

Nernst Equilibrium Potential

Diffusion

The conservation law for a compound with concentration c :
rate change of c = local production + accumulation due to transport.

Model:

$$\frac{d}{dt} \int_{\Omega} c \, dV = \int_{\Omega} p \, dV - \int_{\partial\Omega} \mathbf{J} \cdot \mathbf{n} \, dA$$

Here p represents the production and \mathbf{J} is the flux of c .
The divergence theorem:

$$\int_{\partial\Omega} \mathbf{J} \cdot \mathbf{n} \, dA = \int_{\Omega} \nabla \cdot \mathbf{J} \, dV$$

The law is valid for every volume, thus:

$$\frac{\partial c}{\partial t} = p - \nabla \cdot \mathbf{J}$$

Models for p and \mathbf{J} are needed to compute c .

Fick's Law

$$\mathbf{J} = -D\nabla c$$

The diffusion coefficient D depends upon the solute and the temperature of the embedding fluid:

$$D = \frac{kT}{f}$$

T is the temperature measured on Kelvin, f is a frictional constant and k is the Boltzmann's constant.

The conservation law with this assumption is a reaction-diffusion equation:

$$\frac{\partial c}{\partial t} = \nabla \cdot (D\nabla c) + p$$

1D Diffusion through a pore in the membrane

$$\frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2}$$

Fixed intra and extra cellular concentration:

$$c(0, t) = [C]_i \quad c(L, t) = [C]_e$$

At steady state:

$$\frac{\partial c}{\partial t} = 0 \implies D \frac{\partial^2 c}{\partial x^2} = 0 \implies \frac{\partial c}{\partial x} = a \implies c(x) = ax + b$$

Taking the boundary condition into consideration yields:

$$c(x) = [C]_i + ([C]_e - [C]_i) \frac{x}{L}$$

and a constant flux: $J = -D \frac{\partial c}{\partial x} = \frac{D}{L} ([C]_i - [C]_e)$

Flow through a semi-permeable membrane

Consider two solutions:

- A: Contains 100mM Cl^- ions and 100mM Na^+ ions
- B: Contains 10mM Cl^- ions and 10mM Na^+ ions

Both are neutral. If they are only separated by a membrane permeable to Cl^- but not Na^+ , this will happen:

- Cl^- will diffuse from A to B due the concentration gradient
- $[\text{Cl}^-]_A$ will drop and $[\text{Cl}^-]_B$ will increase
- $[\text{Na}^+]_A$ and $[\text{Na}^+]_B$ will remain fixed (no flow)
- A and B will no longer be neutral
- $[\text{Na}^+]_A > [\text{Cl}^-]_A \Rightarrow A > 0$, $[\text{Cl}^-]_B > [\text{Na}^+]_B \Rightarrow B < 0$.
- Cl^- will be attracted to A and repelled from B

The Nernst Equilibrium Potential

We now have two forces driving Cl^- across the membrane:

- Flow from A to B due to the concentration gradient
- Flow from B to A due to the charge gradient

At some point an equilibrium is reached where the net flow is zero. The transmembrane potential at that point is called the Nernst Equilibrium Potential.

An expression for this potential will now be derived

Plank's equation

Models the ion-flux caused by an electrical field:

$$J = -m \frac{z}{|z|} c \nabla \phi$$

with

m - mobility of the ions in the liquid

$z/|z|$ - sign of the charge of the ion

c - the concentration of the ion

$\nabla \phi$ - the electrical field

Fick's law:

$$J = -D\nabla c$$

Relationship between m and D :

$$m = D \frac{|z|F}{RT}$$

here R is the gas constant and F is Faraday's constant.

Combined effect of concentration gradient and an electric field:

$$J = -D\left(\nabla c + \frac{zF}{RT}c\nabla\phi\right)$$

Nernst Equilibrium Potential

Consider equilibrium in 1D flow:

$$\frac{dc}{dx} + \frac{zF}{RT} c \frac{d\phi}{dx} = 0$$

$$\frac{1}{c} \frac{dc}{dx} + \frac{zF}{RT} \frac{d\phi}{dx} = 0$$

Integrating from inside ($x=0$) to outside ($x=L$) yields:

$$\ln(c) \Big|_{c(0)}^{c(L)} = -\frac{zF}{RT} (\phi(L) - \phi(0))$$

We define the transmembrane potential to be $v = \phi_i - \phi_e$. The value of the transmembrane potential at zero flux is then

$$v_{\text{eq}} = \frac{RT}{zF} \ln\left(\frac{c_e}{c_i}\right) \quad (1)$$

Equation (1) is referred to as the Nernst Equilibrium Potential.

Membrane currents

Accumulation around the membrane

The membrane has properties similar to a capacitor

- Consists of two conducting medias (intra- and extra cellular space)
- These are separated by an insulating material (the membrane)

The potential over a capacitor is proportional to the separated charge (q):

$$v = q/c$$

The factor c is called the capacitance of the capacitor.

The cell membrane modeled as a leaky capacitor

As any real capacitor the membrane conducts some current. The flux of ions (I_{ion}) will cause a change in q and thus v .

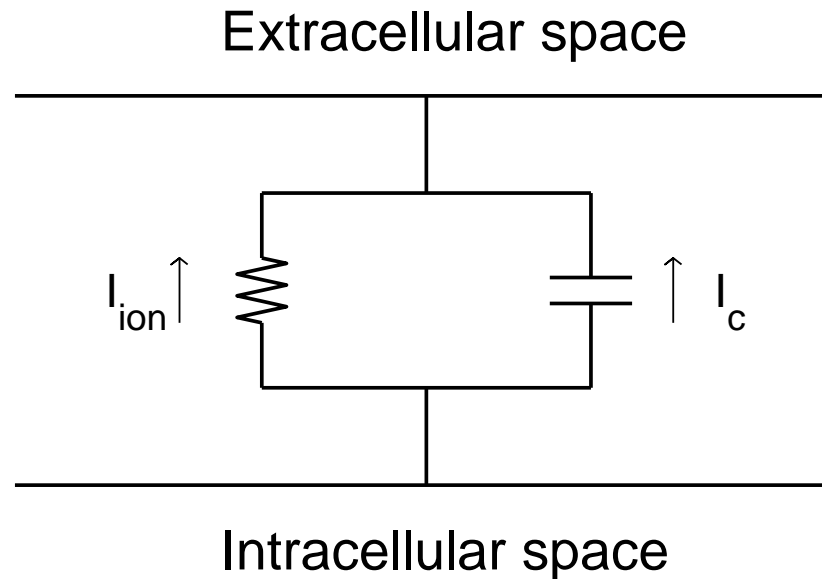
Consider the change over a time interval Δt . It follows that

$\frac{\Delta v}{\Delta t} = \frac{1}{c} \frac{\Delta q}{\Delta t}$ and in the limit we get:

$$\frac{dv}{dt} = \frac{1}{c} \frac{dq}{dt}$$

The term $\frac{dq}{dt}$ is called the capacitive current and is denoted I_c .

Electrical circuit model of the cell membrane



The membrane behaves like resistor and capacitor in parallel:

$$I_t = I_{ion} + I_c$$

If the loop is closed then $I_t = 0$. In that case all the ions passing the membrane accumulate and change the membrane potential accordingly.

Ionic currents

For passive ionic channels the flow through it must obey the equilibrium potential, i.e. be zero when $v = v_{eq}$.

An number of models exists, two common are:

Linear:

$$I(v) = g(v - v_{eq})$$

Here g is the conductance of the channel.

Goldman-Hodgkin-Katz:

$$I(v) = gv \frac{c_i - c_e e^{\frac{-zvF}{RT}}}{1 - e^{\frac{-zvF}{RT}}}$$

Derived from Nernst-Planck equation with assuming a constant (non-zero) field strength.

Nernst-Planck equation:

$$J = -D(\nabla c + \frac{zF}{RT}c\nabla\phi)$$

Consider 1D flow through a channel and assume $\nabla\phi$ is constant in space and that c and ϕ are in steady-state.

$$\frac{d\phi}{dx} = \frac{\Delta\phi}{\Delta x} = \frac{\phi(L) - \phi(0)}{L - 0} = \frac{\phi_e - \phi_i}{L} = -v/L$$

The equation is reduced to an ODE:

$$J/D = -\frac{dc}{dx} - \frac{zF}{RT}c(-v/L) = -\frac{dc}{dx} + kc$$

where $k = \frac{zFv}{RTL}$

The equation

$$J/D = -\frac{dc}{dx} + kc$$

is solved by

$$e^{-kx}c = c_i + \frac{J}{Dk}(e^{-kx} - 1)$$

We determine J by using $c(L) = c_e$:

$$J = Dk \frac{c_i - c(L)e^{-kL}}{1 - e^{-kL}} = D \frac{zFv}{RTL} \frac{c_i - c_e e^{\frac{-zvF}{RT}}}{1 - e^{\frac{-zvF}{RT}}}$$

J has dimension moles per area per time, an expression for current is given by

$$I = zFJ = \frac{D}{L} \frac{z^2 F^2}{RT} v \frac{c_i - c_e e^{\frac{-zvF}{RT}}}{1 - e^{\frac{-zvF}{RT}}}$$

This is the Goldman-Hodgkin-Katz current equation.

Channel gating

Channel gating

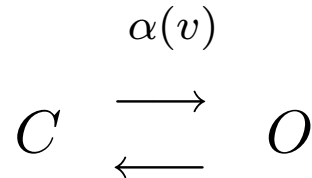
The conductance of a channel varies with time and with transmembrane potential. Model for current per membrane area:

$$I(V, t) = g(V, t)\phi(V) \quad (2)$$

Current through a single open channel is $\phi(V)$ and the amount of open channels per membrane area is $g(V, t)$.

Two State K^+ -channel

Assumes that the channel can exist in two states, closed(C) and open(O):



Applying law of mass action:

$$\frac{d[O]}{dt} = \alpha(v)[C] - \beta(v)[O]$$

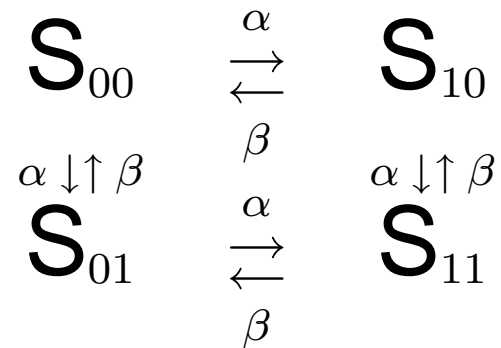
Dividing by the total amount of channels ($[C]+[O]$) yields

$$\frac{dg}{dt} = \alpha(v)(1 - g) - \beta(v)g$$

where g is the portion of open channel ($[O]/([C]+[O])$).

Multiple sub-units

For some channels it is more appropriate to model the gate as series of several sub-gates. Example with two gates:

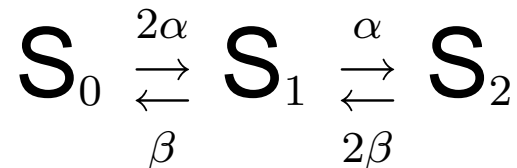


Using law of mass action we get a system of four equation. Will try to reduce this number to one!

Combine the states S_{01} and S_{10} into $S_1 = S_{01} + S_{10}$:

$$\begin{aligned}\frac{S_{01}}{dt} &= \alpha S_{00} + \beta S_{11} - (\alpha + \beta) S_{01} \\ + \frac{S_{10}}{dt} &= \alpha S_{00} + \beta S_{11} - (\alpha + \beta) S_{10} \\ \hline = \frac{S_1}{dt} &= 2\alpha S_{00} + 2\beta S_{11} - (\alpha + \beta) S_1\end{aligned}$$

Define $S_0 = S_{00}$ and $S_2 = S_{11}$, we can then write:



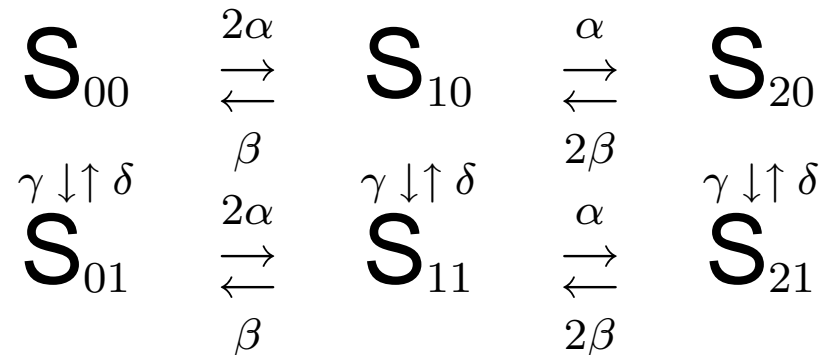
Only two independent variables since $S_0 + S_1 + S_2 = S_T$, constant. Define $x_i = S_i/S_T$. Claim:

$$x_2 = n^2, \text{ with } \frac{dn}{dt} = \alpha(1 - n) - \beta n$$

Sodium

Behavior of the Sodium conductance can not be described by a chain of identical gates.

Two subunits of type m and one of type h .



Here S_{ij} denotes i open m gates and j open h gates. Arguments similar to the one used above leads to these equations for m and h :

$$\frac{dm}{dt} = \alpha(1 - m) - \beta m, \quad \frac{dh}{dt} = \gamma(1 - h) - \delta h$$