the electron microscope following glutaraldehyde fixation, and they are often inhibitory. (From Gershon et al. 1985.)

presynaptic structures for the release of neurochemicals and postsynaptic structures for receiving and responding to those neurochemicals. Evidence is accumulating that signaling between neurons at synapses can be selectively altered by experience (Alkon 1984). Other, structural components of neurons might also be modified through experience, such as the shape and topology of dendrites as well as the spatial distribution of membrane channels (Purves and Voyvodic 1987).

Our understanding of the nervous system at the subcellular level is changing rapidly, and it is apparent that neurons are dynamic and complex entities whose computational properties cannot be approximated by memoryless response functions, a common idealization. It remains an open scientific question how the integrity of memories that span decades can remain intact if the neural substrate is as fluid as preliminary reports indicate, especially if, as it seems, networks of neurons both process and store information.

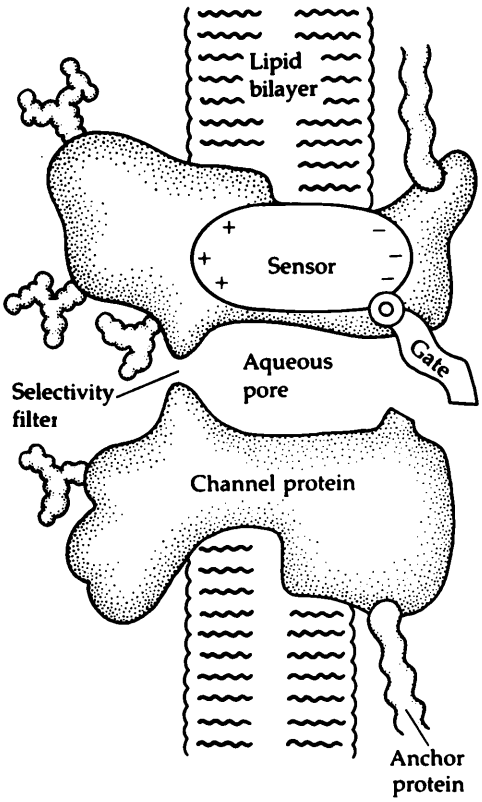

Figure 2.21 Working hypothesis for a voltage-gated channel. The transmembrane protein is shown with a pore that allows sodium ions to flow between the extracellular and intracellular sides of the membrane when the gate is open. (With permission from Hille [1984]. *Ionic Channels of Excitable Membranes*. Sunderland MA: Sinauer Associates.)

Molecules

The integrity of neurons and synapses depends on the properties of membranes and the internal cytoskeleton of the neuron. The membrane serves as a barrier a few nanometers (10^{-9}) thick separating the intracellular and extracellular aqueous compartments. The membrane itself is a two-dimensional fluid medium in which integral membrane proteins and other molecules form associations. Some integral membrane proteins have an important role in maintaining the ionic milieu inside and outside the cell. For example, membrane proteins that serve as ion channels can be voltage sensitive,[9] chemically activated, or both. They may thus permit or prevent the passage of ions across the membrane, which in turn can affect the propagation of a signal down the length of the axon or neurotransmitter release at the presynaptic terminal (figure 2.21). In a sense, the membrane allows the intracellular compartment of a neuron to respond selectively to extracellular signals, and it is this selectivity that endows different neurons with specialized information-processing capabilities. Axon membrane typically contains channels and conductances

that permit it to spike when depolarization reaches a certain threshold. Exactly how dendrite membrane works is much less well understood. Dendrite spiking has been seen in the cerebellum (Llinás and Sugimori 1980), and the conventional wisdom according to which axon membrane is "active" while dendrite membrane is "passive" is undoubtedly a simplification that obscures the subtle, complex, and computationally critical respects in which dendrite membrane is active.

Electrical signaling in neurons is achieved by ionic currents which are regulated by ion channels and ion pumps in the cell membrane. Signaling between neurons is mediated by neurotransmitter receptors in the postsynaptic membrane that respond to particular neurotransmitter molecules by transiently and selectively changing the ionic conductance of the membrane. There are also receptor molecules along the membrane outside of the synaptic site that appear to be functional, but their role is not known (Somogyi et al. 1989). In addition, some receptors can activate one or more second-messenger molecules that can mediate longer-term changes (figure 2.22). Second-messengers in neurons can be activated by more than one receptor. Hence there is a network of interacting chemical systems within a neuron, which can itself be considered a chemical parallel distributed processor.

4 A SHORT LIST OF BRAIN FACTS

A central part of the basic strategy for figuring out how a novel device works is reverse engineering. That is, when a new camera or chip appears on the market, competitors will take it apart to find out how it works. Typically, of course, they already know quite a lot about devices of that general kind, so the problem can be manageable. Although we have to use reverse engineering to study the brain, our starting point is much further back, inasmuch as we know so little about devices of that general kind. From our vantage point, the brain is essentially a bit of alien technology, and hence it is especially difficult to know, among the facts available to us, which are theoretically important and which are theoretically uninteresting. We may actually misunderstand some aspects of brain organization and as a consequence be blocked from having some important insight into mechanisms crucial for cognition. For example, some distinctions made in gross anatomy may turn out to conceal close relationships between distant brain regions, or it may turn out that the functional properties of some synapses in the central nervous system are very different from peripheral synapses in autonomic ganglia and neuromuscular junctions, which have been very well studied.

Since this chapter looks at neuroscience against a background of computational aims, it seems appropriate to raise this question: what are the most basic structural features relevant to neural computation? It goes without saying that many more constraints will be relevant in the context of a specific problem, but we present these 13 as a kind of prolegomenon to problems generally. Short of having formally conducted a proper survey, we conjecture that the following baker's dozen are among those likely to find their way on to a must-know list,

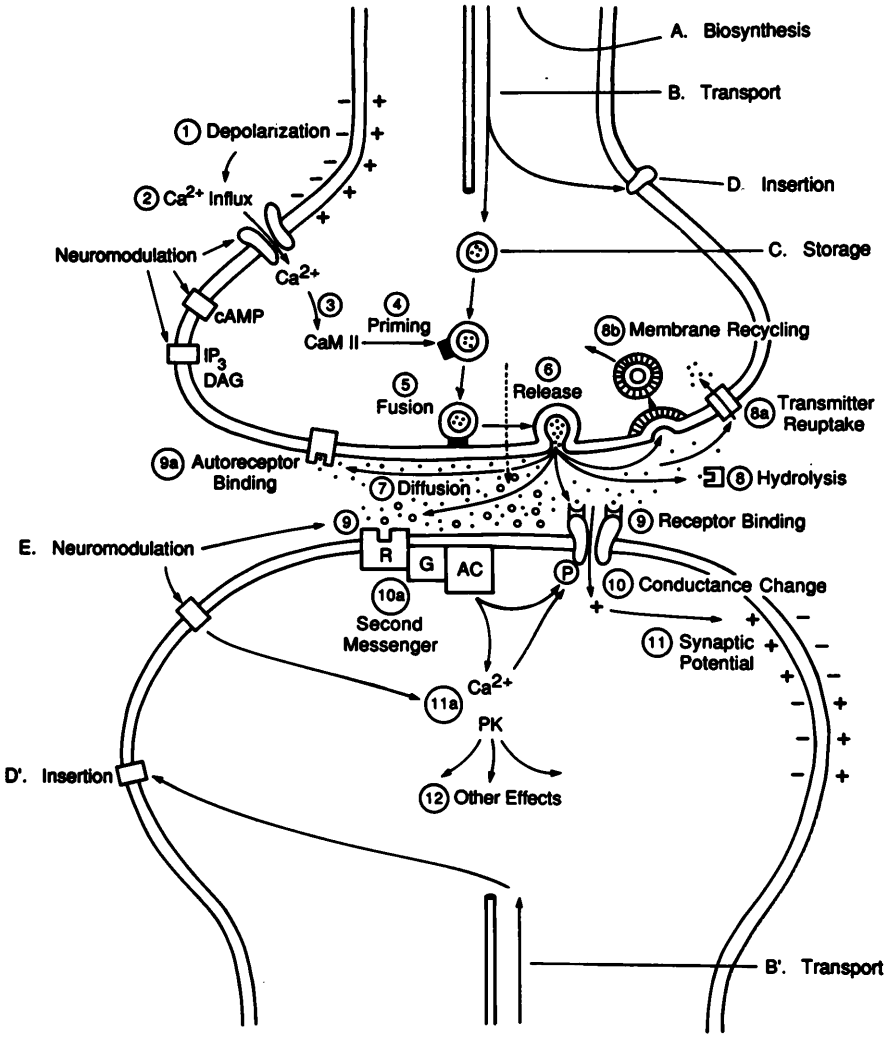

Figure 2.22 Summary of some of the main biochemical mechanisms that have been identified at chemical synapses. A–E, Long-term steps in synthesis, transport, and storage of neurotransmitters and neuromodulators; insertion of membrane channel proteins and receptors, and neuromodulatory effects. 1–12, these summarize the more rapid steps involved in immediate signaling at the synapse. IP_3, inositol triphosphate; CaM II, Ca^{2+}/calmodulin-dependent protein kinase II; DAG, diacylglycerol; PK, protein kinase; R, receptor; G, G protein; AC, adenylate cyclase. (Reprinted with permission from Shepherd 1988.)

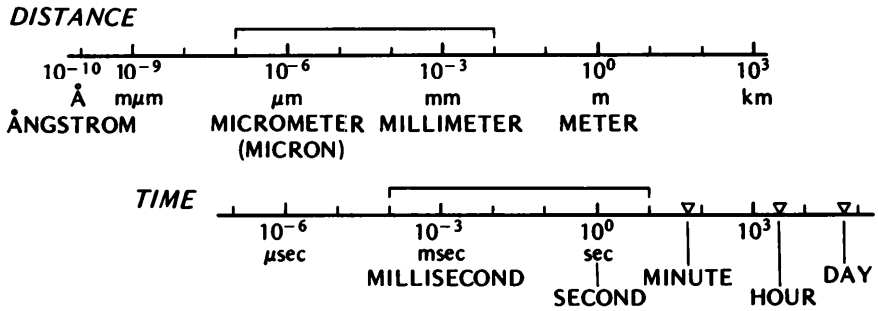

Figure 2.23 Logarithmic scales for spatial and temporal magnitudes. Brackets indicate the scales especially relevant to synaptic processing. (Reprinted with permission from Shepherd 1979.)

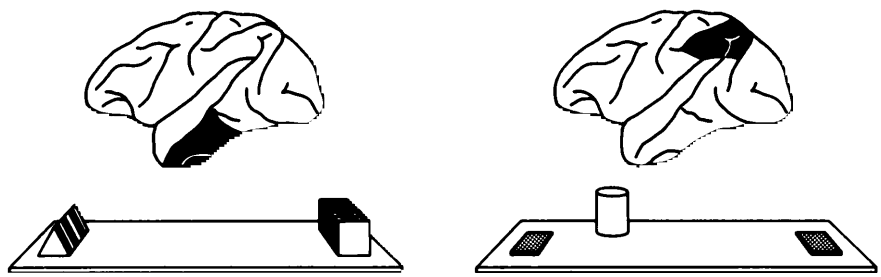

Figure 2.24 Two behavioral tasks that distinguish between the functions of the inferior temporal (IT) and posterior parietal (PP) cortex. (Left) IT lesions, in black, cause a severe impairment in learning to discriminate between two objects based on their features, but the lesions do not affect spatial capacities. (Right) PP lesions cause an impairment to spatial tasks, such as judging which of two identical plaques is closer to a visual landmark (cylinder), but do not affect object discrimination learning. (From Mishkin, Ungerleider and Macko [1983]. Object vision and spatial vision: two cortical pathways. *Trends in Neurosciences* 6: 414–417.)

although we understand very well that opinion can diverge in considerable and surprising ways, and also that a current list will undoubtedly be quickly outdated (for comparable lists, see Crick and Asanuma 1986 and Shepherd 1988). (See figure 2.23 for scales of magnitudes.)

1. *Specialization of Function* There is specialization of function in different regions of nervous systems. This is a ubiquitous and critical feature of nervous system organization, seen in animals from the lowly leech to the human. The specialization enjoyed by regions more distant from the periphery, such as orbitalfrontal cortex of humans, is difficult to determine, though by using a convergence of techniques, including lesions, staining, single-cell recording, evoked potential, and developmental data, the range of likely possibilities can be narrowed (figure 2.24). Specialization so characterized is actually a large-grain feature of an area, based on the statistical distribution of cell response properties and the major input and output pathways. Thus V1, for example, is referred to as a visual area and S1 as a somatosensory area. At a finer grain,

however, the specialization of areas is consistent with the existence of atypical cell types and connectivity. Thus while the preponderance of tested cells in V1 are indeed visually tuned, there exist some cells coding for nonvisual signals, such as eye movement.

2. *Numbers: Neurons and Synapses* The estimated number of neurons in the human nervous system is about 10^{12}; the number of synapses is about 10^{15}. The rat brain has about 10^{10} neurons, and about 10^{13} synapses. In 1 mm^3 of cortical tissue there are about 10^5 neurons and 10^9 synapses. A handy rule of thumb is 1 synapse/μm^3. A single neuron may have thousands or tens of thousands of synapses. Stevens (1989) has calculated that the number of synapses per neuron for a piece of cortex 1 mm thick from a cat or a monkey is 4.12×10^3. The main exception to this is the primary visual cortex of primates, where cells are more densely packed and the number of synapses is about 1.17×10^3 for a piece of cortex 1 mm thick.

3. *Numbers: Connectivity (Who Talks to Whom)* Not everything is connected to everything else. Each cortical neuron is connected to a roughly constant number of other neurons, irrespective of brain size, namely about 3% of the neurons underlying the surrounding square millimeter of cortex (Stevens 1989). Hence, although the absolute number of input lines to a cortical neuron may be quite large, cortical neurons are actually rather sparsely connected relative to the population of neurons in a cell's neighborhood. Most connections are between, not within, cell classes (Sereno 1988). Forward projections to one area are generally matched by recurrent projections back to the area of origin.

4. *Analog Inputs/Discrete Outputs* The input to a neuron is analog (continuous values between 0 and 1), and a neuron's output is discrete (either it spikes or it does not), though some neurons may have analog outputs. Whether a neuron has an output is governed by a threshold rule; that is, whether the cell spikes depends on whether the integration of the inputs exceeds a certain threshold. The profusion of input lines to a single neuron probably represents sensible computational and engineering design for a network of neurons with these properties (Abu-Mostafa 1989a).[10]

5. *Timing: General Considerations* Getting the timing right is an essential feature of nervous systems and, more particularly, of analog computation (Mead 1989). Whether and how dendritic signals traveling soma-wards will interact depends on the time of their arrival at the common node. The magnitude of signals eventually reaching the axon hillock depends on such interactions. In perception, the time scale of the computation must be matched to the time scale of events in the external world, and in motor control it must be matched to the time it takes for the body parts to move (Mead 1989). When outputs of different computational components need to be integrated, the time scales of the various processors contributing values must also match. In short, the system has to operate in real time. Hence nervous systems must be architecturally rigged so that when a process takes time, it takes the right amount of time.

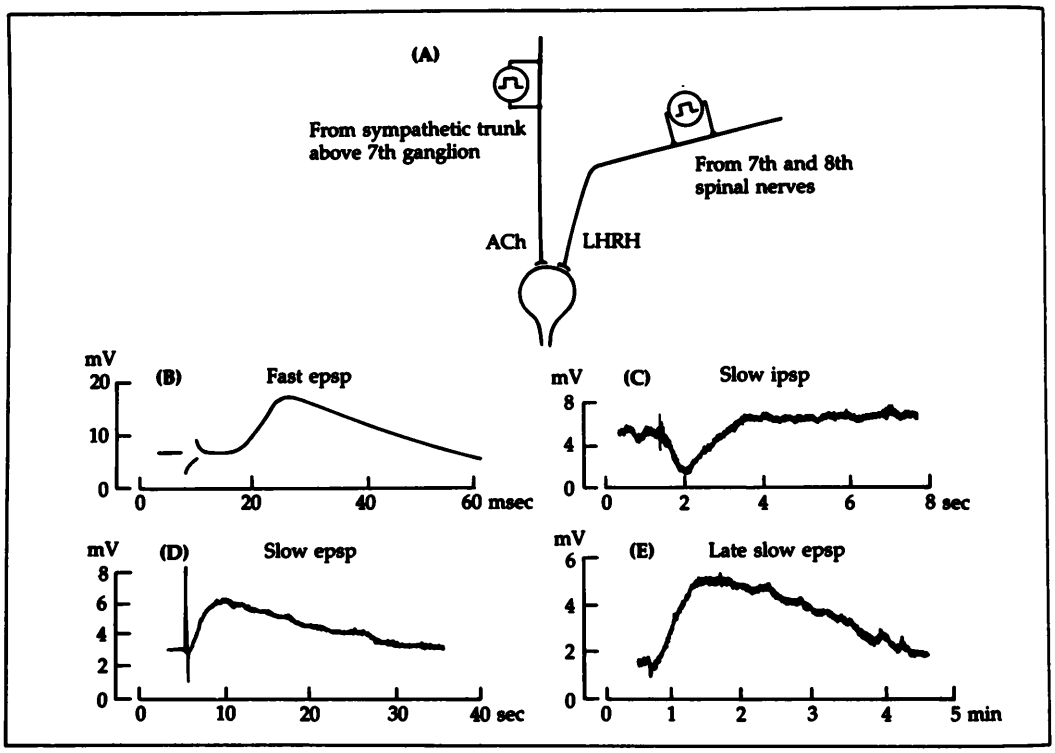

Figure 2.25 Four types of synapses from the sympathetic ganglion of the frog. (A) Innervation of a sympathetic neuron in the ninth ganglion of the paravertebral chain of the bullfrog; the diagram shows the separation of the cholinergic (ACh) and noncholinergic (LHRH) innervation. (B) A single preganglionic stimulus produces a fast EPSP. (C) Repetitive stimulation produces a slow IPSP lasting about 2 sec; the fast EPSP is blocked with a nicotinic blocking agent. (D) Repetitive stimulation also produces a slow EPSP which occurs after the first two responses and lasts about 30 sec. (E) The late slow EPSP, produced by stimulating preganglionic fibers, lasts more than 5 min after repetitive stimulation. (With permission from Kuffler, Nicholls and Martin [1984]. *From Neuron to Brain.* Sunderland MA: Sinauer Associates.)

6. *Timing: Particular Values* An action potential (spike) lasts about 1 msec. Synaptic transmission, including electrotonic conduction in dendrites, takes about 5 msec. Synaptic potentials can last from a millisecond to many minutes (Kuffler 1980) (figure 2.25). Transmission velocity in myelinated axons is about 10–100 meters/sec; in unmyelinated axons it is less than 1 meter/sec. These are general ranges, not precise values.

7. *Cell-to-cell Effects* The effect of an individual synaptic input on a postsynaptic cell is weak, amounting to 1%–5% of the firing threshold. There may be some important exceptions to this trend, such as the strong effects of an individual synapse of a chandelier cell or a basket cell in the cerebral cortex (Martin 1984).

8. *Firing Patterns* Different types of neurons have different firing patterns (figure 2.26). Some neurons in the thalamus have multiple intrinsic firing patterns, and the particular pattern displayed on a given occasion is a function of

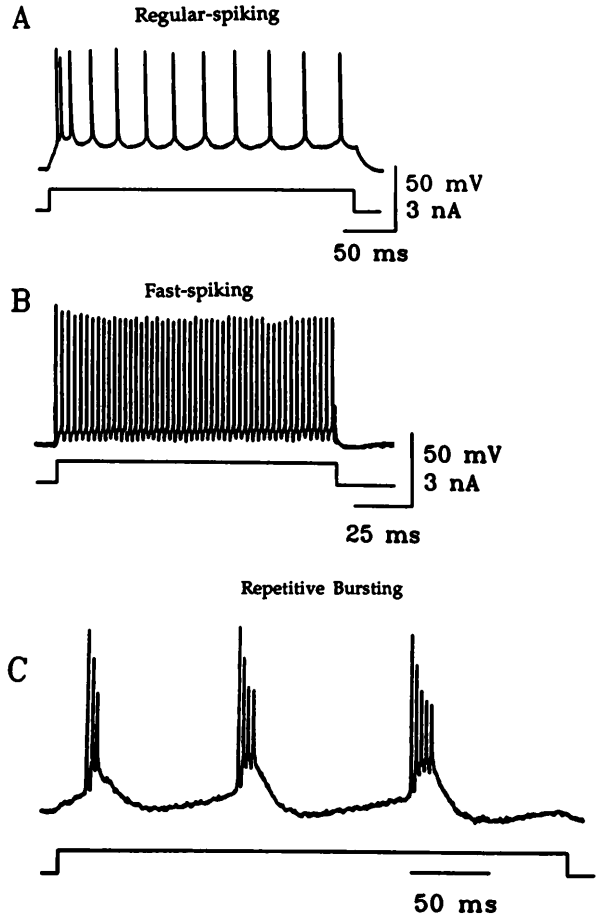

Figure 2.26 Differences in intrinsic firing patterns of cortical neurons. (A) When stimulated with a suprathreshold step of depolarizing current, regular-spiking neurons respond with an initial high-frequency spike output that rapidly declines to much lower sustained frequencies. Intracellular voltages are displayed in the top trace, injected current steps in the bottom trace. (B) Under similar conditions, fast-spiking cells generate high frequencies that are sustained for the duration of the stimulus. (C) Repetitive intrinsic bursting to a prolonged stimulus. Mean interburst frequency was about 9 Hz. (From Connors and Gutnick [1990]. Intrinsic firing patterns of diverse neocortical neurons. *Trends in Neurosciences* 13: 98–99.)

the cell's recent depolarization or hyperpolarization history (Llinás and Jahnsen 1982). The ionic conductances of some cells, for example in the brain stem, endow those cells with oscillatory properties. Such a cell may act as a pacemaker or as a resonator (responding preferentially to certain firing frequencies) (Llinás 1988). Most neurons are spontaneously active, spiking at random intervals in the absence of input. Different neuron types have different characteristic spontaneous rates, ranging from a few spikes per second to about 50 spikes per second.

9. *Receptive Fields: Size and Center-Surround Organization* Under the classical definition, the receptive field is that region of the sensory field from which an adequate sensory stimulus will elicit a response. In the somatosensory system,

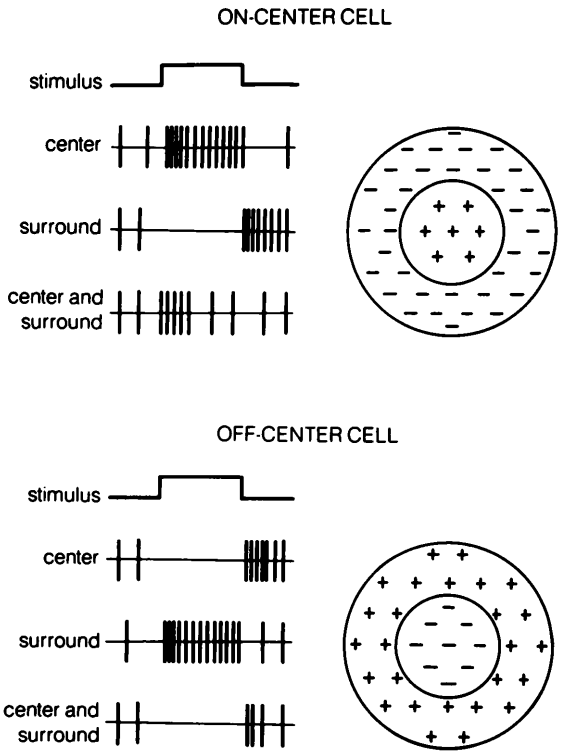

Figure 2.27 Two types of circular center–surround receptive fields in the retina. When the light is shone on the center of the receptive field, the on-center cell responds vigorously, the off-center cell is silent. When the light is shone in the annular surround, the opposite effect is achieved. Under diffuse illumination of both the center and the surround, both cells respond weakly. (With permission from Coren Ward [1989]. *Sensation and Perception*, 3rd ed. Copyright © 1989 Harcourt Brace Jovanovich, Inc.)

the receptive field size varies over the body surface: those for the fingertips are smaller than those for the palm of the hand, and very much smaller than those for the arm. Receptive fields of cells in higher areas of visual cortex tend to be much larger than those in the earlier stages (one sixth of a degree in the foveal region of V1, compared to values ranging from 10 to the whole visual field in inferotemporal cortex). Retinal ganglion cells (cells carrying signals from the retina) have what is called a *center-surround organization* (figures 2.27, 2.28). This organization comes in two variations: (1) a stimulus in the center of the cell's receptive field excites it, but a stimulus in an area surrounding the receptive field inhibits it. This arrangement is known as "on-center/off-surround." (2) The opposite arrangement, namely, a central stimulus inhibits but a surround stimulus excites the cell, is known as "off-center/on-surround." Off-center cells respond maximally to dark spots, while on-center cells respond maximally to light spots. The information carried by the ganglion cells pertains to the comparison between the amount of light falling on the center of the field and the average amount of light falling on the surround, not absolute values of light intensity at the transducer. A center-surround organization is also evident in

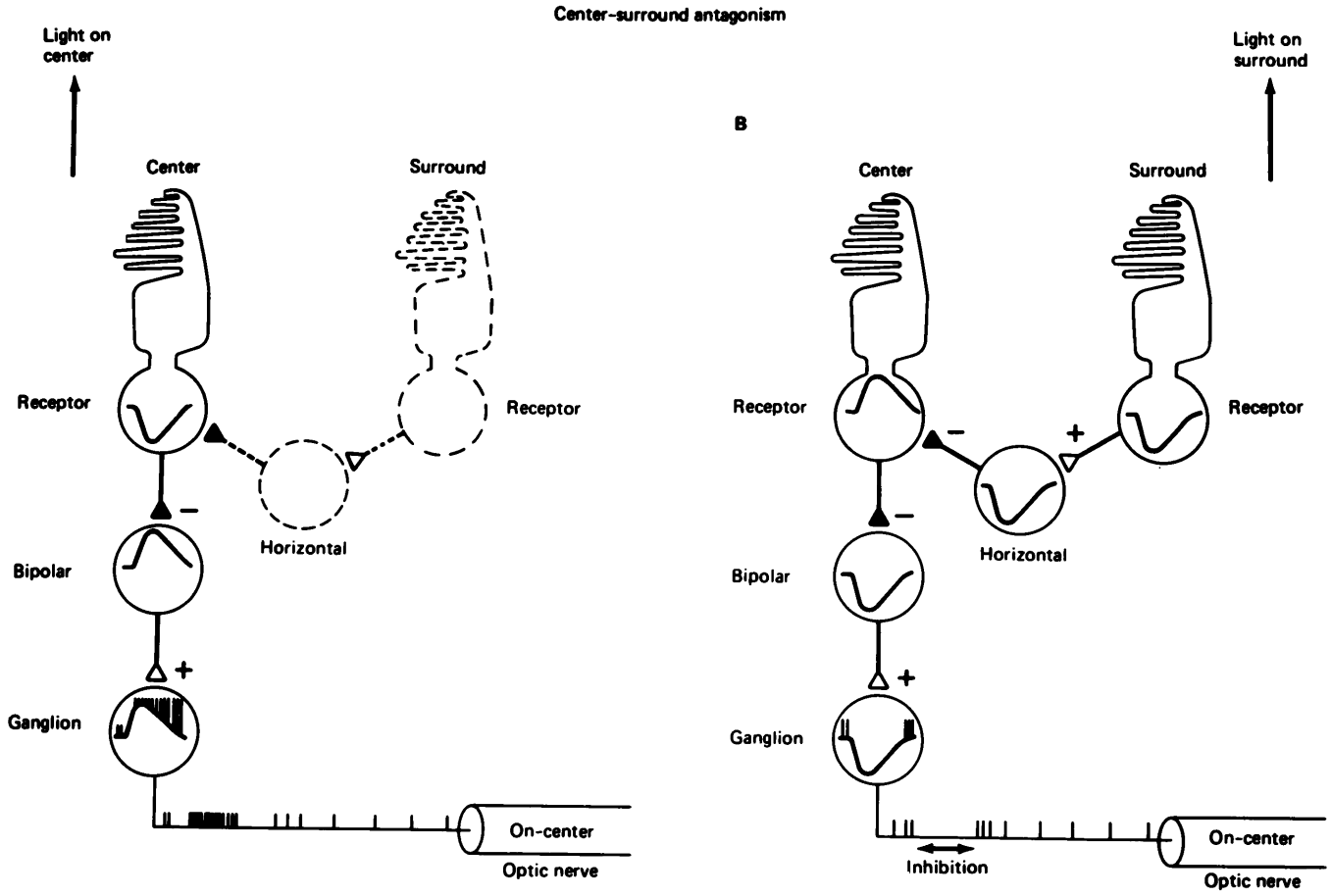

Figure 2.28 In center–surround organization, the response of a ganglion cell to direct light on the center of its receptive field (A) is antagonized by direct light on the surround of its field (B). This antagonistic interaction between neighboring retinal areas is mediated by the inhibitory action of a horizontal cell. (Reprinted with permission from Kandel and Schwartz 1985.)

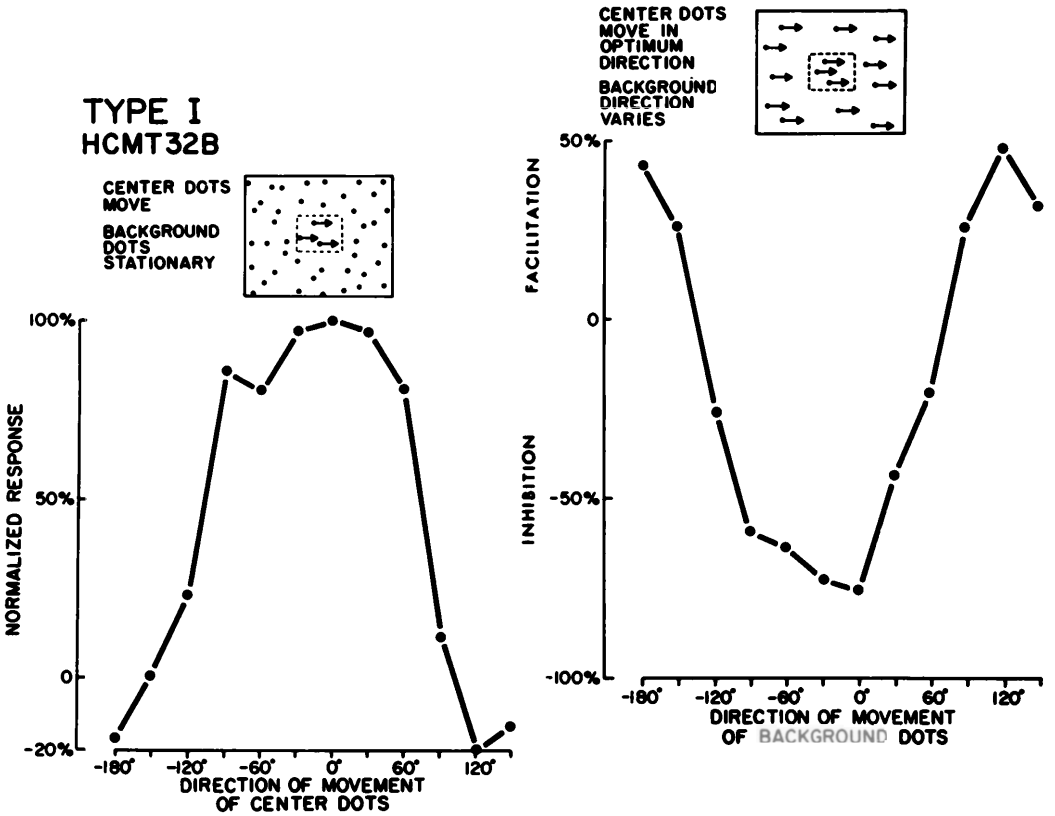

Figure 2.29 Response of a neuron with antagonistic direction-selective surround. (Left) The cell responds vigorously when the dots in the center of the stimulus move (shown above) in the preferred direction but the dots in the surround are stationary. Negative percentages in the graph indicate inhibition relative to the level of spontaneous activity. (Right) The same cell responds very differently to its preferred direction of motion in the center when the dots in the surround also move in the cell's preferred direction. (From Allman et al. 1985.)

the receptive fields of somatosensory neurons in the thalamus and cortex (Mountcastle 1957) (figures 2.27, 2.28).

10. *Receptive Fields: Nonclassical* Events outside the classical receptive field of a cell have been found to modulate selectively the responses of the cell (Nelson and Frost 1978, Allman et al. 1985) (figure 2.29). The effects are selective since they vary as a function of the type of surround stimuli. Nelson and Frost (1985) reported an inhibition as well as a highly specific form of facilitation of the responses of orientation-tuned cells in visual cortex of cats as a nonclassical field effect. Some area 17 cells that were normally responsive to a vertical bar in their receptive fields showed enhanced responses when distant[11] area 17 cells, co-oriented and co-axial to the first, were experimentally stimulated. Zeki (1983) has shown that certain wavelength-dependent neurons in V4 are influenced by the color balance in the surround. The surround effects of cells in the middle temporal (MT) area, where receptive fields are typically 5°–10°, can extend 40°–80° (Allman et al. 1985). Receptive fields are almost certainly more dynamical than previously assumed. For example, repeated stimulation

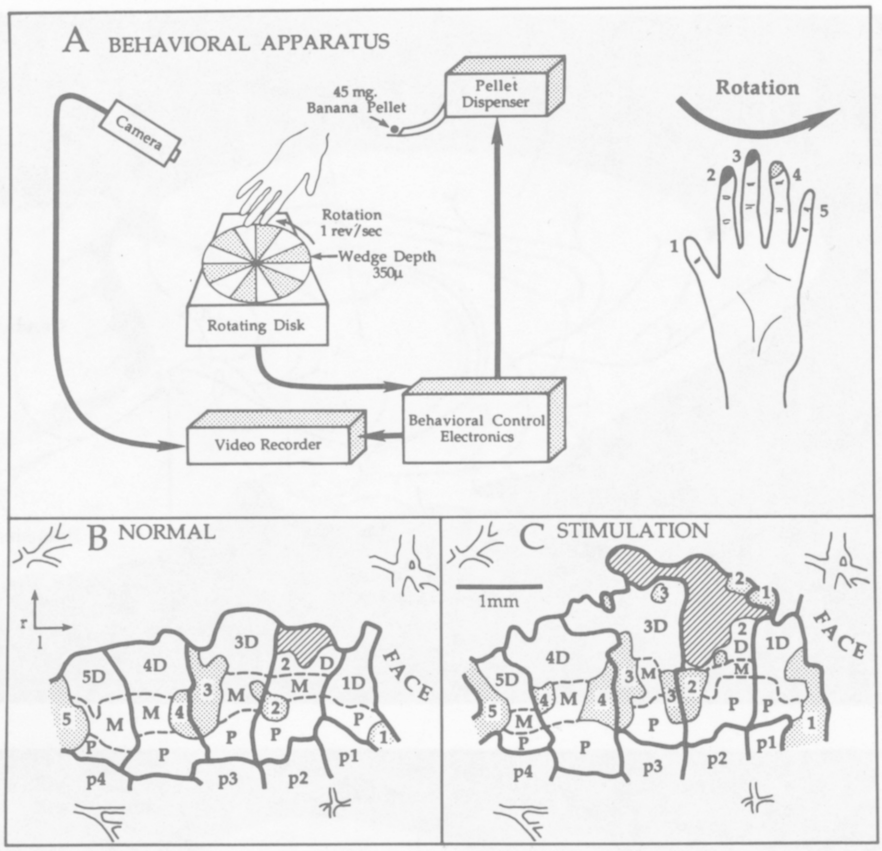

Figure 2.30 Alteration of cortical maps after habitual stimulation. (A) The experimental protocol, showing the fingertips stimulated by the rotating disk. (B) Map in the somatosensory cortex of the left hand of the monkey before the stimulation experiment. Stippled area corresponds to fingertips 2, 3, and 4. (C) Map of the same region after the stimulation experiment. (From Merzenich et al. 1990.)

to the fingertips results in an expansion of the regions of the somatosensory cortex whose neurons have receptive fields in the fingertips (figure 2.30). Recent experiments in in V1 of visual cortex also suggests that receptive fields are labile in that a cell's receptive field may expand when its preferred area on the retina is lesioned (Gibert and Wiesel, in press).

11. *Specific and Nonspecific Systems* In addition to the specific system projecting to the neocortex via the thalamus, such as is seen in the visual, auditory, and somatosensory systems, there are five sources of widely projecting neurons each associated with a specific neurotransmitter, which may play important roles in the sleep–dreaming–waking cycle, in memory, and in awareness and attention. The five are as follows: the locus coeruleus in the brain stem (norepinephrine), the raphe nucleus in the midbrain (serotonin), the substantia nigra in the midbrain (dopamine), the nucleus basalis in the basal forebrain (acetylcholine), and special groups of cells in the mammillary region of the hypothalamus (GABA) (figure 2.31).

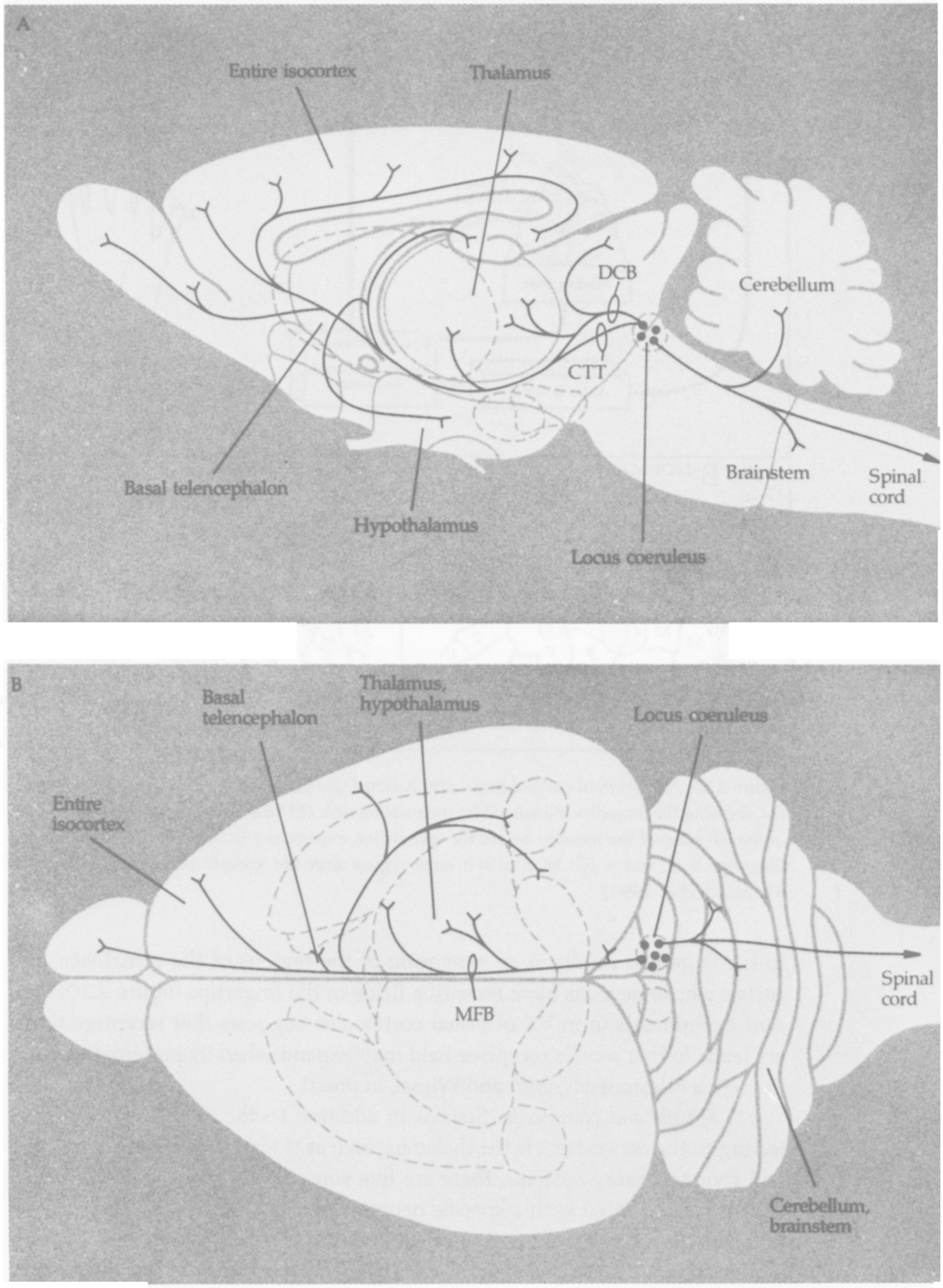

Figure 2.31 Neurons originating in the locus coeruleus project very widely all over the brain, including the cerebellum, brain stem, thalamus, and all over the cerebral cortex. The neurotransmitter they release is norepinephrine. (Reprinted with permission from Angevine and Cotman 1981.)

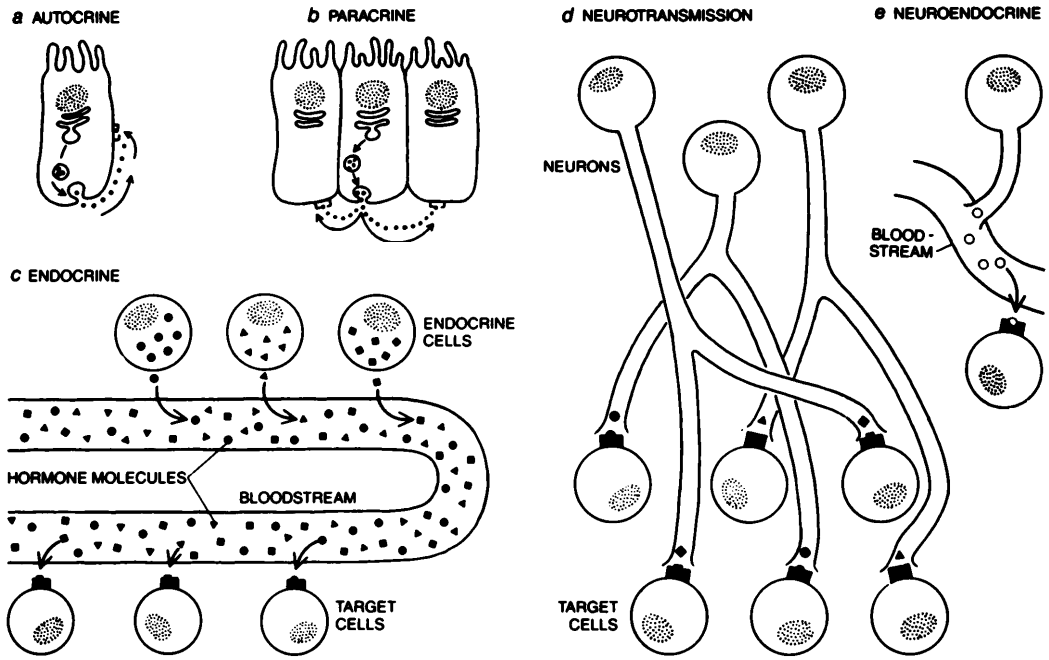

Figure 2.32 Methods of communication of the hormonal and nervous systems. Although autocrine hormones (a) act on the cell that releases them and paracrine hormones (b) act on adjacent cells, most hormones are in the endocrine system and act on cells or organs anywhere in the body. Endocrine glands (c) release hormone molecules into the bloodstream, where they come in contact with receptors on target cells, which recognize the hormones meant to act on those cells and pull them out of the bloodstream. Neurons (d) communicate by releasing neurotransmitters close to target cells. In neuroendocrine action (e) a neuron releases substances that act as hormones directly into the blood. (Reprinted with permission from Snyder 1985.)

12. *Action-at-a-distance* Some neurotransmitters may be released not only at a synaptic site, but may also be dumped into the extracellular space to have an action at a nonsynaptic site some distance from the point of release (Jan et al. 1978) (figure 2.32). Originating in the endocrine system, hormones, such as estradiol, can also reach neurons after traveling through the circulatory system and can alter neural activity.

13. *Parallel Architecture* The brain appears to be highly parallel in that there are many parallel streams of input for a given function. For example, in the monkey two parallel streams from the retina, starting with different types of ganglion cells, project to two distinct sets of layers of the lateral geniculate nucleus—the parvocellular and magnocellular layers, respectively—which in turn project to distinct sublaminae in layer 4 of cortical area V1 of the visual cortex (Hubel and Livingstone 1987, Livingstone and Hubel 1987). The streams are not cleanly segregated, however, and there are probably interactions at every stage (Schiller et al. 1990, Logothetis et al. 1990).

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Selected Journals and Reviews

Current Opinion in Neurobiology. (Current Biology) Review papers on subfields in neuroscience.

Journal of Cognitive Neuroscience. Quarterly journal (MIT Press). Articles on systems neuroscience with emphasis on cognitive processing.

Seminars in Neuroscience. Quarterly journal (Saunders). Each issue is on a special topic in neuroscience.

Trends in Neurosciences. Monthly journal (Elsevier). Contains brief but very useful reviews of special topics and is a good source of up-to-date references to the literature.

Concepts in Neuroscience. (World Scientific). Contains discussions of conceptual issues.

Annual Review of Neuroscience. Palo Alto, CA: (Annual Reviews). Comprehensive reviews of the literature.