5
Electrophysiology

Cochlear implants should aim to reproduce the coding of sound in the auditory system as closely as possible, for best sound perception. The cochlear implant is in part the result of reverse engineering from systems neurophysiology and thus attempts to reproduce the coding of sound. The coding of sound, however, cannot be easily reproduced, as sound produces a complex temporal and spatial pattern of nerve discharges in approximately 20,000 auditory neurons, and only about 22 electrodes can be used with current technology, for example the Nucleus/Cochlear Limited (University of Melbourne/Bionic Ear Institute) systems (Clark 1996, 1997). Nevertheless, by partially reproducing the coding with multiple-electrode stimulation, as well as extracting appropriate information from the speech signal, good speech perception is still possible (Clark 1996, 1997).

General Neurophysiology

The cochlear implant bypasses the transduction of sound vibrations into electrical signals in the cochlea, and directly stimulates cochlear nerve fibers. These in turn excite the higher centers in the central auditory nervous system. Electrical stimulation aims to reproduce the pattern of excitation in the nervous pathways produced by sound, and to manipulate the mechanisms underlying the generation of neural activity to produce this pattern.

Action Potentials

Information is transmitted throughout the central nervous system by action potentials. These electrical events are initiated in dendrites and cell bodies and transmitted along axons, which make connections (synapses) on the dendrites and body of the next cell, as illustrated in Figure 5.1, and so on. The synapses are localized connections that are highly specialized. A more complete account of neural function and the structure of the brain can be found in texts such as Levitan and Kaczmarek (1997) and Shepherd (1998).

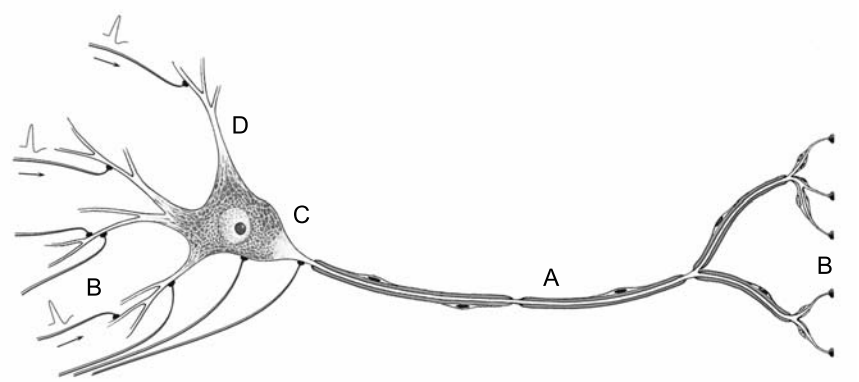

FIGURE 5.1. A diagram of a neuron and connections illustrating the dendrites (D) bringing information to the cell's body (C), and the axons (A) taking information to other neurons via the terminal button-shaped endings or boutons (B).

The action potentials are initiated when the resting potential of the neuron (the voltage across the neural membrane) is decreased (depolarized) to a threshold level as illustrated in Figure 5.2. There is a higher concentration of (K^{1+}) inside and (Na^{1+}) outside the nerve membrane. The resting potential is due to selective permeability of the nerve membrane to the potassium ion (K^{1+}) with a concentration gradient driving it outside the cell membrane. The ion flow across the nerve membrane can be represented as an electrical current that obeys Ohm's law (Mortimer 1990):

$$I_{ion} = g_{ion} (V_m - E_{ion})$$

where I_{ion} is the flow of ions, g_{ion} is the membrane conductance; V_m is the membrane potential; and E_{ion} is the equilibrium potential for a particular ion and given by the Nernst equation:

$$E_{ion} = (RT/zF)\ln(C_o/C_i)$$

where R is the gas constant, T is the absolute temperature, z is the valence of the ion, F is the Faraday constant, C_o is the concentration of the ion on the outside of the membrane, and C_i the concentration on the inside.

Under resting conditions the inward sodium current (I_{Na}) is equal and opposite to the outward potassium current (I_K):

$$I_{Na} = -I_K$$

This can be written as

$$g_{Na}(V_m - E_{Na}) = -g_K (V_m - E_K)$$

where E_{Na} is the equilibrium potential for (Na^{1+}) and E_K for (K^{1+}).
The equation can be solved for V_m:

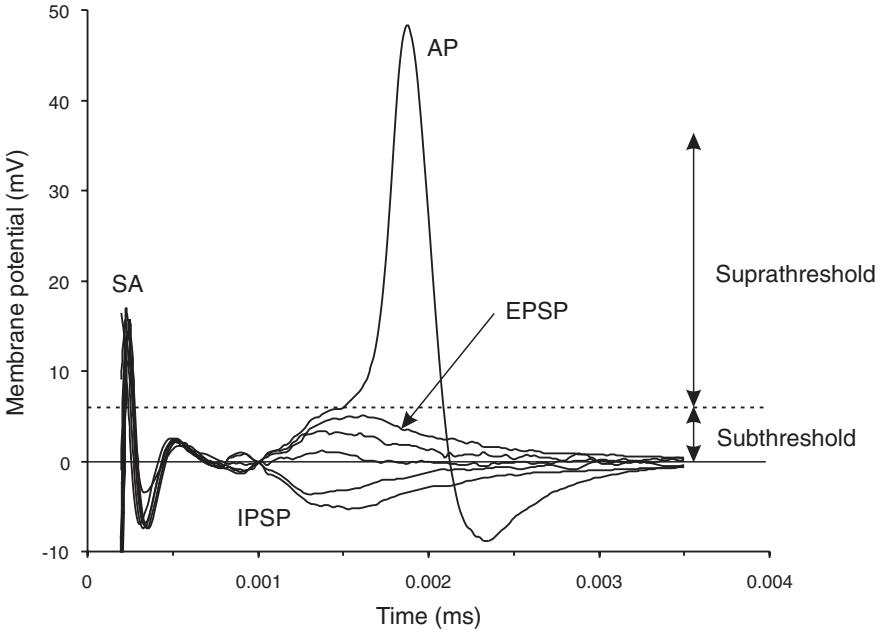

FIGURE 5.2. An intracellular recording of excitatory postsynaptic potentials (EPSPs) and the action potential (AP) generated in a globular bushy cell in the anteroventral cochlear nucleus of the rat. The stimulus artifact (SA) results in EPSPs and when threshold is reached an AP occurs. An inhibitory postsynaptic potential (IPSP) is also shown (Paolini and Clark 1998a).

$$V_m = \frac{E_{Na}\,(g_{Na}/g_K) + E_K}{(g_{Na}/g_K) + 1}$$

Thus the membrane potential is regulated by the ion conductance.

If the sodium conductance is very small during the resting state, the membrane potential approaches -60 mV (i.e., positive outside the membrane), and if the sodium conductance becomes large, the potential approaches the sodium potential of $+55$ mV (i.e., negative outside the membrane).

An excitatory transmitter acts on the postsynaptic membrane to produce an excitatory postsynaptic potential (EPSP), and an inhibitor transmitter an inhibitory postsynaptic potential (IPSP). With excitation when the potential reaches a threshold level the sodium gates in the nerve membrane open and the sodium ions (Na^{1+}), which have a higher concentration outside the cell, rush inward down a potential gradient to produce the action potential. The current due to the passage of (Na^{1+}) produces a further depolarization that in turn increases the conductance of (Na^{1+}). This positive feedback continues until equilibrium is reached with the concentration and voltage gradients of ions balancing each other. The creation of an action potential makes the voltage on the outer surface of the cell membrane negative relative to the inside of the cell. The EPSPs producing an action potential

are generated when acetylcholine and amino acids such as glutamic and aspartic acid are released from the boutons on the presynaptic side of the synaptic space. Hyperpolarization occurs through the release of transmitters that open chloride or potassium channels, and produce IPSPs. In this case chloride ions (Cl^{1-}) move inward or potassium ions (K^{1+}) outward so the outside of the cell membrane becomes more positive relative to the inside. Important inhibitory amino acid transmitters are γ-aminobutyric acid and glycine.

The chemical transmitters for excitation and inhibition are released when an action potential reaches the presynaptic terminal. This induces an increase in the local (Ca^{2+}) concentration close to the open (Ca^{2+}) ion channels. A (Ca^{2+}) sensor binds the (Ca^{2+}) before the release of the transmitter into the synaptic cleft (Bollman et al 2000). The transmitter is released from synaptic vesicles, each being in a docking position close to the presynaptic membrane. The transmitter then initiates an EPSP or IPSP in the postsynaptic membrane.

The EPSPs and IPSPs take a certain period of time to reach a maximum, and then decay over a longer period, as illustrated in Figure 5.2. The postsynaptic potentials sum to produce a potential large enough to initiate an action potential. The summing can be spatial or occur over time as each potential takes a defined period to decay. The response of each neuron is thus the sum total of the excitatory and inhibitory inputs. When the postsynaptic potential reaches a threshold level, the sodium gates in the nerve membrane open wide and sodium ions rush in from the extracellular fluid to produce a rapid voltage change or spike, as illustrated in Figure 5.2. After a short period of time, which depends on the properties of the nerve membrane, the sodium gates close, and the potassium gates open to allow the resting nerve membrane potential to be reestablished. In the meantime, the voltage change or spike is propagated along the neuron by this active self-regenerating process.

If a stimulus arrives during the stage when the sodium gates are open, a second action potential will not occur. The period when a second action potential cannot be initiated is the absolute refractory period. This was shown to be approximately 0.5 ms for the auditory nerve (Moxon 1967). After the absolute refractory period there is a relative refractory period during which time a stronger stimulus is required to excite the neuron. A study by Roberts et al (2000) suggested this can have a mean value of approximately 0.2 ms. During this time the sodium gates have not completely returned to their normal state.

Strength-Duration Curves

A well-defined relation between the electrical current amplitude and the duration of the pulse was found for threshold responses (Hill 1936; Katz 1939). This relationship is a strength-duration curve, and is illustrated for the cat auditory nerve in Figure 5.3. Notice that as the pulse duration decreases, the threshold for an action potential increases in an exponential fashion. A cochlear implant stimulator would need to be able to produce high current amplitudes for the short-

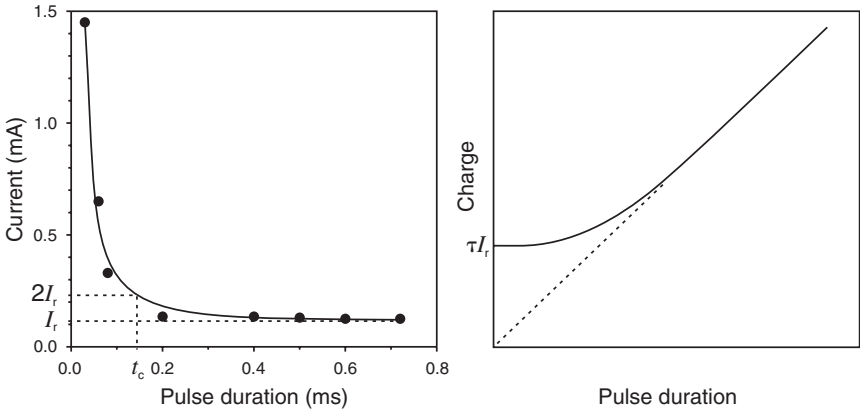

FIGURE 5.3. Left: Strength-duration curve from a cat auditory nerve fiber. I_r, rheobase current; t_c, chronaxie (Clark et al 1977. A multiple electrode hearing prosthesis for cochlear implantation in deaf patients. *Medical Progress through Technology* **5**: 127–140. Reprinted with permission of Springer-Verlag.) Right: Charge-duration curve (Mortimer 1990).

duration pulses required for high stimulus rates. The curve also shows that pulse amplitude and width can be traded in exciting a threshold response. If the current is to be minimized, the pulse duration must be increased. Note that as the pulse duration increases, the threshold current reaches an asymptote—the rheobase.

The mathematical relation between the threshold current (I_{th}) and the stimulus duration (t) can be calculated (Hill 1936; Katz 1939) and the values predicted from the following expression:

$$I_{th} = \frac{I_r}{(1 - e^{-t/\tau})}$$

where I_{th} is the threshold current, I_r the rheobase current, τ the excitation time constant, t the pulse duration and e is the base of natural logarithms. The excitation constant is related to the chronaxie (t_c), which is the pulse width for a current twice the rheobase current.

Depending on the dimensions of the electrode pads and the distance from the cochlear nerve, it may be necessary to minimize charge per phase. The relation between charge per phase and pulse width can be derived from the above equation by multiplying the current by the pulse width. Figure 5.3 shows the amount of charge that must be injected to initiate an action potential. Note that for very short pulse widths the charge approaches an asymptote that has a constant value.

Electrical Models of the Nerve Membrane

The first model of the electrical activity of the nerve membrane was developed by Hodgkin and Huxley (1952). Their studies were undertaken on the squid axon, and the voltage across the membrane could be set and maintained at a constant

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