Physical properties of membranes (Müller & Rudin "black lipid bilayer" model membrane)

capacitance resistance H₂O permeability surface tension

~ 1 μF/cm² ~ 10³ Ω cm² 90–400 μm/sec 0.3–1 dyne/cm

cell membrane

~ 1 μF/cm² 10⁶-10⁹ Ω cm² 17-104 μm/sec 0.5-2 dyne/cm

lipid bilayer



Membrane Electrostatics

DMPC

Complex Electrostatic Environment

- Many atoms
- large density of charges and dipoles
- 10's mV potential across 6 nm!
- large variation in dielectric constant





Transmembrane Potential

The potential difference between two bulk phases.



Charge separation across water ($\varepsilon = 80$) will tend to create a relatively small electric field.

Charge separation across organic phases ($\epsilon = 1.89$) will create large electric fields.

Two parallel planes of opposite charges

The electrical potential difference between the plates is



$$\psi = -\int_{0}^{x} E \, dx = -\int_{0}^{x} \frac{q}{\varepsilon \varepsilon_{0}} \, dx = -q \frac{x}{\varepsilon \varepsilon_{0}} \quad E = \frac{q}{\varepsilon \varepsilon_{0}}$$

$$C = \frac{q}{\Delta \psi} = \frac{A\varepsilon\varepsilon_0}{x}$$

The capacitance of biological membrane is about $1 \ \mu F/cm^2$.

4 Membrane potential is the force that drives ions across the membrane.

4 The membrane potential partly determines the energy stored in ion concentration gradients.

4 The electric field associated with the membrane potential acts on dipolar groups in membrane proteins and may regulate the activities of these proteins.

✤ Voltage-dependent channels open and close in response to changes in the membrane potential.







A charge smoothly distributed on a plane will create an electric field perpendicular to the plane.

$$\psi(x) \approx \psi_{o} e^{-\frac{x}{\lambda}}$$

Surface potential controls protein adsorption and can regulate membrane transport.

Origin of surface charge

4 *Ionisation of surface groups* (ionisation of carboxyl and amino groups to give COO⁻ and NH_3^+ ions)

4 Ion adsorption

➤ Cations more hydrated than anions, have greater tendency to reside in bulk.

> Anions have greater tendency to be specifically adsorbed.

Any ion whose adsorption at surface is influenced by forces other than simple electrostatic potential can be regarded as specifically adsorbed.



The structure of several common mammalian phospholipids that can be found in the plasma membrane along with their charge ranges under physiological conditions.



Membrane surface electrostatic potential

Generally membranes have a negative charge (10 - 20% anionic lipids, charge from gangliosides and proteins)

4 The charge separation depends on:

Diffuse Double- Layer Model

. ⊕

 \oplus

 \odot

OH

-ОH

electrical attraction pulling them toward the surface

 \succ a dynamic tension with diffusion pushing the counterions away from the surface



STERN MODEL (1924)



Strong specific adsorption in the Stern Layer



Electrical double layer



Helmholtz model (1879)

Guoy-Chapman model (1914)

The Gouy-Chapman theory

Assumptions:

- 1. The surface charge is smeared
- 2. Ions are point charges
- 3. No specific ion

adsorption

4. Dielectric constant is constant

The ion distributions as a function of distance from the membrane surface.

> Mean field approximation

Each ion is moving under the influence of an electric potential created by the average charge density of the others $< \rho_q >$.







 $\rho(x) = ze[n_{\perp}(x) - n_{\perp}(x)]$

At a distance x from the surface:

$$\frac{1}{n_{-}(x) = n_{\infty} \exp\left(\frac{+ze\Psi(x)}{k_{B}T}\right)} + \sum_{n_{+}(x) = n_{\infty} \exp\left(\frac{-ze\Psi(x)}{k_{B}T}\right)} + \sum_{n_{+}(x) = n_{\infty} \exp\left(\frac{-ze\Psi(x)$$



Poisson equation

(describes variation of potential in a spatial charge distribution)

$$\frac{d^2\psi}{dx^2} = -\frac{1}{\varepsilon\varepsilon_0}\rho_e \qquad \text{space charge distribution} \\ \sum_{i} z_i en_i(x) \\ \underline{Boltzmann equation} \\ (describes variation of ion concentration)$$

(describes variation of ion concentration in an electric field)

$$\frac{n_{\rm i}(x)}{n_{\rm i}(\infty)} = \exp\left(\frac{-z_{\rm i}\mathrm{e}\psi(x)}{kT}\right)$$

Poisson-Boltzmann equation

$$\frac{d^2\psi}{dx^2} = -\frac{1}{\varepsilon\varepsilon_0} \sum z_i en_i(\infty) \exp\left(\frac{-z_i e\psi}{kT}\right)$$

For a single, symmetric (z-z) electrolyte...

$$\frac{d^2\psi}{dx^2} = -\frac{zen(\infty)}{\varepsilon\varepsilon_0} \left[exp\left(\frac{ze\psi}{kT}\right) - exp\left(\frac{-ze\psi}{kT}\right) \right]$$

for low potentials $|z\psi_0| \le 25 \text{ mV}$, sinh $y \approx y$, and





 $4 1/\kappa$ is a measure of the thickness of the diffuse double layer.



Distance from surface, x (nm)

Surface potential as a function of the surface charge



Univalent electrolyte at 10 mM concentration, $\varepsilon = 80$ and T = 20°C.

The surface charge density = 0.0158 C/m^2 . Univalent electrolyte, $\varepsilon = 80$ and $T = 20^{\circ}\text{C}$. For the aqueous solution ($\varepsilon = 80$) the Debye length for ultrapure water is 190 nm and for 1 mM KCl 9.7 nm.



Surface charge has a number of effects

A negative surface charge attracts cations to the membrane surface

 \succ increaseing the conductance of the membrane to cations

 \succ enhanceing the binding of cations to the membrane surface.

The surface potential has a greater affect on the distributions of divalent ions than on distributions of monovalent ions (high Ca²⁺ concentrations at the membrane surface).

The surface potential changes the pH near the surface of the membrane.

The surface potential may act to repel or attract other surfaces.

How much electrostatic energy is stored in double-layer?

A fully dissociating bilayer membrane can have one unit of charge per lipid headgroup

$$\left|\frac{\sigma_q}{e}\right| = 0.7 nm^{-2}$$

A spherical vesicle of radius 10 μ m then carries stored free energy

$$\Delta G \approx 4\pi (10\,\mu m)^2 \times \frac{0.7}{nm^2} k_B T \approx 10^9 k_B T$$

An entropic force between charged surfaces in solution



> Each surface, together with its counterion cloud, is an electrically neutral object!

> The repulsion of between like-charged surfaces can only arise as an entropic effect.

> The diffused counterion clouds get squeezed; they then resist with an osmotic pressure.

 $\frac{f}{area} = c_0 k_B T$



Opositely charged surfaces attract by counterion release

As the surfaces approach they shed counterion pairs while preserving the system's neutrality.

□ The released ions gain entropy lowering the free energy and driving the surfaces together.



Origin of a dipole potential Ψ_d $\neg P - N^+$ dipole P = O bonds of phosphate groups **Primery determinant** sn_2 -carbonyls Little effect of sn_1 -carbonyls

Dipoles of hydration water which are ordered and oriented at the membrane surface.

<cos(theta)>

Orientational polarization of water





Sketch of typical contributions to the electrostatic potential of a bilayer membrane made of zwiterionic lipids



position

The dipole potential is a major factor in determining the ionic permeability of the lipid bilayer.

Dipole potential modifies the electric field inside the membrane, producing a virtual positve charge in the apolar bilayer center.



Lipid membranes exhibit a substantial (up to six orders of magnitude) difference in the penetration rates between positively and negatively charge hydrophobic ions. The dipole potential $\Delta \psi = \frac{D}{\varepsilon \varepsilon_0}$ D is the surface dipole density in C/m. *A dipole moment of phospholipid* = 1.5 Debyes - 5 x 10⁻³⁰ C/m *Surface area per lipid* = 60 A² *A surface dipole density* = 8.34 x 10⁻¹² C/m *A dipole potential* = 1000/ ε mV

The dipole potential is not a significant component of the membrane potential because the dipoles on opposite surfaces of the membrane are oriented in opposite directions and tend to cancel each other.

Schematics for measuring surface and dipole potentials in lipid monolayers



Dipole potential functions:

Effects the membrane permeability for lipophilic ions and drugs.

Modulates the binding of peptides and biologically active molecules to cell plasma membranes.

Directs the insertion and filding of peptides in the membranes.

Modulates membrane enxymes activities.

Compounds modifying the bilayer dipole potential

Phloretin – strongly reduces the Ψ_d value

Sterols including cholesterol - increases Ψ_d value

6-ketocholestanol – strongly increases Ψ_d value

The removal of sn-carbonyls, which is realized in ether phospholipids decreases Ψ_d .



Fluorescence probes for membrane dipole potential monitoring



Electrochromism (Stark effect)

The shifts of absorption and emission bands caused by the interaction of an electric field with the ground-state and excited state dipole moments of the chromophore.

The spectral shift, $h\Delta v_{obs}$, is proportional to the electric field E, and the change of dipole moment associated with the spectroscopic transition $\Delta \mu$,

$$h\Delta v_{obs} = -\left(\frac{1}{\varepsilon_{ef}}\right) \left|\Delta \vec{\mu}\right| \vec{E} \cos \theta$$

 θ – the angle between $\Delta \mu$ and E vectors, and ε_{ef} is a microscopic analog of dielectric constant, which accounts for dielectric screening.

Sensitivity depends on:

- □ change of the probe dipole moment on electronic excitation
- low-polar environment

□ probe should be oriented parallel ($\cos\theta=1$) or antiparallel ($\cos\theta=1$) to the electric field.



Exited-state charge transfer in styryl dyes



Examples of potential profiles



Negative surface charge on both sides.

➤ A large surface charge on one side.

Surface charge on one side, dipole potential and transmembrane potential.



The electrostatic profile across the plasma membrane and at interfaces.



Long-range van der Waals attraction





attraction constant

Electrostatic repulsion retards aggregation

van der Waals attraction



electrostatic repulsion

Electrostatic repulsion depends on

- 1. The Stern potential, ψ_{δ}
- 2. The thickness of the diffuse double layer, κ^1





Controlling DLVO interactions



Controlling electrolyte valence and concentration



 $\psi_{\delta} = 50 mV; z = 1; \varepsilon = 78.5$



Jar testing of As_2S_3 sol with 1-1 electrolyte.



For z = 2, divide all C's by 64; for z = 3, divide all C's by 729

Controlling effective Stern potential, ψ_{δ}



Examples of surface potential control:

For oxides

$$\psi_0 = 59.2(pH_{\rm pzc} - pH) \,\mathrm{mV}$$

Specific ion adsorption

$$\psi_{\delta} = \psi_{\delta 0} + \frac{z_{i} e \Gamma_{i}}{\varepsilon \varepsilon_{0} \kappa}$$

 $|\psi_{\delta}| < 25 \text{ mV}$ generally inadequate for stability.