The Neuronal Membrane at Rest

Introduction

- The nervous system must be able to collect, distribute, and integrate information.
- The neuron solves the problem of conducting information over a distance by using electrical signals that sweep along the axon.
- Although the axon is like a leaky garden hose, the axonal membrane has special properties that allow it to conduct nerve impulses (action potentials).
- Nerve cells and muscle cells have excitable membranes.
- When a cell with an excitable membrane is not generating impulses, it is said to be at rest; and will have a resting membrane potential.

The Cast of Chemicals

Intracellular Fluid (Cytosol) and Extracellular Fluid

Water (H_2O)

- The two H and the one O are bonded covalently, but O has a greater affinity for electrons.
- H_2O is a polar molecule held together by polar covalent bonds.
- H_2O is an effective solvent for other charged or polar molecules.

Ions

- Are atoms or molecules that have a net charge.
- Ionic molecules (electrolytes) are held together by ionic bonds.
- Cations are positively (+) charges; Anions are negatively charged (-).

The Phospholipid Membrane

- The neuronal membrane is a phospholipid membrane and contributes to the resting membrane potential and to nerve impulses (action potentials) by forming a barrier to water soluble ions, and of course to water itself.

Phospholipid bilayer

- Cell membranes are made predominately of phospholipids.
- Phospholipids are composed of a polar phosphate group and a non-polar lipid group.
- The neuronal membrane consists of a sheet of phospholipids two molecules thick.
    - The polar phosphates face the intracellular and the extracellular fluids.
    - The non-polar lipids face each other in the interior of the membrane
- The phospholipids bilayer effectively isolates the intracellular fluid from the extracellular fluid.

Protein

Enzymes, the cytoskeleton, cellular transporters and receptors, and many chemical messengers are all made of proteins.

Protein Structure

- Proteins have widely varying and different shapes, sizes and chemical characteristics.
- Proteins are composed of various combinations of 20 different amino acids.
  - Amino acids are composed of a combination of NH_2, COOH, and a variable group.
  - Proteins are synthesized by ribosomes of the cell body, where amino acids are sequences and connected by peptide bonds to form a polypeptide.
- The sequence of amino acids determines the Primary structure.
- The coiling / spiraling of the polypeptide determine the Secondary structure.
- The bending / folding of the coiled polypeptide determine the Tertiary structure.
- The bonding of different polypeptide to form a larger protein determines the Quaternary structure.

Ion Pumps

- Some proteins span the cell membrane to form “pumps”, and are called ion pumps.
- ATP is used to change the shape of the protein and the change in shape forces certain ions across the membrane.
- Ion pumps are key to neuron functioning.

Channel Proteins (Ion Channels)

- Other proteins span the cell membrane to form a “pore” and are called channel proteins or ion channels.
- The diameter of the pore and the characteristics of the variables groups of the amino acids determine the ion selectivity of the channel, and allow certain ions to diffuse across the membrane.
- Channels often can be opened and closed by changes in the local microenvironment of the membrane which cause changes in the shape of the proteins.
- Channel proteins (ion channels) are key to neuron functioning.

The Movement of Ions

Diffusion

- The movement of substances from an area of high substance concentration to an area of low substance concentration is called diffusion.
- The difference in concentration, called the concentration gradient, is largely established by ion pumps.

Electricity

- The movement of electrons from an area of high concentration (charge) to an area of low concentration (charge) is the foundation for electricity.
- The difference in charge is called the charge gradient.
- Opposite charges attract (electrons and protons); Like-charges repel (electrons and electrons; or protons and protons).

Electrical Conductance

- Electrical current depends on movement of electrical charge.
  - I = V/R; (I = current, V = voltage, R = resistance)
  - I = g·V; (I = current, g = conductance, V = voltage)

The Ionic Basis of the Resting Membrane Potential

In a typical cell the resting membrane potential (V_m) is about -65 mV.

Equilibrium Potential

- The electrical potential difference (E) that exactly balances an ionic concentration gradient is called the equilibrium potential, and can be determined by the Nerst equation.

Nerst Equation

- At 37C; z = charge (+ or –1or 2)
- $$E_{ion} = \frac{61.54 \text{ mV}}{z} \cdot \text{Log} \frac{[\text{Ion}]_{out}}{[\text{Ion}]_{in}}$$
- The equilibrium potential is easy to calculate for each ion individually

Ion Distribution

- Ions are unevenly distributed between the outside and inside of neurons (as well as other cells), largely due to the actions of ion pumps.

Ion	$[\text{Ion}]_{out}$	$[\text{Ion}]_{in}$	$[\text{Ion}]_{out}$: $[\text{Ion}]_{in}$	E_{ion} @ 37C
K^+	5 mM	100 mM	0.05	-80 mV
Na^+	150 mM	15 mM	10	+62 mV
Ca^{2+}	2 mM	0.0002 mM	10,000	+123 mV
Cl^-	150 mM	13 mM	11.5	-65 mV

Ion Permeabilities

- The permeability of the neuron membrane is different for different ions, largely due to different types of ion channels.

- The resting membrane potential can be determined using the Goldman equation once we know the ions involved and the relative permeability of the membrane to those ions.

Goldman Equation

- At 37C; for K^+ and Na^+;
  P_K = relative permeability to K^+, P_K = relative permeability to Na^+.

$$V_m = \frac{61.54\ \text{mV}}{z} \cdot \quad \text{Log} \frac{P_K[K^+]_{out} + P_{Na}[Na^+]_{out}}{P_K[K^+]_{in} + P_{Na}[Na^+]_{in}}$$

Using the data for ion distribution from the table on the previous page together with the information that the resting membrane is about forty (40) times more permeable to K^+ than to Na^+, we can calculate the resting membrane potential:

$$V_m = \frac{61.54\ \text{mV}}{z} \cdot \quad \text{Log} \frac{40[5]_{out} + 1[150]_{out}}{40[100]_{in} + 1[15]_{in}}$$

$$V_m = \frac{61.54\ \text{mV}}{1} \cdot \quad \text{Log} \frac{350}{4015}$$

$$V_m = 61.54\ \text{mV} \cdot \quad -1.0596$$

$$V_m = -65.2\ \text{mV}$$

Potassium Permeability

- The selective permeability of the resting membrane to K^+ is due to the permeability of K^+ channels and is the key determinant of the resting membrane potential.

Extracellular Potassium

- Increasing extracellular K^+ concentration will depolarize neurons (as well as heart and skeletal muscle).
- The capillary blood-brain barrier limits movement of K^+ into the extracellular fluid of the brain.
- Astrocytes play a critical role in stabilizing extracellular K^+ concentration in the brain by taking up excess K^+.