

# Reading 6: Bioelectrical Signals, Measurements, and Safety

This chapter deals with the genesis of various bioelectric signals that are recorded routinely in modern clinical practice. Given adequate monitoring equipment, many forms of bioelectric phenomena can be recorded with relative ease. These phenomena include the electrocardiogram (ECG), electroencephalogram (EEG), electroneurogram (ENG), electromyogram (EMG), and electroretinogram (ERG).

Engineers generally have a good physical insight into the nature of electromagnetic fields produced by bioelectric sources, and, because of their comprehensive understanding of the physical problem, they may contribute to the solution of biological problems.

This chapter begins by introducing bioelectric phenomena at the cellular level. It proceeds to discuss volume-conductor potential distributions of simple bioelectric sources, and gradually more anatomically complex ones. The volume-conductor electric field problem provides the link (mapping) between microscopic electrical activity generated within the bioelectric source, the flow of action current through the conducting medium, and the macroscopic potential distribution produced at the surface of the body. We continue with a discussion of the functional organization of the peripheral nervous system (outside the brain and spinal cord), which leads to a discussion of the ENG and EMG. Finally, other bioelectric sources (and associated field potentials) are discussed including the active heart (ECG), retina (ERG), and brain (EEG).

## 4.1 ELECTRICAL ACTIVITY OF EXCITABLE CELLS

Bioelectric potentials are produced as a result of electrochemical activity of a certain class of cells, known as *excitable cells*, that are components of nervous, muscular, or glandular tissue. Electrically they exhibit a *resting potential* and, when appropriately stimulated, an *action potential*, as the following paragraphs explain.

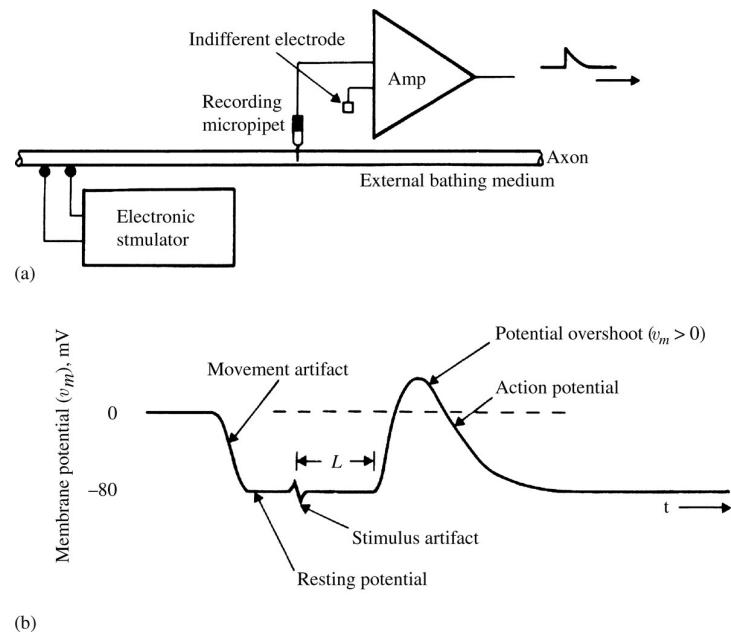
### THE RESTING STATE

The individual excitable cell maintains a steady electrical potential difference between its internal and external environments. This resting potential of the

internal medium lies in the range  $-40$  to  $-90$  mV, relative to the external medium.

Figure 4.1(a) shows how the resting potential is usually measured. A micromanipulator advances a microelectrode (see Section 5.8) close to the surface of an excitable cell and then, by small movements, pushes it through the cell membrane. For the membrane to seal properly around the penetrating tip, the diameter of the tip must be small relative to the size of the cell in which it is placed. Figure 4.1(b) shows a typical electrical recording from a single nerve fiber, including the dc offset potential (resting potential) that occurs upon penetration of the membrane. It also shows the transient disturbance of membrane potential (the action potential) when an adequate stimulus is given.

The cell membrane is a very thin (7 to 15 nm) lipoprotein complex that is essentially impermeable to intracellular protein and other organic anions ( $A^-$ ). The membrane in the resting state is only slightly permeable to  $Na^+$  and rather



**Figure 4.1 Recording of action potential of an invertebrate nerve axon** (a) An electronic stimulator supplies a brief pulse of current to the axon, strong enough to excite the axon. A recording of this activity is made at a downstream site via a penetrating micropipette. (b) The movement artifact is recorded as the tip of the micropipette drives through the membrane to record resting potential. A short time later, an electrical stimulus is delivered to the axon; its field effect is recorded instantaneously at downstream measurement site as the stimulus artifact. The action potential however, proceeds along the axon with a constant conduction velocity. The time period  $L$  is the *latent period* or transmission time from stimulus to recording site.

freely permeable to  $K^+$  and  $Cl^-$ . The permeability of the resting membrane to potassium ion ( $P_K$ ) is approximately 50 to 100 times larger than its permeability to sodium ion ( $P_{Na}$ ).

Typically, the  $K^+$  concentration of the internal medium (cytosol) is 140 mmol/liter, whereas that of the external (bathing) medium is 2.5 mmol/liter. The concentration difference creates a diffusion gradient that is directed outward across the membrane. The movement of the  $K^+$  along this diffusion gradient (while the nondiffusible anion component stays within the cell) is in such a direction as to make the interior of the cell more negative relative to the external medium (that is, positive charge is removed from the interior). Consequently, a transmembrane potential difference is established. Electrically the membrane can be described as a leaky capacitor, since structurally it is comprised of a thin dielectric material (the lipoprotein complex) that acts as a charge separator, and yet it has transmembrane ion channels (pores) of different types, some of which allow a leakage flow of ions across the membrane at rest. The electric field supported by the membrane capacitor at rest is directed inward from positive to negative across the membrane. It tends to inhibit the outward flow of positively charged ions (such as  $K^+$ ), as well as the inward flow of negatively charged ions (such as  $Cl^-$ ). Thus the diffusional and electrical forces acting across the membrane are opposed to one another, and a balance is ultimately achieved. The membrane potential at which such an equilibrium occurs (considering  $K^+$  to be the main ionic species involved in the resting state; that is,  $P_K \gg P_{Na}$ ) is called the *equilibrium potential* for the  $K^+$  ( $E_K$ ). It is measured in volts and is calculated from the Nernst equation,

$$E_K = \frac{RT}{nF} \ln \frac{[K]_o}{[K]_i} = 0.0615 \log_{10} \frac{[K]_o}{[K]_i} \quad (4.1)$$

at 37°C (body temperature). Here  $n$  is the valence of the  $K^+$ ,  $[K]_i$  and  $[K]_o$  are the intracellular and extracellular concentrations of  $K^+$  in moles per liter, respectively,  $R$  is the universal gas constant (Appendix),  $T$  is absolute temperature in K, and  $F$  is the Faraday constant (Appendix). Equation (4.1) provides a reasonably good approximation to the potential of the resting membrane, which indicates that the resting membrane is effectively a *sodium–potassium membrane*. A more accurate expression for the membrane equilibrium potential  $E$ , which accounts for the influence of other ionic species in the internal and external media was first developed by Goldman (1943) and later modified by Hodgkin and Katz (1949), who assumed a constant electric field across the membrane:

$$E = \frac{RT}{F} \ln \left\{ \frac{P_K[K]_o + P_{Na}[Na]_o + P_{Cl}[Cl]_i}{P_K[K]_i + P_{Na}[Na]_i + P_{Cl}[Cl]_o} \right\} \quad (4.2)$$

Here  $E$  is the equilibrium transmembrane (resting) potential when net current through the membrane is zero and  $P_M$  is the *permeability coefficient* of the

membrane for a particular ionic species M. It is called the *Goldman–Hodgkin–Katz (GHK) formulation*.

**EXAMPLE 4.1** For frog skeletal muscle, typical values for the intracellular and extracellular concentrations of the major ion species (in millimoles per liter) are as follows.

Species	Intracellular	Extracellular
$Na^+$	12	145
$K^+$	155	4
$Cl^-$	4	120

Assuming room temperature (20°C) and typical values of permeability coefficient for frog skeletal muscle ( $P_{Na} = 2 \times 10^{-8}$  cm/s,  $P_K = 2 \times 10^{-6}$  cm/s, and  $P_{Cl} = 4 \times 10^{-6}$  cm/s), calculate the equilibrium resting potential for this membrane, using the Goldman equation.

**ANSWER** From (4.2),

$$\begin{aligned} E &= 0.0581 \log_{10} \left[ \frac{P_K(4) + P_{Na}(145) + P_{Cl}(4)}{P_K(155) + P_{Na}(12) + P_{Cl}(120)} \right] \\ &= 0.0581 \log_{10} \left( \frac{26.9 \times 10^{-6}}{790.24 \times 10^{-6}} \right) = -85.3 \text{ mV} \end{aligned}$$

which is close to typical measured values for the resting membrane potential in frog skeletal muscle.

Maintaining the steady-state ionic imbalance between the internal and external media of the cell requires continuous active transport of ionic species against their electrochemical gradients. The active transport mechanism is located within the membrane and is referred to as the *sodium–potassium pump*. It actively transports  $Na^+$  out of the cell and  $K^+$  into the cell in the ratio  $3Na^+ : 2K^+$ . The associated pump current  $i_{NaK}$  is a net outward current that tends to increase the negativity of the intracellular potential. Energy for the pump is provided by a common source of cellular energy, adenosine triphosphate (ATP) produced by mitochondria in the cell.

Thus the factors influencing the flow of ions across the membrane are (1) diffusion gradients, (2) the inwardly directed electric field, (3) membrane structure (availability of pores), and (4) active transport of ions against an established electrochemical gradient. The charge separated by the cell membrane and the structure of this membrane ( $P_K, P_{Na}, P_{Cl}$ ) account for the resting potential.  $K^+$  diffuses outwardly according to its concentration gradient, whereas the nondiffusible organic anion component remains within the cell, creating a potential difference across the membrane. Electroneutrality is maintained within the bulk internal and external media, but due to the membrane capacitance, there

is a monolayer of cations distributed on the outer membrane surface and a monolayer of anions along the inner surface. The number of ions responsible for the membrane potential, however, is very small relative to the total number present in the bulk media. The  $\text{Na}^+$  influx does not compensate for the  $\text{K}^+$  efflux because, in the resting state,  $P_{\text{Na}} \ll P_{\text{K}}$ . Chloride ion diffuses inward down its concentration gradient, but its movement is balanced by the electrical gradient.

**EXAMPLE 4.2** The giant axon of the squid is frequently used in electrophysiological investigations because of its size. Typically it has a diameter of 1000  $\mu\text{m}$ , a membrane thickness of 7.5 nm, a specific membrane capacity of  $1 \mu\text{F/cm}^2$ , and a resting transmembrane potential  $v_m$  of 70 mV. Assume a uniform field within the membrane and calculate the magnitude and direction of the electric field intensity  $\mathbf{E}$  within the membrane.

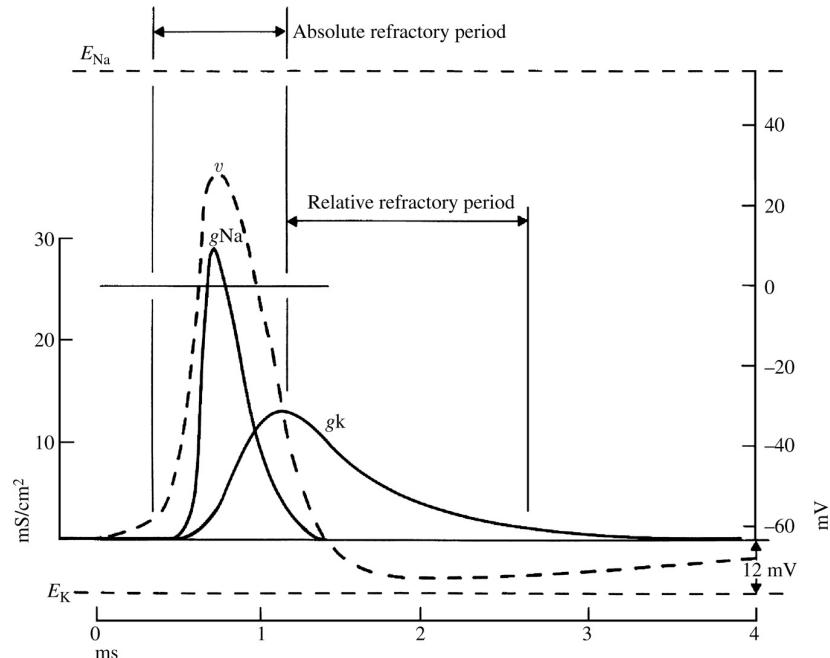
**ANSWER** The membrane is quite thin, serves as a charge separator, and can be represented by a parallel-plate capacitor with  $\mathbf{E}$  directed inward.

$$\mathbf{E} = \frac{v_m}{d} = \frac{70 \times 10^{-3}}{7.5 \times 10^{-9}} = 9.33 \times 10^6 \text{ V/m}$$

## THE ACTIVE STATE

Another property of an excitable cell is its ability to conduct an action potential [Figure 4.1(b)] when adequately stimulated. An *adequate stimulus* is one that brings about the depolarization of a cell membrane that is sufficient to exceed its threshold potential and thereby elicit an all-or-none action potential (brief transient disturbance of the membrane potential), which travels in an unattenuated fashion and at a constant conduction velocity along the membrane. Because of the steady resting potential, the cell membrane is said to be *polarized*. A lessening of the magnitude of this polarization is called *depolarization*, whereas an increase in magnitude is referred to as *hyperpolarization*. The all-or-none property of the action potential means that the membrane potential goes through a very characteristic cycle: a change in potential from the resting level of a certain amount for a fixed duration of time. For a nerve fiber,  $\Delta v \cong 120 \text{ mV}$  and the duration is approximately 1 ms. Further increases in intensity or duration of stimulus beyond that required for exceeding the threshold level produce only the same result.

The origin of the action potential lies in the voltage- and time-dependent nature of the membrane permeabilities (or equivalently, in electrical terms, membrane conductivities) to specific ions, notably  $\text{Na}^+$  and  $\text{K}^+$ . As the transmembrane potential ( $v_m$ ) is depolarized, the membrane permeability to sodium  $P_{\text{Na}}$  (or, equivalently, the conductance of the membrane to sodium  $g_{\text{Na}}$ ) is significantly increased. As a result,  $\text{Na}^+$  rushes into the internal medium of the cell, bringing about further depolarization, which in turn brings about a further increase in  $g_{\text{Na}}$  (i.e.,  $g_{\text{Na}}$  is dependent on transmembrane potential). If the membrane potential threshold is exceeded, this process is self-regenerative

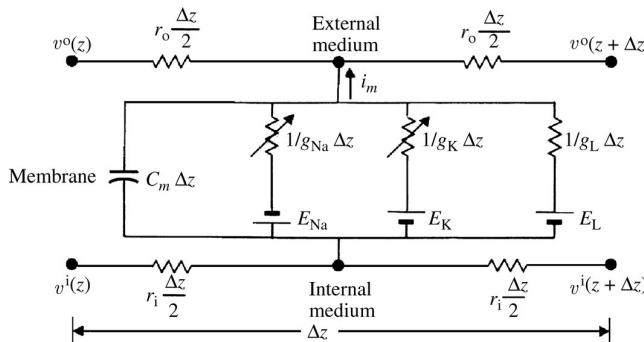


**Figure 4.2** Model-generated transmembrane potential ( $v_m$ ) and membrane ionic conductance changes for sodium ( $g_{\text{Na}}$ ) and potassium ( $g_{\text{K}}$ ) during the action potential. These waveforms are obtained by solving the differential equations developed by Hodgkin and Huxley for the giant axon of the squid at a bathing medium temperature of 18.5 °C.  $E_{\text{Na}}$  and  $E_{\text{K}}$  are the Nernst equilibrium potentials for  $\text{Na}^+$  and  $\text{K}^+$  across the membrane. (Modified from A. L. Hodgkin and A. F. Huxley, “A quantitative description of membrane current and its application to conduction and excitation in nerve.” *Journal of Physiology*, 1952, 117, 530.)

and leads to *runaway* depolarization. Under these conditions,  $v_m$  tends to approach the equilibrium Nernst potential of sodium,  $E_{\text{Na}}$ , which has a value of about +60 mV.

However,  $v_m$  never achieves this level because of two factors: (1)  $g_{\text{Na}}$  is not only voltage dependent but also time dependent, and (as shown in Figure 4.2) it is relatively short-lived compared with the action potential. (2) There is a delayed increase in  $g_{\text{K}}$  that acts as a hyperpolarizing influence, tending to restore  $v_m$  to resting levels (Figure 4.2). As  $v_m$  ultimately returns to the resting level,  $g_{\text{K}}$  is still elevated with respect to its resting value and returns slowly along an exponential time course. Since  $\text{K}^+$  continue to leave the cell during this time, the membrane hyperpolarizes and an undershoot is produced in the transmembrane potential waveform ( $v_m$ ).

The calculated  $g_{\text{Na}}$  and  $g_{\text{K}}$  waveforms of Figure 4.2 are based on *voltage-clamp* data from squid axon. In voltage-clamp experiments, transmembrane potential  $v_m$  is held at prescribed levels via a negative-feedback control circuit.



**Figure 4.3** Diagram of network equivalent circuit of a small length ( $\Delta z$ ) of a cylindrical cell (unmyelinated nerve fiber or skeletal muscle fiber). The membrane proper is characterized by specific membrane capacitance  $C_m$  ( $\mu\text{F}/\text{cm}^2$ ) and specific membrane conductances  $g_{\text{Na}}$ ,  $g_{\text{K}}$ , and  $g_{\text{Cl}}$  in millisiemens/ $\text{cm}^2$  ( $\text{mS}/\text{cm}^2$ ). Here an average specific leakage conductance is included that corresponds to ionic current from sources other than  $\text{Na}^+$  and  $\text{K}^+$  (e.g.,  $\text{Cl}^-$ ). This term is usually neglected. The cell cytoplasm is considered simply resistive, as is the external bathing medium; these media may thus be characterized by the resistance per unit length  $r_i$ , and  $r_o$  ( $\Omega/\text{cm}$ ), respectively. Here  $i_m$  is the transmembrane current per unit length ( $\text{A}/\text{cm}$ ), and  $v^i$  and  $v^o$  are the internal and external potentials at point  $z$ , respectively. Transmembrane potential at each point in  $z$  is given by  $v_m = v^i - v^o$ . (Modified from A. L. Hodgkin and A. F. Huxley, "A quantitative description of membrane current and its application to conduction and excitation in nerve." *Journal of Physiology*, 1952, 117, 501.)

Membrane currents in response to step changes in  $v_m$  are studied in order to determine the voltage- and time-dependent nature of  $g_{\text{Na}}$  and  $g_{\text{K}}$ .

Figure 4.3 shows a network equivalent circuit describing the electrical behavior of a small unit area of membrane. The entire nerve axon membrane can be characterized in a distributed fashion by utilizing an iterative structure of this same basic form.

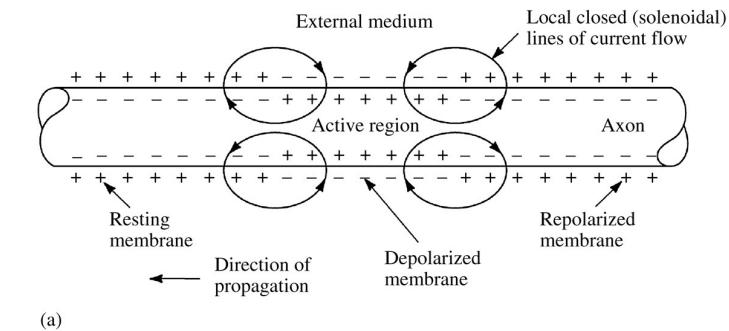
**EXAMPLE 4.3** Suppose that the electrical properties of an elongated excitable cell of cylindrical geometry (such as a nerve or skeletal muscle fiber) can be modeled fairly accurately with a distributed parameter "cable" model such as that of Figure 4.3. What should the temporal-membrane potential response to brief square pulses of stimulating current look like at some fixed distance from a particular stimulating electrode? As the separation distance between the particular stimulating electrode and the exploring micropipette is progressively increased, in what manner should the amplitude of the subthreshold response change?

**ANSWER** Figure 4.3 shows that each section of the distributed parameter model forms an  $R$ - $C$  low-pass filter. Multiple sections form multiple low-pass

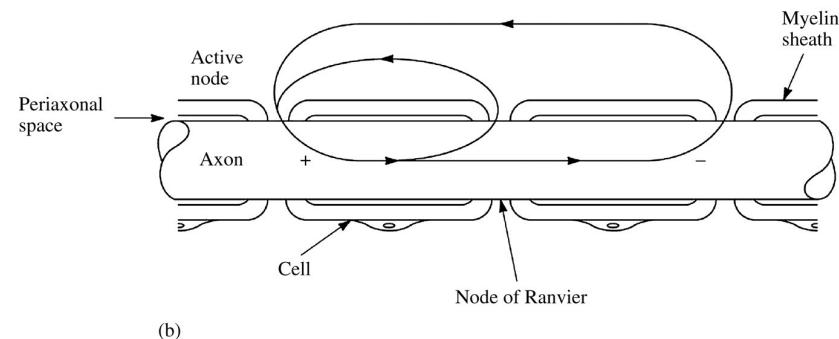
filters. Thus the response due to the stimulating square-wave pulse is progressively smoothed and attenuated as the separation distance increases.

When an excitable membrane produces an action potential in response to an adequate stimulus, the ability of the membrane to respond to a second stimulus of any sort is markedly altered. During the initial portion of the action potential, the membrane cannot respond to any stimulus, no matter how intense. This interval is referred to as the *absolute refractory period*. It is followed by the *relative refractory period*, wherein an action potential can be elicited by an intense superthreshold stimulus (Figure 4.2). The existence of the refractory period produces an upper limit to the frequency at which an excitable cell may be repetitively discharged. For example, if a nerve axon has an absolute refractory period of 1 ms, it has an upper limit of repetitive discharge of less than 1000 impulses/s.

For an action potential propagating along a single unmyelinated nerve fiber, the region of the fiber undergoing a transition into the active state (the *active region*) at an instant of time is usually small relative to the length of the fiber. Figure 4.4(a) shows schematically the charge distribution along the fiber



(a)



**Figure 4.4** (a) Charge distribution in the vicinity of the active region of an unmyelinated fiber conducting an impulse. (b) Local circuit current flow in the myelinated nerve fiber.

in the vicinity of the active region. Note that the direction of propagation of the action potential (considered frozen in time) is to the left, and the membrane lying ahead of the active region is polarized, as in the resting state. A reversal of polarity is shown within the active region because of depolarization of the membrane to positive values of potential. The membrane lying behind the active zone is repolarized membrane.

From the indicated charge distribution, *solenoidal* (closed-path) current flows in the pattern shown in Figure 4.4(a). In the region ahead of the active zone, the ohmic potential drop across the membrane caused by this solenoidal current flowing outward through the membrane is of such a polarity as to reduce the magnitude of  $v_m$  i.e., depolarize the membrane. When  $v_m$  is depolarized to the threshold level (about 20 mV more positive than the resting potential), this region becomes activated as well. The same current pattern flowing behind the active region is ineffective in re-exciting the membrane, which is in the refractory state. The nature of this process is therefore self-excitatory, each new increment of membrane being brought to the threshold level by lines of current from the active source region. The membrane stays in the active state for only a brief period of time and ultimately repolarizes completely. In this way, the action potential propagates down the length of the fiber in an unattenuated fashion, the signal being built up at each point along the way.

Most neurons in invertebrates are unmyelinated, but most vertebrate neurons are myelinated. That is, the axon is insulated by a sheath of myelin, a lipoprotein complex formed from successive wrappings of the axon by a special support cell found along nerve fibers. In peripheral nerves—those that lie outside the central nervous system (CNS)—this support cell is known as a *Schwann cell*. In myelinated CNS neurons, this function is served by a special glial cell known as an *oligodendrocyte*. The myelin sheath is interrupted at regular intervals (1 to 2 mm, depending on the species) by nodes of Ranvier; a single Schwann cell thus provides the insulating myelin sheath covering of the axon between two successive nodes of Ranvier [Figure 4.4(b)]. The tightly wrapped membranes of the Schwann cell closely adhere to the axon membrane and increase its thickness by a factor of 100. This substantially decreases the capacitance of the modified membrane and increases the transverse impedance to current flow in the internodal region of the fiber. Sodium ion channels are distributed in a nonuniform manner in myelinated fibers, being densely clustered at the nodes of Ranvier and very sparsely distributed in the internodal region. Multiple types of potassium channels (fast-gated, slow-gated) are distributed in the paranodal regions lying adjacent to each node of Ranvier. These channels are distributed to a lesser extent throughout the remainder of the internodal region in both amphibian and mammalian species.

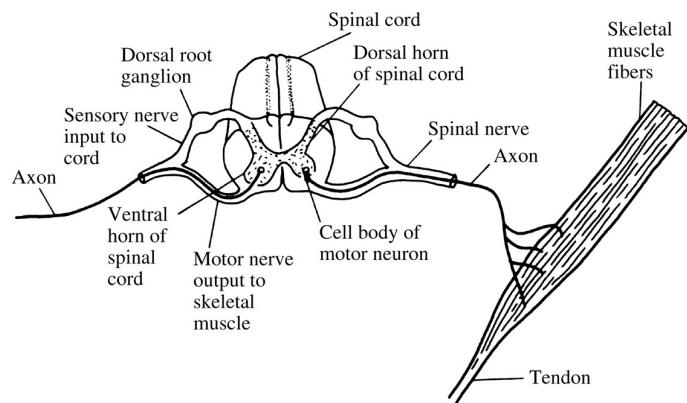
Once the myelinated nerve fiber is activated, conduction proceeds through a process of local circuit current flow, much as in the case of the unmyelinated nerve fiber described earlier [Figure 4.4(a)]. There are differences, however, in that the sources for action current flow are localized at the nodes of Ranvier and are therefore not uniformly distributed along the axonal membrane, as in

the case of the unmyelinated fiber. Myelination of the internode reduces leakage currents, decreases membrane capacitance, and improves the transmission properties of the cable-like myelinated fiber. Local circuit currents emanating from an active node have an exponentially diminishing magnitude over an axial distance spanning several internodal lengths. Accordingly, they contribute to a drop in nodal potential as current passes outward through a given inactive nodal membrane [Figure 4.4(b)].

Thus myelinated nerve fiber conduction proceeds via rapid, sequential activation of the nodes of Ranvier, and local circuit current provides the underlying mechanism for bringing the nodal membrane voltage to threshold. This process is frequently called *saltatory conduction* (from the Latin *saltare*, “to leap or dance”), because action potentials appear to leap from node to node. For an axon of a given diameter, myelination improves the conduction rate by a factor of approximately 20. By reason of its structure, the myelinated nerve fiber represents a more complicated bioelectric action current source than the unmyelinated nerve fiber. Mathematical modeling studies of conduction in both unmyelinated and myelinated nerve fibers have appeared in the literature (Moore *et al.*, 1978; Waxman and Brill, 1978; Halter and Clark, 1991; Moffit *et al.*, 2004).

## 4.5 THE ELECTROMYOGRAM

Skeletal muscle is organized functionally on the basis of the *motor unit* (see Figure 4.10), which consists of a single motor nerve fiber and the bundle of



**Figure 4.10** Diagram of a single motor unit (SMU), which consists of a single motoneuron and the group of skeletal muscle fibers that it innervates. Length transducers [muscle spindles, Figure 4.6(a)] in the muscle activate sensory nerve fibers whose cell bodies are located in the dorsal root ganglion. These bipolar neurons send axonal projections to the spinal cord that divide into a descending and an ascending branch. The descending branch enters into a simple reflex arc with the motor neuron, whereas the ascending branch conveys information regarding current muscle length to higher centers in the CNS via ascending nerve fiber tracts in the spinal cord and brain stem. These ascending pathways are discussed in Section 4.8.

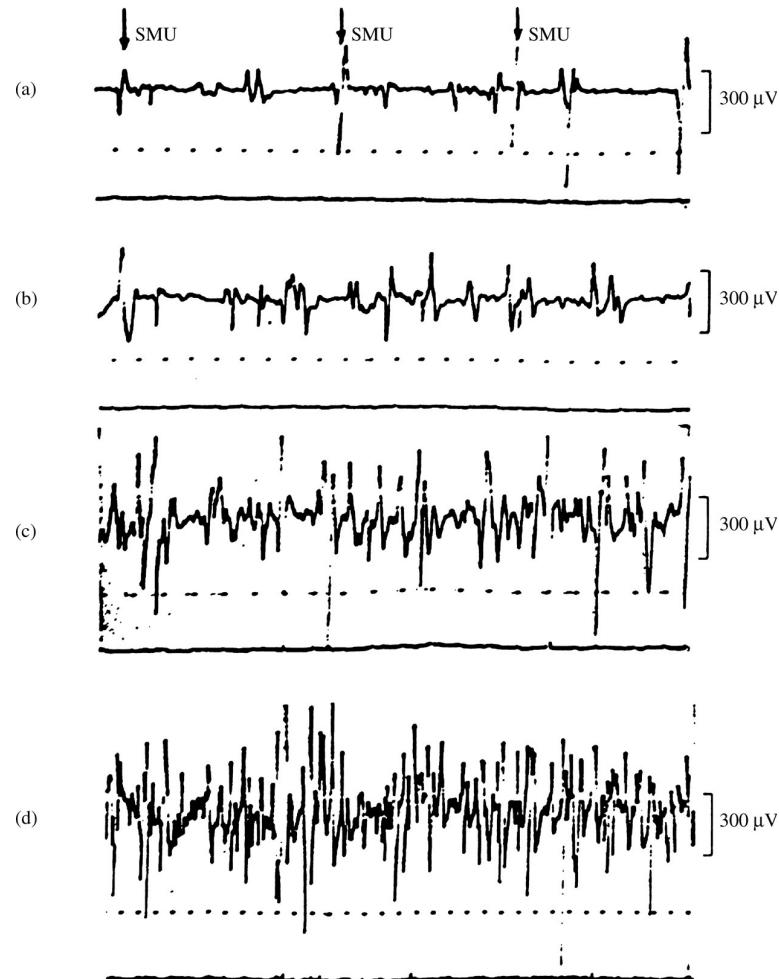
muscle fibers to which it is attached. The motor unit is the smallest unit that can be activated by a volitional effort, in which case all constituent muscle fibers are activated synchronously. The component fibers of the motor unit extend lengthwise in loose bundles along the muscle. In cross section, however, the fibers of a given motor unit are interspersed with fibers of other motor units. Thus, the active muscle fibers of the *single motor unit* (SMU) constitute a distributed bioelectric source located in a volume conductor that consists of all other fibers within the muscle (active and inactive), blood vessels and connective tissue. The evoked field potential from the active fibers of an SMU has a triphasic form of brief duration (3 to 15 ms) and an amplitude of 20 to 2000  $\mu\text{V}$ , depending on the size of the motor unit. The frequency of discharge usually varies from 6 to 30 per second (De Luca, 2006).

One of the disadvantages of recording the EMG by using the convenient surface electrodes is that they can be used only with superficial muscles and are sensitive to electrical activity over too wide an area. Various types of monopolar, bipolar, and multipolar insertion-type electrodes are commonly used in electromyography for recording from deep muscles and from SMUs. These types of electrodes generally record local activity from small regions within the muscle in which they are inserted. Often a simple fine-tipped monopolar needle electrode can be used to record SMU field potentials even during powerful voluntary contractions. Bipolar recordings are also employed. Various types of electrodes are discussed in Chapter 5.

Figure 4.11 shows motor unit potentials from the normal dorsal interosseus muscle under graded levels of contraction. At high levels of effort, many superimposed motor unit responses give rise to a complicated response (the *interference pattern*) in which individual units can no longer be distinguished. In interpreting Figure 4.11, note that when a muscle contracts progressively under volition, active motor units increase their rate of firing and new (previously inactive) motor units are also recruited.

The shape of SMU potentials is considerably modified by disease. In peripheral neuropathies, partial denervation of the muscle frequently occurs and is followed by regeneration. Regenerating nerve fibers conduct more slowly than healthy axons. In addition, in many forms of peripheral neuropathy, the excitability of the neurons is changed and there is widespread slowing of nerve conduction. One effect of this is that neural impulses are more difficult to initiate and take longer in transit to the muscle, generally causing scatter or desynchronization in the EMG pattern.

A number of mathematical modeling studies of single-fiber and multiple-fiber (single motor unit) action potentials have appeared in the literature (Nandedkar *et al.*, 1985; Ganapathy *et al.*, 1987), as well as detailed volume-conductor-based simulations of surface EMG signals (Duchêne and Hogrel, 2000; Farina *et al.*, 2004). Signal processing methods have been



**Figure 4.11** Motor unit action potentials from normal dorsal interosseus muscle during progressively more powerful contractions. (c) In the interference pattern, individual units can no longer be clearly distinguished. (d) Interference pattern during very strong muscular contraction. Time scale is 10 ms per dot. (From J. A. R. Lenman and A. E. Ritchie, *Clinical Electromyography*, 2nd ed., Philadelphia: Lippincott, 1977; reproduced by permission of the authors.)

employed in the analysis of surface EMGs and SMU signals (Reucher *et al.*, 1987; Farina *et al.*, 2003), as have automatic techniques for the detection, decomposition, and analysis of EMG signals (Mambrizo and De Luca, 1984; Stashuk 2001).

## 4.6 THE ELECTROCARDIOGRAM

### ANATOMY AND FUNCTION OF THE HEART

The heart serves as a four-chambered pump for the circulatory system (Figure 4.12). Its main pumping function is supplied by the ventricles. The atria are merely antechambers to store blood during the time the ventricles are pumping. The resting or filling phase of the heart cycle is referred to as *diastole*, whereas the contractile or pumping phase is called *systole*. The smooth, rhythmic contraction of the atria and ventricles has an underlying electrical precursor in the form of a well-coordinated series of electrical events that takes place within the heart. That this set of electrical events is intrinsic to the heart itself is well demonstrated when the heart (particularly that of cold-blooded vertebrates such as the frog or turtle) is removed from the body and placed in a nutrient medium (such as glucose-Ringer solution). The heart continues to beat rhythmically for many hours. Thus, the coordinated contraction of the atria and ventricles is set up by a specific pattern of electrical activation in the musculature of these structures. In humans, these electrical activation patterns in the walls of the atria and ventricles are initiated by a coordinated series of events within the *specialized conduction system* of the heart (Figure 4.12).

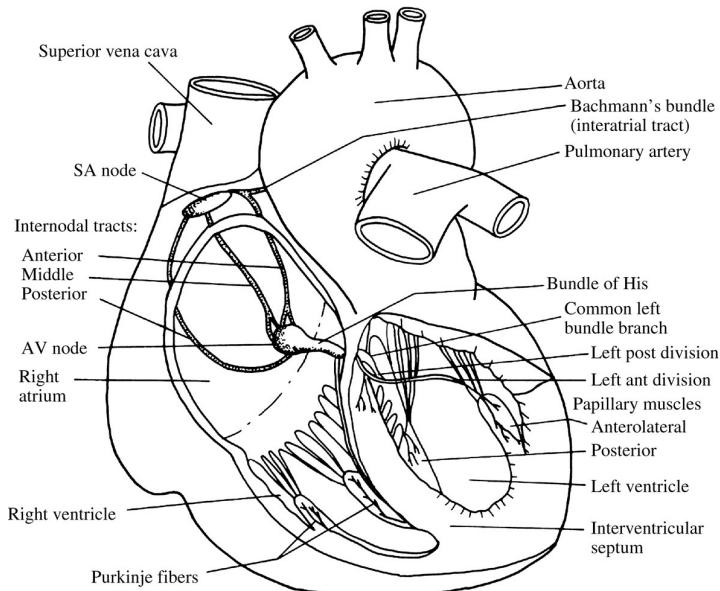
In relation to the heart as a whole, the specialized conduction system is very small and constitutes only a minute portion of the total mass of the heart. The wall of the left ventricle (Figure 4.12) is 2.5 to 3.0 times as thick as the right ventricular wall, and the intraventricular septum is nearly as thick as the left ventricular wall. Thus, the major portion of the muscle mass of the ventricles consists of the free walls of the right and left ventricles and the septum. Considering the heart as a bioelectric source, the source strength at each instant can be expected to be directly related to the active muscle mass at that moment (i.e., to the number of active myocardial cells). Hence, the active free walls of the atria and ventricles and the interventricular septum can be considered the major action current sources responsible for the production of external field potentials recorded from the heart (e.g., recorded within the thoracic volume-conductor medium or at the surface of the body).

### ELECTRICAL BEHAVIOR OF CARDIAC CELLS

The heart comprises several different types of tissues (SA and AV nodal tissue; atrial, Purkinje, and ventricular tissue). Representative cells of each type of tissue differ anatomically to a considerable degree. They are all electrically excitable, and each type of cell exhibits its own characteristic action potential (Figure 4.13).

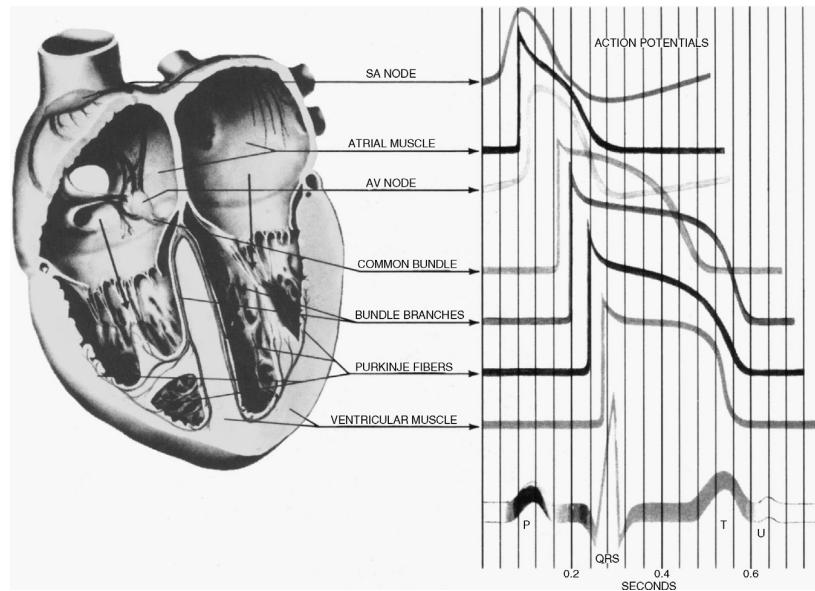
### THE VENTRICULAR CELL

The ventricular myocardium is composed of millions of individual cardiac cells ( $15 \times 15 \times 150 \mu\text{m}$  long). Figure 4.14 is a drawing of a small section of cardiac muscle as seen under light microscopy. The individual cells are relatively long



**Figure 4.12 Distribution of specialized conductive tissues in the atria and ventricles, showing the impulse-forming and conduction system of the heart** The rhythmic cardiac impulse originates in pacemaking cells in the sinoatrial (SA) node, located at the junction of the superior vena cava and the right atrium. Note the three specialized pathways (anterior, middle, and posterior internodal tracts) between the SA and atrioventricular (AV) nodes. Bachmann's bundle (interatrial tract) comes off the anterior internodal tract leading to the left atrium. The impulse passes from the SA node in an organized manner through specialized conducting tracts in the atria to activate first the right and then the left atrium. Passage of the impulse is delayed at the AV node before it continues into the bundle of His, the right bundle branch, the common left bundle branch, the anterior and posterior divisions of the left bundle branch, and the Purkinje network. The right bundle branch runs along the right side of the interventricular septum to the apex of the right ventricle before it gives off significant branches. The left common bundle crosses to the left side of the septum and splits into the anterior division (which is thin and long and goes under the aortic valve in the outflow tract to the anterolateral papillary muscle) and the posterior division (which is wide and short and goes to the posterior papillary muscle lying in the inflow tract). (From B. S. Lipman, E. Massie, and R. E. Kleiger, *Clinical Scalar Electrocardiography*. Copyright © 1972 by Yearbook Medical Publishers, Inc., Chicago. Used with permission.)

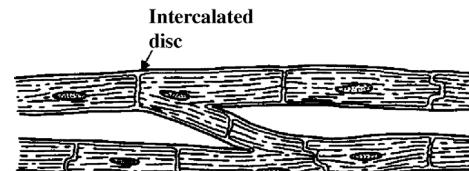
and thin, and although they run generally parallel to one another, there is considerable branching and interconnecting (*anastomosing*). The cells are surrounded by a plasma membrane that makes end-to-end contact with adjacent cells at a dense structure known as the *intercalated disk*



**Figure 4.13 Representative electric activity from various regions of the heart** The bottom trace is a scalar ECG, which has a typical QRS amplitude of 1 to 3 mV. (Copyright © 1969 CIBA Pharmaceutical Company, Division of CIBA-GEIGY Corp. Reproduced, with permission, from *The Ciba Collection of Medical Illustrations*, Frank H. Netter, M.D. All rights reserved.)

(Figure 4.14). Each fiber contains many contractile *myofibrils* that follow the axis of the cell from one end (intercalated disk) to the other. These myofibrils constitute the “contractile machinery” of the fiber. The component cells of cardiac tissue are in intimate contact at the intercalated disks, both electrically and mechanically, so the heart muscle functions as a unit (*a functional syncytium*).

Prior to excitation, the typical ventricular cell has a resting potential of approximately  $-85$  mV. The initial rapid depolarization phase has a rate of rise that is usually greater than  $150$  V/s. This phase is followed by an initial rapid repolarization that leads to a maintained depolarizing plateau region lasting approximately 200 to 300 ms. A final repolarization phase restores membrane potential to the resting level and is maintained for the remainder of the cardiac



**Figure 4.14 The cellular architecture of myocardial fibers** Note the centroid nuclei and transverse intercalated disks between cells.

cycle. The duration of the action potential waveform is collectively referred to as *electrical systole*; the resting phase is referred to as *electrical diastole*.

Most models of membrane excitability that have been used in cardiac electrophysiology are of the Hodgkin–Huxley (HH) type (Hodgkin and Huxley, 1952). The HH formalism was first applied to Purkinje fibers of the specialized conduction system by Noble (1962). This model was later extensively revised by McAllister *et al.* (1975), and variations have been used in simulations of the electrophysiological responses of ventricular (Beeler and Reuter, 1977) and SA pacemaker cells (Yanagihara *et al.*, 1980). These models however, were based on multicellular voltage clamp data that was approximate and contained experimental error. The discovery of (1) enzymatic dispersion techniques suitable for the production of isolated cardiac cells and (2) patch clamp electrode techniques made quantitative whole-cell voltage clamping of individual cells possible (early 1980s). Current–voltage characteristics of different types of ion channels could now be measured accurately and by the 1990s several good mathematical models of different cardiac cell types were available. Importantly, these models contained descriptions for ion pumps (e.g.,  $\text{Na}^+/\text{K}^+$  ATPase,  $\text{Ca}^{2+}$  ATPase) and exchangers (e.g.,  $\text{Na}^+–\text{Ca}^{2+}$ ,  $\text{Na}^+–\text{H}^+$  exchangers), as well as, better fluid compartment models describing ionic content of the internal medium, the sarcoplasmic reticulum (SR), and extracellular restricted diffusion spaces in the intra- and extracellular media. The seminal model initiating these extensive changes in cardiac cell modeling was the Purkinje fiber model developed by DiFrancesco and Noble (1985). It still utilized some ion channel data derived from multicellular voltage clamp experiments, but nevertheless pointed the way to the development of modern day cardiac cell models for all cell types: SA node (Wilders *et al.*, 1991; Demir *et al.*, 1994); atrial cell (Nygren *et al.*, 1998); ventricular cell (Luo and Rudy, 1994; Puglisi and Bers, 2001).

Clearly the P wave is produced by atrial depolarization, the QRS complex primarily by ventricular depolarization, and the T wave by ventricular repolarization. The manifestations of atrial repolarization are normally masked by the QRS complex. The P–R and S–T intervals are normally at zero potential, the P–R interval being caused mainly by conduction delay in the AV node. The S–T segment is related to the average duration of the plateau regions of individual ventricular cells. A small additional wave, called the U wave, is sometimes recorded temporally after the T wave. It is not always present and is believed to be the result of slow repolarization of ventricular papillary muscles.

Section 6.2 describes the 12 standard leads that constitute a diagnostic ECG, so they will not be considered further here.

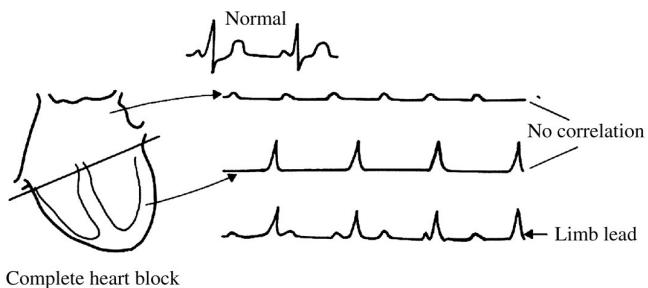
## NORMAL AND ABNORMAL CARDIAC RHYTHMS

Each beat of the normal human heart originates in the SA node. The normal heart rate is approximately 70 beats per minute (bpm). The rate is slowed (*bradycardia*) during sleep and is accelerated (*tachycardia*) by emotion, exercise, fever, and many other stimuli. Detailed aspects of the control that the nervous system has over heart rate are beyond the scope of this book; the reader interested in further discussion is referred to Rowell (1993). Because many parts of the heart possess an inherent rhythmicity (e.g., nodal tissue, Purkinje fibers of the specialized conduction system, and atrial tissues), any part under abnormal conditions can become the dominant cardiac pacemaker. This can happen when the activity of the SA node is depressed, when the bundle of His is interrupted or damaged, or when an abnormal (ectopic) focus or site in the atria or in specialized conduction-system tissue in the ventricles discharges at a rate faster than the SA node.

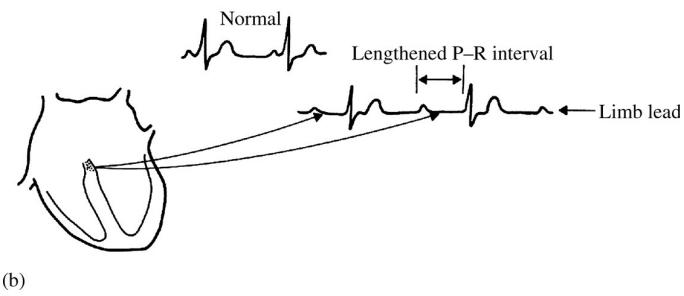
When the bundle of His is interrupted completely, the ventricles beat at their own slow inherent rate (the *idioventricular rhythm*). The atria continue to beat independently at the normal sinus rate, and complete or third-degree block is said to occur [Figure 4.17(a)]. The idioventricular rate in human beings is approximately 30 to 45 bpm.

When the His bundle is not completely interrupted, incomplete heart block is present. In the case of *first-degree heart block*, all atrial impulses reach the ventricles, but the P–R interval is abnormally prolonged because of an increase in transmission time through the affected region [Figure 4.17(b)]. In the case of *second-degree heart block*, not all atrial impulses are conducted to the ventricles. There may be, for example, one ventricular beat every second or third atrial beat (2:1 block, 3:1 block, and so on).

In another form of incomplete heart block involving the AV node, the P–R interval progressively lengthens until the atrial impulse fails to conduct to the ventricle (*Wenckebach phenomenon*). The first conducted beat after the pause (or dropped beat) has a shorter P–R interval (sometimes of normal length) than any subsequent P–R interval. Then the process of the lengthening of the P–R interval begins anew, progressing over several cardiac cycles until another



(a)



(b)

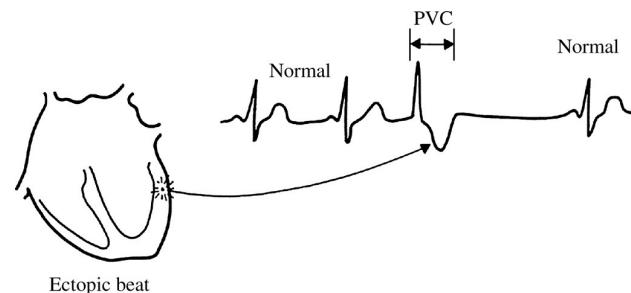
**Figure 4.17 Atrioventricular block** (a) Complete heart block. Cells in the AV node are dead and activity cannot pass from atria to ventricles. Atria and ventricles beat independently, ventricles being driven by an ectopic (other-than-normal) pacemaker. (b) AV block wherein the node is diseased (examples include rheumatic heart disease and viral infections of the heart). Although each wave from the atria reaches the ventricles, the AV nodal delay is greatly increased. This is first-degree heart block. (Adapted from Brendan Phibbs, *The Human Heart*, 3rd ed., St. Louis: The C.V. Mosby Company, 1975.)

beat is dropped. The electrocardiographic sequence starting with the ventricular pause and ending with the next blocked atrial beat constitutes a *Wenckebach period*. The ratio of the number of P waves to QRS complexes determines the block (for example, 6:5 or 5:4 Wenckebach periods).

When one branch of the bundle of His is interrupted, causing right- or left-bundle-branch block, excitation proceeds normally down the intact bundle and then sweeps back through the musculature to activate the ventricle on the blocked side. The ventricular rate is normal, but the QRS complexes are prolonged and deformed.

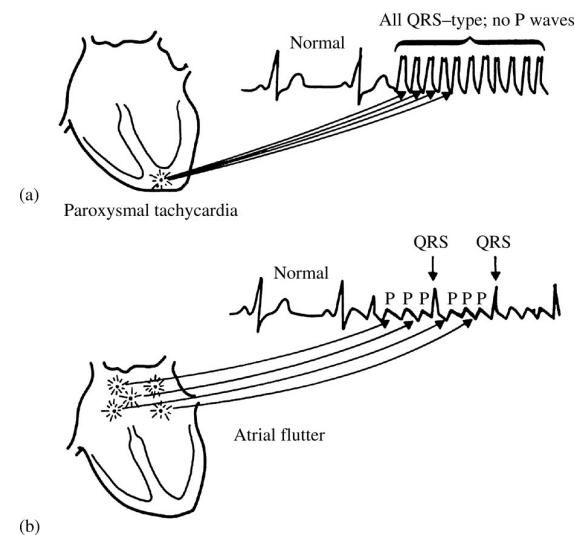
## ARRHYTHMIAS

A portion of the myocardium (or the AV node or specialized conduction system) sometimes becomes “irritable” and discharges independently. This site is then referred to as an *ectopic focus*. If the focus discharges only once, the result is a beat that occurs before the next expected normal beat, and the

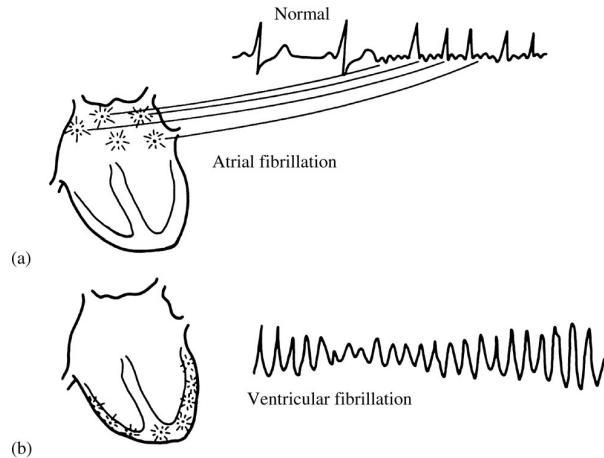


**Figure 4.18 Normal ECG followed by an ectopic beat** An irritable focus, or ectopic pacemaker, within the ventricle or specialized conduction system may discharge, producing an extra beat, or extrasystole, that interrupts the normal rhythm. This extrasystole is also referred to as a *premature ventricular contraction* (PVC). (Adapted from Brendan Phibbs, *The Human Heart*, 3rd ed., St. Louis: The C.V. Mosby Company, 1975.)

cardiac rhythm is therefore transiently interrupted. (With respect to atrial, nodal, or ventricular *ectopic beat*, see Figure 4.18.) If the focus discharges repetitively at a rate that exceeds that of the SA node, it produces rapid regular tachycardia. [With respect to atrial, nodal, or ventricular paroxysmal tachycardia or atrial flutter, see Figure 4.19(a) and (b).] A rapidly and irregularly discharging focus or, more likely, a group of foci in the atria or ventricles may



**Figure 4.19** (a) Paroxysmal tachycardia. An ectopic focus may repetitively discharge at a rapid regular rate for minutes, hours, or even days. (b) Atrial flutter. The atria begin a very rapid, perfectly regular “flapping” movement, beating at rates of 200 to 300 bpm. (Adapted from Brendan Phibbs, *The Human Heart*, 3rd ed., St. Louis: The C.V. Mosby Company, 1975.)



**Figure 4.20** (a) Atrial fibrillation. The atria stop their regular beat and begin a feeble, uncoordinated twitching. Concomitantly, low-amplitude, irregular waves appear in the ECG, as shown. This type of recording can be clearly distinguished from the very regular ECG waveform containing atrial flutter. (b) Ventricular fibrillation. Mechanically the ventricles twitch in a feeble, uncoordinated fashion with no blood being pumped from the heart. The ECG is likewise very uncoordinated, as shown. (Adapted from Brendan Phibbs, *The Human Heart*, 3rd ed., St. Louis: The C.V. Mosby Company, 1975.)

be the underlying mechanism responsible for atrial or ventricular fibrillation [Figure 4.20(a) and (b)].

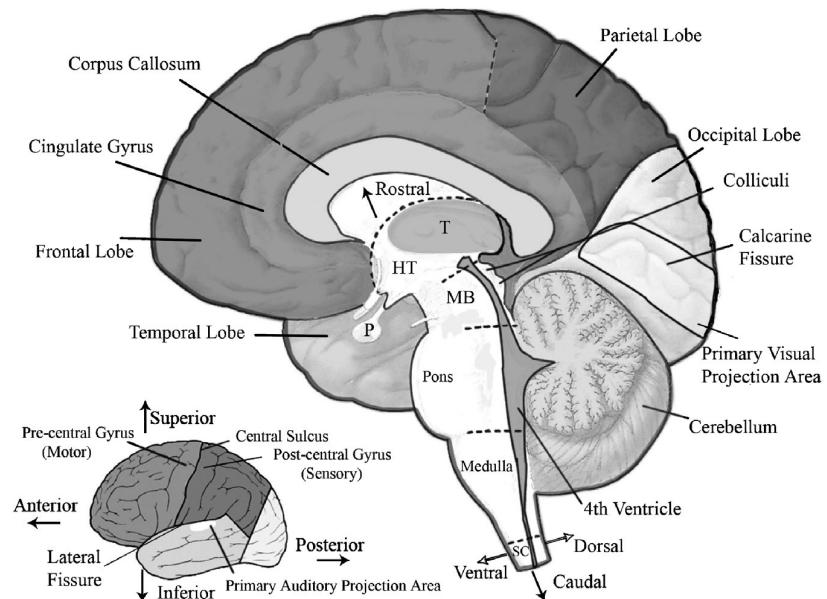
## 4.8 THE ELECTROENCEPHALogram

The background electrical activity of the brain in unanesthetized animals was described qualitatively in the nineteenth century, but it was first analyzed in a systematic manner by the German psychiatrist Hans Berger, who introduced the term *electroencephalogram* (EEG) to denote the potential fluctuations recorded from the brain. Conventionally, the electrical activity of the brain is recorded with three types of electrodes—scalp, cortical, and depth electrodes. When electrodes are placed on the exposed surface (cortex) of the brain, the recording is called an *electrocorticogram* (ECoG). Thin insulated needle electrodes of various designs may also be advanced into the neural tissue of the brain, in which case the recording is referred to as a *depth recording*. (There is surprisingly little damage to the brain tissue when electrodes of appropriate size are employed.) Whether obtained from the scalp, cortex, or depths of the brain, the recorded fluctuating potentials represent a superposition of the field potentials produced by a variety of active neuronal current generators within the volume-conductor medium. Unlike the relatively simple bioelectric source considered in Section 4.2 (the nerve trunk with its enclosed bundles of circular cylindrical nerve axons), the sources generating these field potentials are aggregates of neuronal elements with complex interconnections. The neuronal elements mentioned previously are the dendrites, cell bodies (somata), and axons of nerve cells. Moreover, the architecture of the neuronal brain tissue is not uniform from one location to another in the brain. Therefore, prior to undertaking any detailed study of electroencephalography, we first discuss necessary background information regarding (1) the gross anatomy and function of the brain, (2) the ultrastructure of the cerebral cortex, (3) the field potentials of single neurons leading to an interpretation of extracellular potentials recorded in the cerebral cortex, and (4) typical clinical EEG waveforms recorded via scalp electrodes. We shall then focus on the general volume-conductor problem in electroencephalography and briefly discuss abnormal EEG waveforms (Sherman and Walterspacher, 2006).

## INTRODUCTION TO THE ANATOMY AND FUNCTION OF THE BRAIN

The central nervous system (CNS) consists of the spinal cord lying within the bony vertebral column and its continuation, the brain, lying within the skull [Figure 4.24]. The brain is the greatly modified and enlarged portion of the CNS, surrounded by three protective membranes (the *meninges*) and enclosed within the cranial cavity of the skull. The spinal cord is likewise surrounded by downward continuations of the meninges, and it is encased within the protective bony vertebral column. Both brain and spinal cord are bathed in a special extracellular fluid called *cerebral spinal fluid* (CSF).

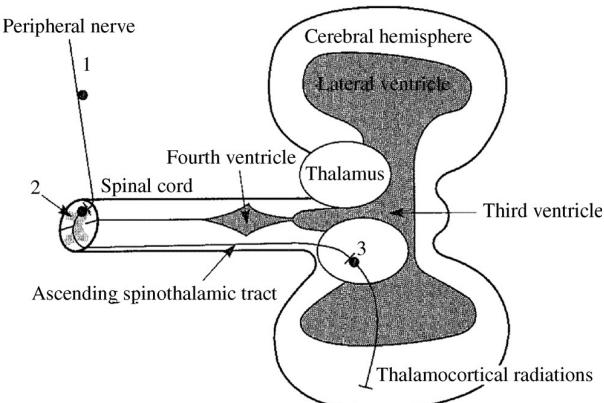
Division of the brain into three main parts—*cerebrum*, *brainstem*, and *cerebellum*—provides a useful basis for the study of brain localization and function (Figure 4.24). The brainstem (*medulla*, *pons*, *midbrain*, *diencephalon*) is the oldest part of the brain. It is actually a short extension of the spinal cord and



**Figure 4.24** Anatomical relationship of brainstem structures [medulla oblongata, pons, midbrain, and diencephalon (thalamus and hypothalamus)] to the cerebrum and cerebellum. General anatomic directions of orientation in the nervous system are superimposed on the diagrams. Here the terms *rostral* (toward head), *caudal* (toward tail), *dorsal* (back), and *ventral* (front) are associated with the brainstem; remaining terms are associated with the cerebrum. The terms *medial* and *lateral* imply nearness and remoteness, respectively, to or from the central midline axis of the brain. Symbols: T (thalamus), HT (hypothalamus), MB (midbrain), SC (spinal cord), P pituitary gland. (Adapted from John H. Martin, *Neuroanatomy: Text and Atlas*, 2nd ed., 1996, pp 14–15, with permission of Appleton and Lange, a Simon and Schuster Company.)

serves three major functions: (1) a connecting link between the cerebral cortex, spinal cord, and cerebellum; (2) an integrative center for several visceral functions (e.g., control of blood pressure and ventilation); and (3) an integration center for various motor reflexes. The *diencephalon* is the most superior portion of the brainstem; its chief component and largest structure is the *thalamus*. The thalamus serves as a major relay station and integration center for all of the general and special sensory systems, sending information to their respective cortical reception areas. It serves as the gateway to the cerebrum. Another major component of the diencephalon is the *hypothalamus*, which integrates functions of the autonomic nervous system and along with the pituitary gland, regulates functions of the thyroid, adrenal, and reproductive glands. The *cerebellum* is a coordinator in the voluntary (somatic) muscle system and acts in conjunction with the brainstem and cerebral cortex to maintain balance and provide harmonious muscle movements. The larger *cerebrum* occupies a special dominant position in the central nervous system, and conscious functions of the nervous system are localized within this structure.

Within the CNS there are *ascending (sensory)* nerve tracts that run from the spinal cord or brain stem to various areas of the brain, conveying information regarding changes in the external environment of the body that are reported by various peripheral biological sensors. There are a variety of such sensors, including the general sensors of temperature, pain, fine touch, pressure, as well as the special senses of vision, audition, equilibrium, taste, and olfaction. Figure 4.25 shows the basic plan associated with the general sense pathways from the periphery (e.g., skin, muscles) to the cortex. A three-neuron chain is involved in conveying information to the cortex where the *primary neuron* has its cell body in a ganglion outside the CNS and makes synaptic contact with a secondary neuron whose cell body is located in a nucleus within



**Figure 4.25** A simplified diagram of the CNS showing a typical general sense pathway from the periphery (neuron 1) to the brain (neuron 3). Note that the axon of the secondary neuron (neuron 2) in the pathway decussates (crosses) to the opposite side of the cord. Descending (motor) pathways are also crossed (see text).

either the spinal cord [e.g., the dorsal horn or the brain stem (Figure 4.25)]. Note from Figure 4.25 that the axon of the *secondary neuron* crosses (decussates) to the other side of the cord and joins a nerve fiber tract bound for the thalamus. The *tertiary neuron* in the pathway is located in a thalamic nucleus, and its axon travels in the *thalamocortical radiations* to the *postcentral gyrus*, which is located just posterior to the *central sulcus* [Figure 4.24 (inset)]. Thus, the postcentral gyrus is the cortical projection area for the general senses.

Neural pathways for the special senses, particularly audition and vision, follow the same general ground plan; however, there are notable deviations from the scheme depicted in Figure 4.25. Usually, more than three neurons are involved in the pathway and not all of the “secondary neurons” decussate. Most of the neurons cross to the opposite (contralateral) side of the body, however a significant number ascend to the thalamus on the same (ipsilateral) side of the body. The auditory and visual pathways have their own special thalamic relay centers—the medial and lateral geniculate bodies, respectively, as well as their own cortical projection areas (Figure 4.24).

Likewise, within the CNS there are *descending (motor)* nerve tracts that originate in various brain structures such as the cerebrum and cerebellum (Figure 4.24) and terminate ultimately on motor neurons in the ventral horn of the spinal cord (Figure 4.10). These motoneurons, in turn, control the contractile activity of the skeletal musculature. For example, the corticospinal tract is a bundle of axons from the primary motor cortex [precentral gyrus, Figure 4.24 (inset)], which projects directly to motor neurons in the spinal cord. Since the ascending general sensory pathways are crossed, the descending corticospinal tracts each cross to the opposite side of the body prior to making synaptic contact with the spinal motor neurons.

Thus, two-way communication links exist between the brain and spinal cord that allow higher centers in the brain to control or modify the behavior of the elemental spinal reflex arc at a given spinal level. By means of these links, the brain is not only informed of a peripheral event but can also modify the response of the spinal reflex to that environmental stimulus. Information is transmitted to the brain by means of a frequency-modulated train of nerve impulses that, upon reaching specific areas of the brain, stimulates the activity of resident neurons. Similarly, the decision to implement a motor action in response to the initial stimulus is manifested in the electrical activity of cortical neurons in specific areas of the brain [e.g., precentral gyrus (primary motor cortex); premotor cortex in frontal lobe]. The pattern of activity is specific to the type of motor action to be taken.

Electrical activity in either ascending or descending nerve fiber tracts may be represented to a first approximation by an action current dipole oriented in the direction of propagation (bioelectric source model). One should be aware that the properties (e.g., size, bulk conductivity) of the volume-conductor medium can change along the length of a particular fiber tract between the spinal cord and the cortex, and the volume-conductor model adopted should be based on the particular measurement considered. The volume-conductor-field potential solutions can be used to both fit and interpret body surface

potential measurements obtained clinically. Recording field potentials non-invasively from the relatively small volume of active nerve trunks, invariably requires the use of cumulative signal averaging techniques. In Figure 4.8, the median nerve was stimulated and compound action potentials were recorded from the subject’s forearm. Although not shown in this figure, sensory fibers in the median nerve thus activated, initiate activity in the general sense pathways to the brain. Averaged field potential recordings can be taken at a variety of points along the ascending pathways [e.g., from spinal cord and brain stem tracts taking note of the crossed nature of the pathway, and finally at the cortex itself (postcentral gyrus)]. The field potentials associated with long nerve tracts depends to a large extent on (a) whether the tract is straight or bent and (b) the resistance (geometry and specific conductivity) of the surrounding volume-conductor media.

This important subject is discussed later; however, for the present, these different types of averaged field potentials are called collectively *somatosensory evoked potentials*. The subject of nerve tracts has been discussed previously; however, the activity of both nuclei in the ascending pathway and clusters of cells in the cortex, depends not only on the ensemble of neurons there, but also on the geometry of the ensemble and the different types of synaptic connections involved.

Averaged sensory evoked potentials in response to brief auditory “clicks” or flashes of light are also routinely recorded as the auditory evoked response (AER) and the visual evoked response (VER), respectively (Jacobson, 1994; Heckenlively and Arden, 1991). Using an electromagnetic stimulating device held over the primary motor cortex (just anterior to the central sulcus), it is also possible to induce currents that activate the corticospinal tract, making possible the recording of averaged field potentials from the descending motor pathways (York, 1987; Geddes, 1987; Esselle and Stuchly, 1992). The same volume-conductor principles are applicable to the analysis of these different types of evoked potential recordings. The cerebrum is a paired structure, with right and left cerebral hemispheres, each relating to the opposite side of the body. That is, voluntary movements of the right hand are “willed” by the left cerebral hemisphere. The surface layer of the hemisphere is called the *cortex*; it receives sensory information from skin, eyes, ears, and other receptors located generally on the opposite side of the body. This information is compared with previous experience and produces movements in response to these stimuli.

Each hemisphere consists of several layers. The outer layer is a dense collection of nerve cells that appear gray in color when examined in a fresh state. It is consequently called *gray matter*. This outer layer, roughly 1 cm thick, is called the *cerebral cortex*. It has a highly convoluted surface consisting of *gyri* (ridges) and *sulci* (valleys), the deeper sulci being termed *fissures*. The deeper layers of the hemisphere (beneath the cortex) consist of myelinated *axons* (or white matter) and collections of cell bodies termed *nuclei*. Some of the integrative functions of the cerebrum can be localized within certain regions of the cortex; others are more diffusely distributed.

A major dividing landmark of the cerebral cortex is the lateral fissure [Figure 4.24], which runs on the lateral (side) surface of the brain from the open end in front, posteriorly and dorsally (backward and upward). The lateral fissure defines a side lobe of cortex inferior to (below) it that is called the *temporal lobe* [Figure 4.24 (inset)]. The superior (upper) part of this lobe contains the *primary auditory cortex*, which is the part of the cortex that receives auditory impulses via neural pathways leading from the auditory receptors in the inner ear.

The visual system is another example of the projection of the senses onto the cerebral cortex. The *occipital lobe* at the back of the head is the primary visual cortex. Light flashed into the eye evokes large electrical potentials from electrodes placed over this area of the cortex.

Another major landmark of the cerebral cortex is the central sulcus [Figure 4.24 (inset)]. However, it is not so prominent and unvarying an anatomical landmark as the lateral fissure. The central sulcus runs from the medial surface (surface along the midline of the brain) over the convexity of the hemisphere to the lateral fissure. It also represents the posterior border of the frontal lobe. The gyrus lying just anterior (forward) to the central sulcus is the *precentral gyrus*, which functions as the *primary motor cortex*. From this gyrus, nerve signals run down through the brainstem to the spinal cord for control of skeletal muscles via neural control of motoneurons in the ventral horn of the spinal cord (Figure 4.10). Lesions (destruction) of part of the precentral gyrus cause partial paralysis on the opposite side of the body.

Immediately posterior to the central sulcus [Fig. 24 (inset)] is the primary *somatosensory cortex*, the *postcentral gyrus*. This region receives impulses from all the general sense receptors from the skin (such as pressure, touch, and pain receptors). Each little area along this gyrus is related to a particular part of the body (for example, the legs on the medial end, the hand in the center, and the face on the end next to the lateral fissure). If a recording electrode is placed appropriately during a neurosurgical procedure, a cortical response can be evoked by tactile stimuli delivered to the *contralateral* (opposite) hand. Likewise, if a stimulus is applied through the same electrode, the subject reports a tingling sensation in the contralateral hand. Higher-order sensory discrimination, such as the ability to recognize a number drawn on the palm of the hand, is organized solely in the parietal lobe of which the postcentral gyrus is a part. Destruction of the parietal lobe results in a loss of this discriminative ability. For example, a subject may still know that he or she is being touched but cannot tell where or what is being drawn on the palm of the hand. The parietal lobe is also responsible for a person's awareness of the general position of the body and its limbs in space.

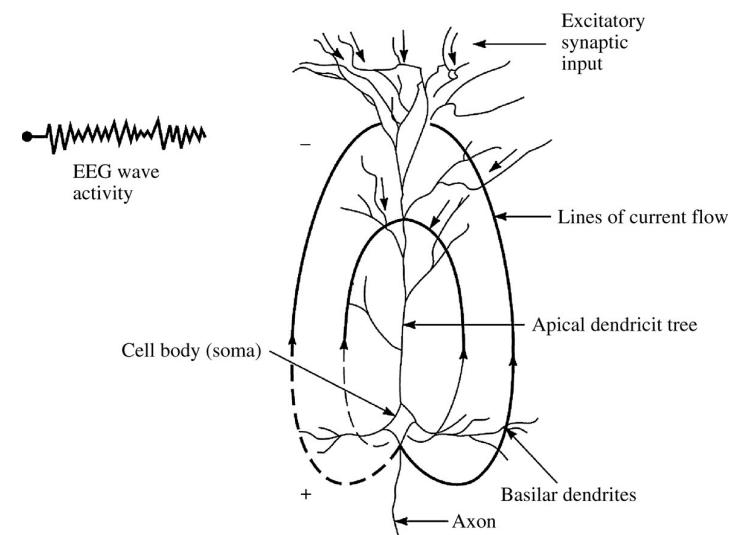
## ULTRASTRUCTURE OF THE CEREBRAL CORTEX

The functional part of the cerebrum is the cerebral cortex (bark, outer covering), a relatively thin layer of gray matter (1.5 to 4.0 mm in thickness) covering the outer surface of the cerebrum, including its intricate convolutions.

Because it is the most recent phylogenetic acquisition of the brain, the cerebral cortex has undergone a relatively greater development than other parts of the brain. The greatest advance in relative growth has been the neocortex, which is present on the superior and lateral aspects of the cerebral hemispheres. The distinctly different type of cortex located on the medial surface and base of the brain is known as the *paleocortex*. We shall use the term *cortex* in this chapter to refer specifically to the neocortex.

Cortical architectures in vertebrates share several common features: (1) stratified layers containing cell bodies and fiber bundles; (2) an outermost layer that lacks neurons (layer I); (3) at least one inner layer containing neurons that give rise to large dendrites, which rise vertically to layer I and travel in that layer forming multiple branches (arborization). The human cortex is generally arranged in six such cortical layers. The neurons are of two main types: *pyramidal* and *nonpyramidal* (many subtypes have been identified). There are also a large number of horizontally oriented layers of nerve fibers that extend between adjacent regions of the cortex, as well as vertically oriented bundles that extend from the cortex to more distant regions of the cortex or downward to the brainstem and spinal cord.

Figure 4.26 shows a schematic drawing of a typical cortical pyramidal cell. The bodies of this type of cell are commonly triangular in shape, with the base down and the apex directed toward the cortical surface. (Pyramidal



**Figure 4.26** Electrogenesis of cortical field potentials for a net excitatory input to the apical dendritic tree of a typical pyramidal cell. For the case of a net inhibitory input, polarity is reversed and the apical region becomes a source (+). Current flow to and from active fluctuating synaptic knobs on the dendrites produces wavelike activity. (See text.)

cell bodies vary greatly in size, from axial dimensions of  $15 \times 10 \mu\text{m}$  up to  $120 \times 90 \mu\text{m}$  or more for the giant pyramids of the motor cortex, which are called *Betz cells* after their discoverer.) These cells usually consist of the following parts: (1) a long apical dendrite (up to 2 mm in length) that ascends from the apex of the cell body through the overlaying cellular layers, and which frequently reaches and branches terminally within the outermost layer of the cortex; (2) dense dendritic arborization occurring at the base of the pyramid-shaped cell (largely horizontally—basilar dendrites); and (3) a single pyramidal cell axon which can emerge from the inner surface of the cortex as projection fibers to other areas of the cortex, or to other structures (e.g., the thalamus, cerebellum, or spinal cord). Frequently these axons send recurrent collateral (feedback) branches back on the cellular regions from which they sprang. Axons of some pyramidal cells turn back toward the cortical surface (never leaving the gray matter) to end via their many branches on the dendrites of other cells.

Nonpyramidal cells of the neocortex differ remarkably from pyramidal cells. Their cell bodies are small, and dendrites spring from them in all directions to ramify in the immediate vicinity of the cell. The axon may arise from a large dendrite; it commonly divides repeatedly to terminate on the cell bodies and dendrites of immediately adjacent cells. The axons of other nonpyramidal cells may turn upward toward the cortical surface, or they may leave the motor cortex (though this is not common).

For a detailed exposition of the various cells, layers, cellular interconnections, inputs, and outputs of the neocortex, see Kandel *et al.* (1991).

## BIOELECTRIC POTENTIALS FROM THE BRAIN

Unipolar recordings of the cortical surface potential relative to that of a remote reference potential may be viewed as a measurement of the integrated field potential at a boundary of a large volume conductor that contains an array of action current sources. Under normal conditions, action potentials conducted by axons in the cortical medium contribute very little to the integrated surface potential, since there are many axons in the cortex which run in many directions relative to the surface and which fire asynchronously. Consequently, their net spatial and temporal influence on the field potential at the surface is negligible. An exception occurs, of course, in the case of a response evoked by the simultaneous (synchronous) stimulation of a cortical input (e.g., direct electrical stimulation of thalamic nuclei or their afferent pathways, which project directly to the cortex via thalamocortical axons—the cortical input). These synchronous responses are called *evoked potentials*, and they are of relatively large amplitude. Synchronicity of the underlying fiber and cortical neuron activity is a major factor influencing surface potential magnitude. Unipolar field potentials recorded within the cortical layers have shown that the cortical surface potential is largely due to the net effect of local postsynaptic potentials of cortical cells (Figure 4.26). These may be of either sign (excitatory or inhibitory) and may occur directly underneath the electrode

or at some distance from it. A potential change recorded at the surface is a measure of the net potential (current resistance  $iR$ ) drop between the surface site and the distant reference electrode. It is obvious, however, that if all the cell bodies and dendrites of cortical cells were randomly arranged in the cortical medium, the net influence of synaptic currents would be zero. This would result in a “closed field” situation that produces relatively small far-field potentials (Lorente de No, 1947). Thus, any electrical change recorded at the surface must be due to the orderly and symmetric arrangement of some class of cells within the cortex.

Pyramidal cells of the cerebral cortex are oriented vertically, with their long apical dendrites running parallel to one another. Potential changes in one part of the cell relative to another part create “open” potential fields in which current may flow and potential differences can be measured at the cortical surface. Figure 4.26 illustrates this concept in diagrammatic fashion. Synaptic inputs to the apical dendritic tree cause depolarization of the dendritic membrane. As a result, subthreshold current flows in a closed path through the cytoplasmic core of the dendrites and cell body of the pyramidal cell, returning ultimately to the surface synaptic sites via the extracellular bathing medium. From the indicated direction of the lines of current flow, the extracellular medium about the soma behaves as a *source* (+), while the upper part of the apical dendritic tree behaves as a *sink* (−).

The influence of a particular dendritic *postsynaptic potential* (PSP) on the cortical surface recording depends on its sign [excitatory (−) or inhibitory (+)] and on its location relative to the measurement site. The effect of each PSP may be regarded as creating a radially oriented current dipole. Therefore, continuing synaptic input creates a series of potential dipoles and resulting current flows that are staggered but overlapped in space and time. Surface potentials of any form can be generated by one population of presynaptic fibers and the cells on which they terminate, depending on the proportion that are inhibitory or excitatory, the level of the postsynaptic cells in the cortex, and so forth.

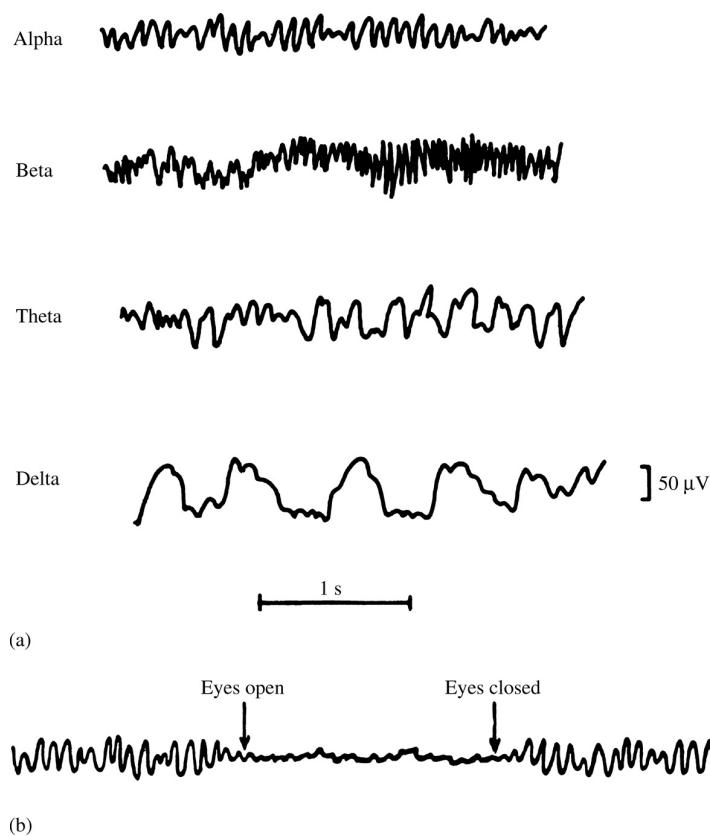
Nonpyramidal cells in the neocortex, on the other hand, are unlikely to contribute substantially to surface records. Their spatially restricted dendritic trees are radially arranged around their cell bodies such that charge differences between the dendrites and the cell body produce fields of current flow that sum to zero when viewed from a relatively great distance on the cortical surface (closed-field situation).

Thus, to summarize, the apical dendrites of pyramidal cells constitute a meshwork of similarly oriented, densely packed units in the outer layers of the cortex. As multiple synaptic endings on the dendritic tree of each cell become active, current can flow in either direction between the dendritic process depending on whether the synapses are excitatory or inhibitory. The source–sink relationship between dendrite and cell is that of a constantly shifting current dipole, where variations in dipole orientation and strength produce wavelike fluctuations in the surface field potential (Figure 4.26). When the sum of dendritic activity is negative relative to the cell, the cell

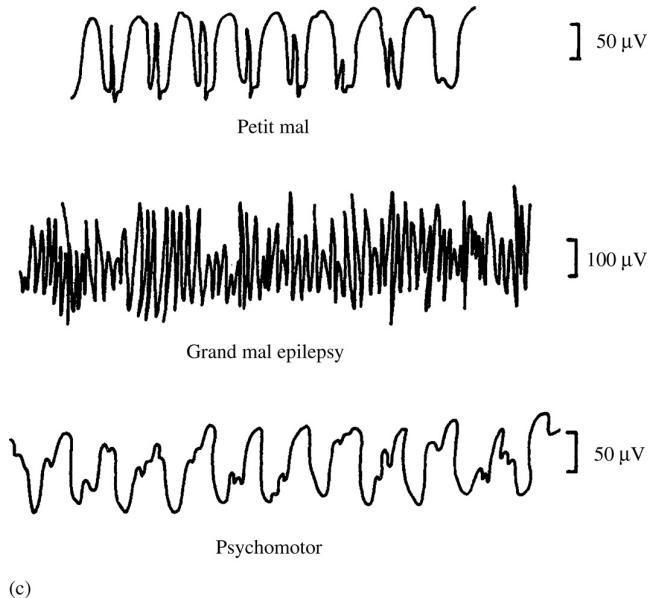
is depolarized and quite excitable. When it is positive, the cell is hyperpolarized and less excitable.

## RESTING RHYTHMS OF THE BRAIN

Electric recordings from the exposed surface of the brain or from the outer surface of the head demonstrate continuous oscillating electric activity within the brain. Both the intensity and the patterns of this electric activity are determined to a great extent by the overall excitation of the brain resulting from functions in the brainstem reticular activating system (RAS). The undulations in the recorded electric potentials (Figure 4.27) are called *brain waves*, and the entire record is called an *electroencephalogram* (EEG).



**Figure 4.27** (a) Different types of normal EEG waves. (b) Replacement of alpha rhythm by an asynchronous discharge when patient opens eyes. (c) Representative abnormal EEG waveforms in different types of epilepsy. (From A. C. Guyton, *Structure and Function of the Nervous System*, 2nd ed., Philadelphia: W.B. Saunders, 1972; used with permission.)



**Figure 4.27** (Continued)

The intensities of the brain waves on the surface of the brain (recorded relative to an indifferent electrode such as the earlobe) may be as large as 10 mV, whereas those recorded from the scalp have a smaller amplitude of approximately 100 µV. The frequencies of these brain waves range from 0.5 to 100 Hz, and their character is highly dependent on the degree of activity of the cerebral cortex. For example, the waves change markedly between states of wakefulness and sleep. Much of the time, the brain waves are irregular, and no general pattern can be observed. Yet at other times, distinct patterns do occur. Some of these are characteristic of specific abnormalities of the brain, such as epilepsy (discussed later). Others occur in normal persons and may be classified as belonging to one of four wave groups (*alpha*, *beta*, *theta*, and *delta*), which are shown in Figure 4.27(a).

Alpha waves are rhythmic waves occurring at a frequency between 8 and 13 Hz. They are found in EEGs of almost all normal persons when they are awake in a quiet, resting state of cerebration. These waves occur most intensely in the occipital region but can also be recorded, at times, from the parietal and frontal regions of the scalp. Their voltage is approximately 20 to 200 µV. When the subject is asleep, the alpha waves disappear completely. When the awake subject's attention is directed to some specific type of mental activity, the alpha waves are replaced by asynchronous waves of higher frequency but lower amplitude. Figure 4.27(b) demonstrates the effect on the alpha waves of simply opening the eyes in bright light and then closing them again. Note that the visual sensations cause immediate cessation of the alpha waves; these are replaced by low-voltage, asynchronous waves.

Beta waves normally occur in the frequency range of 14 to 30 Hz, and sometimes—particularly during intense mental activity—as high as 50 Hz. These are most frequently recorded from the parietal and frontal regions of the scalp. They can be divided into two major types: beta I and beta II. The beta I waves have a frequency about twice that of the alpha waves. They are affected by mental activity in much the same way as the alpha waves (they disappear and in their place appears an asynchronous, low-voltage wave). The beta II waves, on the other hand, appear during intense activation of the central nervous system and during tension. Thus one type of beta activity is elicited by mental activity, whereas the other is inhibited by it.

Theta waves have frequencies between 4 and 7 Hz. These occur mainly in the parietal and temporal regions in children, but they also occur during emotional stress in some adults, particularly during periods of disappointment and frustration. For example, they can often be brought about in the EEG of a frustrated person by allowing the person to enjoy some pleasant experience and then suddenly removing the element of pleasure. This causes approximately 20 s of theta waves.

Delta waves include all the waves in the EEG below 3.5 Hz. Sometimes these waves occur only once every 2 or 3 s. They occur in deep sleep, in infancy, and in serious organic brain disease. They can also be recorded from the brains of experimental animals that have had subcortical transections producing a functional separation of the cerebral cortex from the reticular activating system. Delta waves can thus occur solely within the cortex, independent of activities in lower regions of the brain.

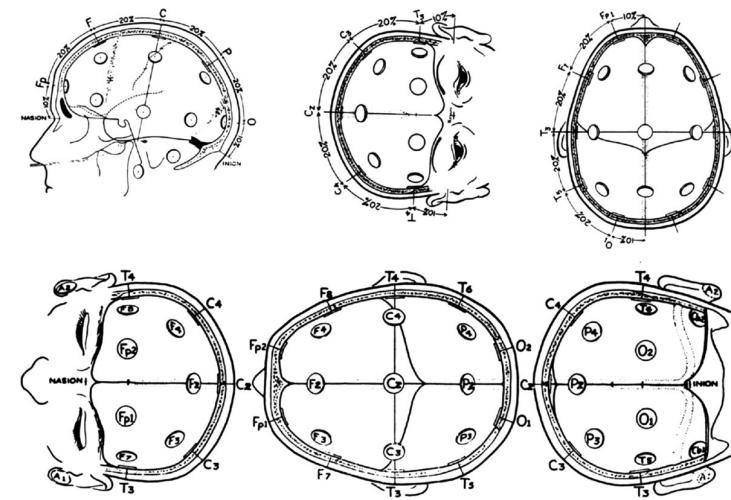
A single cortical cell can give rise only to small extracellular current, so large numbers of neurons must be synchronously active to give rise to the potentials recorded from the cerebral surface. The individual waves of the EEG are of long duration (for example, 30 to 500 ms), and one might well ask how they are produced. They can be long-lasting depolarizations of the cell membranes (for example, of the apical dendrites of pyramidal cells) or a summation of a number of shorter responses. In any event, a sufficiently large number of neurons must discharge together to give rise to these cortical potentials. The term *synchronization* is used to describe the underlying process that acts to bring a group of neurons into unified action. Synaptic interconnections are generally thought to bring about synchronization, although extracellular field interaction between

cells has been proposed as a possible mechanism. Rhythmically firing neurons are very sensitive to voltage gradients in their surrounding medium.

Besides the synchronization required for each wave of resting EEG, the series of repeated waves suggests a rhythmic and a trigger or pacemaker process that initiates such rhythmic action. By means of knife cuts below the intact connective-tissue covering (*meningeal layer or pia matter*) of the brain, one may prepare *chronic islands* of cortex—with all neuronal connections cut, but with the blood supply via surface vessels intact. Only a low level of EEG activity remains in such islands. Though the isolated islands of cortex may not show spontaneous EEG activity, they still have the ability to respond rhythmically, which may be readily demonstrated by the rhythmic responses that are elicited by applying a single electrical stimulus. The inference is that various regions of the cortex, though capable of exhibiting rhythmic activity, require trigger inputs to excite rhythmicity. The RAS, mentioned earlier, appears to provide this pacemaker function.

## THE CLINICAL EEG

The system most often used to place electrodes for monitoring the clinical EEG is the International Federation 10-20 system shown in Figure 4.28. This system uses certain anatomical landmarks to standardize placement of EEG electrodes. The representation of the EEG channels is referred to as a *montage*. In the bipolar montage, each channel measures the difference between two adjacent electrodes. In the referential montage, each channel



**Figure 4.28** The 10-20 electrode system This system is recommended by the International Federation of EEG Societies. [From H. H. Jasper, "The ten-twenty electrode system of the International Federation in Electroencephalography and Clinical Neurophysiology." *EEG Journal*, 1958, 10 (Appendix), 371–375.]

measures the difference between one electrode and a reference electrode, such as on the ear. In the average reference montage, each channel measures the difference between one electrode and the average of all other electrodes. In the Laplacian montage, each channel measures the difference between one electrode and a weighted average of the surrounding electrodes. The differential amplifier requires a separate ground electrode plus differential inputs to the electrode connections. The advantage of using a differential recording between closely spaced electrodes (between successive pairs in the standard system, for example) is cancellation of far-field activity common to both electrodes; one thereby obtains sharp localization of the response. Although the same electric events are recorded in each of the ways, they appear in a different format in each case. The potential changes that occur are amplified by high-gain, differential, capacitively coupled amplifiers. The output signals are recorded and displayed.

In the routine recording of clinical EEGs, the input electrodes are a problem. They must be small, they must be easily affixed to the scalp with minimal disturbance of the hair, they must cause no discomfort, and they must remain in place for extended periods of time. Technicians prepare the surface of the scalp, degrease the recording area by cleaning it with alcohol, apply a conducting paste, and glue nonpolarizable Ag/AgCl electrodes to the scalp with a glue (collodion) and hold them in place with rubber straps, or use a rubber cap that contains all electrodes.

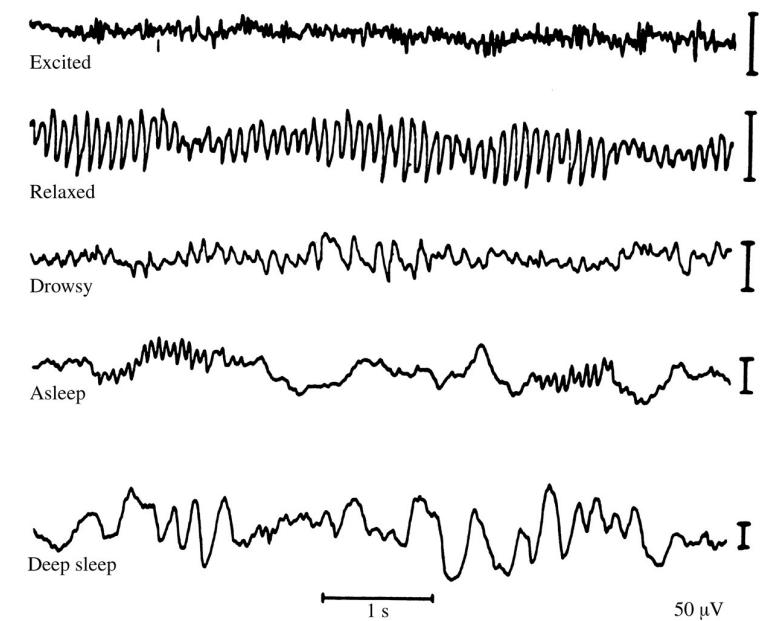
The EEG is usually recorded with the subject awake but resting recumbent on a bed with eyes closed. With the patient relaxed in such a manner, artifacts from electrode-lead movement are significantly reduced, as are contaminating signals from the scalp. Muscle activity from the face, neck, ears, and so on is perhaps the most subtle contaminant of EEG records in the recording of both spontaneous ongoing activity in the brain and activity evoked by a sensory stimulus (*evoked response*). For example, the frequency spectrum of the field produced by mildly contracted facial muscles contains frequency components well within the nominal EEG range (0.5 to 100 Hz). After technicians have achieved resting, quiescent conditions in the normal adult subject, the subject's scalp recordings show a dominant alpha rhythm in the parietal-occipital areas, whereas in the frontal areas, there is a low-amplitude, higher-frequency beta rhythm in addition to the alpha rhythm. In the normal subject there is symmetry between the recordings of the right and left hemispheres. There can be a wide range of EEG measurement artifacts.

In general there is a relationship between the degree of cerebral activity and the average frequency of the EEG rhythm: The frequency increases progressively with higher and higher degrees of activity. For example, delta waves are frequently found in stupor, surgical anesthesia, and sleep; theta waves in infants; alpha waves during relaxed states; and beta waves during intense mental activity. However, during periods of mental activity, the waves usually become asynchronous rather than synchronous, so that the magnitude of the summed surface potential recording decreases despite increased cortical activity.

## SLEEP PATTERNS

When an individual in a relaxed, inattentive state becomes drowsy and falls asleep, the alpha rhythm is replaced by slower, larger waves (Figure 4.29). In deep sleep, very large, somewhat irregular delta waves are observed. Interspersed with these waves—during moderately deep sleep—are bursts of alpha-like activity called *sleep spindles*. The alpha rhythm and the patterns of the drowsy and sleeping subject are *synchronized*, in contrast with the low-voltage *desynchronized*, irregular activity seen in the subject who is in an alert state.

The high-amplitude, slow waves seen in the EEG of a subject who is asleep are sometimes replaced by rapid, low-voltage irregular activity resembling that obtained in alert subjects. However, the sleep of a subject with this irregular pattern is not interrupted; in fact, the threshold for arousal by sensory stimuli is elevated. This condition has therefore come to be called *paradoxical sleep*. During paradoxical sleep, the subject exhibits rapid, roving eye movements. For this reason, it is also called *rapid-eye-movement sleep*, or REM sleep. Conversely, *spindle* or synchronized sleep is frequently called *nonrapid-eye-movement* (NREM), or slow-wave sleep.



**Figure 4.29** The electroencephalographic changes that occur as a human subject goes to sleep. The calibration marks on the right represent 50  $\mu$ V. (From H. H. Jasper, "Electrocephalography." In *Epilepsy and Cerebral Localization*, W. G. Penfield and T. C. Erickson (eds.). Springfield, IL: Charles C. Thomas, 1941.)

Grand mal epilepsy is characterized by extreme discharges of neurons originating in the brainstem portion of the RAS. These discharges then spread throughout the cortex, to the deeper parts of the brain, and even to the spinal cord to cause generalized tonic convulsions of the entire body. They are followed near the end of the attack by alternating muscular contractions, called *clonic convulsions*. The grand mal seizure lasts from a few seconds to as long as 3 to 4 min and is characterized by postseizure depression of the entire nervous system. The subject may remain in a stupor for 1 min to as long as a day or more after the attack is over.

The middle recording in Figure 4.27(c) shows a typical EEG during a grand mal attack. This response can be recorded from almost any region of the cortex. The recorded potential is of a high magnitude, and the response is synchronous, with the same periodicity as normal alpha waves. The same type of discharge occurs on both sides of the brain at the same time, indicating that the origin of the abnormality is in the lower centers of the brain that control the activity of the cerebral cortex, not in the cortex itself. Electrical recordings from the thalamus and reticular formation of experimental animals during an induced grand mal attack indicate typical high-voltage synchronous activity in these areas, similar to that recorded from the cerebral cortex. Experiments on animals have further shown that a grand mal attack is caused by intrinsic hyperexcitability of the neurons that make up the RAS structures or by some abnormality of the local neural pathways of this system.

Petit mal epilepsy is closely allied to grand mal epilepsy. It occurs in two forms, the *myoclonic* form and the *absence* form. In the myoclonic form, a burst of neuronal discharges, lasting a fraction of a second, occurs throughout the nervous system. These discharges are similar to those that occur at the beginning of a grand mal attack. The person exhibits a single violent muscular jerk involving arms or head. The entire process stops immediately, however, and the attack is over before the subject loses consciousness or stops what he or she is doing. This type of attack often becomes progressively more severe until the subject experiences a grand mal attack. Thus the myoclonic form of petit mal is similar to a grand mal attack, except that some form of inhibitory influence promptly stops it.

The absence type of petit mal epilepsy is characterized by 5 to 20 s of unconsciousness, during which the subject has several twitchlike contractions of the muscles, usually in the head region. There is a pronounced blinking of the eyes, followed by a return to consciousness and continuation of previous activities. This type of epilepsy is also closely allied to grand mal epilepsy. In rare instances, it can initiate a grand mal attack.

Figure 4.27(c) shows a typical *spike-and-dome* pattern that is recorded during the absence type of petit mal epilepsy. The spike portion of the record is almost identical to the spikes occurring in grand mal epilepsy, but the dome portion is distinctly different. The spike-and-dome pattern can be recorded over the entire cortex, illustrating again that the seizure originates in the RAS.

Partial epilepsy can involve almost any part of the brain, either localized regions of the cerebral cortex or deeper structures of both the cerebrum and

## THE ABNORMAL EEG

One of the more important clinical uses of the EEG is in the diagnosis of different types of epilepsy and in the location of the focus in the brain causing the epilepsy. Epilepsy is characterized by uncontrolled excessive activity by either a part or all of the CNS. A person predisposed to epilepsy has attacks when the basal level of excitability of all or part of the nervous system rises above a certain critical threshold. However, as long as the degree of excitability is held below this threshold, no attack occurs.

There are two basic types of epilepsy, *generalized epilepsy* and *partial epilepsy*. Generalized epilepsy involves the entire brain at once, whereas partial epilepsy involves a portion of the brain—sometimes only a minute focal spot and at other times a fair amount of the brain. Generalized epilepsy is further divided into *grand mal* and *petit mal* epilepsy.

brainstem. Partial epilepsy almost always results from some organic lesion of the brain, such as a scar that pulls on the neuronal tissue, a tumor that compresses an area of the brain, or a destroyed region of the brain tissue. Lesions such as these can cause local neurons to fire very rapid discharges. When the rate exceeds approximately 1000/s, synchronous waves begin spreading over adjacent cortical regions. These waves presumably result from the activity of localized reverberating neuronal circuits that gradually recruit adjacent areas of the cortex into the “discharge,” or firing, zone. The process spreads to adjacent areas at rates as slow as a few millimeters per minute to as fast as several centimeters per minute. When such a wave of excitation spreads over the motor cortex, it causes a progressive “march” of muscular contractions throughout the opposite side of the body, beginning perhaps in the leg region and marching progressively upward to the head region, or at other times marching in the opposite direction. This is called *Jacksonian epilepsy* or *Jacksonian march*.

Another type of partial epilepsy is the so-called *psychomotor seizure*, which may cause (1) a short period of amnesia, (2) an attack of abnormal rage, (3) sudden anxiety or fear, (4) a moment of incoherent speech or mumbling, or (5) a motor act of rubbing the face with the hand, attacking someone, and so forth. Sometimes the person does not remember his or her activities during the attack; at other times the person is completely aware of, but unable to control, his or her behavior. The bottom tracing of Figure 4.27(c) represents a typical EEG during a psychomotor seizure showing a low-frequency rectangular-wave response with a frequency between 2 and 4 Hz with superimposed 14 Hz waves.

The EEG frequently can be used to locate tumors and also abnormal spiking waves originating in diseased brain tissue that might predispose to epileptic attacks. Once such a focal point is found, surgical excision of the focus often prevents future epileptic seizures.

The EEG is also used to monitor the depth of anesthesia.

The EEG is also used as a brain–computer interface to enable disabled persons to communicate with a computer.

## Biopotential Amplifiers

Amplifiers are an important part of modern instrumentation systems for measuring biopotentials. Such measurements involve voltages that often are at low levels, have high source impedances, or both. Amplifiers are required to increase signal strength while maintaining high fidelity. Amplifiers that have been designed specifically for this type of processing of biopotentials are known as *biopotential amplifiers*. In this chapter we examine some of the basic features of biopotential amplifiers and also look at specialized systems.

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### 6.1 BASIC REQUIREMENTS

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The essential function of a biopotential amplifier is to take a weak electric signal of biological origin and increase its amplitude so that it can be further processed, recorded, or displayed. Usually such amplifiers are in the form of voltage amplifiers, because they are capable of increasing the voltage level of a signal. Nonetheless, voltage amplifiers also serve to increase power levels, so they can be considered power amplifiers as well. In some cases, biopotential amplifiers are used to isolate the load from the source. In this situation, the amplifiers provide only current gain, leaving the voltage levels essentially unchanged.

To be useful biologically, all biopotential amplifiers must meet certain basic requirements. They must have high input impedance, so that they provide minimal loading of the signal being measured. The characteristics of biopotential electrodes can be affected by the electric load they see, which, combined with excessive loading, can result in distortion of the signal. Loading effects are minimized by making the amplifier input impedance as high as possible, thereby reducing this distortion. Modern biopotential amplifiers have input impedances of at least  $10\text{ M}\Omega$ .

The input circuit of a biopotential amplifier must also provide protection to the organism being studied. Any current or potential appearing across the amplifier input terminals that is produced by the amplifier is capable of affecting the biological potential being measured. In clinical systems, electric currents from the input terminals of a biopotential amplifier can result in

microshocks or macroshocks in the patient being studied—a situation that can have grave consequences. To avoid these problems, the amplifier should have isolation and protection circuitry, so that the current through the electrode circuit can be kept at safe levels and any artifact generated by such current can be minimized.

The output circuit of a biopotential amplifier does not present so many critical problems as the input circuit. Its principal function is to drive the amplifier load, usually an indicating or recording device, in such a way as to maintain maximal fidelity and range in this readout. Therefore, the output impedance of the amplifier must be low with respect to the load impedance, and the amplifier must be capable of supplying the power required by the load.

Biopotential amplifiers must operate in that portion of the frequency spectrum in which the biopotentials that they amplify exist. Because of the low level of such signals, it is important to limit the bandwidth of the amplifier so that it is just great enough to process the signal adequately. In this way, we can obtain optimal signal-to-noise ratios (SNRs). Biopotential signals usually have amplitudes of the order of a few millivolts or less. Such signals must be amplified to levels compatible with recording and display devices. This means that most biopotential amplifiers must have high gains—of the order of 1000 or greater.

Very frequently biopotential signals are obtained from bipolar electrodes. These electrodes are often symmetrically located, electrically, with respect to ground. Under such circumstances, the most appropriate biopotential amplifier is a differential one. Because such bipolar electrodes frequently have a common-mode voltage with respect to ground that is much larger than the signal amplitude, and because the symmetry with respect to ground can be distorted, such biopotential differential amplifiers must have high common-mode-rejection ratios to minimize interference due to the common-mode signal.

A final requirement for biopotential amplifiers that are used both in medical applications and in the laboratory is that they make quick calibration possible. In recording biopotentials, the scientist and clinician need to know not only the waveforms of these signals but also their amplitudes. To provide this information, the gain of the amplifier must be well calibrated. Frequently biopotential amplifiers have a standard signal source that can be momentarily connected to the input, automatically at the start of a measurement or manually at the push of a button, to check the calibration. Biopotential amplifiers that need to have adjustable gains usually have a switch by which different, carefully calibrated fixed gains can be selected, rather than having a continuous control (such as the volume control of an audio amplifier) for adjusting the gain. Thus the gain is always known, and there is no chance of its being accidentally varied by someone bumping the gain control.

Biopotential amplifiers have additional requirements that are application-specific and that can be ascertained from an examination of each application. To illustrate some of these, let us first consider the electrocardiogram (ECG), the most frequently used application of biopotential amplifiers.

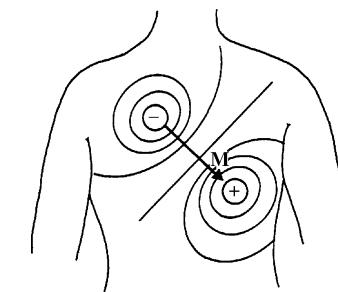
## 6.2 THE ELECTROCARDIOGRAPH

To learn more about biopotential amplifiers, we shall examine a typical clinical electrocardiograph. First, let us review the ECG itself.

### THE ECG

As we learned in Section 4.6, the beating heart generates an electric signal that can be used as a diagnostic tool for examining some of the functions of the heart. This electric activity of the heart can be approximately represented as a vector quantity. Thus we need to know the location at which signals are detected, as well as the time dependence of the amplitude of the signals. Electrocardiographers have developed a simple model to represent the electric activity of the heart. In this model, the heart consists of an electric dipole located in the partially conducting medium of the thorax. Figure 6.1 shows a typical example. Of course in reality the heart is a much more complicated electrophysiological entity, and far more complex models are needed to represent it.

This particular field and the dipole that produces it represent the electric activity of the heart at a specific instant. At the next instant the dipole can change its magnitude and its orientation, thereby causing a change in the electric field. Once we accept this simplified model, we need not draw a field plot every time we want to discuss the dipole field of the heart. Instead, we can represent it by its dipole moment, a vector directed from the negative charge to the positive charge and having a magnitude proportional to the amount of charge (either positive or negative) multiplied by the separation of the two charges. In electrocardiography this dipole moment, known as the *cardiac vector*, is represented by  $\mathbf{M}$ , as shown in Figure 6.1. As we progress through a cardiac cycle, the magnitude and direction of  $\mathbf{M}$  vary because the dipole field varies.



**Figure 6.1 Rough sketch of the dipole field of the heart when the R wave is maximal** The dipole consists of the points of equal positive and negative charge separated from one another and denoted by the dipole moment vector  $\mathbf{M}$ .

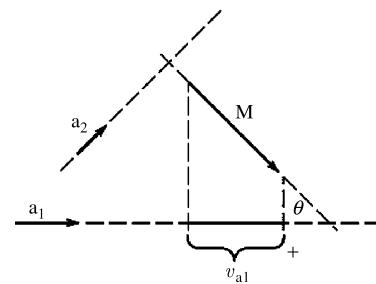
The electric potentials generated by the heart appear throughout the body and on its surface. We determine potential differences by placing electrodes on the surface of the body and measuring the voltage between them, being careful to draw little current (ideally there should be no current at all, because current distorts the electric field that produces the potential differences). If the two electrodes are located on different equal-potential lines of the electric field of the heart, a nonzero potential difference or voltage is measured. Different pairs of electrodes at different locations generally yield different voltages because of the spatial dependence of the electric field of the heart. Thus it is important to have certain standard positions for clinical evaluation of the ECG. The limbs make fine guideposts for locating the ECG electrodes. We shall look at this in more detail later.

In the simplified dipole model of the heart, it would be convenient if we could predict the voltage, or at least its waveform, in a particular set of electrodes at a particular instant of time when the cardiac vector is known. We can do this if we define a *lead vector* for the pair of electrodes. This vector is a unit vector that defines the direction a constant-magnitude cardiac vector must have to generate maximal voltage in the particular pair of electrodes. A pair of electrodes, or combination of several electrodes through a resistive network that gives an equivalent pair, is referred to as a *lead*.

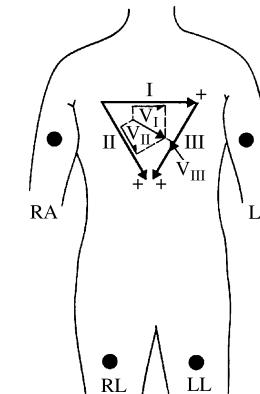
For a cardiac vector  $\mathbf{M}$ , as shown in Figure 6.2, the voltage induced in a lead represented by the lead vector  $\mathbf{a}_1$  is given by the component of  $\mathbf{M}$  in the direction of  $\mathbf{a}_1$ . In vector algebra, this can be denoted by the dot product

$$v_{a1} = \mathbf{M} \cdot \mathbf{a}_1 \quad \text{or} \quad v_{a1} = |\mathbf{M}| \cos \theta \quad (6.1)$$

Where  $v_{a1}$  is the scalar voltage seen in the lead that has the vector  $\mathbf{a}_1$ . Let us consider another lead, represented by the lead vector  $\mathbf{a}_2$ , as seen in Figure 6.2. In this case, the vector is oriented in space so as to be perpendicular to the



**Figure 6.2** Relationships between the two lead vectors  $\mathbf{a}_1$  and  $\mathbf{a}_2$  and the cardiac vector  $\mathbf{M}$ . The component of  $\mathbf{M}$  in the direction of  $\mathbf{a}_1$  is given by the dot product of these two vectors and denoted on the figure by  $v_{a1}$ . Lead vector  $\mathbf{a}_2$  is perpendicular to the cardiac vector, so no voltage component is seen in this lead.



**Figure 6.3** Cardiologists use a standard notation such that the direction of the lead vector for lead I is  $0^\circ$ , that of lead II is  $60^\circ$ , and that of lead III is  $120^\circ$ . An example of a cardiac vector at  $30^\circ$  with its scalar components seen for each lead is shown.

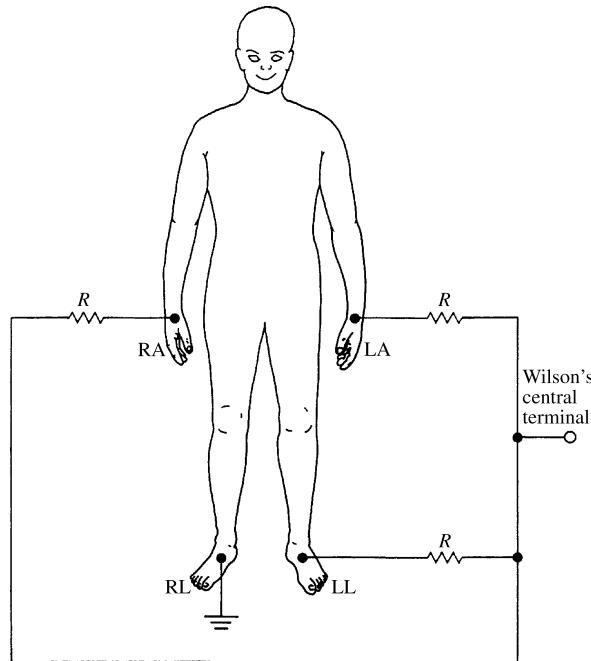
cardiac vector  $\mathbf{M}$ . The component of  $\mathbf{M}$  along the direction of  $\mathbf{a}_2$  is zero, so no voltage is seen in this lead as a result of the cardiac vector. If we measured the ECG generated by  $\mathbf{M}$  using one of the two leads shown in Figure 6.2 alone, we could not describe the cardiac vector uniquely. However, by using two leads with different lead vectors, both of which lie in the same plane as the cardiac vector such as  $\mathbf{a}_1$  and  $\mathbf{a}_2$ , we can describe  $\mathbf{M}$ .

In clinical electrocardiography, more than one lead must be recorded to describe the heart's electric activity fully. In practice, several leads are taken in the *frontal plane* (the plane of your body that is parallel to the ground when you are lying on your back) and the *transverse plane* (the plane of your body that is parallel to the ground when you are standing erect).

Three basic leads make up the *frontal-plane* ECG. These are derived from the various permutations of pairs of electrodes when one electrode is located on the right arm (RA in Figure 6.3), the left arm (LA), and the left leg (LL). Very often an electrode is also placed on the right leg (RL) and grounded or connected to special circuits, as shown in Figure 6.15. The resulting three leads are lead I, LA to RA; lead II, LL to RA; and lead III, LL to LA. The lead vectors that are formed can be approximated as an equilateral triangle, known as *Einthoven's triangle*, in the frontal plane of the body, as shown in Figure 6.3. Because the scalar signal on each lead of Einthoven's triangle can be represented as a voltage source, we can write Kirchhoff's voltage law for the three leads.

$$I - II + III = 0 \quad (6.2)$$

The components of a particular cardiac vector can be determined easily by placing the vector within the triangle and determining its projection along each



**Figure 6.4** Connection of electrodes to the body to obtain Wilson's central terminal

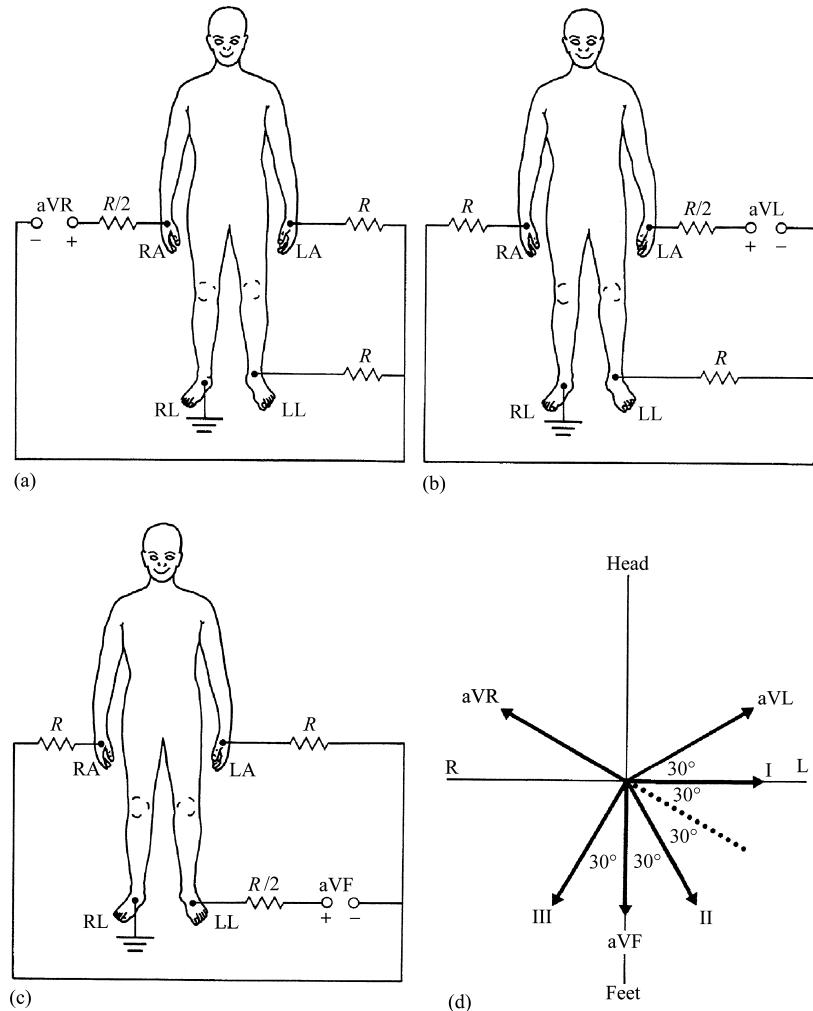
side. The process can also be reversed, which enables us to determine the cardiac vector when we know the components along the three lead vectors, or at least two of them. It is this latter problem that usually concerns the electrocardiographer.

Three additional leads in the frontal plane—as well as a group of leads in the transverse plane—are routinely used in taking clinical ECGs. These leads are based on signals obtained from more than one pair of electrodes. They are often referred to as *unipolar leads*, because they consist of the potential appearing on one electrode taken with respect to an equivalent reference electrode, which is the average of the signals seen at two or more electrodes.

One such equivalent reference electrode is the *Wilson central terminal*, shown in Figure 6.4. Here the three limb electrodes just described are connected through equal-valued resistors to a common node. The voltage at this node, which is the Wilson central terminal, is the average of the voltages at each electrode. In practice, the values of the resistors should be at least  $5\text{ M}\Omega$  so that the loading of any particular lead will be minimal. Thus, a more practical approach is to use buffers (voltage followers, see Section 3.3) between each electrode and the equal-valued resistors. The signal between LA and the central point is known as VL, that at RA as VR, and that at the left foot as VF. Note that for each of these leads, one of the resistances  $R$  shunts the circuit

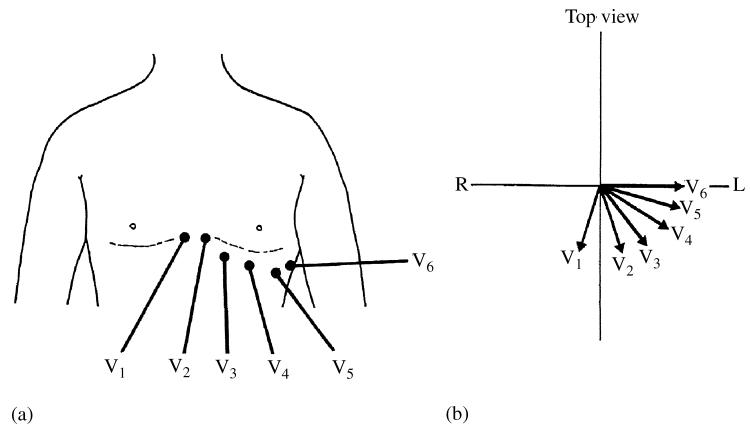
between the central terminal and the limb electrode. This tends to reduce the amplitude of the signal observed, and we can modify these leads to *augmented leads* by removing the connection between the limb being measured and the central terminal. This does not affect the direction of the lead vector but results in a 50% increase in amplitude of the signal.

The augmented leads—known as aVL, aVR, and aVF—are illustrated in Figure 6.5, which also illustrates their lead vectors, along with those of leads I, II, and III. Note that when the negative direction for aVR is considered with



**Figure 6.5** (a), (b), (c) Connections of electrodes for the three augmented limb leads. (d) Vector diagram showing standard and augmented lead-vector directions in the frontal plane.

the other five, all six vectors are equally spaced, by  $30^\circ$ . It is thus possible for the cardiologist looking at an ECG consisting of these six leads to estimate the position of the cardiac vector by seeing which of the six leads has the greatest signal amplitude at that point in the cardiac cycle.



**Figure 6.6** (a) Positions of precordial leads on the chest wall. (b) Directions of precordial lead vectors in the transverse plane.

When physicians look at the ECG in the transverse plane, they use *precordial* (chest) leads. They place an electrode at various anatomically defined positions on the chest wall, as shown in Figure 6.6. The potential between this electrode and Wilson's central terminal is the electrocardiogram for that particular lead. Figure 6.6 also shows the lead-vector positions. Physicians can obtain ECGs from the posterior side of the heart by means of an electrode placed in the esophagus. This structure passes directly behind the heart, and the potential between the esophageal electrode and Wilson's central terminal gives a posterior lead.

### SPECIFIC REQUIREMENTS OF THE ELECTROCARDIOGRAPH

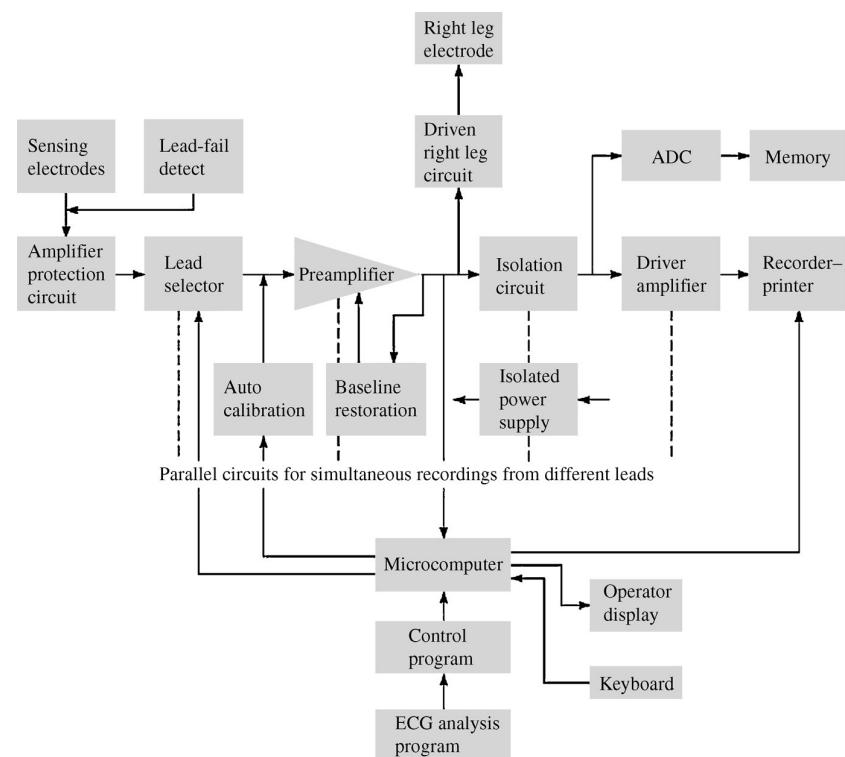
Because the electrocardiograph is widely used as a diagnostic tool and there are several manufacturers of this instrument, standardization is necessary. Standard requirements for electrocardiographs have been developed over the years (Bailey *et al.* 1990; Anonymous, 1991). Table 6.1 gives a summary of performance requirements from the most recent of these (Anonymous, 1991). These recommendations are a part of a voluntary standard. The Food and

Drug Administration is planning to develop mandatory standards for frequently employed instruments such as the electrocardiograph.

## FUNCTIONAL BLOCKS OF THE ELECTROCARDIOGRAPH

Figure 6.7 shows a block diagram of a typical clinical electrocardiograph. To understand the overall operation of the system, let us consider each block separately.

1. *Protection circuit:* This circuit includes protection devices so that the high voltages that may appear across the input to the electrocardiograph under certain conditions do not damage it.
2. *Lead selector:* Each electrode connected to the patient is attached to the lead selector of the electrocardiograph. The function of this block is to determine which electrodes are necessary for a particular lead and to connect them to the remainder of the circuit. It is this part of the electrocardiograph in which the connections for the central terminal are made. This block can be controlled by the operator or by the



**Figure 6.7** Block diagram of an electrocardiograph

microcomputer of the electrocardiograph when it is operated in automatic mode. It selects one or more leads to be recorded. In automatic mode, each of the 12 standard leads is recorded for a short duration such as 10 s.

3. *Calibration signal:* A 1 mV calibration signal is momentarily introduced into the electrocardiograph for each channel that is recorded.
4. *Preamplifier:* The input preamplifier stage carries out the initial amplification of the ECG. This stage should have very high input impedance and a high common-mode-rejection ratio (CMRR). A typical preamplifier stage is the differential amplifier that consists of three operational amplifiers (op amps), shown in Figure 3.5. A gain-control switch is often included as a part of this stage.
5. *Isolation circuit:* The circuitry of this block contains a barrier to the passage of current from the power line (50 or 60 Hz). For example, if the patient came in contact with a 120 V line, this barrier would prevent dangerous currents from flowing from the patient through the amplifier to the ground of the recorder or microcomputer.
6. *Driven-right-leg circuit:* This circuit provides a reference point on the patient that normally is at ground potential. This connection is made to an electrode on the patient's right leg. Details on this circuit are given in Section 6.5.
7. *Driver amplifier:* Circuitry in this block amplifies the ECG to a level at which it can appropriately record the signal on the recorder. Its input should be ac coupled so that offset voltages amplified by the preamplifier are not seen at its input. These dc voltages, when amplified by this stage, might cause it to saturate. This stage also carries out the bandpass filtering of the electrocardiograph to give the frequency characteristics described in Table 6.1. Also it often has a zero-offset control that is used to position the signal on the recorder. This control adjusts the dc level of the output signal.
8. *Memory system:* Many modern electrocardiographs store electrocardiograms in memory as well as printing them out on a recorder. The signal is first digitized by an analog-to-digital converter (ADC), and then samples from each lead are stored in memory. Patient information entered via the keyboard is also stored. The microcomputer controls this storage activity.
9. *Microcomputer:* The microcomputer controls the overall operation of the electrocardiograph. The operator can select several modes of operation by invoking a particular program. For example, she or he can ask the microcomputer to generate the standard 12-lead electrocardiogram by selecting three simultaneous 10 s segments of the six frontal plane leads followed by three 10 s segments of the six transverse plane leads. The microcomputer in some machines can also perform a preliminary analysis of the electrocardiogram to determine the heart rate, recognize some types of arrhythmia, calculate the axes of various features of the electrocardiogram, and determine intervals between these features. A keyboard and an alphanumeric display enable the operator to communicate with the microcomputer.

*High-frequency distortion* rounds off the sharp corners of the waveforms and diminishes the amplitude of the QRS complex.

An instrument that has a frequency response of 1 to 150 Hz shows *low-frequency distortion*. The baseline is no longer horizontal, especially immediately following any event in the tracing. Monophasic waves in the ECG appear to be more biphasic.

## SATURATION OR CUTOFF DISTORTION

High offset voltages at the electrodes or improperly adjusted amplifiers in the electrocardiograph can produce saturation or cutoff distortion that can greatly modify the appearance of the ECG. The combination of input-signal amplitude and offset voltage drives the amplifier into saturation during a portion of the QRS complex (Section 3.2). The peaks of the QRS complex are cut off because the output of the amplifier cannot exceed the saturation voltage.

In a similar occurrence, the lower portions of the ECG are cut off. This can result from negative saturation of the amplifier. In this case only a portion of the S wave may be cut off. In extreme cases of this type of distortion even the P and T waves may be below the cutoff level such that only the R wave appears.

## GROUND LOOPS

Patients who are having their ECGs taken on either a clinical electrocardiograph or continuously on a cardiac monitor are often connected to other pieces of electric apparatus. Each electric device has its own ground connection either through the power line or, in some cases, through a heavy ground wire attached to some ground point in the room.

A *ground loop* can exist when two machines are connected to the patient. Both the electrocardiograph and a second machine have a ground electrode attached to the patient. The electrocardiograph is grounded through the power line at a particular socket. The second machine is also grounded through the power line, but it is plugged into an entirely different outlet across the room, which has a different ground. If one ground is at a slightly higher potential than the other ground, a current from one ground flows through the patient to the ground electrode of the electrocardiograph and along its lead wire to the other ground. In addition to this current's presenting a safety problem, it can elevate the patient's body potential to some voltage above the lowest ground to which the instrumentation is attached. This produces common-mode voltages on the electrocardiograph that, if it has a poor CMRR, can increase the amount of interference seen.

## 6.3 PROBLEMS FREQUENTLY ENCOUNTERED

There are many factors that must be taken into consideration in the design and application of the electrocardiograph as well as other biopotential amplifiers. These factors are important not only to the biomedical engineer, but also to the individual who operates the instrument and the physician who interprets the recorded information. In the following paragraphs, we shall describe a few of the more common problems encountered and shall indicate some of their causes.

### FREQUENCY DISTORTION

The electrocardiograph does not always meet the frequency-response standards we have described. When this happens, frequency distortion is seen in the ECG.

### OPEN LEAD WIRES

Frequently one of the wires connecting a biopotential electrode to the electrocardiograph becomes disconnected from its electrode or breaks as a result of excessively rough handling, in which case the electrode is no longer connected

to the electrocardiograph. Relatively high potentials can often be induced in the open wire as a result of electric fields emanating from the power lines or other sources in the vicinity of the machine. This causes a wide, peak-to-peak deflection of the trace on the recorder at the power-line frequency, as well as, of course, signal loss. Such a situation also arises when an electrode is not making good contact with the patient. A circuit for detecting poor electrode contact is described in Section 6.9.

## ARTIFACT FROM LARGE ELECTRIC TRANSIENTS

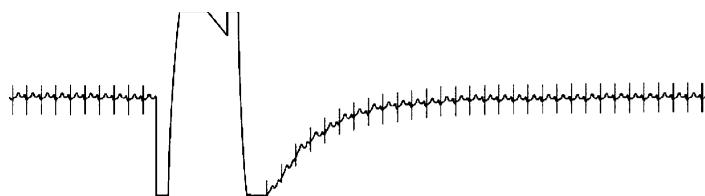
In some situations in which a patient is having an ECG taken, cardiac defibrillation may be required (Section 13.2). In such a case, a high-voltage high-current electric pulse is applied to the chest of the patient so that transient potentials can be observed across the electrodes. These potentials can be several orders of magnitude higher than the normal potentials encountered in the ECG. Other electric sources can cause similar transients. When this situation occurs, it can cause an abrupt deflection in the ECG, as shown in Figure 6.8. This is due to the saturation of the amplifiers in the electrocardiograph caused by the relatively high-amplitude pulse or step at its input. This pulse is sufficiently large to cause the buildup of charge on coupling capacitances in the amplifier, resulting in its remaining saturated for a finite period of time following the pulse and then slowly drifting back to the original baseline with a time constant determined by the low corner frequency of the amplifier. An example of the slowly recovering waveform is shown in Figure 6.8 at a reduced amplitude and time scale to demonstrate the transient.

Transients of the type just described can be generated by means other than defibrillation. Serious artifact caused by motion of the electrodes can produce variations in potential greater than ECG potentials. Another source of artifact is the patient's encountering a built-up static electric charge that can be partially discharged through the body. Older electrocardiographs exhibit a similar transient when they are switched manually from one lead

to another, because there are different offset potentials at each electrode. This is usually not seen on newer machines that switch leads automatically, because voltages due to excess charge are discharged during the switching process.

This problem is greatly alleviated by reducing the source of the artifact. Because we do not have time to disconnect an electrocardiograph when a patient is being defibrillated, we can include electronic protection circuitry, such as that described in Section 6.4, in the machine itself. In this way, we can limit the maximal input voltage across the ECG amplifier so as to minimize the saturation and charge buildup effects due to the high-voltage input signals. This results in a more rapid return to normal operation following the transient. Such circuitry is also important in protecting the electrocardiograph from any damage that might be caused by these pulses.

Artifact caused by static electric charge on personnel can be lessened noticeably by reducing the buildup of static charge through the use of conductive clothing, shoes, and flooring, as well as by having personnel touch the bed before touching the patient. Motion artifact from the electrodes can be decreased by using the techniques described in Chapter 5.



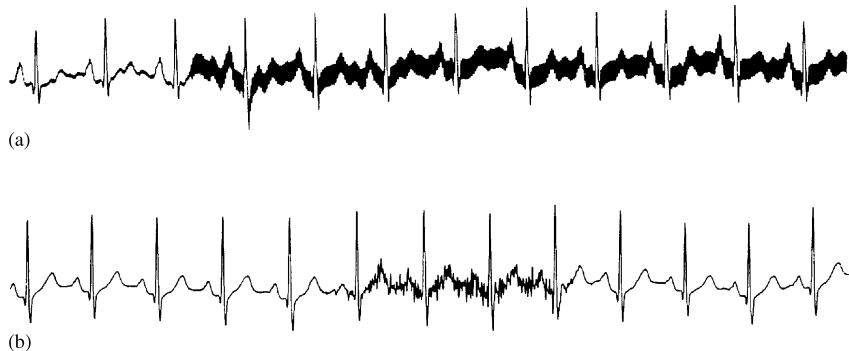
**Figure 6.8** Effect of a voltage transient on an ECG recorded on an electrocardiograph in which the transient causes the amplifier to saturate and a finite period of time is required for the charge to bleed off enough to bring the ECG back into the amplifier's active region of operation. This is followed by a first-order recovery of the system.

## INTERFERENCE FROM ELECTRIC DEVICES

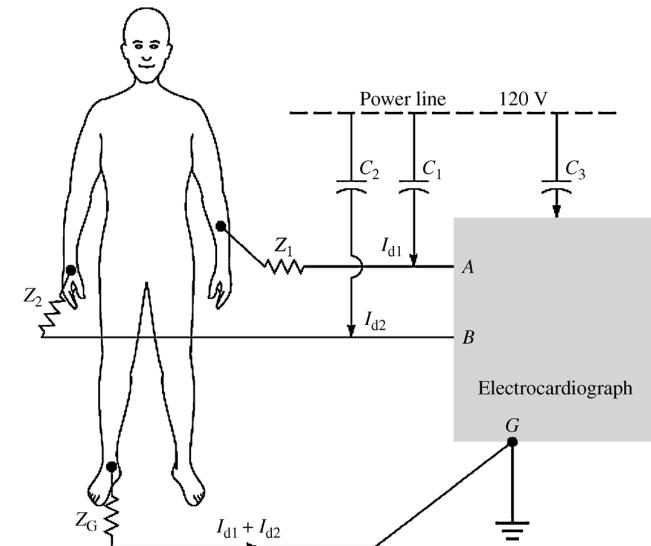
A major source of interference when one is recording or monitoring the ECG is the electric-power system. Besides providing power to the electrocardiograph itself, power lines are connected to other pieces of equipment and appliances in the typical hospital room or physician's office. There are also power lines in the walls, floor, and ceiling running past the room to other points in the building. These power lines can affect the recording of the ECG and introduce interference at the line frequency in the recorded trace, as illustrated in Figure 6.9(a). Such interference appears on the recordings as a result of two mechanisms, each operating singly or, in some cases, both operating together.

*Electric-field coupling* between the power lines and the electrocardiograph and/or the patient is a result of the electric fields surrounding main power lines and the power cords connecting different pieces of apparatus to electric outlets. These fields can be present even when the apparatus is not turned on, because current is not necessary to establish the electric field. These fields couple into the patient, the lead wires, and the electrocardiograph itself. It is almost as though small capacitors joined these entities to the power lines, as shown by the crude model in Figure 6.10.

The current through the capacitance  $C_3$  coupling the ungrounded side of the power line and the electrocardiograph itself flows to ground and does not cause interference.  $C_1$  represents the capacitance between the power line and one of the leads. Current  $i_{d1}$  does not flow into the electrocardiograph because of its high input impedance, but rather through the skin-electrode impedances  $Z_1$  and  $Z_G$  and the subject being measured to ground. Similarly,  $i_{d2}$  flows through  $Z_2$  and  $Z_G$  and the subject to ground. Body impedance, which is about  $500 \Omega$ , can be neglected when compared with the other



**Figure 6.9** (a) A 60 Hz power-line interference. (b) Electromyographic interference on the ECG. Severe 60 Hz interference is also shown on the bottom tracing in Figure 4.13.



**Figure 6.10** A mechanism of electric-field pickup of an electrocardiograph resulting from the power line. Coupling capacitance between the hot side of the power line and lead wires causes current to flow through skin-electrode impedances on its way to ground.

impedances shown. The voltage amplified is that appearing between inputs A and B,  $v_A - v_B$ .

$$v_A - v_B = i_{d1}Z_1 - i_{d2}Z_2 \quad (6.3)$$

Huhta and Webster (1973) suggest that if the two leads run near each other,  $i_{d1} \approx i_{d2}$ . In this case,

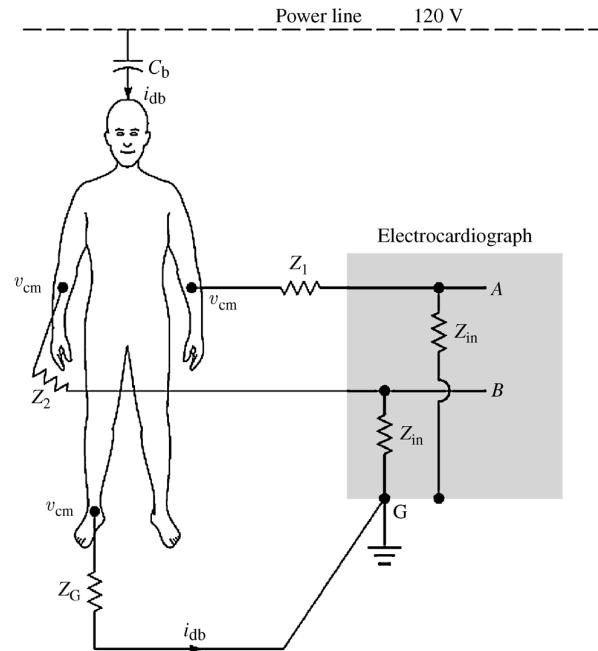
$$v_A - v_B = i_{d1}(Z_1 - Z_2) \quad (6.4)$$

Values measured for 9 m cables show that  $i_d \approx 6 \text{ nA}$ , although this value will be dependent on the room and the location of other equipment and power lines. Skin-electrode impedances may differ by as much as  $20 \text{ k}\Omega$ . Hence

$$v_A - v_B = (6 \text{ nA})(20 \text{ k}\Omega) = 120 \mu\text{V} \quad (6.5)$$

which would be an objectionable level of interference. This can be minimized by shielding the leads and grounding each shield at the electrocardiograph. This is done, in fact, in most modern electrocardiographs. Lowering skin-electrode impedances is also helpful.

Figure 6.11 shows that current also flows from the power line directly into the body. This displacement current  $i_{db}$  flows through the ground impedance



**Figure 6.11** Current flows from the power line through the body and ground impedance, thus creating a common-mode voltage everywhere on the body.  $Z_{in}$  is not only resistive but, as a result of RF bypass capacitors at the amplifier input, has a reactive component as well.

$Z_G$  to ground. The resulting voltage drop causes a common-mode voltage  $v_{cm}$  to appear throughout the body.

$$v_{cm} = i_{db}Z_G \quad (6.6)$$

Substituting typical values yields

$$v_{cm} = (0.2 \mu\text{A})(50 \text{k}\Omega) = 10 \text{mV} \quad (6.7)$$

In poor electrical environments in which  $i_{db} > 1 \mu\text{A}$ ,  $v_{cm}$  can be greater than 50 mV. For a perfect amplifier, this would cause no problem, because a differential amplifier rejects common-mode voltages (Section 3.4). However, real amplifiers have finite input impedances  $Z_{in}$ . Thus  $v_{cm}$  is decreased because of the attenuator action of the skin-electrode impedances and  $Z_{in}$ . That is,

$$v_A - v_B = v_{cm} \left( \frac{Z_{in}}{Z_{in} + Z_1} - \frac{Z_{in}}{Z_{in} + Z_2} \right) \quad (6.8)$$

Because  $Z_1$  and  $Z_2$  are much less than  $Z_{in}$ ,

$$v_A - v_B = v_{cm} \left( \frac{Z_2 - Z_1}{Z_{in}} \right) \quad (6.9)$$

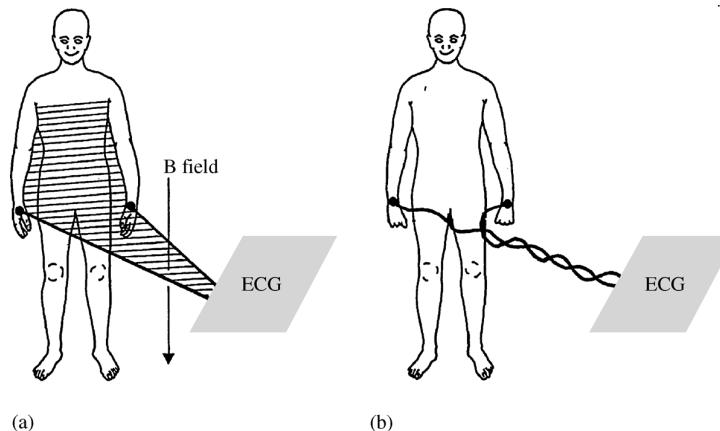
Substituting typical values yields

$$v_A - v_B = (10 \text{mV})(20 \text{k}\Omega / 5 \text{M}\Omega) = 40 \mu\text{V} \quad (E6.10)$$

which would be noticeable on an ECG and would be very objectionable on an EEG. This interference can be minimized by lowering skin-electrode impedance and raising amplifier input impedance.

Thus we see that the difference between the skin-electrode impedances is an important consideration in the design of biopotential amplifiers. Some common-mode voltage is always present, so the input imbalance and  $Z_{in}$  are critical factors determining the common-mode rejection, no matter how good the differential amplifier itself is.

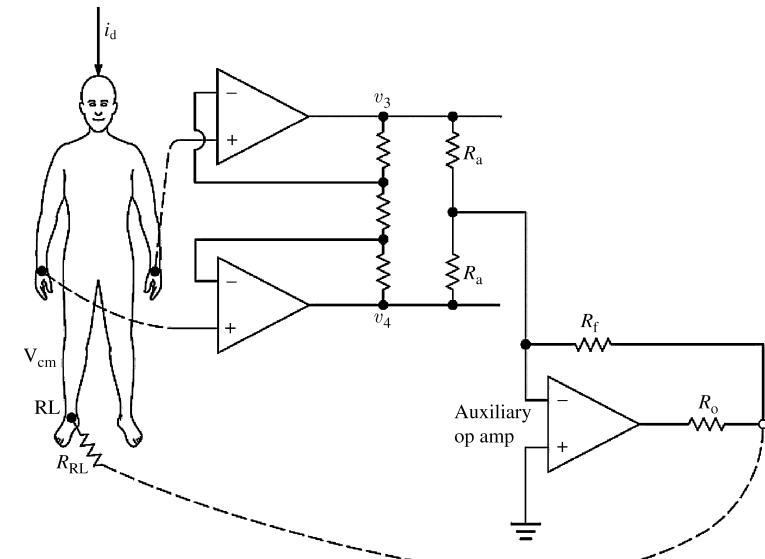
The other source of interference from power lines is magnetic induction. Current in power lines establishes a *magnetic field* in the vicinity of the line. Magnetic fields can also sometimes originate from transformers and ballasts in fluorescent lights or electric appliances and other apparatus. If such magnetic fields pass through the effective single-turn coil produced by the electrocardiograph, lead wires, and the patient, as shown in Figure 6.12, a voltage is induced in this loop. This voltage is proportional to the magnetic-field strength and the area of the effective single-turn coil. It can be reduced (1) by reducing the magnetic field through the use of magnetic shielding, (2) by keeping the electrocardiograph and leads away from potential magnetic-field regions (both of which are rather difficult to achieve in practice), or (3) by reducing the effective area of the single-turn coil.



**Figure 6.12 Magnetic-field pickup by the electrocardiograph** (a) Lead wires for lead I make a closed loop (shaded area) when patient and electrocardiograph are considered in the circuit. The change in magnetic field passing through this area induces a current in the loop. (b) This effect can be minimized by twisting the lead wires together and keeping them close to the body in order to subtend a much smaller area.

## DRIVEN-RIGHT-LEG SYSTEM

In most modern electrocardiographic systems, the patient is not grounded at all. Instead, the right-leg electrode is connected (as shown in Figure 6.15) to the output of an auxiliary op amp. The common-mode voltage on the body is sensed by the two averaging resistors  $R_a$ , inverted, amplified, and fed back to the right leg. This negative feedback drives the common-mode voltage to a



**Figure 6.15 Driven-right-leg circuit for minimizing common-mode interference** The circuit derives common-mode voltage from a pair of averaging resistors connected to  $v_3$  and  $v_4$  in Figure 3.5. The right leg is not grounded but is connected to output of the auxiliary op amp.

low value. The body's displacement current flows not to ground but rather to the op-amp output circuit. This reduces the interference as far as the ECG amplifier is concerned and effectively grounds the patient (Winter and Webster, 1983).

The circuit can also provide some electric safety. If an abnormally high voltage should appear between the patient and ground as a result of electric leakage or other cause, the auxiliary op amp in Figure 6.15 saturates. This effectively ungrounds the patient, because the amplifier can no longer drive the right leg. Now the parallel resistances  $R_f$  and  $R_o$  are between the patient and ground. They can be several megohms in value—large enough to limit the current. These resistances do not protect the patient, however, because 120 V on the patient would break down the op-amp transistors of the ECG amplifier, and large currents would flow to ground.

## Electrical Stimulation

As noted in earlier chapters of this book, a major use of medical electronic instrumentation is in diagnostic medicine. Most instruments sense various physiological signals, carry out some processing of these signals, and display or record them. There is, however, a class of medical electronic devices that are useful therapeutically and as prostheses. Electric stimulators of one form or another represent an important subgroup in this area. Also available are other devices, such as incubators, ventilators, heart-lung machines, artificial kidneys, diathermy devices, and electrosurgical instruments. In this chapter we examine some of these devices and look briefly at their principles of operation.

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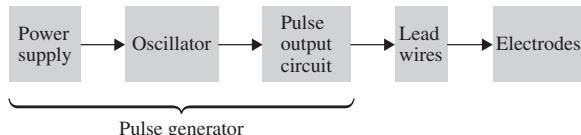
### 13.1 CARDIAC PACEMAKERS AND OTHER ELECTRIC STIMULATORS

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A wide variety of electric stimulators is used in patient care and research. They range from very low-current, low-duty-cycle stimulators, such as the cardiac pacemaker, to high-current single-pulse stimulators, such as defibrillators. In this section, we examine the pacemaker in detail and look at other applications of electric stimulators.

#### CARDIAC PACEMAKERS

The cardiac pacemaker is an electric stimulator that produces periodic electric pulses that are conducted to electrodes normally located within the lining of the heart (the endocardium). The stimulus thus conducted to the heart causes it to contract; this effect can be used prosthetically in disease states in which the heart is not stimulated at a proper rate on its own. The principal pathologic conditions in which cardiac pacemakers are applied are known collectively as *heart block*. These are reviewed by Murray (2006) and Schaldach (1992); Webster (1995) reviews pacemaker design details.



**Figure 13.1** Block diagram of an asynchronous cardiac pacemaker

An *asynchronous* pacemaker is one that is free running. Its electric stimulus appears at a uniform rate regardless of what is going on in the heart or the rest of the body. It therefore gives a fixed heart rate. It was the first type of pacemaker that was developed in the mid-twentieth century (Greatbatch, 2000).

Figure 13.1 is a block diagram of an asynchronous pacemaker. The power supply is necessary to supply energy to the pacemaker circuit. Primary battery sources are used.

The oscillator establishes the pulse rate for the pacemaker; this, in turn, controls the pulse output circuit that provides the stimulating pulse to the heart. This pulse is conducted along lead wires to the cardiac electrodes.

Each of these blocks is important in the construction of the pacemaker, and each must be made highly reliable, because faulty operation of this device can cost a patient's life.

Another component of the overall construction of the pacemaker that is not included in Figure 13.1 is the package itself. Not only must the package of an implanted pacemaker be compatible and well tolerated by the body, but it must also provide the necessary protection to the circuit components in order to ensure their reliable operation. The body is a corrosive environment, so the package must be designed to operate well in this environment, while occupying minimal volume and mass.

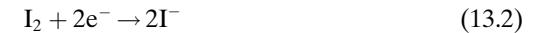
Today, cardiac pacemakers are contained in hermetically sealed metal packages. Titanium and stainless steel are frequently used for the package. Special electron beam or laser welding techniques have been developed to seal these packages without damaging the electronic circuit or the power source. These metal packages take up less volume and are more reliable than the earlier, polymer-based packages.

Although simple, asynchronous pacemakers such as that shown in Figure 13.1 are seldom used anymore, we can learn about pacemakers in general by examining each of the blocks in more detail.

**Power Supply** The usual power supply for implantable pacemakers is a battery made up of primary cells. Customary practice in the early 1970s was to change the pacemaker generator every two years due to limitations of the batteries used at that time. It was not until the lithium iodide battery was introduced into use in pacemakers that the lifetime of the cardiac pacemaker was significantly increased (Greatbatch *et al.*, 1971). The fundamental lithium iodide cell involves the reactions



at the cathode and



at the anode, for the combined reaction



This cell has an open-circuit voltage of 2.8 V and is much more reliable than the batteries that had been used before. Its major limitation is its relatively high source resistance. Essentially all of presently applied pacemakers utilize various forms of lithium batteries as their power source.

**Timing Circuit** The asynchronous pacemaker represents the simplest kind of pacemaker because it provides a train of stimulus pulses at a constant rate regardless of the functioning of the heart. A free-running oscillator is all that is required for the timing pulse in such a system. More advanced pacemakers, such as are used today, still have timing circuits to determine when a stimulus should be applied to the heart, but complex logic circuits, quartz crystal control, and even a microprocessor replace the simple, free-running oscillator. An overview of the function of some of these systems will be presented later in this chapter.

**Output Circuit** The pulse output circuit of the pacemaker generator produces the actual electric stimulus that is applied to the heart. At each trigger from the timing circuit, the output circuit generates an electric stimulus pulse that has been optimized for stimulating the myocardium through the electrode system that is being applied with the generator. Constant-voltage or constant-current amplitude pulses are the two usual types of stimuli produced by the output circuit. Constant-voltage amplitude pulses are typically in the range of 5.0 to 5.5 V with a duration of 500 to 600  $\mu\text{s}$ . Constant-current amplitude pulses are typically in the range of 8 to 10 mA with pulse durations ranging from 1.0 to 1.2 ms. Rates for asynchronous pacemakers range from 70 to 90 beats/min, whereas pacemakers that are not fixed rate typically achieve rates ranging from 60 to 150 beats/min.

## LEAD WIRES AND ELECTRODES

Because, in most pacemaker designs, the generator is located at some position remote from the heart itself, there must be an appropriate conduit to carry the electric stimuli to the heart and to apply them in the appropriate place. The lead wires, in addition to being good electrical conductors, must be mechanically strong. Their distal ends must not only withstand the constant motion of the beating heart, but as the individual in whom the pacemaker is implanted moves about, these lead wires have to be able to withstand the stress of being flexed in various positions. A second requirement of the lead-wire system is

that it must be well insulated. If this is not the case, wherever faults in the insulation occur, there is effectively another stimulating electrode that, in addition to possibly stimulating the tissue in its vicinity, shunts important stimulating current away from its intended point of application on the heart.

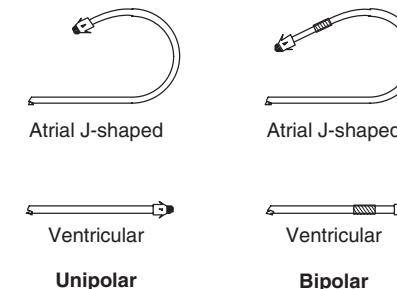
To meet these requirements, the lead wires presently used consist of interwound helical coils of spring-wire alloy molded in a silicone-rubber or polyurethane cylinder. The helical coiling of the wire minimizes stresses applied to it, and the multiple strands serve as insurance against failure of the pacemaker following rupture of a single wire. The soft compliant silicone-rubber or polyurethane encapsulation maintains flexibility of the lead-wire assembly and provides electrical insulation and biological compatibility.

Cardiac pacemakers are either of the *unipolar* or the *bipolar* type. In a unipolar device, a single electrode is in contact with the heart, and negative-going pulses are connected to it from the generator. A large indifferent electrode is located somewhere else in the body, usually mounted on the generator, to complete the circuit. In the bipolar system, two electrodes are placed within the heart, and the stimulus is applied across these electrodes. Both systems of electrodes require approximately the same stimulus for efficient cardiac pacing, as long as negative-going pulses are applied in the unipolar system.

There are clinically applied pacemakers utilizing each system. The electrodes themselves are normally pressed against the inside surface of the heart (endocardial or intraluminal electrodes). It is possible to introduce the electrodes into the heart through a shoulder or neck vein so that it is not necessary to expose the heart surgically during the implantation process.

As with the lead wires, the materials of which electrodes are made are important. The electrodes must be able to stand up to the repeated stress they may encounter as a result of the mechanical activity of the heart, and they must remain in place to provide effective pacing. They must also be made of materials that do not dissolve during long-term implantation, cause undue irritation to the heart tissue adjacent to them, or undergo electrolytic reactions when the stimulus is applied. To avoid any junctional electrolytic corrosion problems, these electrodes are often made of the same materials as the lead wires. Electrodes should also be made of materials that minimize biological interaction such as dense fibrous capsule formation around the electrode. Significant capsule formation can increase the threshold required for stimulation.

Several materials are used for pacemaker electrodes and lead wires. These include platinum and alloys of platinum with other materials: various formulations of stainless steel, carbon, and titanium; and specialized alloys such as Elgiloy (40% cobalt, 20% chromium, 15% iron, 15% nickel, 7% molybdenum, 2% manganese, and traces of carbon and beryllium, originally developed for wrist watch main springs that could endure repeated winding and unwinding without fatigue) and MP35N (35% nickel, 35% cobalt, 20% chromium, 10% molybdenum, and a trace of iron). In early pacemakers, a common type of failure was associated with breakage of the lead wire. Today, thanks to technological advances such as those just described, this problem has been



**Figure 13.2** Unipolar and bipolar implementations of both J-shaped and nonpreshaped leads. All models have distal cathode. Bipolar designs typically have a ring anode proximal 10 to 15 mm on the lead. [From Webster (1995)].

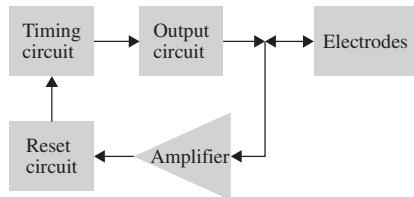
greatly reduced, and lead wires and electrodes usually remain in place when the generator circuit and batteries are replaced.

Figure 13.2 shows the basic structure of typical unipolar intraluminal electrodes where the current travels from the tip to the pacemaker can. The ventricular lead passes through the tricuspid valve and the plastic wings embed in the right ventricle while the conducting bands around the circumference of the solid intraluminal probe contact the endocardium (internal surface of the heart wall) and electrically stimulate it. The atrial lead is J-shaped to contact the atrial wall. For the bipolar leads, the current travels between the tip and the ring.

## SYNCHRONOUS PACEMAKERS

Often patients require cardiac pacing only intermittently, because they can establish a normal cardiac rhythm between periods of block. For these patients, it is not necessary to stimulate the ventricles continuously; in some cases, continuous stimulation can even result in serious complications. For example, if an artificial stimulus falls in the repolarization period following a spontaneous ventricular contraction, ventricular tachycardia or fibrillation can result. Thus it is important in these cases that the artificial pacemaker not compete with the heart's normal pacing action. Such a situation can be achieved with an asynchronous pacemaker by making the rate sufficiently high that the heart does not have a chance to beat on its own between pacemaker stimuli. A better solution, however, involves the use of synchronous pacemakers.

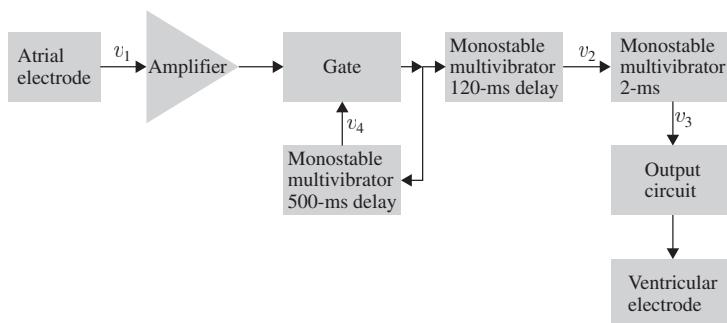
There are two general forms of synchronous pacemakers: the demand pacemaker and the atrial-synchronous pacemaker. Figure 13.3 shows the *demand* pacemaker. It consists of a timing circuit, an output circuit, and electrodes, just like those of the asynchronous pacemaker, but it has a feedback loop as well. The timing circuit is set to run at a fixed rate, usually 60 to 80 beats/min. After each stimulus, the timing circuit resets itself, waits the appropriate interval to provide the next stimulus, and then generates the next pulse.



**Figure 13.3 A demand-type synchronous pacemaker** Electrodes serve as a means of both applying the stimulus pulse and detecting the electric signal from spontaneously occurring ventricular contractions that are used to inhibit the pacemaker's timing circuit.

However, if during this interval a natural beat occurs in the ventricle, the feedback circuit detects the QRS complex of the ECG signal from the electrodes and amplifies it. This signal is then used to reset the timing circuit. It awaits its assigned interval before producing the next stimulus. If the heart beats again before this stimulus is produced, the timing circuit is again reset and the process repeats itself. Thus we see that, when the heart's conduction system is operating normally and the heart has a natural rate that is greater than the rate set for the timing circuit, the pacemaker remains in a standby mode, and the heart operates under its own pacing control. In this way the heart can respond to changing demands of the organism by changing its rate in the usual manner. If, on the other hand, temporary heart block occurs, the pacemaker takes over and stimulates the heart at the fixed rate of the timing circuit.

The *atrial-synchronous* pacemaker is a more complicated circuit, as shown in Figure 13.4. In this case, the pacemaker is designed to replace the blocked conduction system of the heart. The heart's physiological pacemaker, located at the SA node, initiates the cardiac cycle by stimulating the atria to contract and then providing a stimulus to the AV node, which, after appropriate delay,



**Figure 13.4 An atrial-synchronous cardiac pacemaker**, which detects electric signals corresponding to the contraction of the atria and uses appropriate delays to activate a stimulus pulse to the ventricles.

stimulates the ventricles. If the SA node is able to stimulate the atria, the electric signal corresponding to atrial contraction (the P wave of the ECG) can be detected by an electrode implanted in the atrium and used to trigger the pacemaker in the same way that it triggers the AV node. Figure 13.4 shows the voltage  $v_1$  that is detected by the atrial electrodes.

This voltage is a pulse that corresponds to each beat. The atrial signal is then amplified and passed through a gate to a monostable multivibrator giving a pulse  $v_2$  of 120 ms duration, the approximate delay of the AV node. Another monostable multivibrator giving a pulse duration of 500 ms is also triggered by the atrial pulse. It produces  $v_4$ , which causes the gate to block any signals from the atrial electrodes for a period of 500 ms following contraction. This eliminates any artifact caused by the ventricular contraction from stimulating additional ventricular contractions. Thus the pacemaker is refractory to any additional stimulation for 500 ms following atrial contractions.

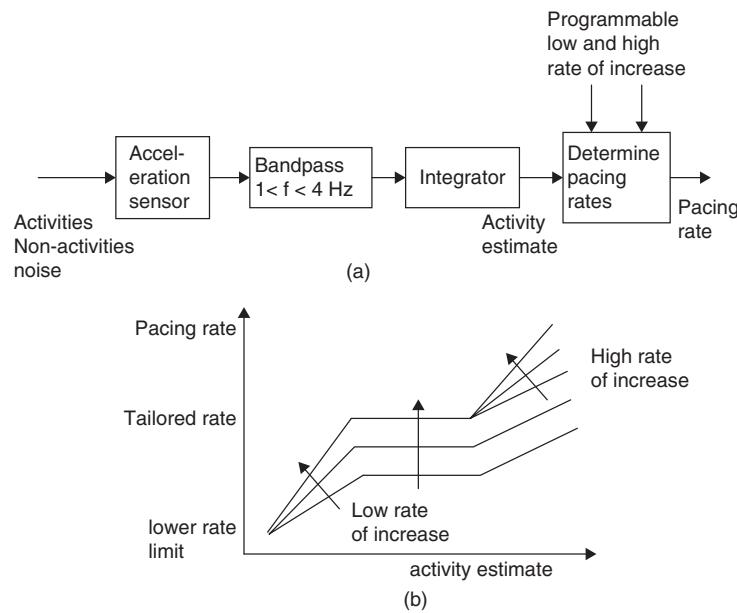
The falling edge of the 120 ms-duration pulse,  $v_2$ , is used to trigger a monostable multivibrator of 2 ms duration. Thus the pulse  $v_2$  acts as a delay, allowing the ventricular stimulus pulse  $v_3$  to be produced 120 ms following atrial contraction. Then  $v_3$  controls an output circuit that applies the stimulus to appropriate ventricular electrodes.

Often atrial-synchronous pacemakers have provisions to run at a fixed rate in case the atrial stimulus is lost. This is achieved by combining the demand-pacemaker system with the atrial-stimulus pacemaker system so that an atrial stimulus disables a fixed-rate timing circuit. If the stimulus is absent, the fixed-rate timing circuit takes over and controls the output circuit in the same way as in the asynchronous pacemaker.

The pacing systems shown in Figures 13.3 and 13.4 are represented as having individual circuit blocks. As with the fixed-rate pacemaker, the blocks in these diagrams illustrate the functions carried out by the pacemaker system. These functions are now carried out by microprocessor systems within the pacemaker. Thus it is not possible to find individual components that make up a specific block in an actual device.

## RATE-RESPONSIVE PACING

Although synchronous pacemakers can meet some of the physiological demand for variation in heart rate and cardiac output, these devices still do not replicate the function of the heart in a physiologically intact individual. The demands of the body during stressful activities such as exercise cannot be fully met by these pacemakers. Figure 13.5 shows that a sensor is used to convert a physiological variable in the patient to an electric signal that serves as an input to the controller circuit. This block of the pacemaker is programmed to control the heart rate on the basis of the physiological variable that is sensed. As with the demand pacemaker, this controller can determine whether any artificial pacing is required and can keep the pacemaker in a dormant state when the patient's natural pacing system is functional. The remainder of the pacing system is the same as described in this chapter for other generators.



**Figure 13.5** (a) The signal from an acceleration sensor within the rate-responsive pacemaker is bandpass filtered to minimize noise, then rectified and low-pass filtered to yield the activity estimate. (b) The physician selects a programmable curve that has a more sensitive acceleration and/or pacing-rate relationship during low and high levels of activity, with a less sensitive intermediate slope to maintain stability during ordinary workloads. [From Webster (1995).].

The sensor can be located within the pacemaker itself, or it can be located at some other point within the body. In the latter case, it is necessary to connect the sensor to the pacemaker by using a lead-wire system.

Many different physiological variables have been used to control rate-responsive pacemakers. Table 13.1 lists some of these variables and, for each, a sensor that can be used to measure that variable in an implanted system. Each of these variables requires a different control algorithm for the control circuit. In some cases, simple proportional control can be used; in other cases, more complex control algorithms are necessary. For example, when the temperature of the venous blood is used as the control variable, derivative control has been found to be important. As a patient begins strenuous exercise, the venous blood temperature begins to decrease because the increased blood flow to the periphery returns cooler blood to the circulation. This decrease lasts for only about a minute, however, and then the venous blood temperature increases, as a result of the increased metabolic activity in the peripheral skeletal muscles, to a temperature that is above the patient's resting body temperature. If it is to perform similarly to the physiologically intact cardiovascular control system,

**Table 13.1** Physiological Variables That Have Been Sensed by Rate-Responsive Pacemakers

Physiological Variable	Sensor
Right-ventricle blood temperature	Thermistor
ECG stimulus-to-T-wave interval	ECG electrodes
ECG R-wave area	ECG electrodes
Blood pH*	Electrochemical pH electrode
Rate of change of right ventricular pressure*	Semiconductor strain-gage pressure sensor
$\left(\frac{dp}{dt}\right)$	
Venous blood oxygen saturation*	Optical oximeter
Intracardiac volume changes	Electric-impedance plethysmography (intracardiac)
Respiratory rate and/or volume	Thoracic electric-impedance plethysmography
Body vibration	Accelerometer

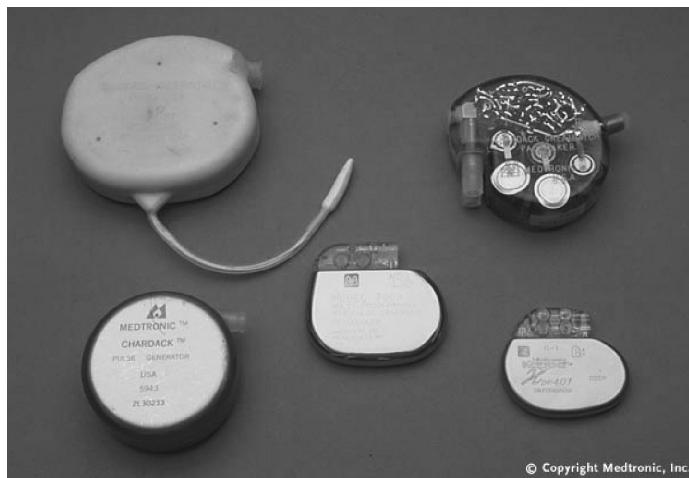
\*Not commercially available.

the pacemaker must have a controller that can recognize these changes and respond to them with an increase in heart rate.

Although we generally think of cardiac pacemakers as implantable devices, there also are external versions of this electric stimulator. Fixed-rate, asynchronous pacemakers are appropriate for external devices, because controls for various pacing functions (such as rate) are located on the circuit and can be adjusted by the clinical staff. Intracardiac electrodes are used, and they are introduced percutaneously through a peripheral vein. The external pacemaker is used for patients who are expected to require pacing for only a few days while they are in the intensive-care unit or who are awaiting implantation of a permanent pacemaker. Frequently, external pacemakers are used for patients recovering from cardiac surgery to correct temporary conduction disturbances resulting from the surgery. As the patient recovers, normal conduction returns and use of the pacemaker is discontinued.

An external transcutaneous cardiac pacemaker can apply 80 mA pulses through  $50 \text{ cm}^2$  electrodes on the chest. But this procedure is painful, so it is used only for emergency or temporary situations (Bocka, 1989).

A typical modern pacemaker is quite small compared to earlier versions. The complete package is about the size of a pocket watch and has a special connector to attach the lead-wire-electrode system. Figure 13.6 shows the evolution of the modern pacemaker. The upper left shows an early form of the pacemaker encapsulated in a biocompatible silicone elastomer. The upper right shows a more recent epoxy resin encapsulated pacemaker. The lifetime of these devices was limited by the battery and the packaging materials. The lower left shows a hermetically sealed metal package in a robust package and



**Figure 13.6** Examples of early pacemakers (top row) and metal encapsulated devices (bottom row). The two units on the bottom right are modern pacemakers that are about the size and mass of a pocket watch. (Photograph courtesy of Medtronic Corp.).

somewhat smaller volume and mass, but the pacemakers were still rather bulky. The advent of lithium batteries and large-scale integrated circuits made it possible for pacemakers to become much lighter and thinner as shown by the remaining two currently used pacemakers in Figure 13.6.

**EXAMPLE 13.1** A cardiac pacemaker delivers 5 V pulses of 2 ms duration to bipolar electrodes, that can be approximated as being a  $2\text{ k}\Omega$ -resistive load. The mean pulse rate of the pacemaker is 70 per min. The pulses represent 25% of the energy consumed by the pacemaker. The pacemaker is powered by two lithium cells connected in series to give a voltage of 5.6 V. As the designer of this circuit, you are called upon to specify a battery capable of operating the pacemaker for 10 years. What is the minimal acceptable capacity for each cell?

**ANSWER** The energy per stimulus pulse will be

$$E_p = \frac{v^2}{R} T = \frac{(5\text{ V})^2}{2\text{ k}\Omega} \times 2\text{ ms} = 25\text{ }\mu\text{J} \quad (\text{E13.1})$$

The number of pulses in 10 years (including 2 leap years) will be

$$\begin{aligned} N &= 70\text{ min}^{-1} \times 60\text{ min/h} \times 24\text{ h/day} \times 365.25\text{ day/year} \times 10\text{ year} \\ &= 3.68 \times 10^8 \text{ pulses} \end{aligned} \quad (\text{E13.2})$$

Thus the total energy will be

$$E_t = NE_p = 3.68 \times 10^8 \times 25\text{ }\mu\text{J} = 9.2\text{ kJ} \quad (\text{E13.3})$$

The energy supplied by the battery must be four times as great

$$E_b = 4E_t = 36.8\text{ kJ} \quad (\text{E13.4})$$

If, for the sake of argument (because it would be unwise to draw such a large current from these cells due to polarization and source resistance effects), we draw a current of 1 A from the battery, it would be supplying a power of 5.6 W. The period of time over which this power would have to be supplied to give an energy  $E_b$  would then be

$$t = \frac{E_b}{5.6\text{ W}} = 6.57\text{ ks} = 1.83\text{ h} \quad (\text{E13.5})$$

Thus, the battery capacity must be at least 1.83 A·h, or rounding off, 2 A·h to operate this pacemaker.

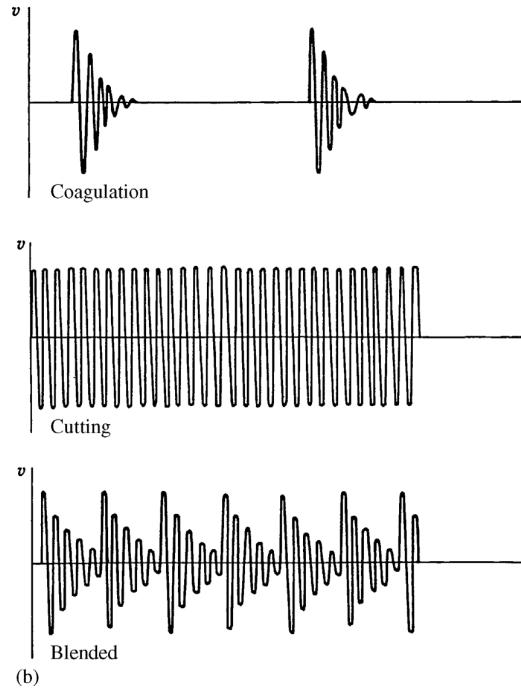
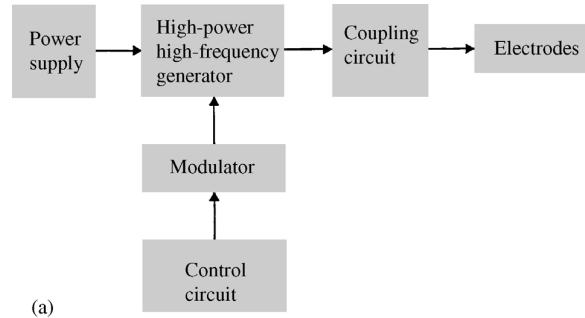
## 13.9 SURGICAL INSTRUMENTS

There are many devices that can be classified as surgical instruments; to consider all of them would require several volumes. There are, however, electric and electronic devices that are important in the surgical care of patients, in addition to those used for monitoring patients in the operating and recovery rooms. In the next two sections, we examine two of these: the electrosurgical unit and the laser.

### ELECTROSURGICAL UNIT

Electric devices to assist in surgical procedures by providing cutting and hemostasis (stopping bleeding) are widely applied in the operating room. These devices are also known as *electrocautery apparatuses*. They can be used to incise tissue, to destroy tissue through desiccation, and to stop bleeding by causing coagulation of blood. The process involves the application of an RF arc between a probe and tissue to cause localized heating and damage to that tissue.

The basic electrosurgical unit is shown in Figure 13.20(a) (Pearce, 2006). The high-frequency power needed to produce the arc comes from a high-power, high-frequency generator. The power to operate the generator comes from a power supply, the output of which may in some cases be modulated to produce a waveform more appropriate for particular actions. In this case, a modulator circuit controls the output of the generator. The application of high-frequency power from the generator is ultimately controlled by the surgeon through a control circuit, which determines when power is applied to the electrodes to carry out a particular action. Often the output of energy from the high-frequency generator needs to be at various levels for various jobs. For this reason, a coupling circuit is inserted between the generator output and the electrodes to control this energy transfer.



**Figure 13.20** (a) Block diagram for an electrosurgical unit. High-power, high-frequency oscillating currents are generated and coupled to electrodes. (b) Three different electric voltage waveforms available at the output of electrosurgical units for carrying out different functions.

The electric waveforms generated by the electrosurgical unit differ for its different modes of action. To bring about desiccation and coagulation, the device uses damped sinusoidal pulses, as shown in Figure 13.20(b). The RF sine waves have a nominal frequency of 250 to 2000 kHz and are usually pulsed at a

rate of 120 per second. Open-circuit voltages range from 300 to 2000 V, and power into a  $500\ \Omega$  load ranges from 80 to 200 W. The magnitude of both voltage and power depends on the particular application.

Cutting is achieved with a CW RF source, as shown in Figure 13.20(b). Often units cannot produce truly continuous waves, as shown in Figure 13.20(b), and some amplitude modulation is present. Cutting is done at higher frequency, voltage, and power, because the intense heat at the spark destroys tissue rather than just desiccating it, as is the case with coagulation. Frequencies range from 500 kHz to 2.5 MHz, with open-circuit voltages as high as 9 kV. Power levels range from 100 to 750 W, depending on the application.

The cutting current usually results in bleeding at the site of incision, and the surgeon frequently requires “bloodless” cutting. Electrosurgical units can achieve this by combining the two waveforms, as shown in Figure 13.20(b). The frequency of this *blended* waveform is generally the same as the frequency for the cutting current. For best results, surgeons prefer to operate at a higher voltage and power when they want bloodless cutting than when they want cutting alone.

Many different designs for electrosurgical units have evolved over the years. Modern units generate their RF waveforms by means of solid-state electronic circuits. Older units were based on vacuum tube circuits and even utilized a spark gap to generate the waveforms shown in Figure 13.20(b).

A block diagram of a typical electrosurgical unit is shown in Figure 13.21. The RF oscillator provides the basic high-frequency signal, which is amplified and modulated to produce the coagulation, cutting, and blended waveforms. A function generator produces the modulation waveforms according to the mode selected by the operator. The RF power output is turned on and off by means of a control circuit connected either to a hand switch on the active electrode or to a foot switch that can be operated by the surgeon. An output circuit couples the power generator to the active and dispersive electrodes. The entire unit derives its power from a power-supply circuit that is driven by the power lines.

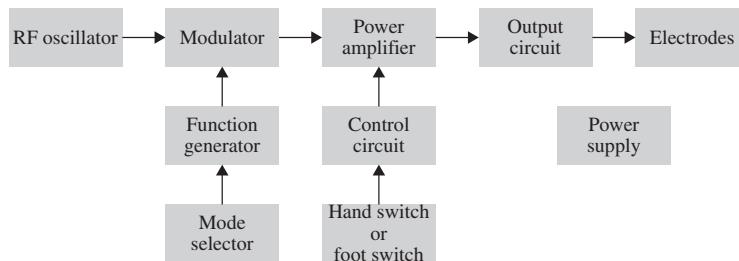
Electrodes used with electrosurgical units come in various sizes and shapes, depending on the manufacturer and the application. The active electrode is a scalpel-like probe that is shaped for the function for which it is intended. The

simplest form consists of a probe that appears to be similar to a test probe used with an electronic instrument such as a multimeter or an oscilloscope. A pointed metallic probe fits into an insulating handle and is held by the surgeon as one would hold a pencil. The finger switch located on the handle is momentarily depressed when the surgeon wants to apply power to the probe.

Whereas the purpose of the active probe is to apply energy to the local tissue at the tip of the probe and thereby to effect coagulation, cutting, or both, the dispersive electrode has a different function. It must complete the RF circuit to the patient without having current densities high enough to damage tissue. The simplest dispersive electrode is a large, reusable metal plate placed under the buttocks or back of the patient. Most procedures use a  $70\text{ cm}^2$  disposable conductive adhesive polymer dispersive electrode placed on the thigh. Another type has a gel-soaked sponge backed by metal foil and surrounded by foam and pressure-sensitive adhesive. Another capacitive type has a thin Mylar insulator backed by foil and its entire face coated with pressure-sensitive adhesive. It is important that this electrode make good contact with the patient over its entire surface so that “hot spots” do not develop.

## RADIO-FREQUENCY CATHETER ABLATION

Extra-conductive accessory pathways between the cardiac atria and ventricles may permit excitation to travel in circles and cause tachycardia. These extra pathway sites can be mapped by inserting a collapsed 64-electrode catheter into the heart chamber and expanding it into a basket to measure conduction times. Then a catheter is introduced to the sites and RF current at about 500 kHz heats the pathways to  $50\text{ }^\circ\text{C}$  to destroy (ablate) the conductive pathways. A temperature sensor at the electrode tip may be used to control the temperature (Huang, 1995).

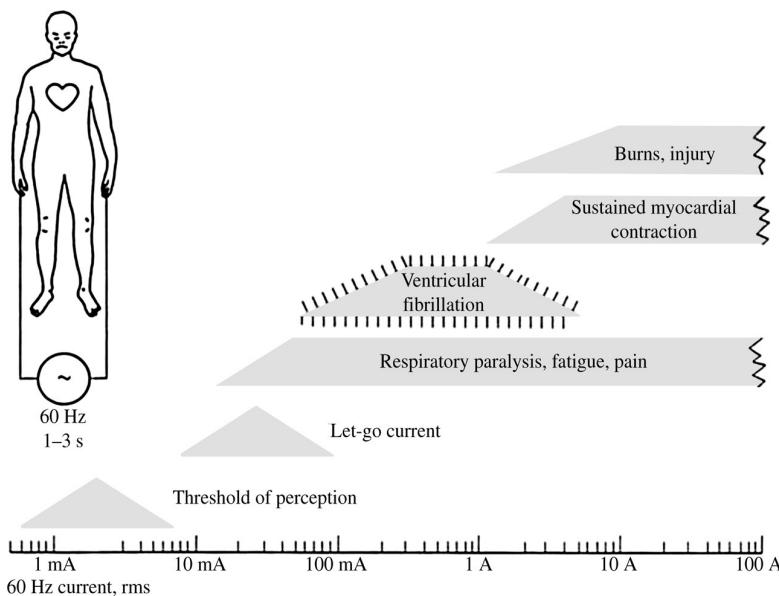


**Figure 13.21** Block diagram of a typical electrosurgical unit

## 14.1 PHYSIOLOGICAL EFFECTS OF ELECTRICITY

For a physiological effect to occur, the body must become part of an electric circuit. Current must enter the body at one point and leave at some other point. The magnitude of the current is equal to the applied voltage divided by the sum of the series impedances of the body tissues and the two interfaces at the entry points. The largest impedance is often the skin resistance at the contact surface. Three phenomena can occur when electric current flows through biological tissue: (1) electric stimulation of excitable tissue (nerve and muscle), (2) resistive heating of tissue, and (3) electrochemical burns and tissue damage for direct current and very high voltages.

Let us now discuss the psychophysical and physiological effects that occur in humans as the magnitude of applied electric current progressively increases. The chart in Figure 14.1 shows the approximate range of currents needed to produce each effect when 60 Hz current is applied for 1 to 3 s via AWG No. 8 copper wires that a 70 kg human holds in each hand. Then, in the section that follows, we will examine the effect of each of these conditions (weight of the individual and so on).



**Figure 14.1** Physiological effects of electricity Threshold or estimated mean values are given for each effect in a 70 kg human for a 1 to 3 s exposure to 60 Hz current applied via copper wires grasped by the hands.

## THRESHOLD OF PERCEPTION

For the conditions just stated, when the local current density is large enough to excite nerve endings in the skin, the subject feels a tingling sensation. Current at the *threshold of perception* is the minimal current that an individual can detect. This threshold varies considerably among individuals and with the measurement conditions. When someone with moistened hands grasps small copper wires, the lowest thresholds are about 0.5 mA at 60 Hz. Thresholds for dc current range from 2 to 10 mA, and slight warming of the skin is perceived.

## LET-GO CURRENT

For higher levels of current, nerves and muscles are vigorously stimulated, and pain and fatigue eventually result. Involuntary contractions of muscles or reflex withdrawals by a subject experiencing any current above threshold may cause secondary physical injuries, such as might result from falling off a ladder. As the current increases further, the involuntary contractions of the muscles can prevent the subject from voluntarily withdrawing. The *let-go current* is defined as the maximal current at which the subject can withdraw voluntarily. The minimal threshold for the let-go current is 6 mA.

## RESPIRATORY PARALYSIS, PAIN, AND FATIGUE

Still higher currents cause involuntary contraction of respiratory muscles severe enough to bring about asphyxiation if the current is not interrupted. During let-go experiments, respiratory arrest has been observed at 18 to 22 mA (Dalziel, 1973). Strong involuntary contractions of the muscles and stimulation of the nerves can be painful and cause fatigue if there is long exposure. (Today's human-subject-research committees probably would not approve these experiments.)

## VENTRICULAR FIBRILLATION

The heart is susceptible to electric current in a special way that makes some currents particularly dangerous. Part of the current passing through the chest flows through the heart. If the magnitude of the current is sufficient to excite only part of the heart muscle, then the normal propagation of electric activity in the heart muscle is disrupted. If the cardiac electric activity is sufficiently disrupted, the heart rate can rise to 300 beats/min as re-entrant wave fronts of depolarization randomly sweep over the ventricles. The pumping action of the heart ceases and death occurs within minutes.

This rapid, disorganized cardiac rhythm is called *ventricular fibrillation*, and unfortunately, it does not stop when the current that triggered it is removed. Ventricular fibrillation is the major cause of death due to electric shock. The threshold for ventricular fibrillation for an average-sized human varies from about 75 to 400 mA. Normal rhythmic activity returns only if a

brief high-current pulse from a defibrillator is applied to depolarize all the cells of the heart muscle simultaneously. After all the cells relax together, a normal rhythm usually returns. In the United States, approximately 1000 deaths per year occur in accidents that involve cord-connected appliances.

## SUSTAINED MYOCARDIAL CONTRACTION

When the current is high enough, the entire heart muscle contracts. Although the heart stops beating while the current is applied, a normal rhythm ensues when the current is interrupted, just as in defibrillation. Data from ac-defibrillation experiments on animals show that minimal currents for complete myocardial contraction range from 1 to 6 A. No irreversible damage to the heart tissue is known to result from brief applications of these currents (Roy et al., 1980).

## BURNS AND PHYSICAL INJURY

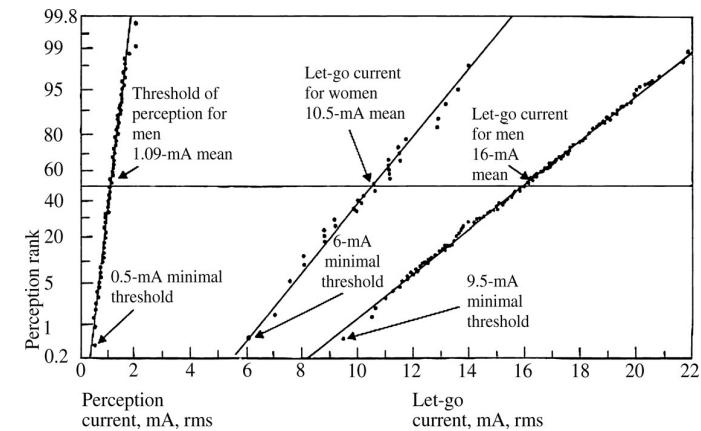
Very little is known about the effects of currents in excess of 10 A, particularly for currents of short duration. Resistive heating causes burns, usually on the skin at the entry points, because skin resistance is high. Voltages greater than 240 V can puncture the skin. The brain and other nervous tissue lose all functional excitability when high currents pass through them. Furthermore, excessive currents may stimulate muscular contractions that are strong enough to pull the muscle attachment away from the bone (Lee et al., 1992).

## 14.2 IMPORTANT SUSCEPTIBILITY PARAMETERS

The physiological effects previously described are for an average 70 kg human and for 60 Hz current applied for 1 to 3 s to moistened hands grasping a No. 8 copper wire. The current needed to produce each effect depends on all these conditions, as explained below. Safety considerations dictate thinking in terms of minimal rather than average values for each condition.

### THRESHOLD AND LET-GO VARIABILITY

Figure 14.2 shows the variability of the threshold of perception and the let-go current for men and women (Dalziel, 1973). On this plot of percentile rank versus rms current in milliamperes, the data are close to the straight lines shown, so a Gaussian distribution may be assumed. For men, the mean value for the threshold of perception is 1.1 mA; for women, the estimated mean is 0.7 mA. The minimal threshold of perception is 500  $\mu$ A. When the current was applied to ECG gel electrodes, the threshold of perception averages only 83  $\mu$ A with a range of 30 to 200  $\mu$ A (Tan and Johnson, 1990). Recent data for surface electrical stimulation of skeletal muscle showed that sensory threshold



**Figure 14.2 Distributions of perception thresholds and let-go currents** These data depend on surface area of contact (moistened hand grasping AWG No. 8 copper wire). (Replotted from C. F. Dalziel, “Electric Shock,” *Advances in Biomedical Engineering*, edited by J. H. U. Brown and J. F. Dickson III, 1973, 3, 223–248.)

was 43% ( $p < 0.001$ ) lower in women and supramotor threshold was 17% ( $p < 0.01$ ) less for women (Maffiuletti et al., 2008).

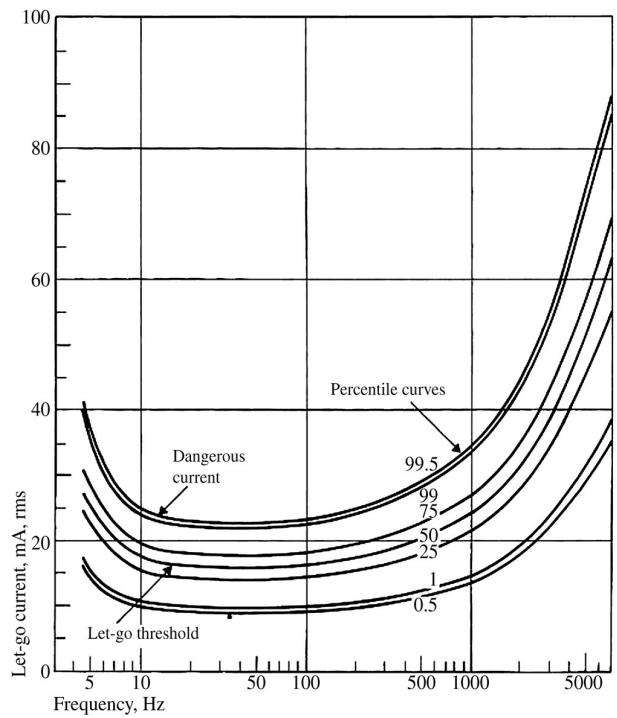
Let-go currents also appear to follow Gaussian distributions, with mean let-go currents of 16 mA for men and 10.5 mA for women. The minimal threshold let-go current is 9.5 mA for men and 6 mA for women. Note that the range of variability for let-go current is much greater than the range for threshold-of-perception current.

### FREQUENCY

Figure 14.3 shows a plot of let-go current versus frequency of the current. Unfortunately, the minimal let-go currents occur for commercial power-line frequencies of 50 to 60 Hz. For frequencies below 10 Hz, let-go currents rise, probably because the muscles can partially relax during part of each cycle. And at frequencies above several hundred hertz, the let-go currents rise again.

### DURATION

To estimate the ventricular fibrillation (VF) risk of electromuscular incapacitation devices (EMDs), it is important to understand the excitation behavior of myocardial cells. Geddes and Baker (1989) presented the cell membrane excitation model by a lumped parallel  $RC$  circuit that represents the resistance and capacitance of the cell membrane. This model determines the cell excitation thresholds that exceed about 20 mV for varying rectangular pulse durations  $d$  by assigning the rheobase currents  $I_r$  (for very long pulse durations) and cell



**Figure 14.3 Let-go current versus frequency** Percentile values indicate variability of let-go current among individuals. Let-go currents for women are about two-thirds the values for men. (Reproduced, with permission, from C. F. Dalziel, “Electric Shock,” *Advances in Biomedical Engineering*, edited by J. H. U. Brown and J. F. Dickson III, 1973, 3, 223–248.)

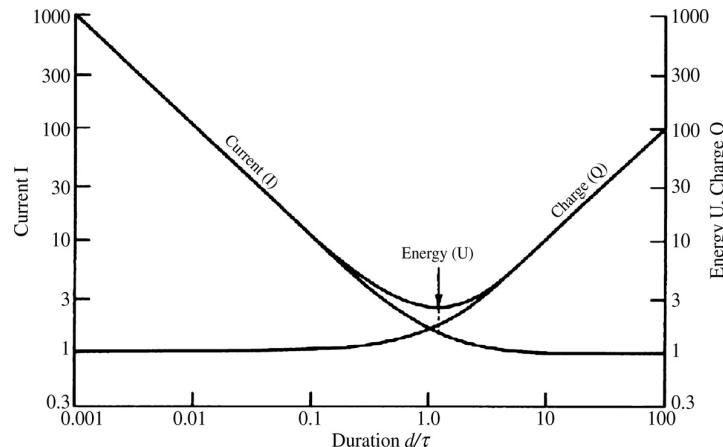
membrane time constant  $\tau = RC$ . Figure 14.4 shows that for short durations the stimulation current threshold  $I_d$  is inversely related to the pulse duration  $d$  by the well-known strength-duration equation

$$I_d = \frac{I_r}{1 - e^{-d/\tau}} \quad (14.1)$$

**EXAMPLE 14.1** A cardiac pacemaker company wants to minimize pacing duration  $d$  while keeping current at 3 times  $I_r$ . Assume cardiac membrane  $\tau = 2\text{ ms}$ , and calculate  $d$ .

**ANSWER** Use (14.1):  $0.33 = 1 - e^{-d/0.002}$ ,  $0.67 = e^{-d/0.002}$ ,  $\ln 0.67 = -d/0.002 = -0.4$ ,  $d = 0.8\text{ ms}$ .

A single electric stimulus pulse can induce VF if it is delivered during the vulnerable period of cardiac repolarization that corresponds to the T wave on



**Figure 14.4** Normalized analytical strength-duration curve for current  $I$ , charge  $Q$ , and energy  $U$ . The  $x$  axis shows the normalized duration of  $d/\tau$ . (From Geddes, L. A., and L. E. Baker, *Principles of Applied Biomedical Instrumentation*, 3rd ed. New York: John Wiley & Sons, 1989).

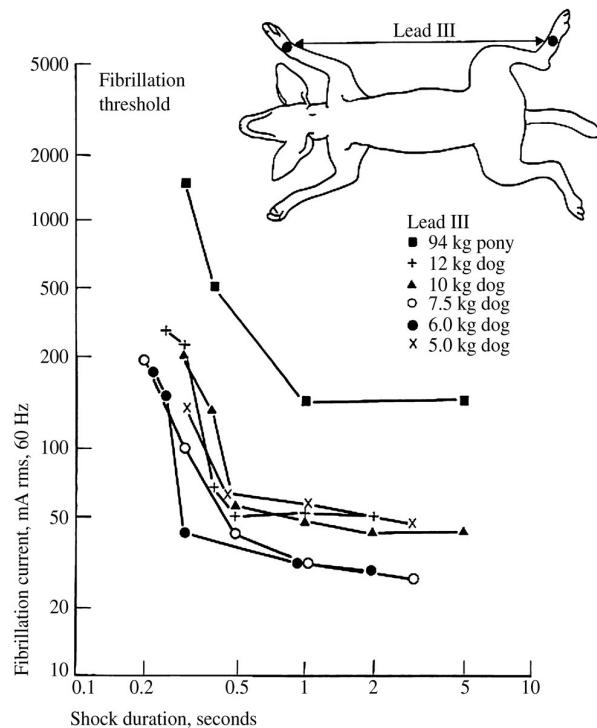
the ECG. For large-amplitude electric transients less than  $100\text{ }\mu\text{s}$  in duration applied directly to the heart, the stimulation threshold approaches a constant charge transfer density of  $3.5\text{ }\mu\text{C}\cdot\text{cm}^{-2}$ . For normal hearts, the ratio of the fibrillation stimulation threshold to the single-beat stimulation threshold is 20:1 to 30:1 for electrodes on the heart and 10:1 to 15:1 for chest surface electrodes (Geddes *et al.*, 1986). For  $60\text{ Hz}$  current applied to the extremities, the fibrillation threshold increases sharply for shocks that last less than about 1 s, as shown in Figure 14.5. Shocks must last long enough to take place during the vulnerable period that occurs during the T wave in each cardiac cycle (Reilly, 1998). For the  $100\text{ }\mu\text{s}$  pulses of electric fences (IEC, 2006) and Tasers, Figure 14.4 shows that much higher currents are required for excitation.

## BODY WEIGHT

Several studies using animals of various sizes have shown that the fibrillation threshold increases with body weight. Fibrillating current increases from  $50\text{ mA rms}$  for  $6\text{ kg}$  dogs to  $130\text{ mA rms}$  for  $24\text{ kg}$  dogs. These findings deserve more study, because they are used to extrapolate fibrillating currents for humans.

## POINTS OF ENTRY

When current is applied at two points on the surface of the body, only a small fraction of the total current flows through the heart, as shown in Figure 14.6(a). These large, externally applied currents are called *macroshocks*.

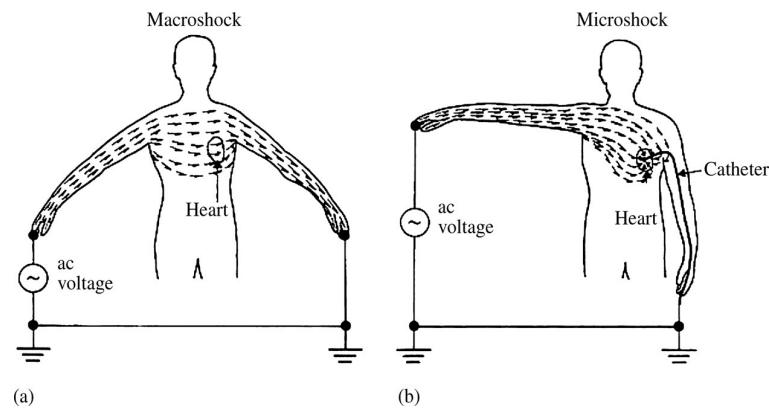


**Figure 14.5** Fibrillation current versus shock duration. Thresholds for VF in animals for 60 Hz ac current. Duration of current (0.2 to 5 s) and weight of animal body were varied. (From L. A. Geddes, *IEEE Trans. Biomed. Eng.*, 1973, 20, 465–468. Copyright 1973 by the Institute of Electrical and Electronics Engineers. Reproduced with permission.)

The magnitude of current needed to fibrillate the heart is far greater when the current is applied on the surface of the body than it would be if the current were applied directly to the heart. The importance of the location of the two macroshock entry points is often overlooked. If the two points are both on the same extremity, the risk of fibrillation is small, even for high currents. For dogs, the current needed for fibrillation is greater for ECG lead I (LA–RA) electrodes than for ECG leads II and III (LL–RA and LL–LA) (Geddes, 1973). The protection afforded by the skin resistance ( $15 \text{ k}\Omega$  to  $1 \text{ M}\Omega$  for  $1 \text{ cm}^2$ ) is eliminated by many medical procedures that require insertion of conductive devices into natural openings, skin incisions, skin abrasion, or electrode gel.

If the skin resistance is bypassed, less voltage is required to produce sufficient current for each physiological effect.

Patients are particularly vulnerable to electric shock when invasive devices are placed in direct contact with cardiac muscle. If a device provides a conductive path to the heart that is insulated except at the heart, then very



**Figure 14.6** Effect of entry points on current distribution (a) *Macroshock*: Externally applied current spreads throughout the body. (b) *Microshock*: All the current applied through an intracardiac catheter flows through the heart. (From F. J. Weibell, “Electrical Safety in the Hospital,” *Annals of Biomedical Engineering*, 1974, 2, 126–148.)

small currents called *microshocks* can induce VF. As Figure 14.6(b) shows, all the current flowing through such a conductive device flows through the heart. The current density at the point of contact can be quite high, and fibrillation in dogs can be induced by total currents as low as  $20 \mu\text{A}$ . [See Roy (1980).] Application of 60 Hz ac for 5 s test periods to a ventricular pacing catheter during implantable cardioverter-defibrillator implant testing in 40 patients showed intermittent capture with a minimum current of  $20 \mu\text{A}$ , continuous capture with hemodynamic collapse with a minimum current of  $32 \mu\text{A}$  and VF persisting after ac termination with a minimum current of  $49 \mu\text{A}$  (Figure 14.7) (Swerdlow *et al.*, 1999.) The other connection can be at any point on the body. The widely accepted safety limit to prevent microshocks is  $10 \mu\text{A}$ .

## **SKIN AND BODY RESISTANCE**

The resistance of the skin limits the current that can flow through a person's body when that person comes into contact with a source of voltage. The resistance of the skin varies widely with the amount of water and natural oil present. It is inversely proportional to the area of contact.

Most of the resistance of the skin is in the outer, horny layer of the epidermis. For  $1 \text{ cm}^2$  of electric contact with dry, intact skin, resistance may range from  $15 \text{ k}\Omega$  to almost  $1 \text{ M}\Omega$ , depending on the part of the body and the moisture or sweat present. If skin is wet or broken, resistance drops to as low as 1% of the value for dry skin. By contrast, the internal resistance of the body is about  $200 \text{ }\Omega$  for each limb and about  $100 \text{ }\Omega$  for the trunk. Thus internal body resistance between any two limbs is about  $500 \text{ }\Omega$ . These values are probably higher for obese patients, because the specific resistivity of fat is high. Actually, the distribution of current in various tissues in the body is poorly understood.

Any medical procedure that reduces or eliminates the resistance of the skin increases possible current flow and makes the patient more vulnerable to macroshocks. For example, biopotential electrode gel reduces skin resistance. Electronic thermometers placed in the mouth or rectum also bypass the skin resistance, as do intravenous catheters containing fluid that can act as a conductor. Thus patients in a medical-care facility are much more susceptible to macroshock than the general population.