Electrical signals are carried by dissociated ions

Different concentrations of four principal types of ions maintain a potential difference across the membrane of neurons: Na\(^+\), K\(^+\), Ca\(^{2+}\) and Cl\(^-\) (Fig. 2A). These ions can move across the cell membrane through ion channels and via ion pumps. The permeability of ion channels can depend on several factors, such as voltage. This gives neurons a rich set of electrical properties.

The Nernst Equation

Ignoring active transport (ion pumps), the flow of ions across the membrane is caused by diffusion (from higher to lower concentration) and by the electrical potential gradient. The “equilibrium” (or “reversal”) potential for each type of ion occurs when these forces balance (Fig. 2B). We can calculate equilibrium potentials as follows.

Fick’s Law for the diffusion flux \( J_{\text{diff}} \) is

\[
J_{\text{diff}} = -D \frac{\partial C}{\partial x}
\]

where \( D \) is the diffusion constant, \( C \) is the concentration, and \( x \) is distance.

Ohm’s law for the flux of charged particles in an electric field \( J_{\text{drift}} \) is

\[
J_{\text{drift}} = -\mu z C \frac{\partial V}{\partial x}
\]

where \( \mu \) is the mobility of the ion, \( z \) is its valence, and \( V \) is the voltage.

Ignoring active transport, there is no net flow when

\[
J_{\text{total}} = J_{\text{diff}} + J_{\text{drift}} = 0
\]

Some physics allows us to write

\[
J_{\text{total}} = -\left(\mu z C \frac{\partial V}{\partial x} + \frac{RT}{F} \frac{\partial C}{\partial x}\right)
\]

where \( T \) is absolute temperature, \( R \) is the universal gas constant, and \( F \) is Faraday’s constant. Thus \( J_{\text{total}} = 0 \) when

\[
\frac{\partial V}{\partial x} = -\frac{RT}{zF} \frac{1}{C} \frac{\partial C}{\partial x}
\]

Therefore

\[
\int_{x_1}^{x_2} \frac{dV}{dx} = -\frac{RT}{zF} \int_{x_1}^{x_2} \frac{1}{C} \frac{dC}{dx}
\]

Change variables:

\[
\int_{V_1}^{V_2} dV = -\frac{RT}{zF} \int_{C_1}^{C_2} \frac{dC}{C}
\]

Therefore

\[
V_2 - V_1 = -\frac{RT}{zF} \ln \frac{C_2}{C_1}
\]

Define the equilibrium potential \( E_i \) of ion \( i \) as the potential across the membrane for which there is no net flow of ions. We then obtain the Nernst Equation:

\[
E_i = \frac{RT}{zF} \ln \frac{C_{\text{out}}}{C_{\text{in}}}
\]

Note the reversal of sign: we have defined the membrane potential \( V_m \) as \( V_{\text{in}} - V_{\text{out}} \), and \( E_i \) as the \( V_m \) for which there is no net flow of that type of ion.
Equilibrium potentials for the squid giant axon

The giant axon of the squid is a very useful experimental preparation for studying the electrical potentials of neurons, much used in the first half of the 19th century.

At 20°C (293K), \( E_i = 58 \text{mV} \log_{10} \frac{C_{\text{out}}}{C_{\text{in}}} \). For the squid giant axon we then have:

<table>
<thead>
<tr>
<th>Ion</th>
<th>Inside (mM)</th>
<th>Outside (mM)</th>
<th>Equilibrium potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>K⁺</td>
<td>400</td>
<td>20</td>
<td>( 58 \log_{10} \frac{20}{400} = -75 \text{mV} )</td>
</tr>
<tr>
<td>Na⁺</td>
<td>50</td>
<td>440</td>
<td>( 58 \log_{10} \frac{440}{50} = +52 \text{mV} )</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>100</td>
<td>560</td>
<td>( -58 \log_{10} \frac{560}{100} = -43 \text{mV} )</td>
</tr>
<tr>
<td>Ca²⁺</td>
<td>( 10^{-4} )</td>
<td>5</td>
<td>( 29 \log_{10} \frac{10^{-4}}{10} = +145 \text{mV} )</td>
</tr>
</tbody>
</table>

Overall resting potential for the squid giant axon is about -70 mV.

Equilibrium potentials for a typical mammalian cell

At 37°C (310K), \( E_i = 62 \text{mV} \log_{10} \frac{C_{\text{out}}}{C_{\text{in}}} \). For a typical mammalian cell we then have:

<table>
<thead>
<tr>
<th>Ion</th>
<th>Inside (mM)</th>
<th>Outside (mM)</th>
<th>Equilibrium potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>K⁺</td>
<td>140</td>
<td>5</td>
<td>( 62 \log_{10} \frac{140}{5} = -90 \text{mV} )</td>
</tr>
<tr>
<td>Na⁺</td>
<td>10</td>
<td>145</td>
<td>( 62 \log_{10} \frac{145}{10} = +72 \text{mV} )</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>4</td>
<td>110</td>
<td>( -62 \log_{10} \frac{110}{4} = -89 \text{mV} )</td>
</tr>
<tr>
<td>Ca²⁺</td>
<td>( 10^{-4} )</td>
<td>5</td>
<td>( 31 \log_{10} \frac{10^{-4}}{10} = +145 \text{mV} )</td>
</tr>
</tbody>
</table>

Overall resting potential for a typical mammalian cell is about -65 mV.

The Goldman-Hodgkin-Katz voltage equation

The ionic gradients described above are maintained by

- Active transport of ions (e.g. Na⁺-K⁺ pump pushes 3 Na⁺ ions out for every two K⁺ in).
- Selective permeability of the membrane to different ions.

The Nernst equation doesn’t take selective permeabilities \( P_i \) into account. But we can make some more assumptions, for example:

- Ions move across membrane independently,
- Electric field in the membrane is constant,
- Electric field in the membrane is constant.

Goldman, Hodgkin and Katz were then able to derive the following equation for the overall resting potential \( V \):

\[
V = \frac{RT}{F} \ln \frac{P_K [K_{\text{out}}]}{P_K [K_{\text{in}}]} + \frac{P_{Na} [Na_{\text{out}}]}{P_{Na} [Na_{\text{in}}]} + \frac{P_{Cl} [Cl_{\text{in}}]}{P_{Cl} [Cl_{\text{out}}]} 
\]

A nice simulator for playing with this and related equations can be found at http://www.nernstgoldman.physiology.arizona.edu.

GHK prediction for the squid giant axon

At rest, the ratio of permeabilities \( P_K: P_{Na}: P_{Cl} \) is 1:0.03 0.1. Combining this with the relevant concentrations gives

\[
V_{\text{rest}} = 58 \log_{10} \frac{1 \times 10 + 0.03 \times 460 + 0.1 \times 40}{1 \times 400 + 0.03 \times 50 + 0.1 \times 540} = -70 \text{mV}
\]

which is in good agreement with experimental data.
What happens during an action potential (spike)?

During an action potential the membrane potential undergoes a short, rapid reversal. This is mainly because Na\(^+\) channels transiently open, increasing their relative permeability from 0.03 to 15 (Fig. 3). We then have

\[
V_m = 58 \log \frac{1 \times 10 + 15 \times 460 + 0.1 \times 40}{1 \times 400 + 15 \times 50 + 0.1 \times 540} = +44\text{mV}
\]

Hodgkin and Huxley developed a seminal mathematical model in the 1940s to describe how action potentials are generated, which we will study in a later lecture.

Summary

- Neurons maintain an electrical potential difference across their membrane.
- The size of this potential difference can be predicted by simple mathematical models of the diffusive and electrical flow of ions across the membrane.

Recommended reading

Figure 2: **A** Four main types of ions are differentially distributed between the inside and outside of neurons. They can move through the membrane via ion channels. These channels have selective permeabilities, which can depend on several variables. **B** There is a particular "equilibrium" electrical potential for each ion at which the flow of ions due to diffusion exactly matches the flow due to the voltage gradient (illustrated here for $K^+$ ions).

Figure 3: Schematic showing how the change in permeability of $Na^+$ channels causes a rapid change in the membrane potential during a spike.