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The Membrane

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ABSTRACT

The characterization of the cell membrane has significantly extended over the past century and continues to be studied. The biological membrane is comprised of numerous amphiphilic lipids, sterols, proteins, carbohydrates, ions and water molecules that result in two asymmetric polar leaflets, in which the interior is hydrophobic due to the hydrocarbon tails of the lipids. The extension of the Fluid Mosaic Model, first proposed by Singer and Nicolson in 1972, has generated a dynamic heterogonous image of the membrane that includes lateral domains and clusters perpetrated by lipid-lipid, protein-lipid and protein-protein interactions. Proteins found within the membrane, which are generally characterized as either intrinsic or extrinsic, have an array of biological functions vital for cell activity. The primary role of the membrane, among many, is to provide a barrier that conveys both separation and protection, thus maintaining the integrity of the cell. However, depending on the permeability of the membrane several ions are able to move down their concentration gradients. In turn this generates a membrane potential difference between the cytosol, which is found to have an excess negative charge, and surrounding extracellular fluid. Across a biological cell membrane, several potentials can be found. These include the Nernst or equilibrium potential, in which there is no overall flow of a particular ion and the Donnan potential, created by an unequal distribution of ions. In addition,

proteins that translocate protons across the membrane generate an electrochemical gradient. In particular, the Proton Motive Force generated across the inner mitochondrial membrane couples the electron transport chain with ATP synthesis. This theory, which has now been experimentally demonstrated, was termed the chemiosmotic hypothesis by Mitchell in 1961. In accordance with transport proteins, channels, particularly those involved in the translocation of Na+ and K-, are essential in nerve stimulation via the depolarization of the membrane, giving rise to the action potential. In general, the depolarization and repolarization of the membrane is a result of the diffusion of Na+ and K- down their concentration gradients through the work of highly coordinated protein channels.

Keywords: Bilayer; Function of the membrane; Fluid Mosaic Model; Lateral domains and clusters; Potentials; Chemiosmotic Hypothesis; Donnan Potential; Proton Motive Force

INTRODUCTION TO THE BIOLOGICAL MEMBRANE

Objectives

- Define the membrane bilayer
- Understand the general characteristics of lipids within the bilayer
- Describe the general regions of the lipid bilayer
- Be able to describe the overall roles of membrane proteins
- Describe the importance of the asymmetry found between the leaflets of the bilayer
- List the general roles of the membrane
- Describe important characteristics of the classical Fluid Mosaic Model proposed by Singer and Nicolson
- Provide an updated version of the Fluid Mosaic Model

INTRODUCTION

During the mid 19th century it was recognized that the plasma membrane of cells is a discrete structure. Physiologists at this time characterized the cell surface as being lipid in nature, measured using the ease or difficulty at which migrant molecules could penetrate. In 1925, Gorter and Grendal proposed that the arrangement of lipids in the membrane was that of a bilayer or leaflet. Later in the mid 1930s, Davson and Danielli extended the image of the membrane to include proteins found on the surface of the membrane and over the next 30 years, the enormous diversity in membrane function developed into a broader image. By 1970s biochemists were becoming considerably more successful at using detergents to dissociate proteins from the membrane, leading to the characterization of many membrane proteins. Additionally, further experimental techniques were developed which revealed the fluid nature of the membrane, characterized by a great deal of dynamic motion and leading to our present view of the membrane. For a more detailed timeline see [1].

Membranes are composed roughly of 20% water with the remaining 80% lipids, sterols, proteins, carbohydrates and ions. The bilayer plays a functional role in both the structure and vitality of cells. This flexible thin layer is the only barrier between the internal components of the cell and the potentially harsh environment. The inside of eukaryotic cells is also sub-divided into a variety of compartments, also surrounded by a membrane. The membranes of distinct organelles, organisms and kingdoms have been found to have large structural similarities that have allowed researchers to apply lessons learned in one system to another.

Structure

Although the membrane is relatively thin compared to the diameter of a cell, it is composed of several distinct regions, which have been characterized over decades using various techniques including X-ray crystallography, neutron scattering and nuclear magnetic resonance. In general, there are roughly 4 regions within the membrane: 1) perturbed water, 2) lipid head groups and bound water, 3) ordered lipid side chains and 4) low chain density or disordered lipid tails (Figure 1).

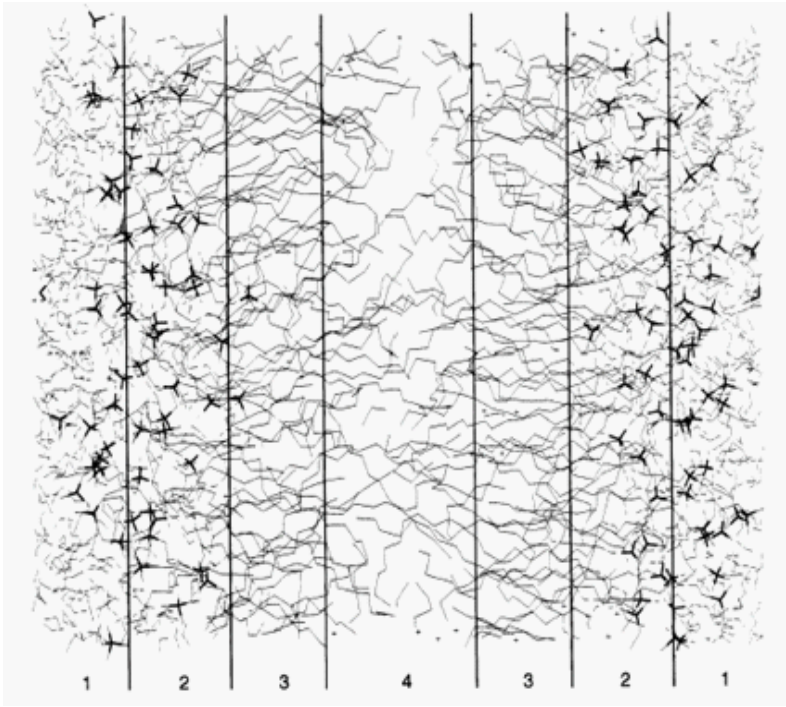

Figure 1: Diagram of the four proposed regions in the bilayer. Region 1 represents the perturbed along the surface of the bilayer. Region 2 is characterized by ordered water molecules surrounded the head groups. Ordered side-chains with low mobility are found in region 3 and region 4 illustrates the low density or disordered ends of the acyl tails. Image provided with permission from Dr. Noskov, University of Calgary.

Lipids, which compose much of biological membranes, are amphiphilic structures with a polar and non-polar region, roughly similar in length. Two tail facing lipid molecules form the bilayer of membranes, resulting in a polar leaflet, in which the hydrophilic head groups extend into the soluble exterior or interior region of the environment or organelle. In general, membranes are able to self-assemble into a bilayer, a consequence of the hydrophobic effect, by which interaction of the hydrophobic tails to the polar environment is unfavorable. The polar molecules drive the hydrophobic heads into compact shapes in order to minimize the total free energy of the system by maximizing the degree of disordered water molecules. Few chemical bonds hold the bilayer together; rather there is a saturation of non-covalent forces between individual molecules.

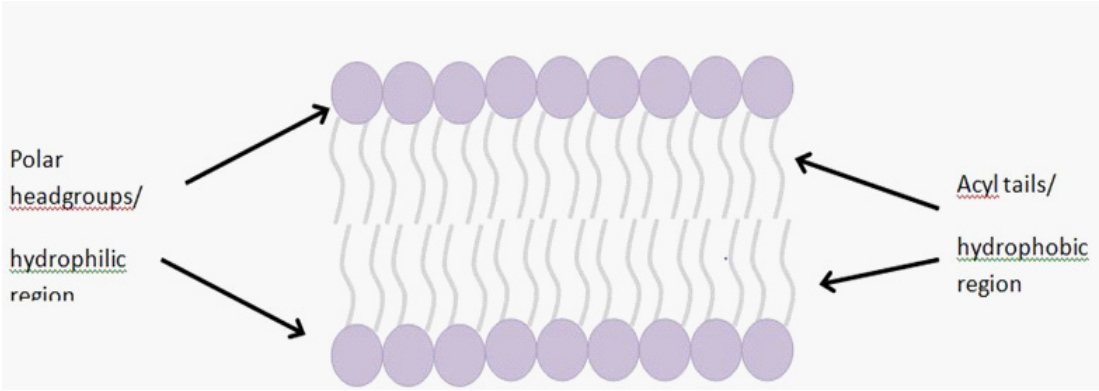

Figure 2: Schematic diagram of the lipid bilayer omitting the presence of other components. The circles in purple represent the polar headgroups and the grey tails represent the acyl tails. Image not drawn to scale.

The bilayer profiles a hydrophobic layer that is approximately 30Å thick. Two head groups are positioned on either side of the membrane, each approximately 15Å thick, in addition, the head groups are also hydrated with water molecules. This leads to an approximate total thickness of 60Å, varying with lipid type. The interior of the membrane has a high dielectric constant, and the hydrophobic center also contains highly ordered water molecules.

One of the most striking features of the membrane bilayer is the enormous diversity of lipids, estimated to be more than 200 per cell. Whereas multiple roles for lipids within the membrane are reasonably clear, the purpose for this great diversity has yet to be fully appreciated, nonetheless may relate to the environment of the cell. Major lipids found in the membrane include: glycerophospholipids, phosphosphingolipids, glycoglycerolipids, glycosphingolipids and sterols. The significance of the headgroup chemistry cannot be undermined as it establishes the chemistry of the bilayer surface. In mammalian cells, the most common lipid is phosphotidylcholine, which has a zwitterionic headgroup with a negative charge on the phosphate group and a positive charge on the choline (Figure 3).

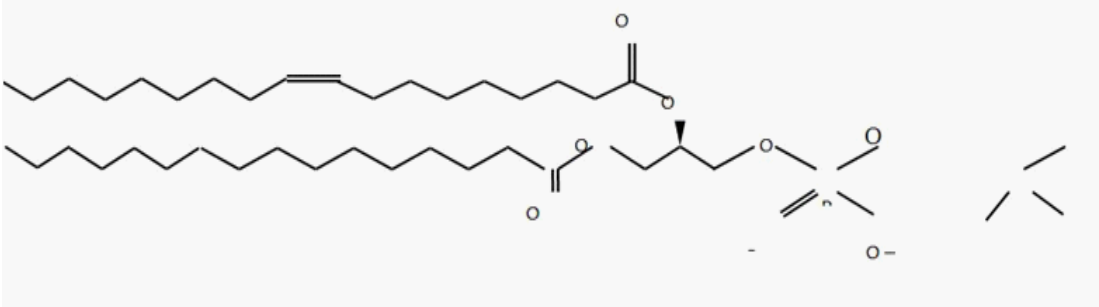

Figure 3: Stick diagram of a phosphotidylcholine derivative, palmitoyl-2-oleoylphosphateidylcholine.

Other dominant lipids include: phosphotidylserine, phosphotidylethanolamine, and phosphotidylglycerol. For a review on lipids in biological membranes see [2].

Membranes contain between 20%-80% (w/w) protein. These amphiphilic proteins are biochemically active components of the membrane and form an abundance and diversity of transporters, enzymes, receptors, pores etc. The knowledge that proteins extended partially or completely into the membrane was supported by insight into the stabilization of the proteins by hydrophobic interactions. This led to a lipid extension of the hydrophobic effect in addition to a better appreciation of the folding mechanisms and driving forces of integral membrane proteins. Proteins found in the membrane are generally viewed as being folded so that a nonpolar region can be presented to the lipid interior while enclosing a polar core.

Membrane proteins can be generally characterized as intrinsic or integral and extrinsic or peripheral, with various topological conformations, number of helices and oligomeric states.

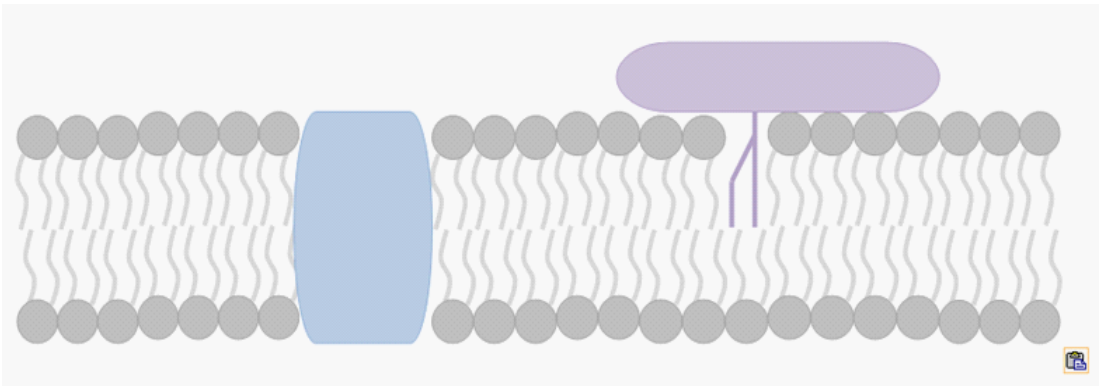

Figure 4a: Schematic diagram of two membrane proteins. The protein in blue represents an integral or intrinsic protein; note the variation in hydrophobicity that the protein would require in order to maintain exposure to both the lipid head groups and acyl tails. The protein in purple represents a peripheral protein that is anchored to the membrane via fatty acid/lipid attachment.

Proteins composed mainly of α-helices are generally found in the inner and outer membranes of chloroplasts and mitochondria, plasma membranes, the endoplasmic reticulum, golgi complex, organelle membranes, viruses and bacterial inner membranes. Beta-barrel proteins are primarily found in the outer membranes of Gram-negative bacteria, chloroplasts and mitochondria. Membranes proteins are also found to associate with the bilayer through hydrophobic stretches of amino acids, and covalent attachment to embedded lipid molecules. (For 3D structures of known membrane proteins: http://blanco.biomol.uci.edu/mpstruc/ and for a comprehensive site on structural and functional information of membrane proteins and peptides: http://www.mpdb.tcd.ie)

A critical feature of biological membranes found in all kingdoms is the asymmetry of the two leaflets. This asymmetry generates different biophysical properties and tasks for the two sides of the membrane. Maintenance of this non-random asymmetry is a consequence of several factors including the physical properties of lipids, giving them very little ability to simply flip their polar head groups across the non-polar core, and thus there is the presence of transporters/enzymes that assist in active lipid translocation across the membrane. This maintenance of asymmetry is essential; for example, the phospholipid phosphotidylserine is located in the cytoplasmic side of the plasma membrane exclusively as a co-factor for a number of membrane-bound enzymes. However, when exposed to the surface, this lipid is a preserved recognition site for phagocytes and stimulates the blood coagulation cascade.

Function

Given the many roles of the membrane, the primary role of a membrane, whether exposed to the cellular exterior environment or not, is to provide a degree of selective separation and protection. As a result of the lipid bilayer, the membrane is selectively permeable to ions and other molecules. This ensures that compounds and compound concentrations remain at appropriate quantities both in and out of the cell.

The plasma membrane plays a role in anchoring the cytoskeleton therefore permitting the integrity of the cell. The membrane also houses many proteins that serve particular functions, some of which include: channel proteins essential in the formation of small openings for the diffusion of molecules, carrier proteins or gated channels that provide a binding site for substrate molecules that are to be exported or imported, receptor proteins that trigger cell responses like the release of hormones, cell recognition proteins, and enzymatic proteins that are able to carry out cellular processes.

In general, the function of the membrane, with the inclusion of proteins includes: a selective barrier, which is critically important in maintaining concentrations of solutes and electrical and chemical potentials, energy generation, lipid production and maintenance, signaling and hormonal control, transport, catalysis, prokaryotic DNA replication, structural support and protection, anchoring and considerably more. Membranes also define the nature of communication between

the outside and the inside of the cell. This may be in the form of actual passage of ions, thus triggering a biological event or conformational changes in membrane proteins.

Fluid Mosaic Model

In 1972, Singer and Nicolson proposed the Fluid Mosaic Model. This concept was grounded on the thermodynamic principles and organization of lipids within the membrane. The Fluid Mosaic Model was also built on the evidence of asymmetry and mobility of the various components of the membrane, determined by several biochemical and biophysical techniques over several decades. Up to this time, the accepted model was that proposed by Robertson or Davidson and Danielle, the Unit Membrane Model or Protein-Lipid-Protein model, respectively.

At first the Fluid Mosaic Model depicted bilayers as a matrix composed of phospholipids, globular integral membrane proteins and glycoproteins integrated into the membrane (Figure 4).

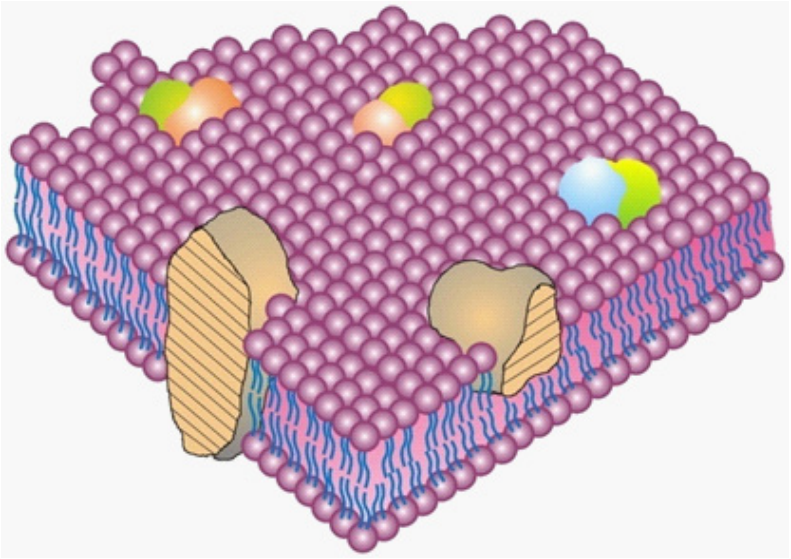

Figure 4b: Schematic diagram of the Fluid Mosaic Model of a biological membrane structure, originally proposed in 1972. Structures coloured in beige represent globular membrane proteins embedded in the fluid bilayer. The figure does not contain variation in lipid composition of membrane domains. Adopted from [3].

Over the years, this depiction was re-established using various biochemical techniques that confirmed the fluidity of the membrane – a dynamic structure in all three axes. However within a few years after its proposal, it became clear that the original model needed to be modified and expanded. The new model included membrane associated cytoskeletal components such as localized proteins or nucleic acids, lipid-lipid, protein-protein or protein-lipid interactions and domains but also an increase and decrease in the mobility of membrane components, among others. This model was much less homogenous than the previously proposed concept, with the inclusion of basic elements of the original model.

The emphasis of this model on biological systems is vital, however in the coming years and by use of various novel biochemical techniques, the Fluid Mosaic Model will continue to undergo an evolution through modifications as our information on this on vital biochemical cellular structure increases. For example, it is now apparent that membrane proteins and other components do not diffuse freely in the fluid bilayer and that there is evidence for lateral domains and clusters within the membrane. In addition, there is also some belief and experimental evidence that supports the arrangement of clusters (domains or rafts) within the membrane as traditional bilayers. Nonetheless, this model still delivers a global illustration of biological membranes for researchers today (Figure 5).

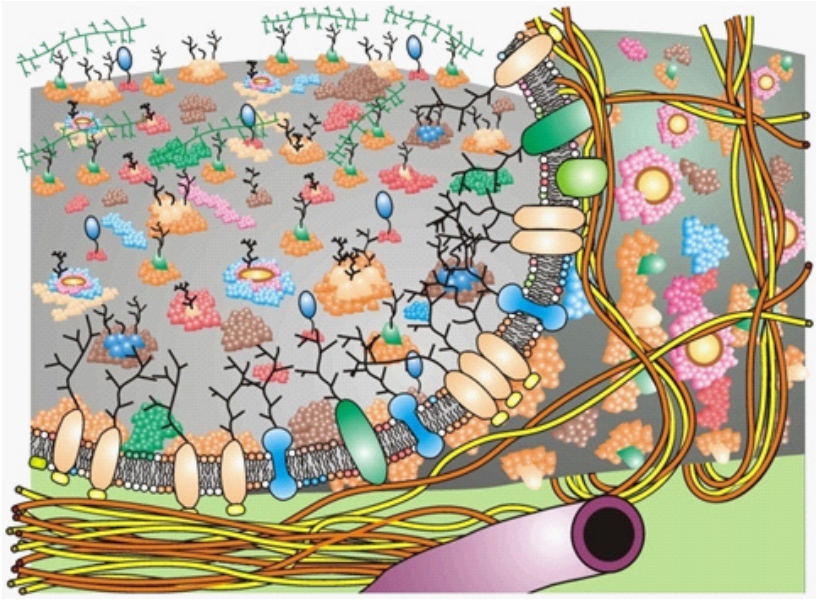

Figure 5: Schematic diagram of an updated version of the Fluid Mosaic Model. Image contains membrane domain structures, membrane-associated cytoskeletal and extracellular structures, different integral proteins, polysaccharide-glycoprotein associations and diverse lipids and oligosaccharides. Restriction on lateral diffusion of some trans-membrane glycoproteins is also represented. Sizes or structures of image components are not drawn to scale. Adapted from [4].

Learning Outcomes

1.Define the membrane bilayer

- Membranes are composed roughly of 20% water and 80% carbohydrates, lipids and proteins
- It is 2D array of amphipathic molecules in which the tails, or acyl chains, associate with each other, out of contact with water, and whose head groups interact with the aqueous solvent
- In addition the interior of the membrane has a high dielectric constant, and the hydrophobic center also contains highly ordered water molecules.

2. Understand the general characteristics of lipids within the bilayer

- Amphipathic compounds that vary greatly in diversity and structure particularly in the headgroup region which establishes the chemistry of the bilayer surface
- Lipids commonly have a polar headgroup and a non-polar tail characterized by an acyl chain

3.Describe the general regions of the lipid bilayer

- The general regions are as follows: perturbed water, bound water that surrounds the headgroups, ordered lipid sidechains, and disordered lipid tails close to the interior of the bilayer

4. Be able to describe the overall roles of membrane proteins

- Proteins within the membrane are biochemically, amphipathic and active components of the membrane that form a diversity of transporters, enzymes, receptors, pores etc.
- Membrane proteins can be vaguely characterized as intrinsic (integral) or extrinsic (peripheral), with various topological conformations, number of helices and oligomeric states

5. Describe the importance of the asymmetry found between the leaflets of the bilayer

- This important characteristic of the membrane generates different biophysical and biochemical properties and tasks for the two sides of the membrane
- This asymmetry is maintained by proteins and their physical properties that do not allow the polar headgroups to diffuse through the hydrophobic core of the bilayer

6. List the general roles of the membrane

- With the inclusion of proteins the general roles are: providing a selective barrier, which is critically important in maintaining concentrations of solutes and electrical and chemical potentials, compartmentalization, energy generation, lipid production and maintenance, signaling and hormonal control, transport, catalysis, prokaryotic DNA replication, structural support and protection, anchoring

7. Describe important characteristics of the classical Fluid Mosaic Model proposed by Singer and Nicolson

- This model is built on the evidence of asymmetry and the mobility of the numerous components of the membrane
- Provides a depiction of a bilayer matrix composed of phospholipids (with no indication of variation), globular integral membrane proteins and glycoproteins

8. Provide an updated version of the Fluid Mosaic Model

- The new model included membrane associated cytoskeletal components such as localized proteins or nucleic acids, lipid-lipid, protein-protein or protein-lipid interactions and domains but also an increase and decrease in the mobility of membrane components

- There is also evidence of lateral domains and clusters that do not diffuse freely, yet there is also belief that the membrane may also contain regions that follow a more traditional description

ENERGETICS OF THE MEMBRANE

Objectives:

- What is the membrane potential?
- What is the role of the cell membrane in maintaining the membrane potential?
- Describe how an action potential is generated and propagated?
- When is the transmembrane movement of a substance thermodynamically favorable?
- Describe the Nernst potential for an ion in terms of electrical and concentration magnitude.
- What is a Donnan potential and what environmental conditions permit its existence?
- If the Donnan potential did not exist, what would happen to ions across the membrane?
- Identify the two main components of the proton motive force.
- Describe the process of the chemiosmotic hypothesis within the membrane.

Membrane Potential

The biological membrane acts as a barrier to prevent movement of solutes from one side of the membrane to the other. However, depending on their permeability, some ions are able to move down their concentration gradient outside of the cell thus generating a voltage across the membrane, the membrane potential ($\Delta\psi$). Most simply, $\Delta\psi$ is a function of the relative concentrations of all ions on either side of the membrane:

$$\Delta\psi = RT/ZF \times \ln([ion]in/[ion]out) \qquad \text{Eq. 2-1}$$

Where R is the gas constant (8.314 J•K-1•mol-1), T is the temperature in Kelvin (25˚C = 298 K), Z is the net charge per ion and F is the Faraday constant, the charge of one mole of electrons (96 485 coulombs•mol^{-1}). Typically, $\Delta\psi$ is expressed in volts (V) or millivolts (mV).

Essentially, the membrane potential is an electrical potential difference between the cytosol of the cell and the surrounding extracellular fluid. This potential can be accounted by the fact that there is a slightly greater number of negative charges than positive charges inside the cell, and a slightly greater number of positive charges than negative charges outside. The resting membrane potential, electrical differences under resting conditions, is typically maintained at about -70 mV (see [5] for further description). By convention the polarity (positive or negative) of the membrane potential is stated in terms of the sign of the excess charge on the inside of cell. Thus, -70 mV indicates an excess of negative charge within the cytosol of the cell.

As sodium, potassium and chloride ions are present in the highest physiological concentrations (Table 1), they play an important role in generation of the membrane potential. However in some specialized organelles other ions play a larger role such as Ca2+ in the sarcoplasmic reticulum or H+ in energized membranes of the mitochondria, chloroplasts and bacterial cytoplasmic membranes. While this potential difference is present in all cells, it is most critical in nerve and muscle cells as changes in their membrane potential are used to code and transmit information.

Table 1

Ion	Extracellular mmol/L	Intracellular mmol/L
Na^+	150	15
K^+	110	10
Cl^-	5	150

Nernst Potential

Walther H. Nernst (1864-1941) received the Nobel prize in 1920 in recognition of his work in thermochemistry. His contribution to the field of chemical thermodynamics led to the generation of an equation correlating chemical energy and the electrical potential of a galvanic cell or battery.

In a biological membrane, the Nernst potential of a specific ion is the membrane potential at which there is no overall flow of that particular ion species from one side of the membrane to the other. The Nernst potential of a cell is commonly referred to as the reversal or equilibrium potential. Reversal here refers to the fact that a change in membrane potential away from that of equilibrium reverses the overall direction of ion flux. See [6] for further description.

The Nernst equation (Eq. 2-2) gives a formula that relates the numerical values of the concentration gradient to the electrical gradient, which balances it.

$$E = RT/ZF \times \ln([ion]in/[ion]out) \qquad \text{Eq. 2-}$$

For example, consider a concentration gradient established by dissolving KCl in half of a divided vessel full of water. If a membrane permeable only to K+ ions is introduced, after a period of time an equilibrium situation will arise where the chemical concentration gradient, which at first forced K+ ions to move down their concentration gradient, is exactly balanced by an electrical gradient opposing the movement of charge.

In summary, the membrane potential at which the electrical force is equal in magnitude but opposite in direction to the concentration force is called Nernst of equilibrium potential for that ion. The magnitude of such equilibrium potential is determined by the Nernst equation.

Donnan Potential

Many cells are composed of membranes with high permeability to both K+ and Na+ ions. Essentially this would prevent establishment of a resting membrane potential as chloride would move down the concentration gradient with potassium, counteracting the positive charge.

However, there exists a phenomenon, discovered by Frederick G. Donnan in 1911, in which ion species from two separated ionic solutions maintain an unequal distribution across a semi selective membrane. The membrane maintains this unequal distribution by acting as a selective barrier to passive ionic diffusion. The electrical potential resultant of this unequal distribution is termed the Donnan potential. See [7] for further description.

For example, if the membrane were completely permeable to both K+ and Cl- ions, movement would exist until relevant concentration gradients were balanced by the membrane potential as given by the Nernst equation. As there can be only one membrane potential at any given time, equilibrium would appear as follows:

$$RT/ZF \times \ln([K+]in/[K+]out) = E = RT/ZF \times \ln([Cl-]in/[Cl-]out) \quad \text{Eq. 2-3}$$

Cancelling out like terms we have:

$$([K+]in/[K+]out) = ([Cl-]in/[Cl-]out) \quad \text{Eq. 2-4}$$

Thus at equilibrium the product of the concentration of diffusible ions on one side of the membrane equals the product of the concentration of diffusible ions on the other side of the membrane.

$$[K+]in \times [Cl-]in = [K+]out \times [Cl-]out \quad \text{Eq. 2-5}$$

In conclusion, the final potassium and chloride ion distribution is irrespective of starting conditions. It does not matter what the initial distribution of these ions is, they will always end up in an equilibrium that obeys the Donnan rule if distribution is passive. However, if the distribution is unequal a Donnon potential will result.

Other more complex contributions to the Donnon potential in a cell include charged biomolecules that accumulate at different concentrations on either side of the cytoplasmic or organelle membranes such as: metabolite molecules, nucleic acids, charge containing carbohydrates, and proteins. Further, it is now also considered that the asymmetric lipid distribution of the bilayer also provides to this potential.

Proton Motive Force

The electron transport system proteins and particular membrane transport proteins are considered as proton pumps, in that they move a proton across the biological membrane from one side to the other. However, protons are hydrogen ions (H^+), and as we have just learned the movement of a charged ion across the membrane results in the generation of an electrochemical gradient. The Proton Motive Force **(PMF)** is therefore a ion chemical gradient and a charge gradient across the lipid bilayer. As the hydrogen ion concentration determines the relative pH of a solution, the chemical distribution from the proton motive force results in differential pH values across the membrane. The creation of this electrochemical gradient across an energy-transducing membrane can be further utilized for chemical, mechanical or osmotic work (Figure 6). See [8] for further description.

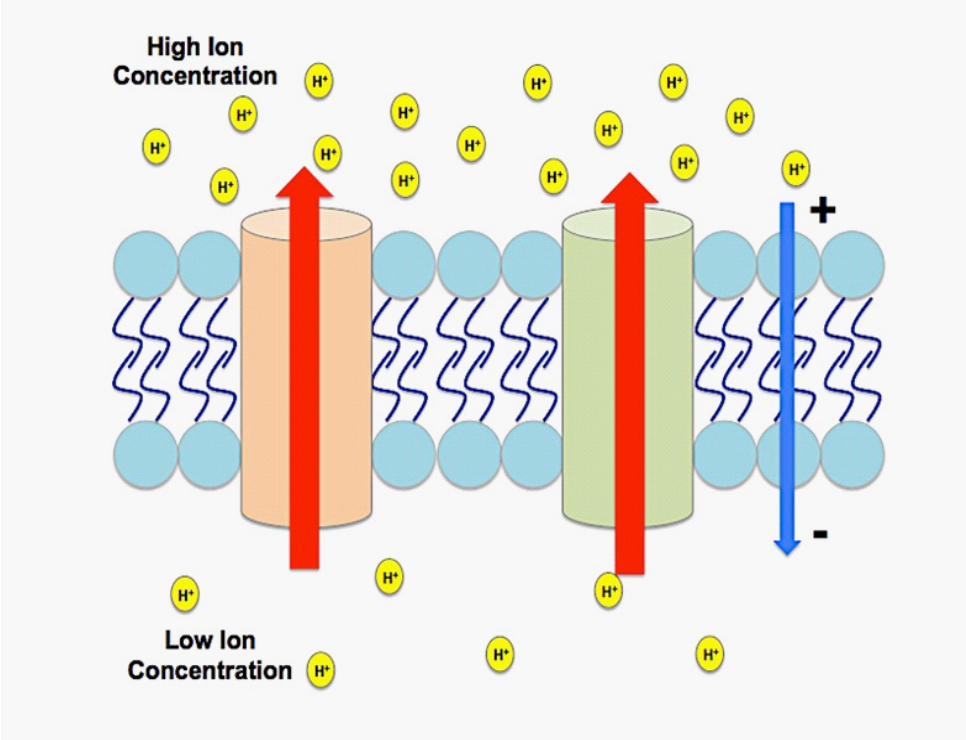

Figure 6: The electrochemical gradient generated by movement of hydrogen ions stores potential energy within the generated concentration difference. This stored energy can be harnessed and used to power chemical reactions. Red arrows depict the movement of hydrogen ions from the inside to the outside of the membrane to form the concentration gradient, which may then be exploited for future work. Blue arrow indicates the generated electrical gradient.

Action Potential

Table 2-1 indicates that the distribution of Na+ and K+ ions are not at equilibrium. To reach equilibrium Na+ would have to enter the cell and K+ would have to exit the cell, both by spontaneously moving down their respective concentration gradients.

Upon nerve stimulation Na+ channels present in the biological membrane open, allowing the inward movement of Na+ to increase the resting membrane potential from -70 mV to as much as +50 mV. This depolarization of the membrane is called an action potential.

The Na+ channels remain open for less than 1 millisecond, however two subsequent effects occur from the formulation of the action potential. Firstly, the membrane depolarization triggers the opening of nearby voltage-gated K+ channels, opening in response to the change in membrane potential. Now K+ ions are permitted to diffuse down their concentration gradient out of the cell, repolarizing the membrane potential back to approximately -70 mV. Secondly, additional Na+ channel farther down the nerve axon are stimulated. This induces another round of depolarization

and repolarization, propagating the action potential down the axon. Action potentials either happen or not, there is no "partial" firing of a neuron. This principle is known as the all or none law. The sequential events of an action potential are summarized in figure 7.

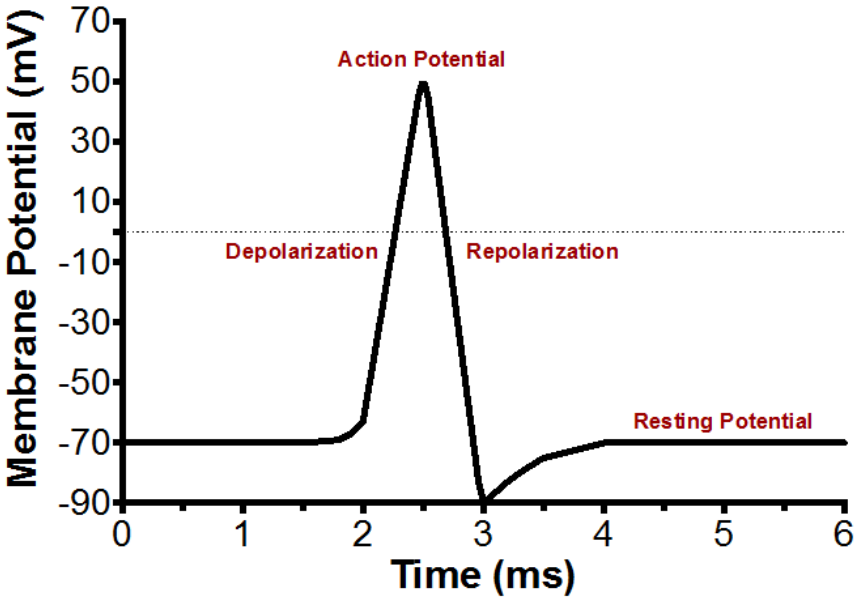

Figure 7a: The action potential. The rapid, temporary change in electrical potential across a membrane is depicted. Influx of Na+ ions depolarize the membrane potential, triggering the action potential. The membrane is repolarized back to resting state upon closing of Na+ and opening of K+ channels. The all or none principle of the action potential completes itself without significant variation in performance.

For a video illustrating the workings of both membrane and action potentials, see https://www.khanacademy.org/science/health-and-medicine/circulatory-system/heart-depolarization/v/membrane-potentials-part-1. This site allows one to browse in depth videos depicting differential ion concentration gradients and propagation of action potentials in relation to the cardiac rhythm of the heart. See also [9,10].

Chemiosmotic Hypothesis

In 1961, Peter Mitchell proposed that a proton gradient across the inner mitochondrial membrane couples the electron transport chain with ATP synthesis [11]. Mitchell's idea, termed the chemiosmotic hypothesis was that the transfer of electrons down the respiratory chain leads to the pumping of protons into the intermembrane space from the mitochondrial matrix. For this concept he was awarded the Nobel Prize in 1978. A lower H+ concentration and negative electrical field is thus generated within the matrix, being the proton motive force. This proton motive force is further harnessed by the ATP synthase protein, phosphorylating ADP to produce ATP. At the

time, Mitchell's hypothesis that oxidation and phosphorylation are coupled by a proton gradient was extremely innovative. Now, a wealth of evidence from biochemical, electron microscopy and crystallographic studies has revealed many details of the ATP synthase structure solidifying Mitchell's theory.

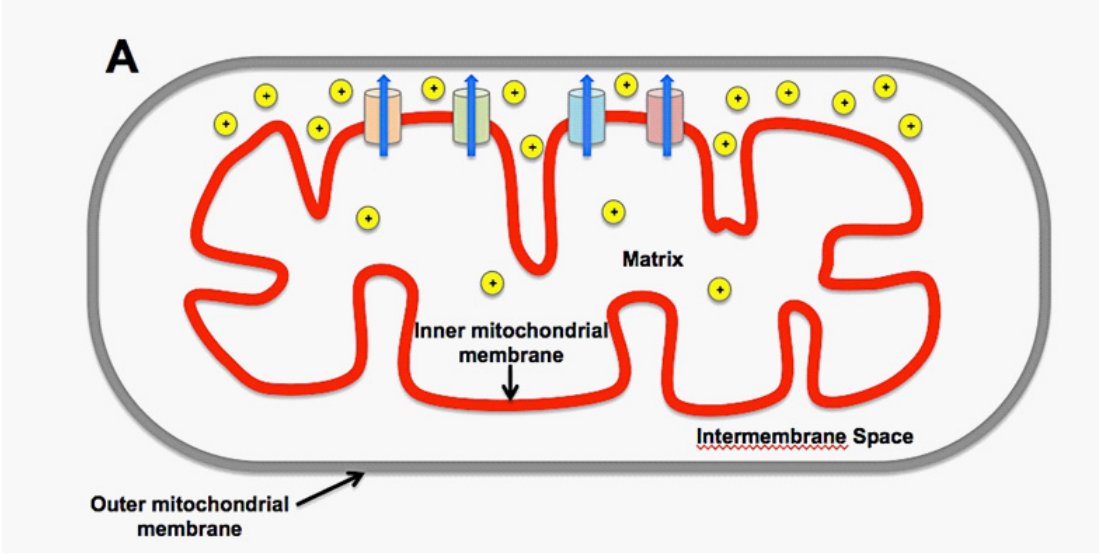

Figure 7b: The Chemiosmotic Hypothesis. Electron transfer down the respiratory chain results in proton pumping into the intermembrane space between the inner and outer mitochondrial membranes. The concentration gradient and membrane potential constituting the proton motive force are harnessed to drive the synthesis of ATP.

***ATP Synthase structure taken from:

http://www.rcsb.org/pdb/101/motm.do?momID=72

Learning Outcomes:

- The membrane potential is the voltage generated from the resulting charge imbalance across the membrane.
- The biological membrane acts as a barrier to prevent the free diffusion of solutes. This generates an electrical potential difference based on the concentration of charged ions on either side of the membrane.
- The Nernst potential for a particular ion is the membrane potential at which the electrical force is equal in magnitude but opposite in direction to the concentration force.
- The Donnan potential is when ion species from two separated ionic solutions maintain an unequal distribution across a semi selective membrane. The Donnan potential is irrespective of starting concentrations and will always exist if the diffusion is passive.

- The transmembrane movement of a solute molecule is thermodynamically favorable (-ΔG) when travelling down its concentration gradient, from an area of high to low concentration.
- An action potential is first started by opening of the sodium channels, permitting flux of sodium ions into the nerve axon to create depolarization. This moves the membrane potential from -70 mV to as much as 50 mV. Closing of the sodium channels and opening of the potassium channels allows potassium movement down its concentration gradient out of the cell, repolarizing the nerve axon.
- The proton motive force is a hydrogen ion electrical and chemical gradient across the lipid bilayer. The creation of this electrochemical gradient across an energy-transducing membrane can be further utilized for chemical, mechanical or osmotic work.
- The chemiosmotic hypothesis is that the transfer of electrons down the respiratory chain leads to the pumping of protons, generating the proton motive force. The proton motive force is further harnessed by the ATP synthase protein, phosphorylating ADP to produce ATP.

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