CHAPTER 4

NEURONS

The basic anatomical unit in the nervous system is a specialized cell called the neuron. An artist's view of a typical neuron is shown in Figure 4.1. Many extensions of the single cell are long and filamentary; these structures are called processes. Every neuron plays several functional roles in a neural system:

1. Metabolic machinery within the cell provides a power source for information-processing functions. In addition, the cell enforces a certain unity for biochemical mechanisms throughout its extent.

2. A tree of processes called dendrites is covered with special structures called synapses, where junctions are formed with other neurons. These synaptic contacts are the primary information-processing elements in neural systems.

3. Processes act as wires, conveying information over a finite spatial extent. The resistance of fine dendrites allows the potential at their tips to be compared with only partial coupling to other computations in the tree.

4. Temporal integration of signals occurs over the short term through charge storage on the capacitance of the cell membrane, and over the longer term by means of internal second messengers and complex biochemical mechanisms.
are equipped with an active amplification mechanism that restores the nerve pulse as it propagates. In lower animals, such as the squid, the restoration is done continuously along the length of the axon. In higher animals, many axons are wrapped with a special insulating material called myelin, which reduces the capacitance between the cytoplasm and the extracellular fluid, and thereby increases the velocity at which signals propagate. The sheaths of these myelinated axons have gaps called nodes of Ranvier few millimeters. These nodes act as repasser sites, where the signal is periodically restored. A single myelinated fiber can carry signals over a distance of 1 meter or more.

Even the most casual exploration of nervous tissue with an electrode reveals a host of signals encoded as trains of action potentials. For this reason, the mechanism of initiation of the nerve pulse, and its restoration as it propagates down the axon, became the center of early physiological investigations. The first quantitative work was carried out by Hodgkin, Huxley, and Katz (Hodgkin et al., 1952a, Hodgkin et al., 1952b, Hodgkin et al., 1952c, Hodgkin et al., 1952d). On the giant axon of the squid an unmyelinated structure nearly 1 millimeter in diameter. This classic investigation revealed the following fascinating story:

1. The cytoplasm in the cell's interior is normally polarized—charged at a potential of approximately —80 millivolts with respect to the extracellular fluid

2. This potential difference is supported across a cell membrane so thin that it can be resolved only by an electron microscope

3. If sufficient current is injected into the cytoplasm in the direction to depolarize the membrane to a threshold potential of approximately —40 millivolts, a nerve pulse is initiated

4. The pulse travels in both directions from the initiation point, and its shape rapidly becomes independent of the mechanism through which the initiation took place

What are the mechanisms by which the axon initiates and propagates the action potential? That question motivated a sustained investigation by many workers over more than 5 decades. In any great scientific detective story, the resolution of a mystery at one level sharpens the focus of the researchers, and creates pressing questions at the next level. In the following sections, we will trace the story of the axon clue by clue. In the process, we will see how the nerve membrane is constructed, and how the electrical mechanisms embedded in that membrane is responsible for the active transmembrane of nerve impulses. Only after we understand the axon will we be in a position to investigate how information processing is done in the dendritic tree of the neuron. That story is still unfolding.

**NERVE MEMBRANE**

All electrical activity in a neuron takes place in the thin membrane that electrically separates the neuron's interior from the extracellular fluid. The nerve membrane is formed from phospholipid molecules arranged in a bilayer about
The permeability of water is about 80 times that of free space, whereas that of the hydrocarbon phase in the interior of the membrane is only about two times that of free space. The energy of a charged ion in either phase can be calculated by integrating the energy required to assemble the charge $q$ in this position from a large number of infinitesimal charges at infinity. The potential for a given accumulated charge can be calculated by integration of Equation 2.1 (p. 13) with respect to $r$, from infinity to the ionic radius $r_i$. The result of this integration is

$$V = \frac{q}{r}$$

The potential computed in this way is also the energy per unit charge required to add an infinitesimal charge dq to the total charge. The total energy $W$ is given by

$$W = \frac{1}{4\pi\varepsilon_0} \int_0^b \frac{dq}{r} = \frac{1}{2} \int_0^b \frac{dq}{r}$$

The energy of an ion such as sodium, which has a 4 Angstrom radius in...
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water, is approximately 0.1 electron volts. In the interior of the bilayer, the energy is approximately 2.4 electron volts, which is approximately 100 kT. The energy barrier that ions must surmount is the energy barrier that ions must cross to pass from one side of the membrane to the other. The energy barrier is determined by the difference in chemical potential between the two sides of the membrane.

ELECTRICAL OPERATION

The energy barrier formed by the nerve membrane is so high that, at room temperature, only very few ions are able to surmount it. For this reason, it is possible to treat the membrane as a perfect insulator. Any current flow through the membrane will have to be mediated by some agent other than the bare ions in the extracellular fluid. The presence of these agents that living systems have in place to allow energy transfer is required for information processing. What kind of agents operate in the nerve membrane, and what operations do they perform?

Power Supply

Before there is gain, there must be a power supply. The most basic charge-transfer agents in all nerve membranes are the metabolically driven pumps that actively extrude sodium ions from the cytoplasm and consignantly import potassium ions from the extracellular fluid. As a result of this pumping process, potassium ions in the cytoplasm are enriched in potassium and depleted of sodium, whereas the extracellular fluid is true of the reverse, as shown in Table 4.1 (Adapted from Katz, 1966.)

A concentration gradient of any charged particles can be used to power an electrochemical reactor. Suppose, for the moment, that the membrane is permeable to only one type of ion—potassium, for example. Due to the gradient in density, potassium ions will diffuse out of the cell, causing an extracellular negative charge to accumulate outside the cell. This negative charge will accumulate on the capacitor of the cell membrane, causing a negative potential in the cytoplasm relative to the extracellular fluid. This situation is an exact analog to the one that created the exponential density gradient in the atmosphere in Chapter 2. The diffusion of ions outward will be exactly counterbalanced by the drift inward when the voltage across the membrane reaches the value $V_c$, such that the relation of Equation 2.15 (p. 25) is satisfied:

$$ V_c = \frac{kT}{N_v} \ln \left( \frac{N_v}{N_s} \right) $$

(4.2)

Here $N_v$ is the ion density in the extracellular fluid, and $N_s$ is the density in the cytoplasm. All voltages are referred to the extracellular fluid. If we artificially raise the potential inside the cell above (more positive than) $V_c$, we will cause a positive current to flow outward. If we reduce the potential inside the cell below (more negative than) $V_c$, we will cause a positive current to flow inward. For this reason, $V_c$ is called the reversal potential for the ion at the ionic concentration ratio given in Equation 4.2. The reversal potentials for the three ion species also are given in Table 4.1. In operational terms, we can think of the sodium reversal potential as the positive power-supply rail for the nerve, and the potassium reversal potential as the negative rail. We should note that the concentrations shown in Table 4.1 are for the giant axon of the squid; they vary considerably among species, and even among cell types in a given organism. There is recent evidence that different regions of the same neuron may have different ion concentrations to achieve different synaptic behavior at different fast electrically related points.

Equivalent Circuit

A schematic diagram that summarizes the contribution of the three ions:

![Equivalent Circuit](image)

**FIGURE 4.3** Equivalent circuit of a patch of nerve membrane. The buffers represent the reversal potentials for particular ions; the conductances represent the membrane permeability for the same ion. The membrane capacitance is shown as a lumped capacitor.

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TABLE 4.1 Typical concentrations of ions inside neural processes and in the extracellular fluid (Source: Adapted from Katz, 1966.)

<table>
<thead>
<tr>
<th>Ion</th>
<th>Inside (mM)</th>
<th>Outside (mM)</th>
<th>Reversal potential (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺</td>
<td>140</td>
<td>15</td>
<td>-92</td>
</tr>
<tr>
<td>K⁺</td>
<td>50</td>
<td>490</td>
<td>5</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>40</td>
<td>540</td>
<td>-40</td>
</tr>
</tbody>
</table>

* Na⁺: sodium; K⁺: potassium; Cl⁻: chloride.
gradients to the membrane current is shown in Figure 4.3. From it, we can visualize the operation of the membrane over a wide range of conditions. In this diagram, the Vm are the reversal potentials of the ions, and the Gs are the conductances of the membrane for the flow of those ions. Using Figure 4.3, we can compute the membrane current I for any given cytoplasmic potential V, and for any values of ionic conductances:

\[ I = (V_K - V)G_K + (V_M - V)G_M + (V_Na - V)G_{Na} \]  

(4.3)

Any set current will charge or discharge the capacitance of the membrane until the current is reduced to zero. Hodgkin et al. (Hodgkin et al., 1962b) found that, under normal conditions, the chloride current can be neglected. Making this assumption, we can solve Equation 4.3 for the voltage Vm at which the current is zero:

\[ V_m = \frac{V_K G_K + V_M G_M}{G_K + G_M} \]

V_m is called the resting potential of the cytoplasm, because it is the potential at which the cell will come to rest if left electrically uncontrolled. In a typical neuron, G_K is approximately 1000 times G_M. Using that value, and the concentrations given in Table 4.1, V_m is about -80 millivolts. The resting potential can vary considerably from one set of experimental conditions to another.

We have come to a solution of the first riddle in the axon story: A neuron at rest is polarized to a negative potential because its membrane is selectively permeable to potassium. A nerve pulse is a transient excitation of the cytoplasmic potential in a positive direction; it is an example of an excitatory signal because it depolarizes the membrane. If the membrane is charged more negatively than its resting voltage, it is said to be hyperpolarized, in which case the signal is inhibitory.

We achieve electrical activity in a patch of nerve membrane by making one or more of the ionic conductances dependent on some control quantity. That quantity can be the voltage (as in the axon), the concentration of a chemical substance (as in chemical synapses), the intensity of light (as in photoreceptors), or the degree of mechanical deformation (as in the hair cells in the ear). We will first see how these conductances are responsible for the generation and propagation of the action potential in an axon. In later sections, we will consider other ways that the potential inside the neuron is manipulated by the nervous system to accomplish information-processing tasks.

THE ACTION POTENTIAL

We have seen that the membrane potential can be manipulated by any agent that selectively increases the permeability of the membrane to one ionic species. How can agents of this kind be employed to initiate and propagate an action potential?

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FIGURE 4.4 Response of the axon to stimulation by 2-millisecond current pulses of increasing magnitude. When the pulse drives the potential of the cytoplasm higher than -40 millivolts relative to the extracellular fluid, an action potential is generated. Once this action potential is triggered, it acquires a constant shape, independent of the circumstances under which it was generated. Marginal cases result in either a delayed action potential or a delayed to long transient, as shown by the rightmost two curves. [Source: Adapted from Katz, 1968]

Initiation of the Action Potential

If we inject small pulses of current into the cytoplasm, the potential will respond as shown in Figure 4.4. For current levels that depolarize the membrane less than approximately 20 millivolts from its resting state, the potential shows a somewhat sluggish response that saturates after a few milliseconds. This type of response is characteristic of any circuit consisting of a capacitance in parallel with a conductance, as we will discuss in Chapter 8. In the case of the axon, the capacitance is that of the membrane, and the conductance is due to the potassium permeability. At higher current levels, we observe an exponential increase in the cell potential, culminating in the explosive generation of an action potential. If we terminate the current pulse before the potential has reached approximately -40 millivolts, the membrane recovers, and no pulse is generated. Once the potential is more positive than approximately -40 millivolts, however, a pulse is generated even if the driving current is terminated. That potential is therefore a threshold, beyond which a self-reinforcing reaction is underway, and no recovery is possible.

All the information we have presented so far was known by 1950. The key question was, what mechanism was responsible for the self-reinforcing reaction? That question was unraveled by the detective work for which Hodgkin and Huxley received the Nobel Prize in 1963. The giant axon of the squid is large enough
In response to a depolarization of the membrane, there is a transient increase in the sodium conductance, followed by a delayed but prolonged increase in the potassium conductance. The currents through these conductances, setting on the capacitance of the membrane, create the action potential. Although this picture explains the qualitative shape of the action potential once the pulse is triggered, it tells us nothing about the mechanism that leads to the dashed, and to the all-or-nothing response. To understand that behavior, we must know how the conductances depend on the membrane potential.

**Voltage Dependence of the Conductances**

By carrying out similar experiments at several depolarizing potentials, Hodgkin and Huxley gathered data on the time course of the two currents as a function of the membrane potential. From these data, they reconstructed the time dependence of the sodium and potassium conductances for different membrane potentials. Plots of the peak sodium conductance and the sustained potassium conductance as functions of the membrane potential are sketched in Figure 4.6. At current levels, both conductances are exponential functions of the membrane potential, increasing by a factor of e for every approximately 4-millivolt increase in voltage. At higher current levels, both curves saturate—albeit more rapidly in the dendritic of the transient current on gate voltage shown in Figure 3.7 (p. 38). The quantitative difference between the transient current and the nerve current is that the latter has an exponential characteristic that is six times wider.

**Figure 4.5** Schematic of the arrangement used by Hodgkin, Huxley, and Katz to measure the current through a membrane of a squid axon under conditions where the membrane potential was controlled externally. The sensory electrode assumes the potential of the cytoplasm. The amplifier generates a current proportional to the potential of the cytoplasm. This current is the difference between the actual potential at the outside of the axon and the measured potential. This current is in the direction to move the actual potential toward the assisted value. The current is sensed by an oscilloscope, shown as a meter on the diagram; the extracellular fluid is in ground for the entire arrangement. (Source: Hodgkin et al., 1952a.)

The waveforms shown are a simplification of records taken, using this apparatus, for a step increase in membrane potential. The initial transient is the current required to charge the membrane capacitance. Curve A is the total current as a function of time. Curve B is the potassium current alone. The difference, A - B, is thus attributed to the sodium current, which rises to a maximum and then decays.

When a voltage step from approximately -60 millivolts to near 0 millivolts was applied to the axon, the current waveform labeled A in Figure 4.5 was observed. A transient inward current was followed by a sustained outward current. From Figure 4.3, we can see that there is only one source of inward-directed current—the sodium gradient. To check this conjecture, Hodgkin and Huxley replaced most of the sodium ions in the extracellular fluid with choline—large organic ions that cannot pass through the membrane. In this way, the researchers could approximately equalize the sodium concentration on the two sides of the membrane, thereby reducing the sodium reversal potential to zero and eliminating the sodium current at this voltage. Hodgkin and Huxley attributed the resulting current waveform (labeled B in Figure 4.5) to potassium. The difference between the two waveforms had to be the sodium current under normal conditions, as shown in the bottom trace in Figure 4.5.

**Figure 4.6** Exponential current-voltage characteristic of voltage-dependent channels. At high voltages, the fraction of channels that are open approaches unity, causing a saturation of the current. (Source: Hodgkin et al., 1952a, p. 464.)
time steeper than that of the former! It is this exponentially increasing current that gives the axon membrane the gain required to produce the self-reinforcing reaction leading to the all-or-nothing response.

Although Hodgkin and Huxley did not address the mechanism by which this remarkable exponential dependence comes about, their findings did allow them to reconstruct the initiation and propagation of the action potential. The summary in their 1952 paper is still the best short description of the phenomenon extent:

When the membrane potential is suddenly reduced (depolarisation), the initial pulse of current through the capacity of the membrane is followed by large currents carried by ions (chiefly sodium and potassium), moving down their own electrochemical gradients. The current carried by sodium ions rises very fast to a peak and then decays to a low value, that carried by potassium ions rises much more slowly along an S-shaped curve, reaching a plateau which is maintained with little change until the membrane potential is restored to its resting value. These two components of the membrane current are enough to account qualitatively for the propagation of an action potential, the sequence of events at each point on the nerve fibre being as follows: (1) Current from a neighboring active region depolarizes the membrane by spread along the cable structure of the fibre (local circuits). (2) As a result of this depolarization, sodium current is allowed to flow. Since the external sodium concentration is several times greater than the internal, this current is directed inwards and depolarizes the membrane still further, until the membrane potential reverses its sign and approaches the value at which sodium ions are in equilibrium. (3) As a delayed result of the depolarization, the potassium current increases and the ability of the membrane to pass sodium current decreases. Since the internal potassium concentration is greater than the external, the potassium e rents is directed outwards. When it exceeds the sodium current, it repolarizes the membrane, raising the membrane potential to the neighbourhood of the resting potential, at which potassium ions inside and sodium ions outside are nearly to equilibrium. (Hodgkin et al., 1952a, p. 470)

**IONIC CHANNELS**

The question of electrical activity in the axon has been sharpened still further what is the mechanism by which the membrane conductance achieves its remarkable exponential dependence? To find the answer, we need to take a close look at the sodium current.

**Channel Conductance**

A closer look at the sodium current, finally captured in 1986 by Keller et al. (1986) and his coworkers, is shown in Figure 4.7. The ion-specific conductance changes in discrete steps, the height of each step is approximately linear in the membrane potential relative to the reversal potential of the ion. At low currents, the number of steps and the width of each step are both exponential functions of the membrane potential. At any given voltage, the steps are all the same height. This remarkable finding suggests that each step is the result of an allosteric action on the part of a single molecular entity. The molecular entities responsible for selective permeability of nerve membranes to specific ions are aggregates called channels. The channels responsible for propagating the nerve pulse in an axon are voltage-controlled.

Because the detailed structure has not been worked out for either the sodium or the potassium channels, we will exercise a bit of artistic license to visualize how one of these channel's might operate. The result of this creative endeavor is shown in Figure 4.8.

Imagine a molecule about 50 angstroms long, with two positive charges on one end of a long hydrocarbon backbone and two negative charges on the other. The backbone is sprinkled with occasional polar groups along its length. We suppose that, in their normal stable configuration (shown in the highly schematized

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**FIGURE 4.7** Current through nerve membrane as a function of time, for several membrane voltages. Several steps are due to formation of sodium channels, downward steps are due to channel disappearance. The height of a single step is the current in a single channel, which increases approximately linearly with applied voltage, measured with respect to the sodium resting potential.

Several charges are pulled through the membrane when a channel is formed, hence, the average number of channels penetrating the membrane decreases exponentially with applied voltage. (Source: Adapted from Keller et al., 1986)
resides in Figure 4.8a), triads of these molecules are lying on one surface of the membrane in the form of a Y-structure. The positive end of one triad and the negative end of another are neighboring. The hydrophobic backbone of all these are buried in the membrane and are away from the water. A single molecule would be capable of penetrating the membrane, placing the positively charged head-group on the opposite side of the membrane. The negatively charged tail-group.

The energy of such an isolated molecule in this new configuration would be much higher than that of the molecule in the original state, because the polar groups in the hydrophobic backbone would be directly confronted with the low-permittivity membrane. The triad of molecules could penetrate the membrane if the energy barrier were sufficiently lowered. The energy that the others must pay to get through the membrane. The symmetry would allow each molecule to turn its backbone to the membrane’s hydrophobic interior and share polar groups with the other ones in the triangular space between them. This configuration of our hypothetical triad (shown in Figure 4.8b) would have six positive charges on one side of the membrane, and six negative charges on the other. Transition from the outside configuration to the penetrating configuration would carry six charges from one side of the membrane to the other.

If it were indeed possible to construct a triad capable of this type of behavior, many of such triads would be formed in the long course of evolution. Some, in other words, would have a little space running down the center through which some electronegative ion might pass, in contact with a polar group from one molecule or another. In other words, the penetrating configuration of the triad might function as a channel for ions to flow through the membrane. If the ion were too small, its energy in the center of the membrane would be too high, as per Equation 4.1. If the ion were too large, it could not fit through the space between polar groups. But an ion of just the right size might squeeze through, nicely shielded from the hostile hydration of the polar groups of the molecules in the triad. In this way, a particular molecule could form channels with a high degree of specificity for one ion.

The foregoing dissection is highly idealized, and in detail it is certainly not correct for any particular channel. It is, however, consistent in broad outline with the known properties of voltage-dependent channels. A detailed discussion of the known properties of channels can be found in Hille [Hille, 1984].
a number of gating charges is involved in the reaction that opens the channel. For Figure 4.6, taken from the giant axon of the squid, there are approximately six gating charges involved. Recent work on the node of Ranvier of the frog suggests that three molecules form a channel in that system [DuBois et al., 1983]. The voltage dependence of Figure 4.7 gives approximately four gating charges. It thus seems that vertebrates employ approximately twice as many channels per axon as the squid, each carrying two charges through the membrane. If the charges in the reaction do not go all the way through the membrane, the energy they contribute is only a fraction of eV, and hence measurable quantities often are observed.

The exponential dependence of conductance on membrane potential is a result of the behavior of the population of channels, rather than of the conduction property of any given channel. As can be seen from the current in Figure 4.7, a discrete increase in current as each channel opens, and an equal decrease as each channel closes. The size of an individual step is roughly linear in the voltage between the membrane voltage and the reversal potential for the selected ion, indicating that an individual channel is ohmic (current proportional to voltage). The rate at which channels open increases, and at which they close decreases, with voltage. Both dependencies are exponential, and can be seen clearly in Figure 4.7, where the number of channels open at any time is a result of the balance of these two processes. The exponential current-voltage relation in the nerve is a result of the same physical laws responsible for the exponential transistor characteristic. There is an energy barrier between a state in which current can flow and one in which current cannot flow. The height of that barrier is dependent on a control voltage. The Boltzmann distribution determines the fraction of the total population that is in the conducting state. In the transistor, the electrons in the channel form the population in question, and these same electrons carry the current. In the nerve membrane, the channels form the population in question, and ions in the channels carry the current. In both cases, the number of individual changes in transistors are exponential in the control voltage, and the transport of these changes results in a current that varies exponentially with the control voltage.

COMPUTATION

We have traced the ideas elucidated in one of the great endeavors in intellectual history; in the process, we have learned a great deal about the electrical machinery in the neuron. At one time, people might have supposed that understanding the action potential would be the key that would unlock a full understanding of neural information processing in the brain. It is now clear that, although we have a good understanding of how the nervous system transmits information over large distances, this knowledge does not shed much light on how the information is computed. We have yet to test a single unifying principle in neural computation that shines with the same clarity as the axon story does; that work is ahead of us. The balance of this book describes one approach (of many) to a deeper understanding of the basic principles underlying neural computation. This quest will require the work of specialists in many fields over many years.

A few comments may serve to render our task a bit less daunting. Computation in neural systems uses the same kind of machinery that we have already encountered in the axon story. Once we can control the ionic conductances, we can manipulate the resting potential of the membrane. An increase in sodium conductance depolarizes the membrane, and an action potential for initiation of a nerve pulse. An increase in potassium conductance can hyperpolarize the membrane, and hence acts as an inhibitory influence.

If the chloride reversal potential is near the resting potential, as is often the case, an increase in chloride conductance will not have much effect on the potential of the membrane, but can decrease the effect of either sodium or potassium conductance by requiring more current for a given excursion in potential. This reduction in the sensitivity of the membrane by increasing its conductance to the resting potential is called shunting inhibition. These and other methods of manipulating the membrane potential operate in the richly branched tree of dendrites to produce the complex interaction of electrical and chemical signals that is neural computation. Interactions are the dendritic tress can all work in a continuous analog fashion, as indicated by Equation 4.3. They neither require nerve pulses for their operation, nor necessarily result in the generation of a nerve pulse. In fact, the vast majority of computations in the nervous system is done with slowly varying analog potentials in the dendritic trees of neurons. These signals come about through the actions of synaptic contacts with other neurons. The result of the computation is not always discrete, but may instead be converted into an action potential to be transmitted to the far reaches of the brain.

The synapses provide an entirely new class of function in dendritic computations. We can say that the synapses is to the nerve membrane as the voltage-controlled channel is to communication. The story of the synapse is still being worked out, and the following section gives only the briefest account of this fascinating and rapidly evolving field.

SYNAPSES

We have seen how the potential across a nerve membrane can cause an exponential change in current through the same membrane. This is appropriate for the propagation of an action potential, but is not sufficient for general compu-
tation. What we need is the ability to control the conductance through a second membrane. The ability to control the current into or out of one electrical node by the potential on another node is the key ingredient that makes all information processing possible. This capability results in a natural direction in the flow of information; in neural systems, it is provided by synapses. These specialized structures are the central information-processing devices in neural systems.

![Figure 4.9](image)

**Figure 4.9** Simplified sketch of a synapse. Depolarization of the presynaptic membrane results in neurotransmitter release. Neurotransmitter diffuses across the synaptic cleft, resulting in the opening of receptor channels in the postsynaptic membrane. Postsynaptic current flows from the cytoplasm to the extracellular fluid.

![Figure 4.10](image)

**Figure 4.10** Experimental dependence of postsynaptic current on presynaptic membrane potential. The frequency of miniature chloride events (plotted vertically) is a measure of current through the postsynaptic membrane. The current is extremely noisy, due to the quasimolecular nature of neurotransmitter release. The solid line is an exponential fit to the experimental data filled circles. (Source: Adapted from Shepherd, 1979.)

A drawing depicting a typical synaptic arrangement is shown in Figure 4.9. The function of a synapse is to control the conductance of the membrane separating the interior of the postsynaptic cell from the extracellular fluid. That conductance is controlled by the potential across the presynaptic membrane. The detailed mechanism by which synapses operate is extremely interesting, and will no doubt be the subject of study for many years. We will present here only the essential principles of synapse operation. There are several excellent reviews of the subject at various levels of detail (Shepherd, 1979).

Inside the presynaptic membrane is a high concentration of specific neurotransmitter molecules. When the presynaptic membrane is depolarized, calcium ions allow calcium ions \((Ca^{2+})\) to flow into the presynaptic cell from the synaptic cleft. The calcium ions activate the subcellular machinery that causes release of neurotransmitter molecules into the synaptic cleft, where these molecules diffuse to the postsynaptic membrane and initiate a chain of events that results in the opening of ion-specific channels. The amount of neurotransmitter released, and therefore the change in conductance of the postsynaptic membrane, is an exponential function of the postsynaptic potential, as shown in Figure 4.10.
If the channels opened by the neurotransmitter are specific for sodium, for example, a depolarization of the presynaptic membrane will result in a depolarization of the postsynaptic membrane, and the synapse is said to be excitatory. If the neurotransmitter leads to the opening of potassium-specific channels, the postsynaptic membrane will be hyperpolarized, and the synapse is said to be inhibitory. As we have noted previously, chloride channels can act to increase the conductance of the membrane without appreciable change in potential—synapses leading to this behavior are called shunting. Within these broad categories, many variations are possible. In addition, synapses are known that open channels for molecules other than sodium, potassium, or chloride. We shall not discuss any of these complexities here.

A single synapse is the neural counterpart of a transistor. The tip of every neural process ends in a synapse, and there are many synaptic contacts along the branches of the dendritic tree as well. As in electronic computational machinery, synapses occur not in isolation, but rather in circuit arrangements. Dendrites form a wide variety of synaptic connections with dendrites and axons of other neurons. The specialization of function of the many areas in the nervous system is largely a result of these synaptic circuit arrangements. Cross-sections through several representative synaptic structures are shown in Figure 4.11. Specific circuits for many parts of the brain are discussed in Gordon Shepherd's excellent book The Synaptic Organization of the Brain (Shepherd, 1979). In addition, a lucid popular account has appeared in Scientific American (Shepherd, 1978). Many of these arrangements have (not altogether by accident) parallel or circuits in we will discuss in subsequent chapters.

REFERENCES