Biomedical Instrumentation

The Origin of Bio-Potentials

Winter 1393
Bonab University
Bioelectric Signals

• Bioelectrical potential is a result of electrochemical activity across the membrane of the cell.

• Bioelectrical signals are generated by excitable cells such as nervous, muscular, and glandular cells.

• The resting potential of the cell is -40 to -90 mV relative to the outside and +60 mV during action potential.

• Volume conductor electric field is an electric field generated by many excitable cells of the specific organ such as the heart.

Typical types of bioelectric signals
- Electrocardiogram (ECG, EKG)
- Electroencephalogram (EEG)
- Electromyogram (EMG)
- Electroretinogram (ERG)
L: latent period = transmission time from stimulus to recording site.

Potential inside cells -40 to -90 mV relative to the outside.

Cell membrane is lipoprotein complex that is impermeable to intracellular protein and other organic anions (A⁻)
The Resting State

Membrane at resting state is
-slightly permeable to Na\(^+\) and freely permeable to K\(^+\) and Cl\(^-\)
-permeability of potassium \(P_K\) is 50 to 100 times larger than the permeability to sodium ion \(P_{Na}\).

Frog skeletal muscle membrane

Internal media

External media

2.5 mmol/liter of K\(^+\)

Cl\(^-\)

140 mmol/liter of K\(^+\)

K\(^+\)

Diffusional force > electrical force

2.5 mmol/liter of K\(^+\)

Cl\(^-\)

140 mmol/liter of K\(^+\)

K\(^+\)

Electric Field

Diffusional force = electrical force
**Sodium-Potassium Pump**

Keeping the cell at resting state requires active transport of ionic species against their normal electrochemical gradients.

Sodium-potassium pump is an active transport that transports Na\(^+\) \textbf{out} of the cell and K\(^+\) \textbf{into} the cell in ratio \(3\text{Na}^+:2\text{K}^+\).

Energy for the pump is provided by a cellular energy adenosine triphosphate (ATP).

\[2\text{K}^+ \leftrightarrow 3\text{Na}^+\]

2.5 mmol/liter of K\(^+\)  
140 mmol/liter of K\(^+\)

Electric Field

External media \hspace{1cm} Internal media

Frog skeletal muscle membrane
Equilibrium Potential- Nernst Equation

Approximate: Resting membrane \(-=\) Potassium membrane

\[
E_k = \frac{RT}{nF} \ln \left( \frac{[K]_o}{[K]_i} \right) = 0.0615 \log_{10} \left( \frac{[K]_o}{[K]_i} \right)
\]

At 37 °C

Where \(n\) is the valence of \(K^+\).

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

E: Equilibrium transmembrane resting potential (V), net current is zero

\(P_M\): permeability coefficient of the membrane for ionic species \(M\)

\([M]_i\) and \([M]_o\): the intracellular and extracellular concentrations of \(M\) in moles/liter

R: Universal gas constant (8.31 J/mol.k)

T: Absolute temperature in K

F: Faraday constant (96500 C/equivalent)
### Example 4.1

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

<table>
<thead>
<tr>
<th>Species</th>
<th>Intracellular</th>
<th>Extracellular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺</td>
<td>12</td>
<td>145</td>
</tr>
<tr>
<td>K⁺</td>
<td>155</td>
<td>4</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>4</td>
<td>120</td>
</tr>
</tbody>
</table>

Assuming room temperature (20 °C) and typical values of permeability coefficient for the frog skeletal muscle:

\( P_{Na} = 2 \times 10^{-8} \text{ cm/s}, \ P_{k} = 2 \times 10^{-6} \text{ cm/s}, \text{ and } P_{Cl} = 4 \times 10^{-6} \text{ cm/s} \), calculate the equilibrium resting potential for this membrane, using the Goldman equation.
\[
E = \frac{RT}{F} \ln \left\{ \frac{P_K[K]_o + P_{Na}[Na]_o + P_{Cl}[Cl]_i}{P_K[K]_i + P_{Na}[Na]_i + P_{Cl}[Cl]_o} \right\} 
\] (4.2)

**ANSWER** From (4.2),

\[
E = 0.0581 \log_{10} \left[ \frac{P_K(4) + P_{Na}(145) + P_{Cl}(4)}{P_K(155) + P_{Na}(12) + P_{Cl}(120)} \right]
\]

\[
= 0.0581 \log_{10} \left( \frac{26.9 \times 10^{-6}}{790.24 \times 10^{-6}} \right) = -85.3 \text{ mV}
\]

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

Membrane at resting state is polarized (more negative inside the cell)

**Depolarization**: lessening the magnitude of cell polarization by making inside the cell less negative.

**Hyperpolarization**: increasing the magnitude of cell polarization by making inside the cell more negative.

A stimulus that depolarize the cell to a potential higher than the **threshold potential** causes the cell to generate an action potential.

**Action Potential**:
- Rate: 1000 action potential per second for nerve
- All-or-none
- $\Delta v = 120$ mV for nerve (duration $\approx 1$ ms)
If stimulus depolarize the cell such that $V_{\text{cell}} > V_{\text{threshold}}$ an action potential is generated.
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 Na\(^+\) and K\(^+\). As the transmembrane potential \(v_m\) is depolarized, the membrane permeability to sodium \(P_{Na}\) (or, equivalently, the conductance of the membrane to sodium \(g_{Na}\)) is significantly increased. As a result, Na\(^+\) rushes into the internal medium of the cell, bringing about further depolarization, which in turn brings about a further increase in \(g_{Na}\) (i.e., \(g_{Na}\) is dependent on transmembrane potential). If the membrane potential threshold is exceeded, this process is self-regenerative and leads to runaway depolarization. Under these conditions, \(v_m\) tends to approach the equilibrium Nernst potential of sodium, \(E_{Na}\), which has a value of about +60 mV.

However, \(v_m\) never achieves this level because of two factors: (1) \(g_{Na}\) 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 \(g_K\) 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, \(g_K\) is still elevated with respect to its resting value and returns slowly along an exponential time course. Since K\(^+\) continue to leave the cell during this time, the membrane hyperpolarizes and an undershoot is produced in the transmembrane potential waveform (\(v_m\)).
When action potential happens:
The ability of membrane to respond to 2\textsuperscript{nd} stimulus is greatly reduced

**Absolute refractory period**: membrane can not respond to any stimulus.

**Relative refractory period**: membrane can respond to intense stimulus.

The upper limit of repetitive discharge?
Action potential travel at one direction.

Myelination reduces leakage currents and improve transmission rate by a factor of approximately 20.
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 $g_{Cl}$ 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 $r_i$ and $r_o$ ($\Omega/cm$), respectively. Here $i_m$ is the transmembrane current per unit length (A/cm), and $v_i$ and $v_o$ are the internal and external potentials at point $z$, respectively.
Volume Conductor Fields

Volume conduction: Transmission of an electric field generated by active cell (current source) or cells immersed in a volume conductor medium of resistivity $\rho$ such as the body fluids. (ENG, EMG, ECG are other examples)

Potential Waveform at the outer surface of membrane for monophasic action potential:
1- tri-phasic in nature
2- greater spatial extent than the action potential
3- much smaller in peak to peak magnitude
4- relatively constant in propagation along the excited cell.

- Potential in the extracellular medium of a single fiber fall off exponentially in magnitude with increasing radial distance from the fiber (potential zero within 15 fiber radii)
- Potential depends on medium Properties.
Volume Conductor Fields

Local closed (solenoidal) lines of current flow

Repolarized membrane

Axon

Active region

Direction of propagation

Depolarized membrane

Resting membrane

External medium

Local closed (solenoidal) lines of current flow

A. Biphasic action potential

B. Monophasic action potential

C. Triphasic action potential
Volume Conductor Fields

The extracellular field of an active nerve trunk with its thousands of component nerve fibers simultaneously activated is similar to the field of a single fiber.

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 ($S_s$).
Peripheral Nervous System Function (somatic)

Spinal nervous system is functionally organized on the basis of what is called the reflex arc:

1. A sense organ: (ear-sound, eye-light, skin-temperature)

2. A sensory nerve: (transmit information to the CNS)

3. The CNS: serves as a central integrating station

4. Motor nerve: communication link between CNS and peripheral muscle

5. Effector organ: skeletal muscle fibers
**Example of reflex arc**

- The **crossed extensor reflex** is a **withdrawal reflex**.
- When the reflex occurs, the **flexors** in the withdrawing limb contract and the **extensors** relax, while in the other limb, the opposite occurs.

- An example of this is when a person steps on a **nail**, the leg that is stepping on the nail pulls away, while the other leg takes the weight of the whole body.
Muscle length control

Schematic diagram of a muscle-length control system for a peripheral muscle (biceps)

(a) Anatomical diagram of limb system, showing interconnections.

(b) Block diagram of control system.
Junctional Transmission

**Synapses**: intercommunicating links between neurons

**Neuromuscular junctions**: communicating links between neurons and muscle fibers at *end-plate region*.

Neuromuscular junction (20nm thickness) release neurotransmitter substance Acetylcholine (Ach)

Time delay due to **junction** is 0.5 to 1 msec

*Excitation-contraction time* delay due to muscle contraction

At high **stimulation rates**, the mechanical response fuse into one continuous contraction called a **tetanus** (mechanical response summates).
Neuromuscular junction

Axon of motor neuron
Myelin sheath
Action potential propagation in motor neuron

Voltage-gated calcium channel
Action potential propagation in muscle fiber

Terminal button
Vesicle of acetylcholine
Voltage-gated Na⁺ channel

Plasma membrane of muscle fiber
Acetylcholine receptor site
Acetylcholinesterase
Chemically gated cation channel

Motor end plate
Contractile elements within muscle fiber

Local current flow between depolarized end plate and adjacent membrane opens voltage-gated Na⁺ channels, reducing the potential to threshold and initiating an action potential in the adjacent membrane.
Electroneurogram (ENG)

Recording the field potential of an excited nerve.

**Neural field potential is generated by**
- Sensory component
- Motor component

**Parameters for diagnosing peripheral nerve disorder**
- Conduction velocity
- Latency
- Characteristic of field potentials evoked in muscle supplied by the stimulated nerve (temporal dispersion)

Amplitude of field potentials of nerve fibers < extracellular potentials from muscle fibers.
Conduction Velocity of a Nerve

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.

\[
\text{Velocity} = u = \frac{D}{L_1 - L_2}
\]

Subtraction of longer latency and shorter
Extracellular field response from the sensory nerves of the median or ulnar nerves

To excite the large, rapidly conducting sensory nerve fibers but not small pain fibers or surrounding muscle, apply brief, intense stimulus (square pulse with amplitude 100-V and duration 100-300 μsec). To prevent artifact signal from muscle movement position the limb in a comfortable posture.

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.
Nerve repair

Median nerve repair

Ulnar artery

Ulnar nerve repair
Some times when a peripheral nerve is stimulated, two evoked potentials are recorded in the muscle the nerve supplies. The time difference between the two potentials determined by the distance between the stimulus and the muscle.

Stimulated nerve: posterior tibial nerve
Muscle: gastrocnemius
Electromyogram (EMG)

Skeletal muscle is organized functionally on the basis of the single motor unit (SMU).

SMU is the smallest unit that can be activated by a volitional effort where all muscle fibers are activated synchronously.

SMU may contain 10 to 2000 muscle fibers, depending on the location of the muscle.

Factors for muscle varying strength
1. Number of muscle fibers contracting within a muscle
2. Tension developed by each contracting fiber
Muscle Fiber (Cell)

http://www.blackwellpublishing.com/matthews/myosin.html
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.