Appendix 4

The action of nerves

The structure of a typical nerve cell or neuron is shown in Fig. A4.1. The nucleus of the cell is found in the large cell body situated at one end of the neuron. Small arms (dendrites) radiate from the cell body and receive messages from other neurons. These messages either stimulate or de-stimulate the neuron. The cell body 'collects' the sum total of these messages.

Ion channels are selective for different ions. There are cationic ion channels for Na^+, K^+, and Ca^{2+} ions. When these channels are open, they are generally excitatory and lead to depolarization of the cell.

It is worth emphasizing that the cell body of a neuron receives messages not just from one other neuron, but from a range of different neurons. These pass on different messages (neurotransmitters). Therefore, a message received from a single neuron is unlikely to stimulate a neuron signal by itself, unless other neurons are acting in sympathy.

Assuming that the overall stimulation is great enough, an electrical signal is fired down the length of the neuron (the axon). The axon is covered with sheaths of lipid (myelin sheaths), which act to insulate the signal as it passes down the axon.

The axon leads to a knob-shaped swelling (synaptic button) if the neuron is communicating with another neuron. Alternatively, if the neuron is communicating with a muscle cell, the axon leads to what is known as a neuromuscular endplate, where the end plate is spread like an amoeba over an area of the muscle cell.

Within the synaptic button or neuromuscular endplate there are small globules (vesicles) containing the neurotransmitter chemical. When a signal is received from the axon, the vesicles merge with the cell membrane and release their neurotransmitter into the gap between the neuron and the target cell (synaptic gap). The neurotransmitter binds to a receptor, as described in Chapter 4, and passes on its message. Once the message has been received, the neurotransmitter leaves the receptor and is either broken down enzymatically (e.g. by acetylcholine) or taken up intact by the presynaptic neuron (e.g. noradrenaline). Either way, the neurotransmitter is removed from the synaptic gap and is unable to bind with its receptor a second time.

To date, we have talked about nerves 'firing' and the generation of 'electrical signals' without really considering the mechanism of these processes. The secret behind nerve transmission lies in the movement of ions across cell membranes, but there is an important difference in what happens in the cell body of a neuron compared with the axon. We shall consider what happens in the cell body first.

All cells contain sodium, potassium, calcium, and chloride ions, and it is found that the concentration of these ions is different inside the cell compared with outside. The concentration of potassium inside the cell is larger than the surrounding medium, whereas the concentration of sodium and chloride ions is smaller. Thus, a concentration gradient exists across the membrane.

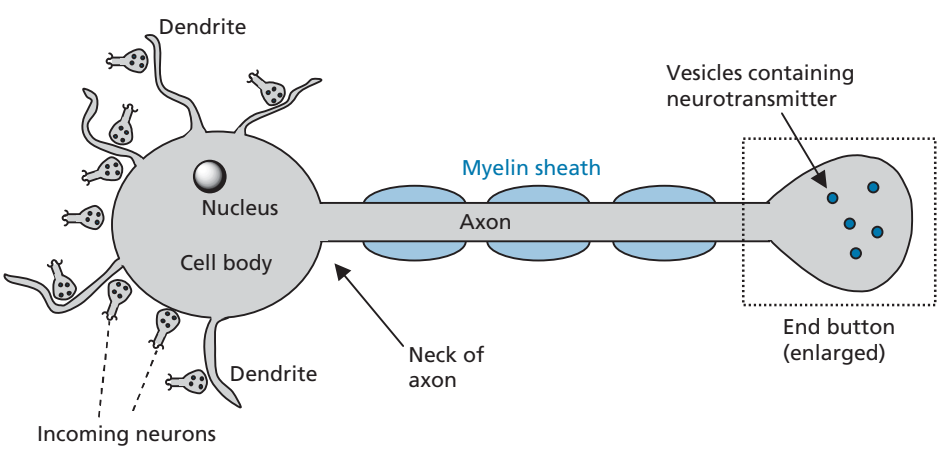

FIGURE A4.1 Structure of a typical nerve cell (neuron).

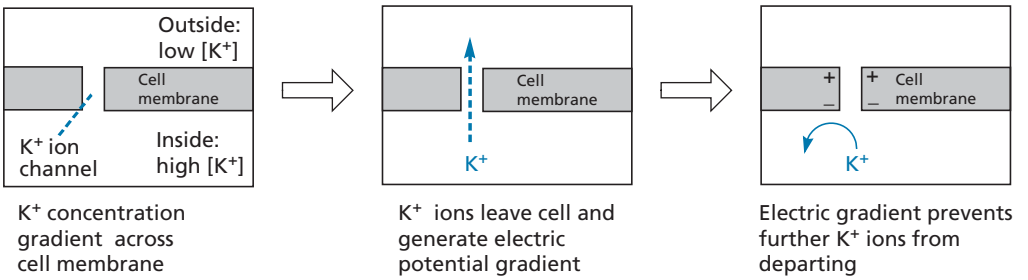

FIGURE A4.2 Generation of electric potential across a cell membrane.

Potassium is able to move down its concentration gradient (i.e. out of the cell), as it can pass through the potassium ion channels (Fig. A4.2). But, if potassium ions can move out of the cell, why does the potassium concentration inside the cell not fall to equal that of the outside? The answer lies in the fact that potassium is a positively charged ion and, as it leaves the cell, an electric potential is set up across the cell membrane. This would not happen if a negatively charged counterion could leave with the potassium ion. However, the counterions in question are large proteins which cannot pass through the cell membrane. As a result, a few potassium ions are able to escape down the ion channels out of the cell and an electric potential builds up across the cell membrane such that the inside of the cell membrane is more negative than the outside. This electric potential (50–80 mV) opposes, and eventually prevents, the flow of potassium ions.

But what about the sodium ions? Could they flow into the cell along their concentration gradient to balance the charged potassium ions that are departing? The answer is that they cannot because they are too big for the potassium ion channels. This appears to be a strange argument, as sodium ions are smaller than potassium ions, but it has to be remembered that we are dealing with an aqueous environment where the ions are solvated (i.e. they have a 'coat' of water molecules). Sodium, being a smaller ion than potassium, has a greater localization of charge and is able to bind its solvating water molecules more strongly. As a result, sodium, along with its water coat, is bigger than a potassium ion with or without its water coat.

Ion channels for sodium do exist, and these channels are capable of removing the water coat around sodium and letting it through. However, the sodium ion channels are mostly closed when the neuron is in the resting state. As a result, the flow of sodium ions across the membrane is very small compared to potassium. Nevertheless, the presence of sodium ion channels is crucial to the transmission of a nerve signal.

To conclude, the movement of potassium across the cell membrane sets up an electric potential across the cell membrane which opposes this flow. Charged protein structures are unable to move across the membrane, while sodium ions cross very slowly and so an equilibrium is established. The cell membrane is polarized and the electric potential at equilibrium is known as the resting potential.

The number of potassium ions required to establish that potential is of the order of a few million compared with the several hundred billion present in the cell. Therefore, the effect on concentration is negligible.

As mentioned above, potassium ions are able to flow out of potassium ion channels, but not all of these channels are open in the resting state. What would happen if more were to open? The answer is that more potassium ions would flow out of the cell and the electric potential across the cell membrane would become more negative to counter this increased flow. This is known as **hyperpolarization** and the effect is to de-stimulate the neuron (Fig. A4.3).

Suppose, instead, that a few sodium ion channels were to open up. In this case, sodium ions would flow into the cell and, as a result, the electric potential would become less negative. This is known as **depolarization** and results in a stimulation of the neuron.

If chloride ion channels are opened, chloride ions flow into the cell, and the cell membrane becomes hyperpolarized, de-stimulating the neuron.

Ion channels do not open or close by chance. They are controlled by the neurotransmitters released by communicating neurons. The neurotransmitters bind with their receptors and this leads to the opening or closing of ion channels. Such ion channels are known as **ligand-gated ion channels**. For example, acetylcholine controls the sodium ion channel, whereas γ-aminobutyric acid (GABA) and glycine control chloride ion channels. The resulting flow of ions leads to a localized hyperpolarization or depolarization in the area of the ion channel. The cell body collects and sums all this information such that the neck of the axon experiences an overall depolarization or hyperpolarization depending on the sum total of the various excitatory or inhibitory signals received.

We shall now consider what happens at the axon of the neuron (Fig. A4.4). The cell membrane of the axon also has sodium and potassium ion channels, but they are different in character from those in the cell body. The axon

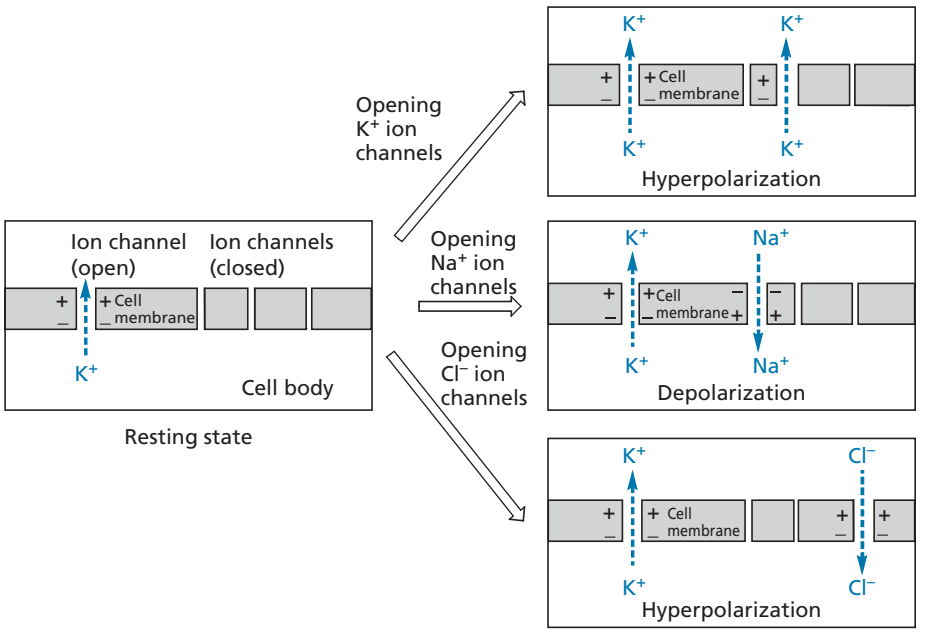

FIGURE A4.3 Hyperpolarization and depolarization.

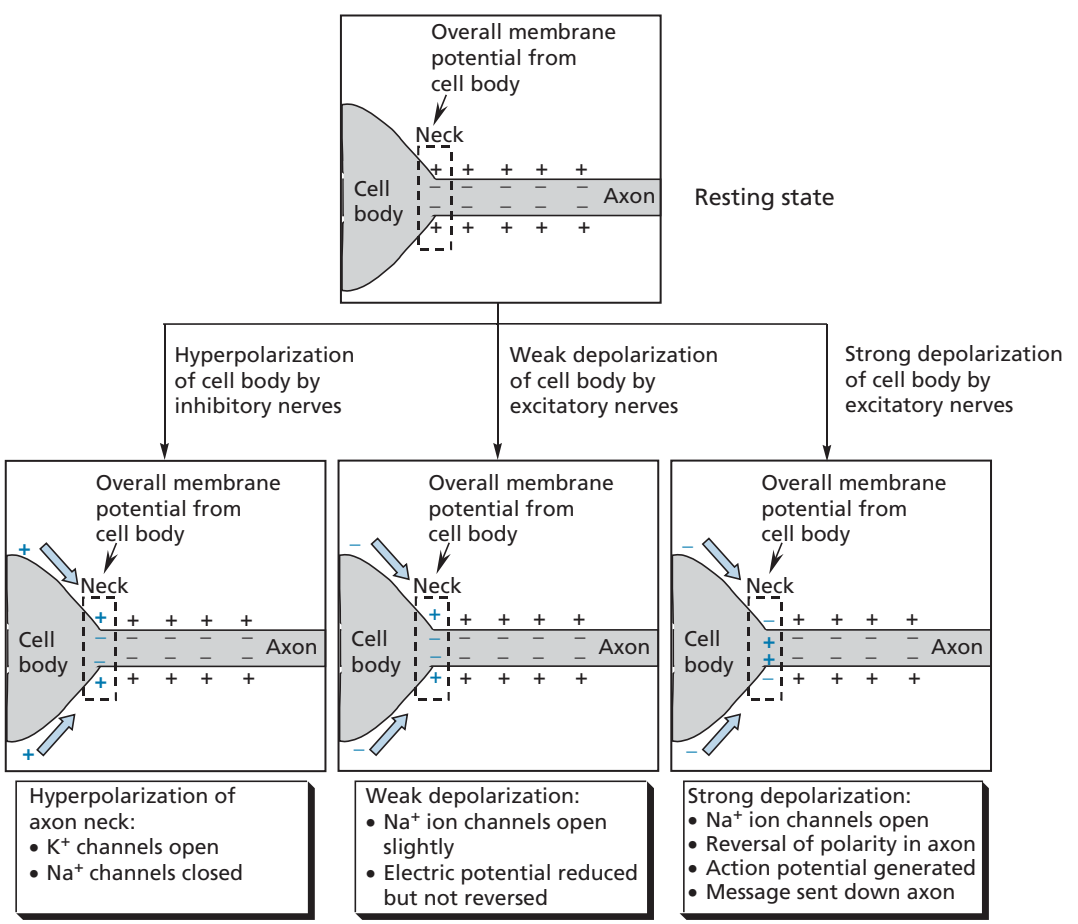

FIGURE A4.4 Hyperpolarization and depolarization effects at the neck of the axon.

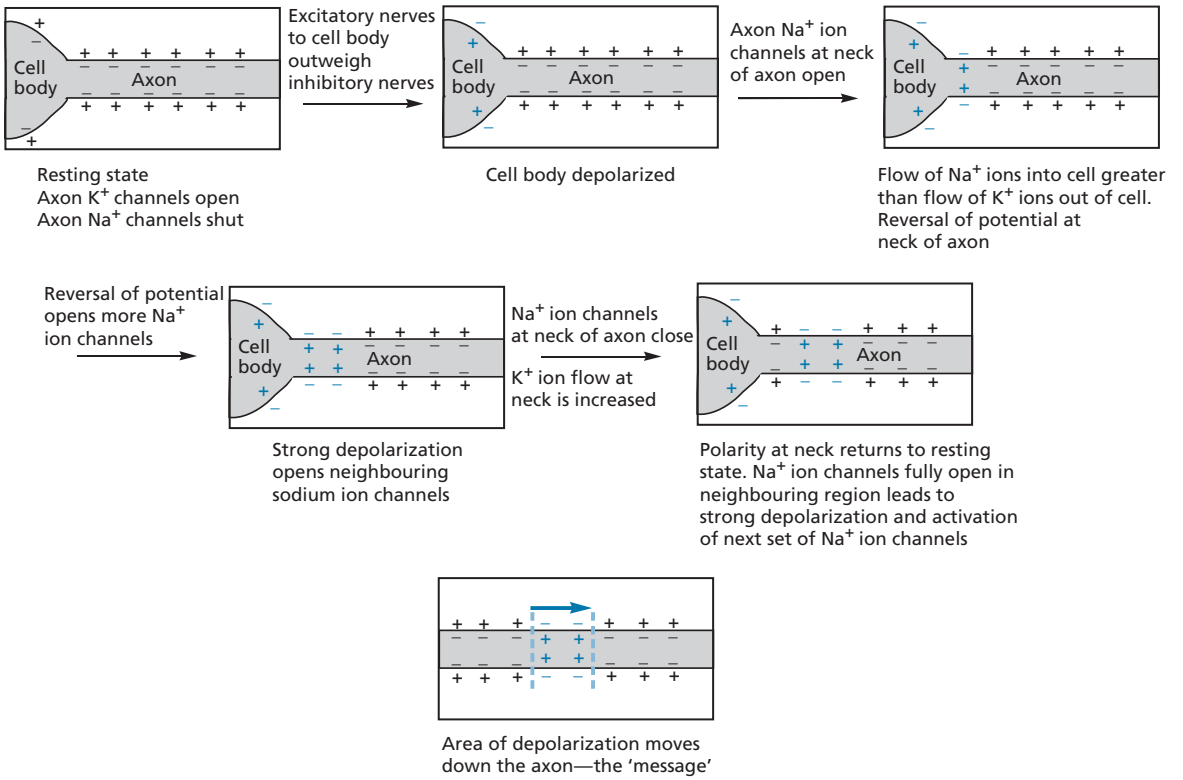

FIGURE A4.5 Generation of an action potential.

ion channels are not controlled by neurotransmitters, but by the electric potential of the cell membrane. Therefore, they are known as **voltage-gated ion channels**.

The sodium ion channels located at the junction of the nerve axon with the cell body are the crucial channels as they are the first channels to experience whether the cell body has been depolarized or hyperpolarized.

If the cell body is strongly depolarized then a signal is fired along the neuron. A specific threshold value has to be reached before this happens, however. If the depolarization from the cell body is weak, only a few sodium channels open up and the depolarization at the neck of the axon does not reach that threshold value. The sodium channels then reclose and no signal is sent.

With stronger depolarization, more sodium channels open up until the flow of sodium ions entering the axon becomes greater than the flow of potassium ions leaving it. This results in a rapid increase in depolarization, which, in turn, opens up more sodium channels, resulting in very strong depolarization at the neck of the axon. The flow of sodium ions into the cell increases dramatically, such that it is far greater than the flow of potassium ions out of the axon, and the electric potential across the membrane is reversed, such that it is positive inside the cell and negative outside the cell. This process lasts less than a millisecond before the sodium channels reclose and sodium permeability returns to its normal state. More potassium channels then open and permeability to potassium ions increases for a while to speed up the return to the resting state.

The process is known as an action potential and can only take place in the axon of the neuron. The cell membrane of the axon is said to be excitable, unlike the membrane of the cell body. The important point to note is that once an action potential has fired at the neck of the axon it has reversed the polarity of the membrane at that point. This, in turn, has an effect on the neighbouring area of the axon and depolarizes it beyond the critical threshold level. It, too, fires an action potential and so the process continues along the whole length of the axon (Fig. A4.5). The number of ions involved in this process is minute, such that the concentrations are unaffected. Once the action potential reaches the synaptic button or the neuromuscular endplate it causes an influx of calcium ions into the cell and an associated release of neurotransmitter into the synaptic gap. The mechanism of this is not well understood.