Chapter 4. Origin of Biopotentials

- Biopotentials
  - Electrocardiogram (ECG)
  - Electroencephalogram (EEG)
  - Electroneurogram (ENG)
  - Electromyogram (EMG)
  - Electroretinogram (ERG)
  - Others

4.1 Electrical Activity of Excitable Cells

Resting State

- RMP (resting membrane potential): -50 to -100 mV w.r.t external medium (extracellular fluid)
- Measurement of RMP

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 micropipet. (b) The movement artifact is recorded as the tip of the micropipet 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 proceeds along the axon at a constant propagation velocity. The time period \( L \) is the latent period or transmission time from stimulus to recording site.
• Cell membrane
  ▫ 7 to 15 nm, lipoprotein complex
  ▫ Impermeable to intracellular protein and A⁻
  ▫ \( P_K \approx (50 – 100) \times P_{Na} \Rightarrow \) potassium membrane

• Concentration imbalance (frog skeletal muscle)

<table>
<thead>
<tr>
<th>Ion</th>
<th>Intracellular [mmol/liter]</th>
<th>Extracellular [mmol/liter]</th>
<th>Permeability [cm/s]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺</td>
<td>12</td>
<td>145</td>
<td>( P_{Na} = 2 \times 10^{-8} )</td>
</tr>
<tr>
<td>K⁺</td>
<td>155</td>
<td>4</td>
<td>( P_{K} = 2 \times 10^{-6} )</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>4</td>
<td>120</td>
<td>( P_{Cl} = 2 \times 10^{-6} )</td>
</tr>
</tbody>
</table>

• Equilibrium potential
  ▫ Diffusion vs. electric force
    ▫ Nernst equation: \( E_K = \frac{RT}{nF} \ln \frac{[K_i]}{[K_o]} = 0.0615 \log_{10} \frac{[K_i]}{[K_o]} \) [V] at 37 °C

    ▫ More accurately, Goldman-Hodgkin-Katz equation:
      \[
      E = \frac{RT}{F} \ln \left( \frac{P_K [K_i]_o + P_{Na} [Na_i]_o + P_{Cl} [Cl_i]_o}{P_K [K_i]_o + P_{Na} [Na_i]_o + P_{Cl} [Cl_i]_o} \right)
      \]

• Sodium-potassium pump
  ▫ Maintain steady-state ionic imbalance using ATP
    ▫ 3Na⁺ out and 2K⁺ in (3Na⁺:2K⁺)

• Cl⁻ diffuses inward but its movement is balanced by the electric field

• Factors influencing RMP
  ▫ Active transport of ions (sodium-potassium pump) \( \Rightarrow \) concentration gradient
  ▫ Diffusion \( \Leftarrow \) concentration gradient
  ▫ Electric field \( \Leftarrow \) organic anions (A⁻) do not diffuse
  ▫ Membrane structure \( \Rightarrow \) different permeability
Active State

- Adequate stimulus
  - Depolarization that is sufficient to exceed threshold voltage (about 20 mV more positive than RMP)
  - All-or-none or binary
- Action potential
  - Stimulus $\Rightarrow$ threshold
  - Voltage- and time-dependency of membrane permeability (Fig. 4.2 and 4.3)
  - RMP(polarization) $\Rightarrow$ depolarization $\Rightarrow$ repolarization $\Rightarrow$ hyperpolarization $\Rightarrow$ RMP
  - Absolute refractory period and relative refractory period (if absolute refractory period is 1 ms, action potential discharge is limited by 1000 impulses/s)
- Action potential propagation (Fig. 4.4a)
  - Without attenuation
  - Constant conduction velocity
  - Depolarized active region $\Rightarrow$ current loop $\Rightarrow$ ohmic voltage drop $\Rightarrow$ depolarization of neighboring region
- Unmyelinated neuron (Fig. 4.4a): in invertebrates, not saltatory
- Myelinated neuron (Fig. 4.4b): in invertebrates
  - Schwann cell and node of Ranvier
  - Saltatory conduction: about 20 times faster
Figure 4.2 Theoretical action potential $\nu$ and membrane ionic conductance changes for sodium ($g_{Na}$) and potassium ($g_{K}$) 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. $E_{Na}$ and $E_{K}$ are the Nernst equilibrium potentials for sodium and potassium 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, p. 530.)

Figure 4.3 Diagram of network equivalent circuit of a small length ($\Delta z$) of an unmyelinated nerve fiber or a skeletal muscle fiber. The membrane proper is characterized by specific membrane capacitance $C_m$ ($\mu F/cm^2$) and specific membrane conductances $g_{Na}$, $g_{K}$, and $g_{L}$ in mS/cm² (millisiemens/cm²). Here an average specific leakage conductance is included that corresponds to ionic current from sources other than Na⁺ and K⁺ (for example, 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 $r_1$ and $r_2$ ($\Omega/cm$), respectively. Here $i_m$ is the transmembrane current per unit length ($\Lambda/cm$), and $\nu_i$ and $\nu_o$ are the internal and external potentials $\nu$ at point $z$, respectively. (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, p. 501.)
4.2 Volume Conductor Fields

- Volume conductor: a salt solution simulating the composition of body fluids
- Simplest and fundamental problem in electrophysiology: single excitable cell immersed in a volume conductor
  - Bioelectric source: active cell, constant current source
  - Electrical load: bathing medium:
- Potential in the extracellular medium due to a simple monophasic action potential from a single active cell in a volume conductor
  - Triphasic
  - Greater spatial extent than the action potential
  - Smaller magnitude: exponentially falls off, about tens of μV at the membrane surface
- Potential in the extracellular medium due to thousands of action potentials simultaneously fired from compound nerve fibers in an infinite homogeneous volume conductor (Fig. 4.5)
  - Superposition
• Triphasic
• About a few μV
• Both magnitude and frequency are reduced at larger radial distance from the sources
• Potential differences measured at various locations: biopotentials

Figure 4.5 Extracellular field potentials (average of 128 responses) were recorded at the surface of an active (1-mm-diameter) frog sciatic nerve in an extensive volume conductor. The potential was recorded with (a) both motor and sensory components excited ($S_m + S_s$), (b) only motor nerve components excited ($S_m$), and (c) only sensory nerve components excited ($S_s$).

4.3 Functional Organization of Peripheral Nervous System

*Reflex Arc*
• Sense organ: sense receptors for pressure, temperature, touch, pain, etc.
• Sensory nerve
• CNS: brain and spinal cord
• Motor nerve
• Effector organ: skeletal muscle
Junctional Transmission

- Communicating links
  - Synapse: neuro-neuro junction
  - End-plate region: neuromuscular junction
- Junctional transmission process: electrochemical
  - Acetylcholine (Ach): neurotransmitter substance
  - Delay of 0.5 – 1.0 ms
- Muscle
  - Excitation-contraction time (delay)
  - Tetanus or tetanic contraction: at high stimulation rate

4.4 Electroneurogram (ENG)

- Conduction velocity and latency
- Characteristics (morphology) of field potentials: sensory and motor

Field Potentials of Sensory Nerves

- Stimulus
- Need to excite large and rapidly conducting sensory fibers
- Try to avoid exciting pain fibers and surrounding muscle
- Brief and intense: square pulse of 100 V amplitude and 100 – 300 $\mu$s duration

- **Stimulus isolation unit**
  - Isolate stimulating electrodes from ground
  - Minimize the stimulus artifacts

- Patient ground electrode is placed between stimulating electrodes and recording electrodes

- **Recording**
  - High-gain high-input-impedance differential amplifier
  - High CMRR and low noise
  - ENG ~ 10 $\mu$V
  - Signal averaging is often used

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**Motor-Nerve Conduction Velocity**

- Fig. 4.7: recording or stimulating at two sites of known distance
- Bigger amplitude than sensory signal

![Diagram](image)

**Figure 4.7** Measurement of neural conduction velocity via measurement of latency of evoked electrical response in muscle. The nerve was stimulated at two different sites a known distance $D$ apart.
Reflexly Evoked Field Potentials

- Stimulation of a peripheral nerve
  - Motor nerve action potential propagates distally to muscle and generate the first response with smaller latency ⇒ M wave
  - Sensory nerve action potential propagates proximally to CNS and elicit a spinal reflex to generate the second response with greater latency ⇒ H wave

- Move stimulation point toward muscle
  - Latency of M wave decreases
  - Latency of H wave increases since it is a reflex

- Sensory nerve fibers have larger diameter and lower threshold (Fig. 4.9)
  - Small stimulus ⇒ only H wave
  - Medium stimulus ⇒ both M and H wave
  - Large stimulus ⇒ mostly M wave (M wave produces refractory period to prevent H wave from occurring)

Figure 4.8 Sensory nerve action potentials evoked from median nerve of a healthy subject at elbow and wrist after stimulation of index finger with ring electrodes. The potential at the wrist is triphasic and of much larger magnitude than the delayed potential recorded at the elbow. Considering the median nerve to be of the same size and shape at the elbow as at the wrist, we find that the difference in magnitude and waveshape of the potentials is due to the size of the volume conductor at each location and the radial distance of the measurement point from the neural source. (From J. A. R. Lenman and A. E. Ritchie, Clinical Electromyography, 2nd ed., Philadelphia: Lippencott, 1977; reproduced by permission of the authors.)
4.5 Electromyogram (EMG)

- Single motor unit (SMU, Fig. 4.10) of skeletal muscle
  - Smallest unit that can be activated by a volitional effort
  - All constituent muscle fibers are stimulated synchronously
  - Can be modeled as a unit bioelectric source in a volume conductor
  - SMU potential: evoked extracellular potential, triphasic, 3 – 15 ms, 20 – 2000 μV, 6 – 30 pps, measured by a fine-tipped needle electrode
- EMG (Fig. 4.11)
  - Many superimposed motor unit responses
  - Complicated interference pattern
- Diagnostic features
  - Shape of SMU potential
  - Conduction velocity
  - EMG pattern: detection, decomposition, and analysis of EMG
  - Gross EMG activity
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, while 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.

Figure 4.11 Motor unit action potentials from normal dorsal interosseus muscle during progressively more powerful contractions. In the interference pattern (c), 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.)
4.6 Electrocardiogram (ECG)

Anatomy and Function of the Heart

- Four-chamber pump: Fig. 4.12
- Two phases
  - Diastole: resting or filling phase
  - Systole: contractile or pumping phase
- Intrinsic specialized conduction system ⇒ coordinated contraction of atria and ventricles
- Atria and free walls and septum of ventricles ⇒ major part of bioelectric source

Electrical Behavior of Cardiac Cells

- Conduction system: SA node ⇒ atria ⇒ AV node ⇒ His bundle ⇒ Purkinje fiber ⇒ ventricular muscle
- Each cell has its own characteristic action potential
- SA node is the primary pacemaker and its rhythm is called as sinus rhythm
- Any other heart cell could also be a pacemaker
Ventricular Cell

- Ventricular myocardium is composed of millions of cardiac cells (15×15×150 μm)
- Action potential
  - RMP is about –90 mV
  - Initial depolarization is rapid (150 V/s) with following plateau of 200 – 300 ms
  - Repolarization restores RMP

Ventricular Activation

- Isochronous excitation surfaces in Fig. 4.15
- Activation sequence: septal surface of LV (5 ms into QRS) ⇒ from left to right across septum ⇒ at 20 ms, several regions of RV and LV ⇒ at 30 ms, nearly closed activation surface is formed ⇒ move uniformly toward epicardium ⇒ at 30 – 40 ms, apex and other sites of RV and LV walls ⇒ toward posterior-basal region finally
- In general, endocardium ⇒ epicardium and apex ⇒ base
Body-Surface Potentials

- Heart as an equivalent bioelectric source ⇒ a net equivalent current dipole at the electrical center of the heart ⇒ magnitude and center of the dipole changes with time
- Equivalent cardiac generator in a volume conductor ⇒ potential difference on the body surface ⇒ ECG (Fig. 4.16)
- ECG (Fig. 4.13 bottom)
  - P wave: atrial depolarization
  - QRS complex: ventricular depolarization, atrial repolarization is masked by QRS
  - T wave: ventricular repolarization
  - U wave: sometimes appear after T wave, small, maybe due to slow repolarization of ventricular papillary muscle
  - P-R interval: normally at zero potential, conduction delay at AV node
  - S-T interval: normally at zero potential, average duration of plateau regions of ventricular cells
Normal and Abnormal Cardiac Rhythms

- **Normal heart rhythm**
  - Pacemaker is SA node with sinus rhythm of about 70 bpm
  - Bradycardia: slow rhythm, during sleep
  - Tachycardia: fast rhythm, by emotion, exercise, fever, other stimuli

- **Abnormal heart rhythm**
  - SA node is depressed
  - His bundle or some other part of conduction system is damaged
  - Ectopic focus in atria or ventricles discharges faster than SA node

- **Heart block**
  - Third degree or complete heart block: His bundle is completely interrupted, atria beat at normal sinus rhythm, ventricles beat independently at idioventricular rhythm (30 – 45 bpm)
  - Second degree heart block: 2:1 block or 3:1 block
  - Wenckebach phenomenon: gradual lengthening of P-R interval until the pause (dropped beat), 6:5 or 5:4 Wenckebach period
  - First degree heart block: incomplete block of His bundle, all atrial pulses reach
ventricles, P-R interval is abnormally prolonged
- Bundle branch block: LBBB or RBBB, blocked side is excited later by the conduction from the normal side, QRS complexes are prolonged and deformed

**Arrhythmias**
- Ectopic focus: a portion of myocardium or AV node or a part of conduction system becomes irritable and discharges independently
  - Discharge once: atrial, nodal, or ventricular ectopic beat, extra systole or PVC
  - Repeated faster discharge: paroxysmal tachycardia, atrial flutter
  - Rapid and irregular discharge of a group of foci: atrial or ventricular fibrillation
- Reentry or circus re-excitation
  - Ischemic region ⇒ depressed conductivity ⇒ slow conduction ⇒ re-excite other normal areas recovered from initial excitation ⇒ re-excite slow region ⇒ …
  - Intermittent reentry ⇒ extrasystole
  - Continuous reentry ⇒ tachyarrhythmia

**Alteration of Potential Waveforms in Ischemia**
- Ischemia ⇒ change in intracellular and extracellular potential waveform (Fig. 4.21)
  ⇒ change in QRS complex, S-T segment, and T wave (ST elevation and TQ depression)
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.

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.)
**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 beats/min. (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.)
4.7 Electroretinogram (ERG)

**Anatomy of Vision**

- Spherical, 24 mm diameter
- Light path: cornea $\Rightarrow$ anterior chamber filled with aqueous humor (fluid) $\Rightarrow$ lens $\Rightarrow$ vitreous chamber filled with vitreous body (gel) $\Rightarrow$ retina (sensory part)
  - Aqueous humor
    - 20 to 25 mmHg: keeps correct geometry
    - Nutrient and gas transport: circulatory system $\leftrightarrow$ aqueous humor $\leftrightarrow$ lens and cornea
  - Glaucoma: not enough flow of aqueous humor
    - Damages of lens and cornea
    - Development of high pressure $\Rightarrow$ damage of retina
- Retina
  - Photoreceptors
    - Photoelectric sensor: photons $\Rightarrow$ breakdown of photopigments (photolabile)
      $\Rightarrow$ transmitter ions released $\Rightarrow$ change in membrane potential
    - Rods: vision in dim light, photopigment is rhodopsin
• Cones: color vision in bright light, 1 to 3 photopigments
  □ Biopolar cells
    • Contact photoreceptors in the external plexiform layer
  □ Horizontal cells
    • Interconnect rods and cones in the external plexiform layer
  □ Amacrine cells
    • Second horizontal network in the internal plexiform layer
  □ Ganglion cells
    • Contact bipolar cells in the internal plexiform layer
    • Fire and transmit action potentials down the optic nerve

\[\text{Figure 4.22} \text{ The transparent contact lens contains one electrode, shown here on horizontal section of the right eye. Reference electrode is placed on the right temple.}\]
Electrophysiology of the Eye

- Electroretinogram (ERG)
  - Exploring electrode
    - On the inner surface of the retina
    - On the cornea: Ag/AgCl electrode embedded in a special saline-filled contact lens
  - Indifferent electrode: temple, forehead, or earlobe
- ERG response to light flash (a few seconds) ⇒ flash ERG
  - Early-receptor potential (ERP): no latency, from photopigments, linear with light intensity
  - Late-receptor potential (LRP: 1 to 5 ms latency, from outputs of photoreceptors, logarithmic with light intensity
  - ERP and LRP form a leading edge of ‘a’ wave followed by ‘b’, ‘c’, and ‘d’ waves.

![ERG Response](image)

**Figure 4.23 Vertebrate electroretinogram**

Spatial Properties of the ERG

- Linear superposition: ERG due to many stimuli at different regions = sum of ERG’s due to each stimulus
- Stimulus: light scattering within the eye ⇒ low-intensity stimulus with high-background illumination is preferred to achieve a localized stimulus
- Signal averaging technique
- Assessment of functional retinal behavior
• Independent of optic nerve or optical pathways

**The Electro-oculogram (EOG)**

• Steady corneal-retinal potential
• Measure of eye position or movement
• Electrodes: recessed Ag/AgCl
  - Left and right of the eye or on the nose and the temple
  - Above and below the eye
• EOR
  - Cornea is positive: gaze shift to left (right) ⇒ left (right) electrode becomes more positive
  - μm range, dc amplifier
  - Noise (EEG, EMG, etc.) ≈ 1° eye movement ⇒ > 2° resolution
  - Range < ±30° eye movement
• Applications
  - Sleep and dream research
  - Eye movements of infants and children
  - Reading ability or visual fatigue valuation

### 4.8 Electroencephalogram (EEG)

#### EEG

• Potential fluctuations recorded from the brain, Hans Berger
• Superposition of volume conductor fields due to aggregates of dendrites, cell bodies (somata), and axons with complex interconnections

#### EEG
- EEG: scalp electrodes
- ECoG (electrocorticogram): cortical electrodes
- Depth recording: depth electrodes (needle electrodes)

**Introduction to the Anatomy and Function of the Brain**

< **Central nervous system (CNS)** >

• **Brain**: skull ⊆ menings (3 protective membranes) ⊆ CSF ⊆ brain
• **Spinal cord**: vertebral column ⊆ menings ⊆ CSF ⊆ spinal cord
• Cerebral spinal fluid (CSF): bathing solution of brain and spinal cord

< **Brain** >
• **Brainstem**: short extension of spinal cord
  □ Major functions
    • Connection link among cerebral cortex, spinal cord, cerebellum
    • Integration center for several visceral functions (heart rate, respiratory rate)
    • Integration center for various motor reflexes
  □ Diencephalon: the most superior portion
  □ Thalamus: chief component and largest structure
    • Major relay station and integration center for all sensory systems
    • Relay sensory information to their respective cortical reception areas
    • Gateway to cerebrum

• **Cerebellum**
  □ Coordinator in voluntary (somatic) muscle system
  □ Maintain balance in conjunction with brainstem and cerebral cortex
  □ Provide harmonious muscle movements
  □ Conscious function of nervous system

• **Cerebrum**:
  □ Paired structure
    • Right cerebral hemisphere is related to the left side of body
    • Left cerebral hemisphere is related to the right side of body
  □ Cerebral cortex (gray matter)
    • < 1 cm thick outer layer of each hemisphere of cerebrum
    • Receives sensory information from skin, eyes, ears, and other receptors
    • Dense collection of nerve cells
    • Highly convoluted surface: gyri (ridges), sulci (valleys), fissures (deeper sulci)
  □ Deeper layers
    • Axons (white matter)
    • Collection of cell bodies (nuclei)
Figure 4.24 (a) Anatomical relationship of brainstem structures (medulla oblongata, pons, midbrain, and diencephalons) to the cerebrum and cerebellum. General anatomic directions of orientation in the nervous system are superimposed on the diagram. Here the terms rostral (toward heard), 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. (b) 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 (2) in the pathway decussates (crosses) to the opposite side of the cord. [Part (A) modified from Harry E. Thomas, Handbook of Biomedical Instrumentation and Measurement, 1974, p.254. Reprinted with permission of Reston Publishing Company, Inc. a Prentice-Hall company, 11480 Sunset Hills Road, VA 22090.]

Figure 4.25 The cerebrum, showing the four lobes (frontal, parietal, temporal, and occipital), the lateral and longitudinal fissures, and the central sulcus. (From A. B. McNaught and R. Callander, Illustrated Physiology, 3rd ed., 1975. Edinburgh: Churchill Livingstone. Used with permission of Churchill Livingstone.)
<Nerve pathways: two-way communication links between brain and spinal cord>

- Signals: frequency-modulated train of nerve impulses (action potentials)
- Sensory (ascending) nerve pathways
  - General sensors: temperature, pain, touch, pressure
    • Three-neuron chain: primary neuron (sensor → spinal cord or brainstem) ⇒ secondary neuron (spinal cord or brain stem → thalamus) ⇒ third neuron (thalamus → post-central gyrus)
    • Secondary neurons decussate
  - Special sensors: vision, audition, equilibrium, taste, olfaction
    • Usually more than three-neuron chain
    • Some secondary neurons decussate (not all of them)
    • Audition: auditory sensor ⇒ medial geniculate bodies (in thalamus) ⇒ visual cortex (in occipital lobe of cerebrum)
    • Vision: visual sensor ⇒ lateral geniculate bodies (in thalamus) ⇒ auditory cortes (in temporal lobe of cerebrum)
- Motor (descending) nerve pathways
  - Cerebrum or cerebellum ⇒ motor neurons in ventral horn of spinal cord ⇒ skeletal muscle
  - Descending corticospinal tracts decussate

<Evoked potentials>
- Somatosensory evoked potential
- Auditory evoked potential (AEP) or response (AER)
- Visual evoked potential (VEP) or response (VER)

<Cerebral cortex>
- Divided by major fissures
- Temporal lobe
  • Side lobe of cortex inferior to lateral fissure
  • Superior (upper) part contains primary auditory cortex
- Occipital lobe
  • Back of the head
  • Primary visual cortex
- Precentral gyrus
  • Primary motor cortex
  • Lesions of a part of precentral gyrus can cause partial paralysis on the opposite side of body
- Premotor cortex: more complex motor movements such as speech
• Frontal lobe
  □ Anterior and inferior portions: control of emotional behavior
  □ Prefrontal lobe: higher intellectual functions (?)

• Parietal lobe
  □ Primary somatosensory cortex
    • Receives impulses from all general sensors
    • Each small portion corresponds to a certain part of body
  □ Higher order sensory discrimination
  □ Awareness of the general position of body and limbs

Ultrastructure of the Cerebral Cortex
• Cerebral cortex: functional part of cerebrum, gray matter, 1.5 to 4 mm thick
• Neocortex and paleocortex
• Cortex (neocortex) is generally arranged in six layers of neurons and fiber bundles
• Two major types of cells in cortex
  □ Pyramidal
  □ Nonpyramidal

Bioelectric Potentials from the Brain
• Action potentials in axons: little contribution to surface recordings
  □ Normal circumstances
    • Action potentials in axons are asynchronous in time
    • Axons run in many directions relative to surface
  □ Exceptions: evoked potential due to direct stimulation
• Local postsynaptic potentials of cortical cells ⇒ surface potential
  □ Pyramidal cells: nonzero sum potential, major contribution to surface potential
    • Similarly oriented, densely packed (orderly and symmetric arrangement)
    • Active excitatory and inhibitory synaptic ending of dendrite ⇒ local postsynaptic potential (PSP) ⇒ current flow
    • Cell-dendrite relationship ⇒ current dipole
    • Variations in orientation and strength of dipole ⇒ volume conductor ⇒ potential waveform
  □ Nonpyramidal cells: zero sum potential, little influence on surface potential

Resting Rhythms of the Brain
• Continuous oscillating electrical activity within the brain ⇒ brain waves
Brainstem reticular activating system (RAS) ⇒ overall excitation of the brain ⇒ intensity and pattern of brain waves
  • Synchronization of a group of neurons ⇒ enough amplitude
  • RAS as a pacemaker ⇒ rhythmicity

Electroencephalogram (EEG): entire record of brain waves

Intensity of brain waves
  □ From the surface of the brain: 10 mV
  □ From the scalp: 100 μV

Frequency of brain waves: 0.5 – 100 Hz

Waveform
  □ Depends on the degree of activity of the cerebral cortex
  □ Usually, irregular and no general pattern
  □ Sometimes, distinct patterns occur such as epileptic spikes

Types of EEG waves

Alpha wave
  • Normal person, awake in a quite and resting state
  • Most strong in occipital region
  • Also measured in parietal and frontal region
  • Frequency: 8 – 13 Hz
  • Amplitude: 20 – 200 μV
  • Completely disappear when the subject is asleep
  • Attention to some type of mental activity ⇒ alpha wave is replace by asynchronous waves with higher frequency and lower amplitude

Beta wave
  • Measured in parietal and frontal region
  • Frequency: 14 – 30 Hz, up to 50 Hz with intense mental activity
  • Beta I wave: twice the frequency of alpha, attention to some type of mental activity ⇒ beta I wave is replace by asynchronous waves with lower amplitude (similar to alpha)
  • Beta II wave: during intense activation of CNS or tension
  • Mental activity inhibits beta I and elicits beta II.

Theta wave
  • Measured in parietal and temporal region from children or adults with emotional stress (disappointment and frustration)
  • Frustrate a person suddenly ⇒ 20 s of theta waves
  • Frequency: 4 – 7 Hz
- Delta wave
  - Frequency: < 3.5 Hz
  - Sometimes, occur once every 2 or 3 s
  - Occur in deep sleep
  - Measured from infant
  - Occur in serious organic brain disease
  - Occur solely within the cortex

**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 wave-like activity. See text.
Clinical EEG

- International Federation 10 – 20 system: electrode attachment
  - Small Ag/AgCl electrodes
  - Glue electrodes on scalp using collodion or hold them with rubber straps
- Differential amplifier: high gain, capacitive coupling
  - Between each member of a pair of electrodes: bipolar mode
    - Far field activities are cancelled
  - Between one electrode and reference electrode at earlob(s): monopolar mode
  - Between one electrode and the average of others: average reference mode
- Patients: awake, resting, eyes closed
- Noise: muscle activities from face, neck, ears, etc
- EEG from normal subject at resting state
  - Parietal – occipital areas: dominant alpha rhythm
  - Frontal areas: alpha rhythm and low-amplitude high-frequency beta rhythm
  - Symmetry of recordings between right and left hemispheres
- EEG from normal subject with increased cerebral activity
  - Increase in frequency of brain waves
  - Decrease in amplitude of brain waves since waves become asynchronous
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.)

Sleep Patterns

- Change of EEG pattern during sleep
  - Alert: low voltage, desynchronized wave
  - Resting: alpha wave, synchronized wave
  - Drowsy ⇒ fall asleep: slower and larger wave, synchronized wave
  - Moderately deep sleep: very large and irregular delta wave, sleep spindles (burst of alpha-like activity)
  - Deep sleep: very large and irregular delta wave
- Paradoxical sleep or rapid-eye-movement (REM) sleep
  - Rapid, low-voltage irregular activity
  - Threshold for arousal by sensory stimuli is even elevated
  - Rapid, roving eye movements
  - Marked reduction in muscle tone
  - Dreaming
- Nonrapid-eye-movement (NREM) sleep or slow wave sleep
  - Spindle or synchronized sleep
Without dreaming

Figure 4.29 The electroencephalographic changes that occur as a human subject goes to sleep. The calibration marks on the right represent 50 μV. (From H. H. Jasper, "Electroencephalography," in Epilepsy and Cerebral Localization, edited by W. G. Penfield and T. C. Erickson. Springfield, IL: Charles C. Thomas, 1941.)

Volume-Conductor Problem in Electroencephalography
- Brain: complicated geometry, inhomogeneous, anisotropic, distributed current dipoles
- Focal EEG sources due to stimulus ⇒ equivalent dipole model
- Localization of intracerebral potential sources (inverse problem)
  - Assume a model (such as an equivalent dipole generator in a homogeneous, isotropic conducting sphere)
  - Solve forward problem: calculate a potential from the model
  - Calculate error between measured potential and calculated potential
  - Iteratively adjust model parameters to minimize the error in least squares sense

Abnormal EEG
- Epilepsy: uncontrolled excessive activity by a part of all of CNS
  - Increased basal level of activity ⇒ attact
  - Activity below threshold ⇒ no attact
- Generalized epilepsy: entire brain at once
Grand mal epilepsy

- Intrinsic hyperexcitability of neurons in the brainstem portion of RAS or abnormal local neural pathways ⇒ extreme discharges of these neurons ⇒ cortex ⇒ deeper parts of brain ⇒ spinal cord ⇒ generalized tonic convulsions of the entire body following clonic convulsions
- Grand mal seizure lasts for a few seconds to 3 – 4 min
- Post-seizure depression of the entire nervous system
- Stupor for 1 min or a day or more
- EEG: high amplitude, synchronous, same periodicity as alpha, from any region, same discharges on both sides of the brain at the same time

Petit mal epilepsy

- Myoclonic form: a burst of neuronal discharges, for a fraction of a second, throughout the nervous system, single violent muscular jerk (arms or head), similar to a very short grand mal attack, no loss of consciousness, may lead to grand mal attack progressively
- Absence form: 5 – 20 s of unconsciousness, several twitchlike muscle contractions (usually head), pronounced blinking of eyes, return to consciousness, may lead to grand mal attack progressively, spike-and-dome pattern EEG over entire cortex, origin in RAS

Partial epilepsy: a portion (any part) of the brain

- Jacksonian epilepsy or Jacksonian march: organic lesion of the brain (scar, tumor, destroyed tissue) ⇒ rapid discharge of local neurons, > 1000 pps ⇒ spread with mm/min to cm/min ⇒ motor cortex ⇒ progressive march of muscular contractions throughout the opposite side of the body (leg → head or head → leg)
- Psychomotor seizure: low frequency (2 – 4 Hz) rectangular wave with superimposed 14 Hz waves, awareness but loss of control, sometimes without awareness
  - A short period of amnesia
  - An attack of abnormal rage
  - Sudden anxiety or fear
  - A moment of incoherent speech or mumbling
  - A motor act of rubbing the face with hand, attacking someone, etc

Diagnosis of tumors or diseased brain tissues

4.9 Magnetoencephalogram (MEG)
Active bioelectric source ⇒ magnetic as well as electric field
- Alpha wave ⇒ 0.1 pT at 5 cm from the scalp
- Biomagnetic field is 100 million times weaker than magnetic field of the earth (~ 50 μT)

SQUID (Superconducting Quantum Interference Device)
- Magnetometer with a sensitivity of 0.01 pT
- Gradiometer technique removes background noise (~ 10 – 100 nT)

MEG
- Advantages
  - Brain is homogeneous and isotropic in terms of magnetic permeability
  - Noncontact measurements
- Multi-channel MEG
  - > 100 channels
  - Mapping of biomagnetic field changing with time
  - Smaller SQUID detectors ⇒ better spatial resolution ⇒ more precise localization of intracerebral sources