Electrical Signaling

Neurons: major task is signaling

- Electrical signal for long distance with speed
- Communication with electrical and chemical synapses

Electrical signaling is based on electrical excitability of the cell.

**FIGURE 1.** Excitable cells generate a wide variety of electrical signals. Some signals are large (e.g., A, B, H), while others are small (e.g., C). Some are depolarizing (C), while others are hyperpolarizing (D). Some last seconds (I), while others last only milliseconds (A). Some have complex waveforms (E, H), while others are relatively simple (F). Finally, some signals are periodic (J, K, L).
What is the molecular basis of membrane excitability?
Neurons and muscle fibers exhibit membrane excitability.
- Respond to specific stimuli
- Generate the action potentials
- Propagate the signal

Ionic movements across the cell membrane.
- Such as K\(^+\), Na\(^+\), Ca\(^{2+}\), Cl\(^-\)

Ability of the membrane from a resting to an active state.

The cell membrane
Cell membrane-phospholipid bilayer
- Integral and peripheral proteins
  - Phospholipid bilayer: a strong barrier to ions
  - Pores or channels that span the cell membrane: permeate ions
    - Protein
      - Ionic selectivity
        - Example: K\(^+\) channels, Na\(^+\) channels
        - Either Non-gated (unregulated and always open)
        - or Gated (regulated)
Membrane potential ($V_m$) results from the separation of charge across the membrane.

High electrical resistance of membrane

Transfer of very few ions through non-gated ion channels

Neuron: selective for $\text{Na}^+$, $\text{K}^+$, $\text{Cl}^-$

Glia: selective only for $\text{K}^+$

Thus, membrane conductance is a function of density and permeability of the non-gated ion channels.
Equilibrium potential for K+ can be calculated by the Nernst equation

\[ E_K = \frac{RT}{zF} \ln \left( \frac{[K^+]_o}{[K^+]_i} \right) \]

\[ = (58 \text{ mV}) \log \left( \frac{[K^+]_o}{[K^+]_i} \right) \]

\[ = -58 \text{ mV (inside negative to the outside)} \]
2. An imaginary cell with Na+ leak channels
Na⁺ outside: \([\text{Na}^+]_o = 100 \, \text{mM}\)
Na⁺ inside: \([\text{Na}^+]_i = 10 \, \text{mM}\)

Calculate equilibrium potential for Na⁺

3. An imaginary cell with K⁺ and Na⁺ leak channels
Na⁺ outside \([\text{Na}^+]_o = 100 \, \text{mM}, \quad \text{K}^+ \text{ outside} = 10 \, \text{mM}\)
Na⁺ inside \([\text{Na}^+]_i = 10 \, \text{mM}, \quad \text{K}^+ \text{ inside} = 100 \, \text{mM}\)

What is the movement of these ions?

What is the membrane potential of this cell?
Fluxes for Na\(^+\), K\(^+\), and Cl\(^-\) at the resting membrane potential

Resting potential is not an equilibrium potential

\[\downarrow\]

Steady state fluxes of ions

<table>
<thead>
<tr>
<th>Driving force</th>
<th>Net driving force</th>
<th>Net flux</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chem.</td>
<td>Elec.</td>
<td></td>
</tr>
<tr>
<td>Extracellular side</td>
<td>Na(^+)</td>
<td>(\times P_{Na})</td>
</tr>
<tr>
<td>Cytoplasmic side</td>
<td>Na(^+)</td>
<td>(\downarrow)</td>
</tr>
<tr>
<td>Extracellular side</td>
<td>K(^+)</td>
<td>(\uparrow)</td>
</tr>
<tr>
<td>Cytoplasmic side</td>
<td>K(^+)</td>
<td>(\downarrow)</td>
</tr>
<tr>
<td>Extracellular side</td>
<td>Cl(^-)</td>
<td>(\times P_{Cl})</td>
</tr>
<tr>
<td>Cytoplasmic side</td>
<td>Cl(^-)</td>
<td>(\downarrow)</td>
</tr>
</tbody>
</table>

**Figure 6-6**

The fluxes for Na\(^+\), K\(^+\), and Cl\(^-\) across the cell membrane are a result of their chemical and electrical driving forces and the permeability of the membrane. The fluxes shown here are for a cell with a membrane potential of \(-60\) mV and the ionic gradients shown in Table 6-1. (Horizontal arrows signify no net driving force or no net flux.)

**Deviation from Nernst equation**

The relationship between membrane potential and external K\(^+\) concentration [log scale] in nerve cells and glia. The calculated Nernst potential for K\(^+\) (solid line) matches the observed membrane potential in glia (open circles) over a wide range of extracellular K\(^+\) concentration. In nerve cell membranes, however, the observed potential deviates from the theoretical curve at relatively low values of extracellular K\(^+\) (dashed line). (Adapted from Orkand, 1977.)
Equation for the membrane potential

At steady state: \( i_K + i_{Na} = 0 \)

\( i_K = g_K (V_m - E_K), \quad i_{Na} = g_{Na} (V_m - E_{Na}) \)

\[
V_m = E_{Na} \left( \frac{g_{Na}}{g_{Na} + g_K} \right) + E_K \left( \frac{g_K}{g_{Na} + g_K} \right)
\]

Goldman Equation

\[
V_m = \frac{RT}{F} \ln \frac{P_K [K^+]_o + P_{Na} [Na^+]_o + P_{Cl} [Cl^-]_o}{P_K [K^+]_i + P_{Na} [Na^+]_i + P_{Cl} [Cl^-]_o}
\]

at resting,

\( P_K : P_{Na} : P_{Cl} = 1 : 0.04 : 0.45 \)
Unequal distribution of ions and membrane potential

<table>
<thead>
<tr>
<th>Ion</th>
<th>Intracellular</th>
<th>Extracellular</th>
<th>$E_{ion}$</th>
<th>Intracellular</th>
<th>Extracellular</th>
<th>$E_{ion}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frug muscle fiber</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>K⁺</td>
<td>140</td>
<td>2.5</td>
<td>-102 mV</td>
<td>400</td>
<td>10</td>
<td>-93 mV</td>
</tr>
<tr>
<td>Na⁺</td>
<td>10</td>
<td>120</td>
<td>+63 mV</td>
<td>50</td>
<td>460</td>
<td>+56 mV</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>1.5</td>
<td>77.5</td>
<td>-99 mV</td>
<td>100</td>
<td>540</td>
<td>-42 mV</td>
</tr>
<tr>
<td>Organic anions</td>
<td>86</td>
<td>40</td>
<td>—</td>
<td>360</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Squid giant axon</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Membrane potential</td>
<td>—</td>
<td>—</td>
<td>-90 mV</td>
<td>—</td>
<td>—</td>
<td>-70 mV</td>
</tr>
</tbody>
</table>

Role of Na\(^+\)/K\(^+\) pump

At a steady state potential, there exist constant ionic movements (Na\(^+\) in, K\(^+\) out). Even though this is extremely small, but eventually concentration gradient will run down and Vm becomes 0.

How do neurons maintain concentration gradient of Na\(^+\) and K\(^+\)?
⇒ Na\(^+\)/K\(^+\) pump moves 3 Na\(^+\) out and 2 K\(^+\) in (ATP-dependent)

![Diagram of Na+/K+ pump](image)

The pump is electrogenic and hyperpolarizes the cell.

$$E_{Na} = 56\text{mV}$$

$$E_K = -93\text{mV}$$

potential due to non-gated channel

Hyperpolarization by Na\(^+\)/K\(^+\) pump