27. The Goldman-Hodgkin-Katz equation:

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27.1. Definition of variables and formulas

The Goldman-Hodgkin-Katz equation:

\[ \Delta \psi = E_m = -\frac{RT}{zF} \ln \frac{p_K[K]_i + p_{Na}[Na]_i + p_{Cl}[Cl]_o}{p_K[K]_o + p_{Na}[Na]_o + p_{Cl}[Cl]_i} \]

\( \Delta \psi \): electric potential difference between the two sides, the membrane potential of the cell (V)
R: universal gas constant: 8.31 J/(molK)
T: absolute temperature (K)
z: charge of the ion (in this form \( z = +1 \))
F: Faraday's constant, 96485 C/mol
[X]_i: intracellular concentration of ion X (mol/dm³)
[X]_o: extracellular concentration of ion X (mol/dm³)
ln: natural logarithm
\( p_x \): permeability of ion X, which can be increased by the opening of channels selective for that ion. The relative values of \( p \) of the various ions compared to each other is significant.

Interpretation of the GHK equation: The value of the membrane potential (MP) depends on the concentrations of the main permeating ions and their permeabilities through the membrane, which is mainly determined by the opening / closing of the channels selective for that ion. The greater the permeability for a given ion (many channels open), the closer the MP will be to the equilibrium (Nernst) potential for that ion. For example, opening of many K+ channels will shift the MP toward -89 mV, while opening of many Na+ channels will shift the MP toward +60 mV.

The actual MP is the average of the Nernst-potentials of the permeating ions weighted by the permeabilities.
27.2. Sample exercises with solutions

Table for the sample exercises:

<table>
<thead>
<tr>
<th>I.C. conc (mM)</th>
<th>E.C. conc (mM)</th>
<th>Nernst-pot. (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>K⁺</td>
<td>140</td>
<td>5</td>
</tr>
<tr>
<td>Na⁺</td>
<td>10</td>
<td>140</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>20</td>
<td>120</td>
</tr>
</tbody>
</table>

27.2.1. Exercise

Based on the ion concentrations and equilibrium potentials shown in the table what is the value of the membrane potential if the relative permeabilities are p_K : p_Na : p_Cl = 150:3:10? (T = 37°C)

\[ \Delta \psi = E_m = -\frac{8.31 \times 310 \ln 150 \times 140 + 3 \times 10 + 10 \times 120}{+1 \times 96485 \ln 150 \times 5 + 3 \times 140 + 10 \times 20} = -0.0267 \times \ln(16.22) = -74.4 mV \]

27.2.2. Exercise

How will the current membrane potential of -74.4 mV change if p_K decreases due to the closing of K⁺ channels?

If p_K decreases, the weight of E_K in setting the MP decreases, thus, the MP will move away from -89 mV becoming more positive. (= The outflow of K⁺ decreases, fewer positive charges leave the cell, the MP becomes more positive.)

27.2.3. Exercise

How will the current membrane potential of -74.4 mV change if p_Cl increases due to the opening of Cl⁻ channels?

If p_Cl increases, the weight of E_Cl in setting the MP increases, thus, the MP will move toward -48 mV becoming more positive. (= The outflow of Cl⁻ increases, more negative charges leave the cell, the MP becomes more positive.)

27.2.4. Exercise

Based on the ion concentrations and equilibrium potentials shown in the table what is the value of the membrane potential if the relative permeabilities are p_K : p_Na : p_Cl = 150:5:10? (T = 37°C)
\[ \Delta \psi = E_m = -\frac{8.31 \times 310 \ln \frac{100 \times 140 + 5 \times 10 + 10 \times 120}{100 \times 5 + 5 \times 140 + 10 \times 20}}{+1 \times 96485} = -0.0267 \ln(10.89) = -63.8 mV \]

### 27.2.5. Exercise

Based on the ion concentrations and equilibrium potentials shown in the table what is the value of the membrane potential if the relative permeabilities are \( p_K : p_{Na} : p_{Cl} = 10:1:2 \) (\( T = 37^\circ C \))

\[ \Delta \psi = E_m = -\frac{8.31 \times 310 \ln \frac{10 \times 140+1 \times 10 + 2 \times 120}{10 \times 5 + 1 \times 140 + 2 \times 20}}{+1 \times 96485} = -0.0267 \ln(7.17) = -52.6 mV \]

### 27.3. Practice exercises

Based on the ion concentrations and equilibrium potentials shown in the table answer the questions below (\( T = 37^\circ C \)).

<table>
<thead>
<tr>
<th></th>
<th>I.C. conc (mM)</th>
<th>E.C. conc (mM)</th>
<th>Nernst-pot. (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( K^+ )</td>
<td>145</td>
<td>4.5</td>
<td>-93</td>
</tr>
<tr>
<td>( Na^+ )</td>
<td>15</td>
<td>120</td>
<td>+56</td>
</tr>
<tr>
<td>( Cl^- )</td>
<td>30</td>
<td>110</td>
<td>-35</td>
</tr>
</tbody>
</table>

1. What is the value of the membrane potential if the relative permeabilities are: \( p_K : p_{Na} : p_{Cl} = 30:1:2 \)?
   (a) -75.6 mV    (b) -62.4 mV    (c) -58.7 mV    (d) -46.8 mV

2. Around what value will the membrane potential stabilize if it is currently -70 mV, and the permeability of \( Cl^- \) significantly increases compared to the other ions?
   (a) -93 mV    (b) -35 mV    (c) 0 mV    (d) +25 mV

3. How will the membrane potential change from the current -70 mV if the extracellular \( K^+ \) concentration is significantly elevated and the \( K^+ \) permeability remains high?
   (a) shifts in the negative direction    (b) does not change    (c) shifts in the positive direction

4. What value will the membrane potential approach from the current -70 mV if the extracellular \( K^+ \) concentration is raised to 145 mM and the \( K^+ \) permeability remains high?
   (a) -93 mV    (b) does not change    (c) 0 mV    (d) +56 mV

Multiple choice (more than one answer possible)
5. Based on the above data what new value can the membrane potential assume from the current -62 mV value if we block the K\(^+\) channels by inhibitor compounds?

(a) -52 mV  (b) -15 mV  (c) -73 mV  (d) +68 mV

6. Based on the above data what new value can the membrane potential assume if a high number of voltage-gated Na\(^+\) channels open and \(p_{\text{Na}}\) becomes dominant?

(a) -52 mV  (b) -15 mV  (c) -73 mV  (d) +52 mV

7. What is the value of the membrane potential if the relative permeabilities are: \(p_K : p_{\text{Na}} : p_{\text{Cl}} = 120:1:2\)?

(a) -79,8 mV  (b) -65,4 mV  (c) -58,4 mV  (d) -49,8 mV

8. How will the membrane potential change from the current -60 mV if the extracellular Cl\(^-\) concentration is decreased and the Cl\(^-\) permeability remains high?

(a) shifts in the negative direction  (b) does not change  (c) shifts in the positive direction

9. A cell has a membrane potential of -40 mV and high K\(^+\) and Cl\(^-\) conductance. How will the membrane potential change if we block the Cl\(^-\) channels with inhibitors?

(a) shifts in the negative direction  (b) does not change  (c) shifts in the positive direction

10. Based on the data in the table what is the value of the membrane potential if the relative permeabilities are: \(p_K : p_{\text{Na}} : p_{\text{Cl}} = 100:1:6\)?

(a) -77,8 mV  (b) -66,2 mV  (c) -53,2 mV  (d) -47,8 mV

11. True or false
Based on the GHK equation, a large change in the MP can only occur if the concentration of the permeating ions changes to a great extent relative to each other on the two sides of the membrane.

12. True or false
Based on the GHK equation, opening of Cl\(^-\) channels shifts the membrane potential toward the equilibrium potential of Cl\(^-\).