

MEMBRANE POTENTIAL, ACTION POTENTIAL

Some Thermodynamics Background

Free enthalpy (denoted: G , also called Gibbs free energy or Gibbs energy) is the thermodynamic potential which shows the amount of useful work obtainable from a thermodynamic system at constant pressure and temperature. In thermodynamic systems which are at constant pressure and temperature, the free enthalpy is minimum at equilibrium.

The chemical potential (μ) is the rate of change of the free enthalpy (G) of the system with respect to the change in the number of moles of the constituent particles (v):

$$\mu = \frac{\Delta G}{\Delta v}.$$

For ideal solutions the chemical potential can be calculated as follows:

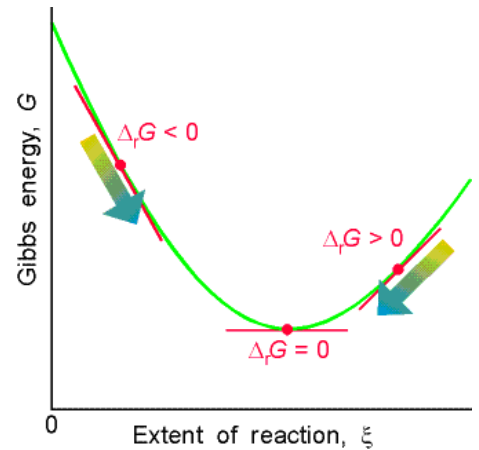
$$\mu = \mu_0 + R \cdot T \cdot \ln(c)$$

where μ_0 is the chemical potential of one mole substance, T is the absolute temperature, R the gas constant.

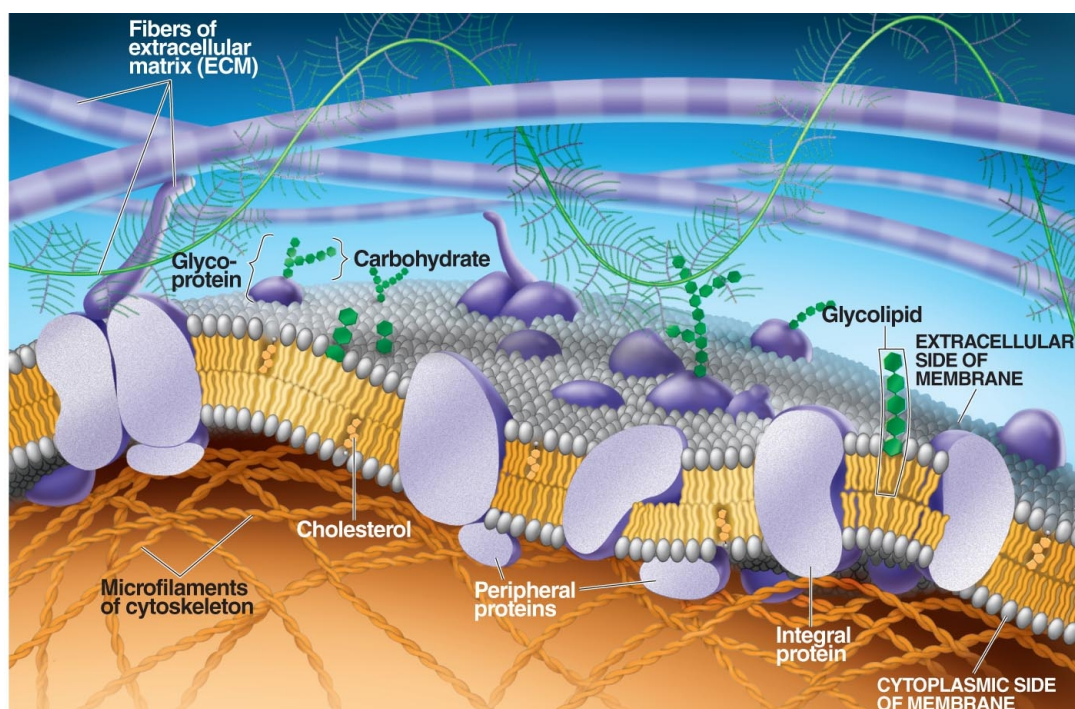
If electrostatic fields are also present, the chemical potential is:

$$\mu = \mu_0 + R \cdot T \cdot \ln(c) + z \cdot F \cdot \varphi,$$

where z denotes the valency of the particles, φ the electric potential, $F = N_A \cdot e$ is the Faraday constant, N_A denotes Avogadro's number, e the elementary electric charge. To emphasize the last term that describes the electric interactions, the above expression is often called electrochemical potential.



Membrane Transport

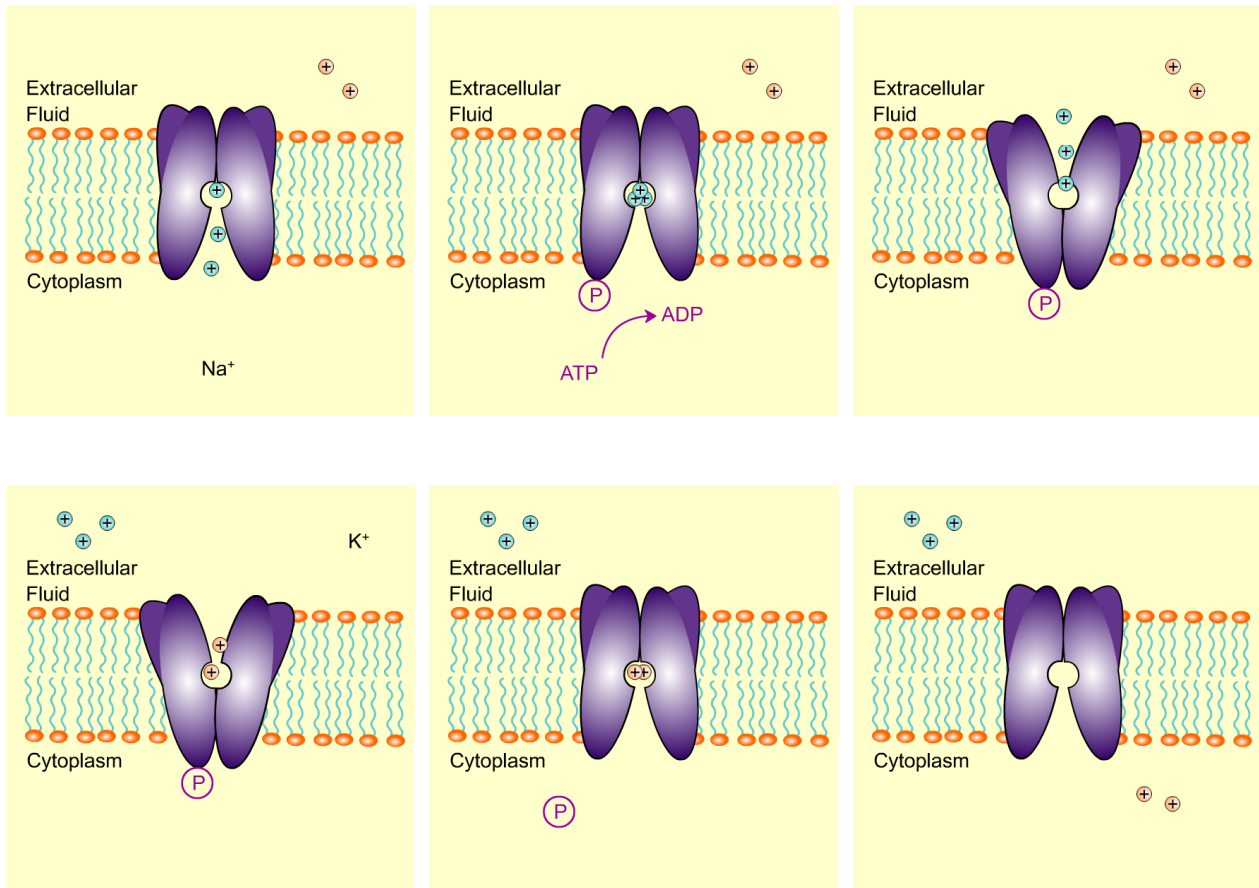


Definition of membrane transport: moving of biochemicals and other atomic or molecular substances across biological membranes.

Three types are distinguished: passive transport, facilitated transport, active transport.

Active Transport

Active transport is done by transporter proteins, which use chemical energy (e.g. $\text{ATP} \rightarrow \text{ADP}$, $\Delta\mu_{H^+}$, $\Delta\mu_{Na^+}$) to pump the substance to higher electrochemical potential. Active transport is limited at high substance concentrations by the number of protein transporters present.



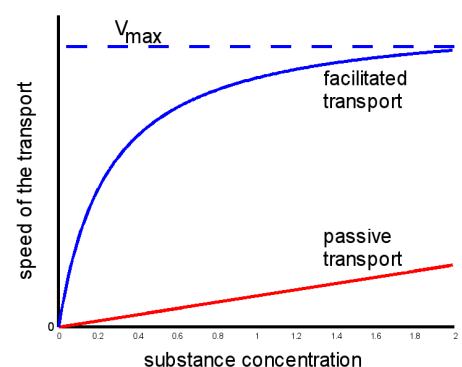
Facilitated Transport

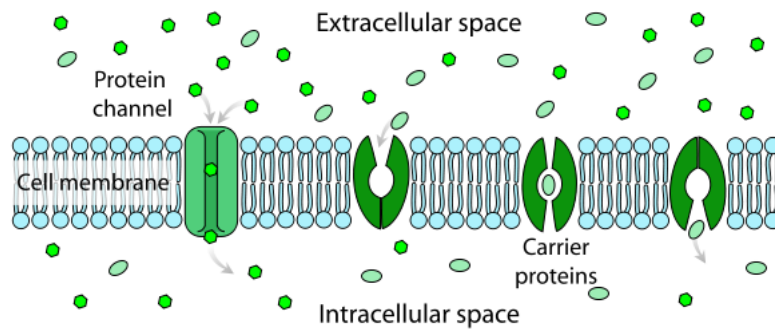
Facilitated transport does not require energy, and it only transports from higher to lower electrochemical potential, but it does require a carrier or a channel protein. Carrier proteins bind the substance and carry it across the membrane. Ion channels do not bind the solute, but form hydrophilic pores through the membrane that allow certain types of solutes (usually inorganic ions) to pass through.

The facilitated transport can be described very similarly to the enzyme catalyzed reactions. The speed of the transport is proportional to the amount of the activated carrier protein (P) - substrate (S) complex (PS):

$$v = k \cdot [\text{PS}] = \frac{k \cdot [\text{P}] \cdot [\text{S}]}{K_M + [\text{S}]}$$

At large substrate concentrations the speed of facilitated transport is limited by the number of carrier or channel proteins available.





Passive Transport

Passive transport happens by simple diffusion. It does not require energy or specialized molecules, and it only transports from higher to lower electrochemical potential. (Remember: diffusion is the tendency of molecules to spread into an available space. This tendency is a result of the intrinsic thermal movement of the molecules at temperatures above absolute zero.) Many small, uncharged molecules (e.g. water, oxygen, carbon dioxide, ethanol) readily cross the cell membrane by simple diffusion. Ions and charged molecules diffuse across the lipid bilayer of cell membranes very, very poorly.

The diffusion of uncharged molecules within the membrane is described by Fick's law:

$$J = -D_m \cdot \frac{c_{m1} - c_{m2}}{d},$$

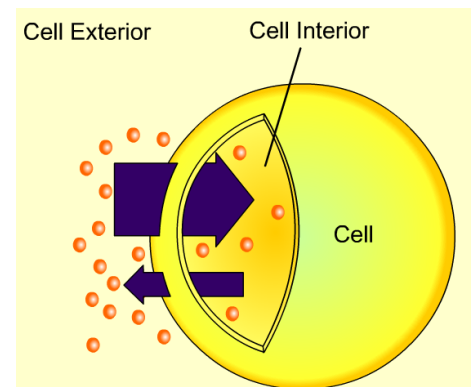
where J is the matter flow density, D_m is the diffusion constant in the membrane, c_{m1} and c_{m2} are the concentrations of the substance at the two surfaces, inside the membrane, and d is the thickness of the membrane. We know that:

$$\frac{c_{m1}}{c_1} = \frac{c_{m2}}{c_2} = K,$$

where c_1 and c_2 are the substance concentrations at the two surfaces of the membrane in the aqueous phase, and K is the partition coefficient of the substance between the aqueous phase and the membrane. We can now write:

$$J = -p \cdot (c_2 - c_1) = -p \cdot \Delta c,$$

where the quantity $p = K \cdot \frac{D_m}{d}$ is called the permeability constant.



Nernst Equation

The transport of small charged ions is of outstanding biological importance. There is an electric potential difference between the two sides of the membranes of the living cells. Let us consider the diffusional equilibrium of a single charged particle across this membrane.

In equilibrium the electrochemical potential on the two sides of the membrane will be the same:

$$\mu_0 + R \cdot T \cdot \ln(c_1) + z \cdot F \cdot \phi_1 = \mu_0 + R \cdot T \cdot \ln(c_2) + z \cdot F \cdot \phi_2.$$

Rearranging the equation we get:

$$\phi_2 - \phi_1 = \frac{R \cdot T}{z \cdot F} \cdot \ln\left(\frac{c_1}{c_2}\right).$$

The above equation is called Nernst equation, and describes the equilibrium of one single species of ion. In living cells, however, the transport of several different ions contributes to the equilibrium, and the Nernst equation can not adequately describe the membrane potential.

Goldman-Hodgkin-Katz Equation

The Goldman-Hodgkin-Katz equation is used in cell physiology to determine the potential across a cell's membrane taking into account all of the ions that are permeant through the membrane.

Onsager's law can be used to describe the diffusion of the charged molecules. Writing up Onsager's equation for the k^{th} ion:

$$J_k = -L_k \cdot \frac{\Delta\mu_k}{\Delta x},$$

where L_k is the conductivity coefficient of the k^{th} ion, $\Delta\mu_k$ is the electrochemical potential difference of the k^{th} ion between the two sides of the membrane, and Δx the thickness of the membrane.

From the definition of the electrochemical potential:

$$\mu_k = \mu_{k0} + R \cdot T \cdot \ln(c_k) + z_k \cdot F \cdot \phi, \text{ we can derive that:}$$

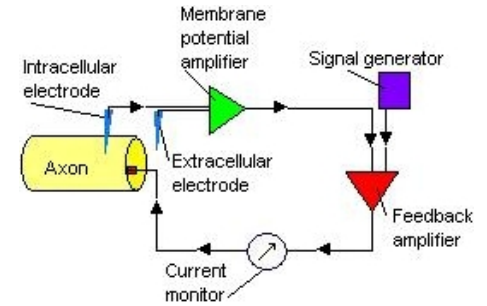
$$J_k = -p_k \cdot \frac{\Delta c_k}{\Delta x} - p_k \cdot \frac{z_k \cdot F}{R \cdot T} \cdot c_k \cdot \frac{\Delta \phi}{\Delta x}.$$

Knowing that in equilibrium the net electric current through the membrane is 0 ($\sum_k J_k = 0$), and assuming that only the one valent ions are important for the equilibrium, we get the Goldman-Hodgkin-Katz equation:

$$U = \Delta\phi_k = \phi_{k2} - \phi_{k1} = \frac{R \cdot T}{F} \cdot \ln\left(\frac{\sum p_k^+ \cdot c_{k2}^+ + \sum p_k^- \cdot c_{k1}^-}{\sum p_k^- \cdot c_{k2}^- + \sum p_k^+ \cdot c_{k1}^+}\right).$$

The most important ions that build up the membrane potential of the cell are K^+ , Na^+ , Cl^- . Considering only these in the Goldman-Hodgkin-Katz equation:

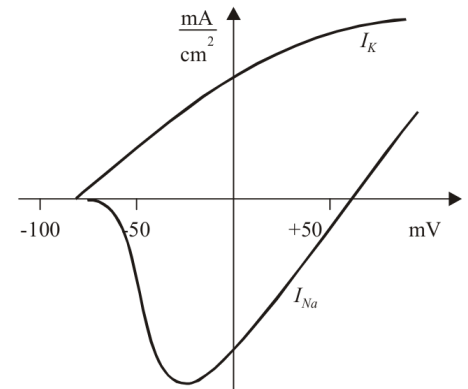
$$U = \Delta\phi_k = \phi_{k2} - \phi_{k1} = \frac{R \cdot T}{F} \cdot \ln\left(\frac{p_K \cdot [K^+]_2 + p_{Na} \cdot [Na^+]_2 + p_{Cl} \cdot [Cl^-]_1}{p_K \cdot [K^+]_1 + p_{Na} \cdot [Na^+]_1 + p_{Cl} \cdot [Cl^-]_2}\right).$$



Ion Currents in the Membrane

The voltage clamp method is used by electrophysiologists to measure the ion currents across a membrane while holding the membrane voltage at a set level.

Neuronal membranes contain many different kinds of ion channels, some of which are voltage gated. The voltage clamp allows the membrane voltage to be manipulated independently of the ionic currents, allowing the current-voltage relationships of membrane channels to be studied.



Action Potential

Action potentials are pulse-like self-regenerating waves of voltage that travel along several types of cell membranes. The action potential arises from changes in the permeability of the cell's membrane to specific ions. The best-understood example of an action potential is generated on the membrane of the axon of a neuron, but also appears in other types of excitable cells, such as muscle cells, and even some plant cells.

The action potential is initiated when the membrane is sufficiently depolarized. As the membrane potential is increased, both the sodium and potassium ion channels begin to open. This increases both the inward sodium current and the balancing outward potassium current. For small voltage increases, the potassium current triumphs over the sodium current and the voltage returns to its normal resting value.

Before the threshold is reached, the axon membrane behaves like an ordinary inactive electric circuit with a certain resistance and capacitance:

$$U(t) = U_{max} \cdot (1 - e^{-\frac{t}{RC}}),$$

where R and C denote the capacity and the resistance characteristic of the membrane.

Similarly, when the voltage returns to equilibrium:

$$U(t) = U_{max} \cdot e^{-\frac{t}{RC}},$$

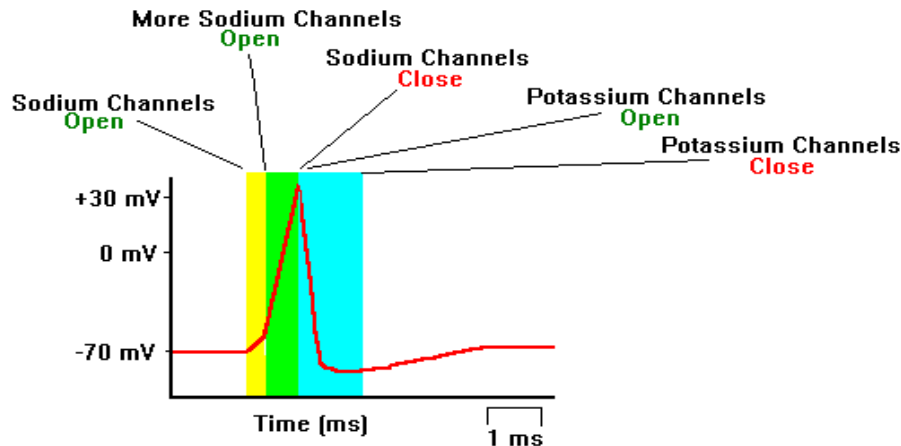
where U_{max} is the deviation from the resting potential at time $t = 0$.

The disturbance in the membrane potential decays exponentially in space as well:

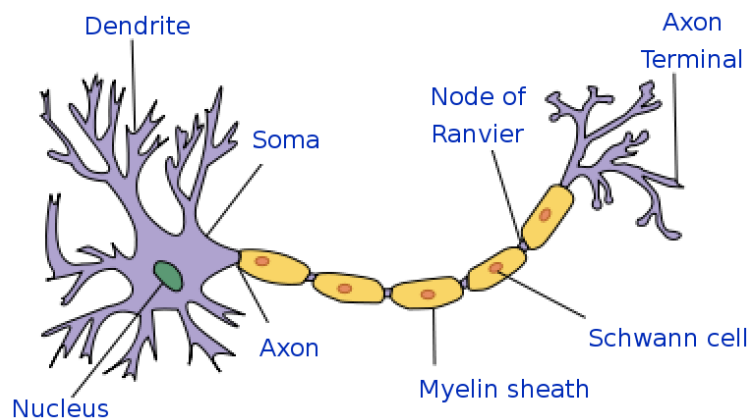
$$U(x) = U_{max} \cdot e^{-\frac{x}{\lambda}},$$

where x is the distance in the membrane from the site of the disturbance, and U_{max} is the deviation from the resting potential at $x = 0$.

If the voltage increases past a critical threshold, typically 15 mV higher than the resting value, the sodium current dominates. This results in a positive feedback, since the sodium current depolarizes the membrane even more, which activates more sodium channels. Thus, the cell "fires", producing an action potential.



When the sodium channels open during the depolarization, Na^+ rushes in because both of the greater concentration of Na^+ on the outside and the more positive voltage on the outside of the cell. When the Na^+ channels close and the K^+ channels open, the K^+ now leaves the axon due both to the greater concentration of K^+ on the inside and the reversed voltage levels.



Once initiated, the action potential travels through the axon. Since the axon is insulated, the action potential can travel through it with small signal decay. Nevertheless, to ensure the signal does not fail, regularly spaced patches, called the nodes of Ranvier, help boost the signal. The action potential depolarizes the membrane patch at the node of Ranvier, sparking another action potential. In effect, the action potential is created afresh at each node of Ranvier.

The opening and closing of the sodium and potassium channels may leave some of them in a "refractory" inactive state, in which they are unable to open again until the membrane potential returns to a sufficiently negative value for a long enough time. Shortly after "firing" an action potential, in the refractory period, so many ion channels are refractory that no new action potential can be fired. This ensures that the action potential travels in only one direction along the axon.