

Biophysical Chemistry for Life Scientists

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Lecture 11

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Diffusion

Real processes, such as those that go on continually in biological systems are always attended by a free energy decrease for the system. One of the simplest ways to describe this approach of the system towards a state of lower free energy is by way of the concept of the thermodynamic force. We can illustrate the power of this approach first by deriving Fick's Law of Diffusion.

You might recall from elementary mechanics in physics that a particle in a mechanical or gravitational field always moves from a point of high potential energy to one of lower potential energy. Another way of stating this fact is that there is a force on the particle given by

$$\vec{F}(\vec{r}) = -\vec{\nabla}V(\vec{r})$$

or in one dimension

$$F_x = -\frac{dV}{dx} \quad \text{or} \quad -\frac{\partial V}{\partial x}$$

However, in contrast to motion in free space or a vacuum, motion of molecules in a gas or liquid involves resistance or frictional forces. A particle moving in such a medium must cause displacement and separation of these interacting molecules. Force is required and the net result is an expenditure of energy. When the path of a particle involves the separation of two or more molecules, work is done by the particle on these two or more molecules. This work or energy expenditure by the particle is not recovered by the particle when the two or more molecules again return to their average intermolecular distances. Instead, this work of separation is dissipated as heat characteristic of irreversible processes. In fact, the rate of energy dissipation by the moving particle is proportional to its velocity.

One frequently speaks of this rate of energy dissipation as a frictional force. This frictional force is not only a property of the particular medium through which the particle is moving, but is also dependent on the particle size and shape. The larger the size, the greater the resistance encountered. The inherent property of the medium which determines the friction force is called the viscosity η , and is related, in part, to the degree of molecular interaction and molecular size and shape. In 1850, Stokes showed that for a sphere

$$\vec{F}_f = -6\pi\gamma\eta\vec{v}$$

where

$\vec{F}_f$ = frictional force

γ = radius of sphere

η = viscosity

$\vec{v}$ = velocity of motion of sphere

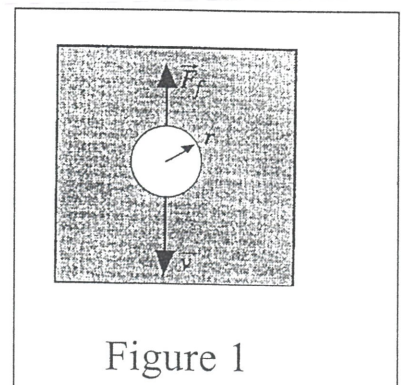


Figure 1

The quantity $6\pi\eta\bar{v}$ is often referred to as the frictional coefficient, i.e.,

$$f = 6\pi\eta\bar{v}$$

Since the frictional force encountered by a particle moving in a viscous medium is proportional to the velocity of the particle, it is evident that a driving force acting on the particle cannot lead to its continual acceleration. The particle will reach a velocity such that the frictional force opposing the motion becomes equal to the driving force. Given a constant driving force, the velocity of motion of a particle in a viscous medium will be a constant, and is obtained by equating

$$\vec{F}_f = -\vec{F}_d$$

where $\vec{F}_d \equiv$ driving force on particle

or $\vec{F}_d = 6\pi\eta\bar{v}$

$$\bar{v} = \frac{1}{f} \vec{F}_d = \lambda \vec{F}_d$$

$\lambda = f^{-1} \equiv$ mobility $\equiv$ velocity of particle assumed when unit driving force is acting on it

Concept of a Flux

Now consider a large number of molecules k moving with an average velocity $\bar{v}_k$ as a result of this driving force $\vec{F}_d$.

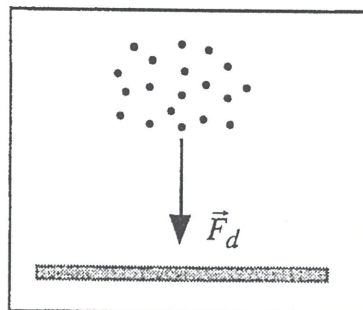


Figure 2

Let us calculate the number of such molecules crossing 1 cm^2 of this imaginary boundary $\perp$ flow per unit time or sec. This quantity is called the flux.

$$\vec{J}_k = C_k \vec{v}_k$$

where $C_k \equiv$ concentration of moles / cm^3

Substituting for $\vec{v}_k$,

$$\vec{J}_k = \lambda_k C_k \vec{F}_{d_k} \quad \text{flux moles / cm}^2 \text{ / sec}$$

Derivation of Fick's Law of Diffusion (First Law)

The above discussion assumes that the particles are subjected to gravitational potential. However, $\vec{F}_d$ need not be mechanical in origin. $\vec{F}_d$ could be the thermodynamic force. For neutral solutes, we can define a thermodynamic force

$$\vec{F}_{d_k} = -\vec{\nabla} \mu_k(\vec{r}) \cdot \frac{1}{N_A}$$

or in 1-D,

$$(F_{d_k})_x = -\frac{\partial \mu_k(\chi)}{\partial \chi} \cdot \frac{1}{N_A}$$

Now

$$\mu_k(\chi) = \mu_k^0 + RT \ln C_k(\chi)$$

Therefore,

$$(F_{d_k})_x = -\frac{1}{N_A} \cdot RT \frac{d \ln C_k(x)}{dx} = -k_B T \frac{1}{C_k} \left[\frac{dC_k(x)}{dx} \right]$$

From this result, we see that a concentration gradient provides a thermodynamic force for the particles or molecule to diffuse. Also, particles diffuse from higher μ_k to lower μ_k , or from higher C_k to lower C_k .

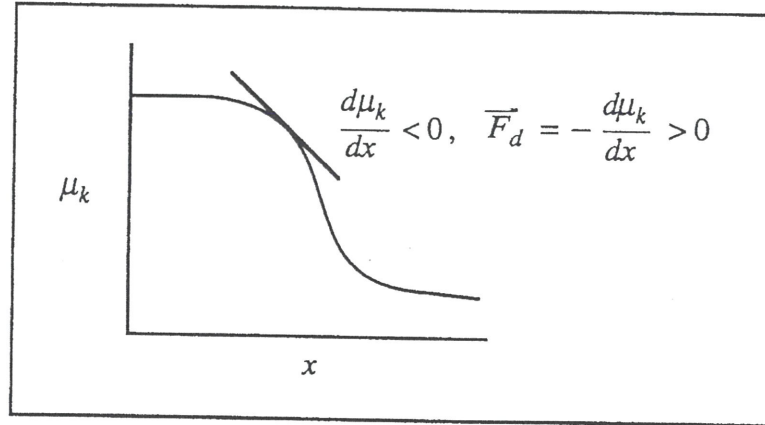


Figure 3

With this result, we can obtain the flux:

$$\begin{aligned}\bar{J}_k &= \lambda_k C_k \bar{F}_{d_k} \\ J_k &= -\lambda_k C_k k_B T \frac{1}{C_k} \frac{dC_k(x)}{dx} \\ J_k &= -\lambda_k k_B T \frac{dC_k(x)}{dx} = -D_k \frac{dC_k}{dx} \quad \text{Fick's Law (First Law)}\end{aligned}$$

where $D_k \equiv$ diffusion coefficient of species k

$$= \frac{k_B T}{f} = k_B T \lambda_k \quad (\text{cm}^2 / \text{sec})$$

Table 1. Typical Diffusion Coefficients at 20 °C in H₂O (cm²/sec)

Glycine	9.5 x 10 ⁻⁶
Leu-Gly-Gly	4.6 x 10 ⁻⁶
Ribonuclease	10.2 x 10 ⁻⁷
Human Serum Albumin	6.1 x 10 ⁻⁷
Human Hb	6.8 x 10 ⁻⁷
Tobacco Mosaic Virus	3.0 x 10 ⁻⁸
H ₂ O	10 ⁻⁶
Phospholipids in Bilayer Membrane	10 ⁻⁷ to 10 ⁻⁸
Membrane Proteins	10 ⁻¹⁰ or lower

Diffusion of Electrolytes

For charged species k (as opposed to neutral solutes discussed above)

$$\vec{F}_{d_k} = -\vec{\nabla}\mu_k(\vec{r}), \quad \mu_k = \text{electrochemical potential}$$

where $\bar{\mu}_k(x) = \mu_k^0(T, P) + RT \ln C_k(x) + z_k F \Phi(x)$

From this

$$\begin{aligned} J_k &= -\lambda_k C_k \left(\frac{1}{N_A} \right) \frac{d\bar{\mu}_k}{dx} \\ &= -\lambda_k C_k \left(\frac{1}{N_A} \right) \left[\frac{RT}{C_k} \frac{dC_k}{dx} + z_k F \frac{d\Phi(x)}{dx} \right] \\ &= -\lambda_k k_B T \left[\frac{dC_k(x)}{dx} + \frac{z_k |e| C_k}{k_B T} \frac{d\Phi(x)}{dx} \right] \end{aligned}$$

which shows that the flux is controlled by both the concentration and the electrical potential gradient. Now $\frac{d\Phi}{dx}$ may exist purely as a result of diffusion of the electrolyte (or free diffusion of ions), or it may be imposed on the system from an external source, with the use of appropriate electrodes. For example:

(1) Free Diffusion

You cannot have macroscopic separation of charges in space. Accordingly, there is no net charge flow

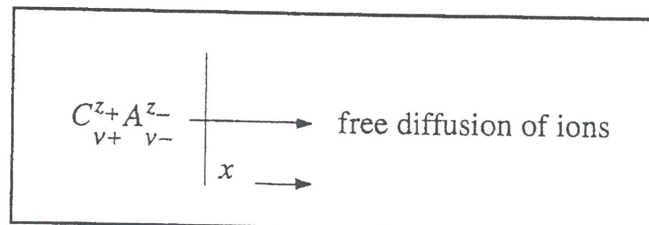


Figure 4

Therefore

$$\sum_k z_k J_k = 0 \quad \text{for all values of } k$$

For simplicity, consider a binary electrolyte:

Conditions for Free Diffusion:

$$0 = z_+ \lambda_+ \frac{dC_+(x)}{dx} + \frac{\lambda_+ z_+^2 F}{RT} C_+ \frac{d\Phi(x)}{dx} + z_- \lambda_- \frac{dC_-(x)}{dx} + \frac{\lambda_- z_-^2 F}{RT} C_- \frac{d\Phi(x)}{dx}$$

Since for binary electrolytes

$$C_k = \nu_k C$$

where $\nu_k \equiv$ stoichiometric number of ions

We obtain

$$\frac{d\Phi}{dx} = -\frac{RT}{F} \left[\frac{z_+ \nu_+ \lambda_+ + z_- \nu_- \lambda_-}{z_+^2 \nu_+ \lambda_+ + z_-^2 \nu_- \lambda_-} \right] \frac{d \ln C(x)}{dx}$$

This result shows that in general one expects some electrical potential gradient to be associated with the simple diffusion of an electrolyte. $\frac{d\Phi}{dx}$ depends on:

(a) $z_+ \nu_+ \lambda_+ + z_- \nu_- \lambda_-$

(b) $\frac{d \ln C(x)}{dx}$

Only if $z_+ \nu_+ \lambda_+ + z_- \nu_- \lambda_- = 0$ would $\frac{d\Phi}{dx} = 0$ in the presence of $\frac{d \ln C}{dx}$.

For a simple univalent-univalent electrolyte, where

$$z_+ = 1, \quad z_- = -1, \quad \nu_+ = 1, \quad \nu_- = 1$$

$$\frac{d\Phi}{dx} = -\frac{RT}{F} \frac{(\lambda_+ - \lambda_-)}{(\lambda_+ + \lambda_-)} \frac{d \ln C}{dx}$$

Thus, if the mobility of the cation λ_+ is larger than that of the anion λ_- , then the resulting electrical potential gradient has the opposite sign to the concentration gradient, or in other words, opposes the motion of cations.

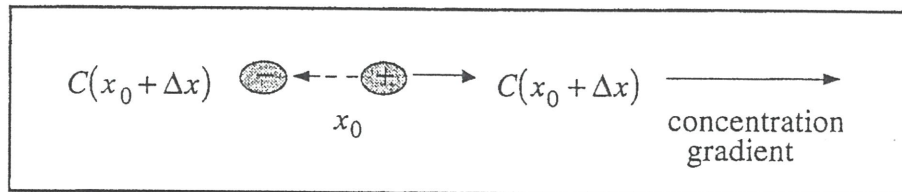


Figure 5

If λ_- is greater than λ_+ , then $\frac{d\Phi}{dx}$ has the same sign as $\frac{dC}{dx}$, and tends to oppose the motion of anions. In effect, what exists in a diffusion system is a slight displacement of charge; the more mobile charge leads the less mobile one by a slight amount, just enough to give rise to $\frac{d\Phi}{dx}$ observed. The diffusion of cations and anions are coupled together in this fashion by their electrical attraction for each other.

(2) Electrophoresis

Discuss later.

Passive Transport Across Membranes

Neutral Solutes

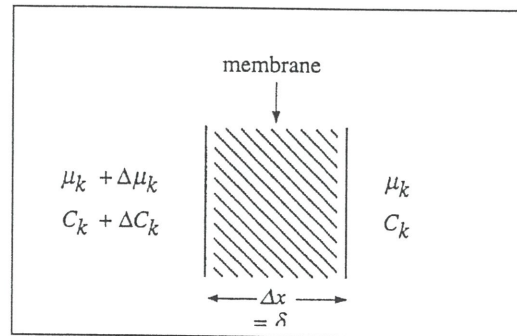


Figure 6

General Equation

$$J_k = -\lambda_k C_k \left(\frac{1}{N_A} \right) \frac{d\mu_k}{dx} \quad \text{moles / cm}^2 \text{ / sec}$$

where $\lambda \equiv$ mobility

Take an imaginary boundary inside a membrane.

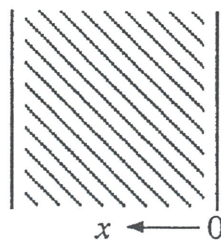


Figure 7

We may write:

$$\begin{aligned}
 J_k^m(x) &= -\lambda_k^m C_k^m(x) \frac{1}{N_A} \frac{d\mu_k^m(x)}{dx} \equiv \text{flux of species } k \text{ at point } x \text{ in the membrane} \\
 &= -\lambda_k^m C_k^m(x) \frac{1}{N_A} RT \frac{1}{C_k^m} \frac{dC_k^m(x)}{dx} \\
 &= -\lambda_k^m k_B T \frac{dC_k^m(x)}{dx}
 \end{aligned}$$

Invoke the steady state approximation and assume that there is no accumulation of solute at each boundary. Then $J_k^m(x) =$ constant for every point x in the ' membrane, and if λ_k^m is independent of x , $\frac{dC_k^m(x)}{dx}$ must be constant across the membrane as well for each species. We shall of course assume that the concentrations all remained outside the membrane so that

$$C_k(x=0) \text{ and } C_k(x+\Delta x) \text{ are } C_k \text{ and } C_k + \Delta C_k$$

on the right and left boundaries, respectively.

Define the partition coefficient such that

$$C_k^m = k_k^p C_k$$

where $k_k^p \equiv$ partition coefficient for k th species
 $\equiv$ equilibrium distribution coefficient

Then at the two membrane boundaries

$$C_k^m(x=0) = k_k^p C_k(x=0)$$

$$C_k^m(x+\Delta x) = k_k^p C_k(x+\Delta x) = k_k^p C_k(x=0) + k_k^p \Delta C_k$$

Substituting into the flux equation:

$$\begin{aligned}
 J_k^m(x) &= -\lambda_k^m k_B T \frac{dC_k^m(x)}{dx} \\
 &= -\lambda_k^m k_B T \frac{\Delta C_k^m}{\Delta x} \\
 &= -\lambda_k^m k_B T \frac{C_k^m(x = \Delta x) - C_k^m(x = 0)}{\Delta x} \\
 &= -\lambda_k^m k_B T k_k^p \frac{\Delta C_k}{\Delta x} \\
 &= -\lambda_k^m k_B T k_k^p \frac{1}{\delta} \Delta C_k \\
 &= -p_k^m \Delta C_k
 \end{aligned}$$

Where $p_k^m \equiv$ permeability coefficient of species k

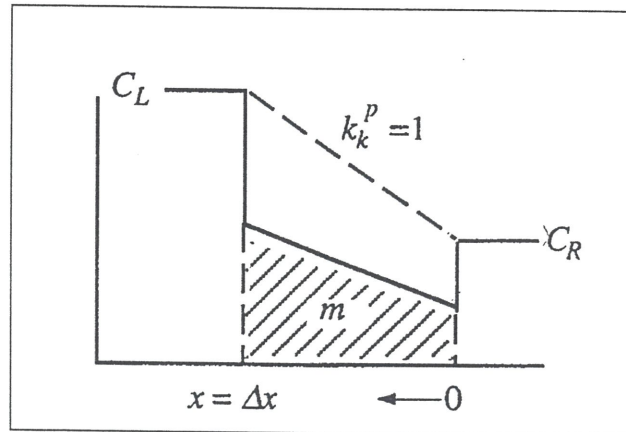


Figure 8

Water Transport Across Membranes

(This has been an active field in biophysics for many years!)

You have to worry about a difference in the hydrostatic pressure across the membrane, in addition to the activity difference, i.e.,

$$\frac{\Delta P}{\Delta x} \text{ in addition to } \frac{\Delta \ln x_s}{\Delta x}$$

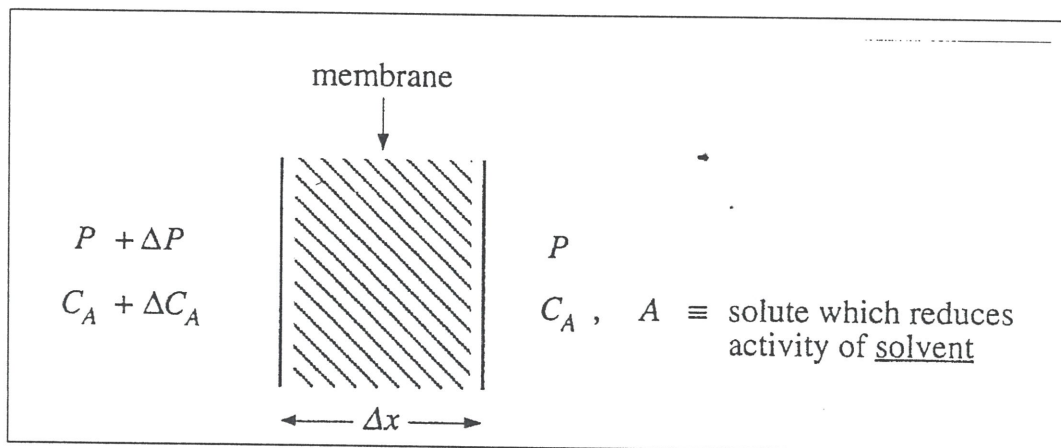


Figure 9

Start with the Magic Formula

$$\begin{aligned} J_s^m &= \text{water flux across the membrane} \\ &= -\lambda_s^m C_s^m \frac{1}{N_A} \frac{d\mu_s^m}{dx} \end{aligned}$$

As before, assume the driving force is constant across each imaginary boundary within the membrane.

Then

$$J_s^m = -\lambda_s^m C_s^m \frac{1}{N_A} \frac{\mu_s^m(x = \Delta x) - \mu_s^m(x = 0)}{\delta}$$

Now

$$\begin{aligned}\mu_s^m(x=0) &= \mu_s^l(x=0) = \mu_s^{0l}(P) + RT \ln x_s \quad \text{and} \\ \mu_s^m(x=\Delta x) &= \mu_s^l(x=\Delta x) = \mu_s^{0l}(P + \Delta P) + RT \ln x'_s\end{aligned}$$

Therefore

$$\begin{aligned}\mu_s^m(x = \Delta x) - \mu_s^m(x = 0) &= \mu_s^{0l}(P + \Delta P) - \mu_s^{0l}(P) + RT \ln x'_s - RT \ln x_s \\ &= \left(\frac{\partial \mu_s^{0l}}{\partial P} \right) \Delta P + RT \Delta \ln x_s \\ &= \bar{V}_s^* \Delta P - RT \bar{V}_s^* \Delta C_A, \quad \bar{V}_s^* = \text{average molar vol. of solvent}\end{aligned}$$

Therefore

$$\begin{aligned}J_s^m &= -\lambda_s^m C_s^m \frac{1}{N_A} \frac{1}{\delta} (\bar{V}_s^* \Delta P - RT \bar{V}_s^* \Delta C_A) \\ &\equiv -\lambda_s^m k_s^P \bar{C}_s \frac{1}{N_A \delta} \bar{V}_s^* (\Delta P - RT \Delta C_A) \\ &\equiv -\lambda_s^m k_s^P \frac{1}{N_A \delta} (\Delta P - RT \Delta C_A) \quad \text{as } \bar{C}_s \bar{V}_s^* \equiv 1 \text{ for dilute solutions}\end{aligned}$$

Note at equilibrium $J_s^m = 0$ so that $\Delta P = RT \Delta C_A = \pi$ as expected.

Electrodifusion (Diffusion of Ions Across Membranes)

$$J_k^m(x) = -\lambda_k^m C_k^m(x) \frac{1}{N_A} \frac{d\bar{\mu}_k^m(x)}{dx}$$

where $\bar{\mu}_k^m(x) = \bar{\mu}_k^{0m} + RT \ln C_k^m(x) + z_k F \Phi^m(x)$

Now

$$\frac{d\bar{\mu}_k(x)}{dx} = \frac{RT}{C_k^m} \frac{dC_k^m}{dx} + z_k F \frac{d\Phi^m(x)}{dx}$$

Assume a steady state with:

- (1) linear concentration gradient
- (2) constant potential gradient

over the region of the membrane (Δx).

Then

$$\frac{dC_k^m(x)}{dx} = k_k^p \frac{dC_k}{dx} = k_k^p \frac{\Delta C_k}{\Delta x} \quad \text{and}$$

$$\frac{d\Phi^m(x)}{dx} = \frac{\Delta \Phi}{\Delta x}$$

so that

$$\begin{aligned} J_k^m(x) &= -\lambda_k^m C_k^m \left(\frac{k_B T}{C_k^m} k_k^p \frac{\Delta C_k}{\Delta x} + \frac{z_k F}{N_A} \frac{\Delta \Phi}{\Delta x} \right) \\ &= -\frac{\lambda_k^m k_k^p k_B T}{\delta} \left(\Delta C_k + \frac{z_k F}{RT} \bar{C}_k \Delta \Phi \right) \end{aligned}$$

where $\frac{\lambda_k^m k_k^p k_B T}{\delta} = P_k^m$ and $\bar{C}_k$ = center of membrane

for each ionic species.

Consider Two Types of Membranes

- (1) If a membrane is permeable to only one ionic species, say k , then without any external electrical connection, no electric current can flow (hence no flux in this case). Thus, $J_k = 0$ and we can solve for $\Delta\Phi$.

$$\Delta\Phi = \frac{-RT}{z_k F} \left[\frac{\Delta C_k}{\bar{C}_k} \right] \text{ or more exactly}$$
$$\frac{-RT}{z_k F} \ln \frac{C_L}{C_R} = \Phi_L - \Phi_R \text{ (Gibbs - Donnan potential)}$$

- (2) If, on the other hand, a membrane is permeable to a variety of ions present, each with its own permeability coefficient, then the condition of no net electric current flow gives the following

$$\sum_{k=1}^n z_k J_k^m = 0, \text{ for all ions}$$

In this case, ionic fluxes are possible,

$$\text{or } - \sum_{k=1}^n z_k P_k^m \Delta C_k - \frac{F}{RT} \sum_{k=1}^n z_k^2 P_k^m \bar{C}_k \Delta\Phi = 0$$
$$\text{or } \Delta\Phi = - \frac{RT}{F} \frac{\sum_{k=1}^n z_k P_k^m \Delta C_k}{\sum_{k=1}^n z_k^2 P_k^m \bar{C}_k} \quad (\text{steady state potential})$$

This is the approximate Goldman equation.

Biological Membranes

For biological membranes, the ionic permeability of many ions is small, so a few ions dominate. Therefore, you need to sum over the principal ions whose permeabilities and conductances across the membrane are significant.

Resting Nerve

Only the permeability of K^+ is significant, so $\Delta\Phi \approx$ Gibbs-Donnan potential applied to K^+ .

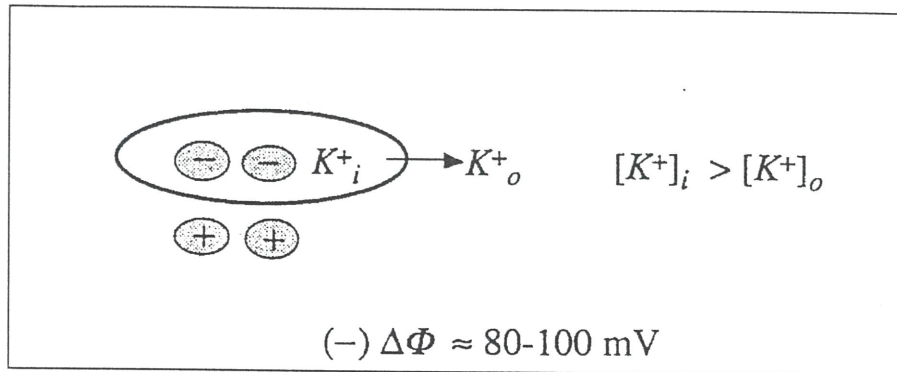


Figure 10

Excited Nerve

The permeabilities of K^+ and Na^+ are significant. During impulse transmission, changes occur in the membrane so that the conductances of both K^+ and Na^+ are important. A transient point is reached where the Na^+ permeability coefficient or conductance is much greater than that for K^+ .

Thus far, we have derived Fick's First Law and have shown how it could be used to describe the passive transport of molecules across membranes.

Fick's First Law

$$J_k^x = -D \frac{dC_k(x)}{dx} \quad \text{flux of species } k \text{ along } x - \text{direction}$$

where $D \equiv$ diffusion coefficient

According to Einstein,

$$D = \frac{k_B T}{f} \quad \text{where } f \equiv \text{frictional coefficient}$$

$$= \lambda_k k_B T \quad \lambda_k \equiv \text{mobility of species } k$$

Extend to 3-Dimensions

$$\bar{J}_k = -D \nabla C_k \quad \text{if diffusion is isotropic.}$$

If the medium is anisotropic, then

$$\begin{pmatrix} J_k^x \\ J_k^y \\ J_k^z \end{pmatrix} = \begin{pmatrix} D_{xx} & 0 & 0 \\ 0 & D_{yy} & 0 \\ 0 & 0 & D_{zz} \end{pmatrix} \begin{pmatrix} \frac{dC_k}{dx} \\ \frac{dC_k}{dy} \\ \frac{dC_k}{dz} \end{pmatrix}$$

$\Uparrow$
 Diffusion tensor $\underline{D}$