# Electrical properties of cell membrane

The fundamental unit of all biological life is the cell, a mass of biomolecules in watery solution surrounded by a **cell membrane**. One of the characteristic features of a living cell is that it controls the exchange of electrically charged ions across the cell membrane and therefore the electrical potential of its interior relative to the exterior.

## Cells and cell membrane

All cells are surrounded by a cell membrane. We will neglect all the complexities of the metabolic and structural apparatus found in the interior of the cell and simply consider it as a little bag, formed by the cell membrane, and filled with saline (i.e., water with ions dissolved in it). Likewise, we will assume that the exterior of the cell is a bath of saline. This approximation is drastic but not unreasonable, particularly since we are here only interested in the basis of electrical information processing within the neuron and between neurons.

The crucial element (i.e., the *only* one that we did not abstract away!) is thus the cell membrane. In its simplest form, it is a *phospholipid bilayer,* i.e. a layer which is only two phospholipid molecules thick. Each of these molecules has two ends (one is a phosphate group, the other a hydrocarbon chain, i.e. a lipid) and these two ends have very different properties. The phosphate end is **hydrophilic** (it likes to be in a watery environment and to be surrounded by water molecules). In contrast, the lipid end is **hydrophobic** (it hates to be close to water; remember that oil is a hydrocarbon!). *Love* and *hate* for molecules means that they will achieve a lower energy if they attain the *loved* state and are able to avoid the *hated* states. Each molecule attempts to get into the lowest-energy state possible.
How can a phospholipid molecule be immersed in water at one of its ends and, at the same time, avoid to be in water at its other end? The answer is, as so often, team work! If enough phospholipid molecules get together, they can bundle up their oily (hydrocarbon) ends together, forming a double-layered sheet with the hydrocarbon ends in the center, and, at the same time, bath their phosphate ends in water on the *outside* of the sheet. This does not work at the borders of the sheet so it is best to have no ends, i.e., to close the sheet on itself, forming a closed sphere. The result is a certain volume of water (or saline) enclosed by a double layer of phospolipid molecules and -- Voilà! -- a *cell*! In fact, such *artificial cells* can be made from its constituent phospolipid molecules (for references see Scott 1975).

## Conductance

From the mentioned work on artificial membranes we know that *pure* phospholipid bilayers are quite good insulators (this is not surprising: there are no free ions in the membrane so

there are no carriers to transport charges). Their specific conductance per unit area is only about $g_{pure}=10^{-13}\Omega^{-1}m^{-2}$ (Goldup et al, 1970).

The conductance of biological membranes is much higher, typically by several orders of magnitude even *at rest* (i.e., without synaptic influences etc). The reason is that there are all kinds of ion channels and other *pores* penetrating the membrane and allowing additional currents to flow. It is these currents that make cells behave in complex and interesting ways. We will discuss some of them below.

## Capacitance

According to our simplification, the inside and the outside of the cell are both solutions of various salts in water. As opposed to the cell membrane, salt water constitutes quite a good conductor because there are free ions that can transport electrical charges. What we have then is two conductors (the inside and the outside of the cell), separated by an insulator (the membrane). This makes it possible to have different amounts of electrical charges inside and outside the cell. If we can separate a charge $Q$ by applying an electrical potential $V$ across the membrane, the membrane has by definition a capacitance $C=Q/V$. In fact, because the membrane is so thin (only two molecules thick, with a total thickness of about $6\times10^{-9}m$), we don't need much voltage to separate the charges and therefore the membrane capacitance is quite high; per unit area, it is

$$c=C/S\approx10^{-2}Fm^{-2} \quad \text{.....(1)}$$

where F is the unit of capacitance ("Farad").

The specific capacitance of biological membranes is very close to what is obtained simply from the dielectric constant of lipids and the thickness of the bilayer (for a simple derivation see Hobbie, 1997) and, unlike the conductance, the capacitance is very little influenced by all the complexities of biology.

## Electrical potentials across the membrane

Our interest is mainly on the function of neurons which is a class of cells that uses electrical signals for information processing. How can a cell generate such signals? The first thing we need is some way of generating different voltages at different parts of the system, in particular, inside and outside of each cell. Like all cells, neurons generate this difference by separating different ion species. More specifically, in the cell membrane of each neuron are **ion pumps**, which are protein molecules that span the membrane and use metabolic energy to transport some ions inside the cell and others outside. A typical one is the $Na^+$ $K^+$ pump which moves two potassium ions into the cell and, at the same time, three sodium

ions out of the cell. After this pump has been running for some time, the concentration of potassium inside the cell becomes larger than that outside, and the concentration of sodium becomes larger outside than inside. Running the pump requires energy, which is provided to the pump in the usual energy currency of the cell, the ATP→ADP process.

How does this generate an electric potential? Let us assume we are in thermodynamic equilibrium which means in this context that the net flux of ions is vanishing. (Of course, this is a *dynamic* equilibrium, meaning that ions cross the membrane in both directions but on average, the number of ions flowing in the cell is the same as the number of ions flowing out of the cell. Therefore, the *net* flux, i.e. the *difference* between the numbers of ions going each direction, is zero but the numbers themselves are not). Then, the probability $P_{in}$ of finding a specific ion inside the cell, as compared to the probability $P_{out}$ of finding it outside, depends on the energy the ion has inside ($E_{in}$) *vs*. outside ($E_{out}$). From statistical mechanics, we know that the relation between these probabilities is given by the Boltzmann distribution:

$$P_{in}/P_{out}=\exp(-E_{in}/kT)/\exp(-E_{out}/kT) \quad \text{.....(2)}$$

where $k$ is a constant called the **Boltzmann factor** and $T$ is the temperature (in Kelvin). The energy of an ion is certainly a very complicated quantity, with all the interactions and biochemical complexities going on in a living system. Fortunately, the details are not important for our purposes: We can rewrite eq. (2) in the form

$$P_{in}/P_{out} = \exp\{-(E_{in}-E_{out})/kT\} \quad (3)$$

and we see that only the *difference* of energies counts. The biochemical milieu is not very different inside the cell from outside the cell. Therefore, the chemical energies of ions inside and outside the cell are about the same, and the only real difference between the energy of the ions inside and outside is their electrical energy. This is computed directly as $zeV$, where $z$ is the valence of the ion, $e$ the electric unit charge (the charge of one electron), and $V$ the electrical potential. Therefore, all other energy terms cancel out and we are left with

$$P_{in}/P_{out} = \exp\{-ze(V_{in}-V_{out})/kT\}$$

Now we can turn things around: Instead of computing the probabilities from the voltages, we can obtain the voltages from the probabilities: The voltage difference between the inside and the outside of the cell is obtained as

$$\Delta V=V_{in}-V_{out} = (kT/ze)\ln(P_{out}/P_{in}) \quad \text{.....(4)}$$

This relation is known as the **Nernst Equation**. Usually, it is expressed in terms of the ion concentrations but since the probability of finding an ion at some location is proportional to its concentration at this location, the formulations are equivalent. It is also customary to set the voltage scale such that $V_{out}$=0 (the choice of the electric 'ground' is arbitrary; note that this convention changed over time and that in the classical papers by Hodgkin and Huxley which are cited below, the opposite sign is used).

We thus find that each ion species has its own voltage at which it is in statistical equilibrium. This voltage is commonly called the "reversal potential" of this ion because the current generated by these ions reverses its sign when this voltage is applied to the membrane.

## Membrane patch in equilibrium

If we consider a patch of cell membrane which may contain many ion channels but which is small enough such that the transmembrane voltage is approximately the same everywhere in the patch. Electrically, one single ion channel is equivalent to a resistance in series with a voltage source: The resistance $r_{channel}$ is simply the inverse of the conductance of the ion channel pore (let us assume for simplicity that the channel is permeable to a single ion species only), and the voltage $V_i$ is the reversal potential of the ion species $i$ which can pass through the channel. If we have many channels, say $N$, they are electrically all in parallel, so their total resistance is $R= r_{channel}/N$. Likewise, if we have an ion channel that selectively lets different ions pass, it can be considered as several one-ion-only channels in parallel.

Let us start by assuming that there is only one ion species, say sodium. The reversal potential $V_{Na}$ for sodium is computed from the Nernst equation, eq. (4). The conductance for sodium $g_{Na}=R^{-1}{}_{Na}$ is, as just discussed, the sum of the conductances of all channels that allow sodium ions to pass. According to Ohm's Law, the current across these channels is proportional to the difference in electrical potential (voltage) across the membrane, and the proportionality factor is just the conductance. Keeping in mind our convention that the outside voltage is zero (ground), the current flowing across the membrane is thus

$$I_{Na}=V_{Na}/R_{Na}=g_{Na}V_{Na} \quad \text{.....(5)}$$

What if there is more than one type of ion, e.g. sodium *and* potassium? Currents will then flow across both types of channels until an equilibrium is established, with the voltage inside the cell somewhere between the reversal potentials of these two ion species. Common names for this equilibrium potential are **resting potential** or **leakage potential**, $V_L$ .

In order to compute $V_L$ , we assume that the system is already in equilibrium, with the inside of the cell at this potential (which is so far unknown). In order to compute the sodium current, we thus have to modify eq. (5) as follows,

$$I_{Na} = (V_{Na} - V_L)/R_{Na} = g_{Na}(V_{Na} - V_L) \quad \text{.....(6)}$$

since the difference between the outside (at zero voltage) and the inside (at voltage $V_L$) is $V_{Na} - V_L$ . By exactly the same argument, the current of $K^+$ ion is

$$I_K = (V_K - V_L)/R_K = g_K(V_K - V_L) \quad \text{.....(7)}$$

where, of course, $G_K = R^{-1}{}_K$ is the conductance across the potassium channels.
We can now compute $V_L$ from the requirement that the system is in equilibrium. If that is the case, then conservation of charge requires that all currents cancel each other out, or, in other words, that the sum of all currents is zero (this is known as **Kirchhoff's Current Law**), thus $I_{Na} + I_K = 0$. Together with eqs. (6) and (7), we therefore have

$$g_K V_K - g_K V_L + g_{Na} V_{Na} - g_{Na} V_L = 0 \quad \text{.....(8)}$$

The only unknown in this equation is $V_L$ and we can solve for it to obtain

$$V_L = (g_{Na} V_{Na} + g_K V_K)/(g_{Na} + g_K) \quad \text{.....(9)}$$

Of course, voltages have to be entered in this equation with their correct signs, as they are obtained from eq. (4). In most physiological conditions, $V_{Na} > 0$ and $V_K < 0$ .
So far we have focused only on two ion species, sodium and potassium, just as as Hodgkin and Huxley did when they developed their famous model of the giant squid axon (Hodgkin et al, 1952; Hodgkin and Huxley, 1952a-d). However, it can be easily seen that equation (9) can be generalized for more than two ion species. The resting potential is then given by the quotient of two sums over all ion species,

$$V_L = \sum_i g_i V_i / \sum_i g_i$$

where, of course, $V_i$ is the reversal potential of ion species $i$ and $g_i$ is its transmembrane conductance. It is found that for many neurons, the resting potential is close to $-70mV$ .

## Donnan membrane equilibrium

(1) The **Gibbs–Donnan effect** (also known as the Donnan's effect, Donnan law, Donnan equilibrium, or Gibbs–Donnan equilibrium) is a name for the behaviour of charged particles near a semi-permeable membrane that sometimes fail to distribute evenly across the two sides of the membrane. The usual cause is the presence of a different charged substance that is

unable to pass through the membrane and thus creates an uneven electrical charge.For example, the large anionic proteins in blood plasma are not permeable to capillary walls. Because small cations are attracted, but are not bound to the proteins, small anions will cross capillary walls away from the anionic proteins more readily than small cations. Thus, some ionic species can pass through the barrier while others cannot. The solutions may be gels or colloids as well as solutions of electrolytes, and as such the phase boundary between gels, or a gel and a liquid, can also act as a selective barrier. The electric potential arising between two such solutions is called the Donnan potential. The effect is named after the American physicist Josiah Willard Gibbs who proposed it in 1878 and the British chemist Frederick G. Donnan who studied it experimentally in 1911. The Donnan equilibrium is prominent in the triphasic model for articular cartilage proposed by Mow and Lai, as well as in electrochemical fuel cells and dialysis. The Donnan effect is tactic pressure attributable to cations ($Na^+$ and $K^+$) attached to dissolved plasma proteins.

The presence of a charged impermeant ion (for example, a protein) on one side of a membrane will result in an asymmetric distribution of permeant charged ions. The Gibbs–Donnan equation at equilibrium states (assuming permeant ions are $Na^+$ and $Cl^-$):

$[Na^+]\alpha/[Na^+]\beta = [Cl^-]\beta/[Cl^-]\alpha$ where $\alpha$, $\beta$ represent the number of ions moving in/out through the membrane from beginning till the end of equilibrium

**Physiological applications**

Red blood cells

When tissue cells are in a protein-containing fluid, the Donnan effect of the cytoplasmic proteins is equal and opposite to the Donnan effect of the extracellular proteins. The opposing Donnan effects cause chloride ions to migrate inside the cell, increasing the intracellular chloride concentration. The Donnan effect may explain why some red blood cells do not have active sodium pumps; the effect relieves the osmotic pressure of plasma proteins, which is why sodium pumping is less important for maintaining the cell volume.

Neurology

Brain tissue swelling, known as cerebral oedema, results from brain injury and other traumatic head injuries that can increase intracranial pressure (ICP). Negatively charged molecules within cells create a fixed charge density, which increases intracranial pressure through the Donnan effect. ATP pumps maintain a negative membrane potential even though negative charges leak across the membrane; this action establishes a chemical and electrical gradient.

The negative charge in the cell and ions outside the cell creates a thermodynamic potential; if damage occurs to the brain and cells lose their membrane integrity, ions will rush into the cell to balance chemical and electrical gradients that were previously established. The membrane voltage will become zero, but the chemical gradient will still exist. To neutralize the negative charges within the cell, cations flow in, which increases the osmotic pressure inside relative to the outside of the cell. The increased osmotic pressure forces water to flow into the cell and tissue swelling occurs

(2) **Gibbs adsorption isotherm**

It is an equation to relate the changes in the concentration of the component in contact with the surface with changes in surface tension; resulting in changes in surface energy. It represents the relationship between adsorption and change in surface tension of a solvent due to the presence of solutes. This equation is true for relatively solute solutions, hydrated organic compounds, amphipathic species. It was discovered by J.W. Gibbs in 1878 and separately by J.J. Thompson in 1888.

$dG = -SdT + Vdp + \mu_1 dn_1 + \mu_2 dn_2 + \gamma dA$

where, $\gamma$ = surface tension; dA = increase in surface area; S = entropy; p = pressure; V = volume