Membrane potential

Resting membrane potential


Action potential

http://cognitiveconsonance.info/2013/03/21/neuroscience-the-action-potential/
Resting membrane potential

Inside of each cell is negative as compared with outer surface: negative resting membrane potential (between -30 and -90 mV)

Examination with microelectrode (Filled with KCl solution– Same mobility , There is not disturbing diffusion potential)

All living cells maintain a potential difference across their cell membranes. The inside usually negative relative to the outside.

Membrane potential

The electrical potential difference (voltage) across a cell's plasma membrane.
Why is the membrane potential formed?

- Unequal distribution of ions on two sides of the membrane: in the cell – high $K^+$ and low $Na^+$ concentration
- Constantly active K-Na pump: $Na^+$ moves out, $K^+$ moves in
- Selectively permeable membrane: the cell membrane is more permeable for Potassium ions than Sodium ions
- Non-diffusible ions (proteins and nucleic acids) with negative charge are in the cell

Intracellular Extracellular

<table>
<thead>
<tr>
<th>Ion</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>$Na^+$</td>
<td>10 mM</td>
</tr>
<tr>
<td>$K^+$</td>
<td>140</td>
</tr>
<tr>
<td>$Ca^{2+}$</td>
<td>$&lt;10^{-1}$</td>
</tr>
<tr>
<td>$Cl^-$</td>
<td>3-4</td>
</tr>
<tr>
<td>$A^{-}$</td>
<td>140</td>
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</tr>
<tr>
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<td>2.5</td>
</tr>
<tr>
<td>$Ca^{2+}$</td>
<td>2</td>
</tr>
<tr>
<td>$Cl^-$</td>
<td>120</td>
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Forces controlling the movements of charged particles

„Drive forces“:

1) The difference of the ions concentration - Concentration gradient (diffusion: moving the particles from a high concentration area to a low one):
   Chemical potential

2) Charge difference between two sides of the membrane – electrical gradient:
   Electric potential

In equilibrium the change of free energy of the chemical and electrical concentration gradient equal and different direction.

The resting membrane potential can be calculated.
The origin of the resting membrane potential

- **Bernstein potassium** hypothesis

- **Nernst** equilibrium potential (electro-chemical potential)

- **Donnan** equilibrium: the membrane is **impermeable** for some components (e.g. intracellular proteins).

- **Goldman** equation: The membrane potential is the result of a „compromise” between the various equilibrium potentials, each weighted by the membrane permeability and absolute concentration of the ions.

### Nernst equation

Chemical potential \( \Rightarrow W_{chem} = NRT \ln \frac{X_1}{X_2} \)

- \( N \) = number of moles associated with the concentration gradient
- \( R \) = gas constant
- \( T \) = absolute temperature
- \( X_1 / X_2 \) = concentration gradient

Electrical potential \( \Rightarrow W_{elect} = NzFE \)

- \( N \) = number of moles of the charged particles
- \( z \) = valency
- \( F \) = Faraday’s number
- \( E \) = strength of the electric field (V)
Equilibrium potential

**Nernst equation:**
What membrane potential (E) balances the concentration gradient ($X_1/X_2$).

$$E = \frac{RT}{zF} \ln \frac{X_1}{X_2}$$

The inward and outward flows of the ions are balanced
(net current = zero → equilibrium = stable, balanced, or unchanging system).

Equilibrium potential

$$[K^+] \Rightarrow E_{mV} = -\frac{58}{1} \log \left(\frac{139}{2.5}\right) = -101.2 \text{ mV}$$

$K^+ = 2.5 \text{ mM} \leftrightarrow K^+ = 139 \text{ mM}$

$E_{mV} = -101.2 \text{ mV} \rightarrow$ no net movement (equilibrium)
$E_{mV} > -101.2 \text{ mV} \rightarrow K^+$ moving out
$E_{mV} < -101.2 \text{ mV} \rightarrow K^+$ moving in

A voltage value of the ion for which the balance between the concentration gradient.
Ionic concentrations inside and outside of a muscle cell

\[ \begin{align*}
Na^+ & : 120 \text{ mM} \\
K^+ & : 2.5 \text{ mM} \\
Cl^- & : 120 \text{ mM} \\
\end{align*} \]

\[ \begin{align*}
Na^+ & : 20 \text{ mM} \\
K^+ & : 139 \text{ mM} \\
Cl^- & : 3.8 \text{ mM} \\
\end{align*} \]

\[ [K^+] \Rightarrow E_{mv} = \frac{-58}{1} \log \left( \frac{2.5}{1} \right) = -101.2 \text{ mV} \]

\[ [Na^+] \Rightarrow E_{mv} = \frac{-58}{1} \log \left( \frac{20}{120} \right) = +45.1 \text{ mV} \]

\[ [Cl^-] \Rightarrow E_{mv} = \frac{-58}{1} \log \left( \frac{3.8}{120} \right) = +86.9 \text{ mV} \]

\[ E_{mv} = -92 \text{ mV} \]

- The Nernst equation is not suitable for determining the membrane potential.
- The calculated values differ from the measured values.
- Behavior of the ions are not independent.
- It is not a closed system.
The origin of the resting membrane potential

- **Bernstein** potassium hypothesis

- **Nernst**-equilibrium potential (electro-chemical potential)

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**Donnan equilibrium, Donnan-potential:**

Frederick George Donnan
(1870-1956; irish chemist)

- different diffusion agility through the semipermeable membrane →
  
  **diffusion potential**

- one of the particels cannot move through the membrane (intracellular proteins) →

  *Equilibrium concentration difference*
Rule of Donnan-equilibrium

- Diffusible ions: $K^+, Cl^-$

\[
\frac{RT}{zF} \ln \left( \frac{K_{in}}{K_{out}} \right) = E = \frac{RT}{zF} \ln \left( \frac{Cl_{out}}{Cl_{in}} \right)
\]

\[
\frac{[K_{in}]}{[K_{out}]} = \frac{[Cl_{out}]}{[Cl_{in}]}
\]

\[
[K_{in}] [Cl_{in}] = [K_{out}] [Cl_{out}]
\]

Only valid if the ions diffuse **passively** through the membrane!

What if the Donnan rule is not valid??

*Goldman-Hodgkin-Katz equation*

David E. Goldman (USA)
Alan Lloyd Hodgkin (England)
Bernard Katz (England).

To be able to determine the potential the permeability must be considered for each ion!!!!!!!
Goldman equation

N positively charged, and M negatively charged ion:

\[
E_m = \frac{RT}{F} \ln \left( \frac{\sum_j^N P_{M_j^+} [M_j^+]_{out} + \sum_j^M P_{A_j^-} [A_j^-]_{in}}{\sum_j^N P_{M_j^+} [M_j^+]_{in} + \sum_j^M P_{A_j^-} [A_j^-]_{out}} \right)
\]

- Every ion.
- Good agreement with reality.

Goldman equation

Membrane potential is the result of a compromise. Membrane potential is the average of the equilibrium potential of each ion with the weightened membrane permeabilities and absolute concentrations of the ions.
"Leakage" through the cell membrane

→ a membrane-potential is not equal with any of the equilibrium potentials for the different ions
  - $E_{mV}^{K^+} = -101.2$ mV <
  - $E_{mV}^{Na^+} = +45.1$ mV >
  - $E_{mV}^{Cl^-} = +86.9$ mV >

$\sum E_{mV} = -92$ mV

→ the ions are trying to get (move) through the membrane
  - $K^+$ is trying to get out
  - $Na^+$ is trying to get in
  - $Cl^-$ is trying to get in

$\Rightarrow$ "leakage"

Ion channels

◆ Resting or non-gated
  their opening and closing are not affected by the membrane potential (e.g. resting $K^+$ channels; potassium-sodium ($K^+$-$Na^+$) "leak" channel)

◆ Gated channels
  open in response to specific ligands or changes in the membrane potential (e.g. voltage-gated $K^+$ and $Na^+$ channels)
Na-K ATP-ase

- The passive flux of Na$^+$ and K$^+$ (leakage) is **balanced** by the active work of Na-K pump → contribution to the membrane potential.

- 3 Na$^+$ move out vs. 2 K$^+$ move in (exchanger)

- **ATP** is the energy source

Action potential
Action potential

♦ It can be developed on the membrane of nerve cells or muscle cells

♦ Typical for a given cell type

♦ Required stimulation above the voltage threshold

Action potential

♦ **Action potential**: a momentary reversal of membrane potential (-70 mV to +40 mV) that will be followed by the restoration of the original membrane potential after a certain time period (1-400ms).

♦ Action potentials happens in different **phases**.

♦ Action potentials are triggered by the depolarization of the membrane (local disturbances) if it can reach a critical value (**voltage threshold**).

♦ Action potentials are **all or none** phenomena
  ◦ any stimulation above the voltage threshold results in the same action potential response.
  ◦ any stimulation below the voltage threshold will not result action potential response.
1. Resting phase

Equilibrium situation

2. Rising phase

The voltage gated sodium channels will open-up if the voltage threshold was reached by the stimulus.

→ Na\(^+\) will move into the cell.

→ the inner surface of the cell will be positively charged.

K\(^+\) channels are starting to open-up
3. **Overshoot**

The movement of the Na\(^+\) will slow down

\[ \text{EmV}_{\text{Na}} = +45.1 \text{ mV (Nernst equilibrium potential)} \]

Na\(^+\) channels will start to form an inactive conformation

4. **Falling phase**

All the voltage gated K\(^+\) channels are open

\[ \rightarrow \text{K}^+ \text{ move out from the cell} \]

Sodium channels are closed down (inactivation)

\[ \rightarrow \text{refractory period} \]
5. **Falling phase**

The movement of the K⁺ ions will slow down

\[ \text{EmV}_{K^+} = -101.2 \text{ mV} \] (Nernst equilibrium potential)

The K⁺ channels will get into a closed conformation

The numerous and slowly inactivating K⁺ channels will cause some hyperpolarisation

6. **Resting phase**
The formation of a new AP is totally blocked.

- Absolute refractory period
- Relative refractory period

Larger depolarisation is needed than the threshold to initialize an AP.

http://www.youtube.com/watch?v=7EyhsOewnH4
The Action Potential Types

- Nerve Action Potential
- Heart Action Potentials
- Smooth Muscle Action Potential
- Skeletal Muscle Action Potential

Propagation of action potential

- Unmyelinated axon
- Myelinated axon

Slow propagation
Saltatory propagation- fast

The propagation speed increase with increasing fibre cross section.