

Membrane Potentials

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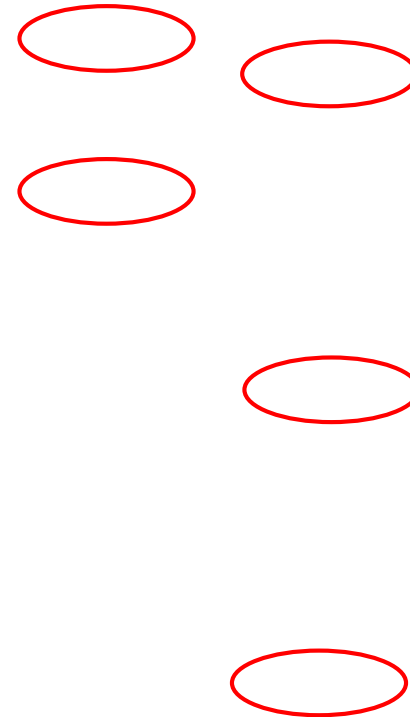
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- Extracellular fluid

- Na^+ , Cl^-

- Intracellular fluid

- K^+ , phosphate compounds,
proteins with negatively charged
side chains



Potential Difference (Electrical Potential)

- Separated electrical charges of opposite sign have the potential to do work if they are allowed to come together
- The units are volts
 - In biological systems mV

Membrane Potential

- Electrical charge difference across the membrane
- Membrane potential (V_m)

$$V_m = V_{in} - V_{out}$$

- Resting membrane potential (V_r): The membrane potential of a cell at rest
 - $V_{out} = 0$ (reference)
 - $V_m = V_{in} \approx -70$ mV
(V_m in neurons = -40 to -90)

Resting membrane potential

- The resting membrane potential is the result of the passive flux of individual ion species through several classes of resting channels
- The magnitude of the resting membrane potential depends mainly on two factors:
 - differences in specific ion concentrations in the intracellular and extracellular fluids
 - differences in membrane permeabilities to the different ions, which reflect the number of open channels for the different ions in the plasma membrane

Membrane Potential

- electrochemical driving force
(the sum of the electrical and
chemical driving forces)
- the conductance of the
membrane to the ion

*ion flux = (electrical driving force + chemical
driving force) × membrane conductance*

Membrane Potential

- *Equilibrium potential*: The membrane potential at which electrical and chemical fluxes become equal in magnitude but opposite in direction
 - The larger the concentration gradient, the larger the equilibrium potential
- *Nernst equation*

Membrane Potential

- The resting potential of a cell is determined by the proportions of different types of ion channels that are open, together with the value of their equilibrium potentials

- Goldman-Hodgkin-Katz Equation

$$V_m = 61 \log \frac{P_K [K_{out}] + P_{Na} [Na_{out}] + P_{Cl} [Cl_{in}]}{P_K [K_{in}] + P_{Na} [Na_{in}] + P_{Cl} [Cl_{out}]}$$

- P_{ion} = relative membrane permeability

Resting membrane potential

- Resting potential is generated largely because of the movement of K^+ out of the cell down its concentration gradient through K^+ leak channels
- Inside of the cell becomes negative with respect to the outside
- Resting membrane potential is not equal to the K^+ equilibrium potential because a small number of open leak channels for Na^+ does pull the membrane potential slightly toward the Na^+ equilibrium potential

Na⁺/K⁺ Pumps

- The concentrations of intracellular sodium and potassium ions do not change, because of the action of the Na⁺/K⁺-ATPase pump.
 - In a resting cell, the number of ions the pump moves equals the number of ions that leak down their electrochemical gradient
- Electrogenic pump
 - Moves three Na⁺ out of the cell for every two K⁺ that it brings in
 - Unequal transport of positive ions makes the inside of the cell more negative than it would be from ion diffusion alone
 - Very small contribution

Graded potentials and Action potentials

- All cells have a resting membrane potential due to the presence of ion pumps, ion concentration gradients, and leak channels in the cell membrane
- What makes a cell excitable?
 - Gated ion channels
 - Gated channels give a cell the ability to produce electrical signals (*excitability*) that can transmit information between different regions of the membrane (*excitable membranes*-neurons and muscle cells)
- Graded potentials → short distance signaling
- Action potentials → long-distance signaling

- **Polarized:**
 - outside and inside of a cell have a different net charge
- **Depolarization:**
 - reduction in charge separation
 - less negative potential
- **Overshoot:**
 - reversal of the membrane potential polarity—when the inside of a cell becomes positive relative to the outside.
- **Repolarization:**
 - returning of membrane potential to the resting value
- **Hyperpolarization:**
 - increase in charge separation
 - more negative membrane potential

Graded Potentials

- Graded potentials are changes in membrane potential that are confined to a relatively small region of the plasma membrane.
 - the magnitude of the potential change can vary
 - Receptor potential, synaptic potential, pacemaker potential
- Charge flows between the place of origin of the potential and adjacent regions of the plasma membrane, which are still at the resting potential

Graded potentials

- Can be either depolarizing or hyperpolarizing
- Magnitude is related to the magnitude of the initiating event (graded)
- Charge is lost with the distance
 - Leak channels (predominantly K⁺)

Action Potential

- Large alterations in the membrane potential (up to 100 mV)
- Very rapid (1-4 msec)
- Voltage-gated Na⁺ and K⁺ channels that mediate most neuronal action potentials

Voltage-gated channels

- Have sequences of charged amino acids that make the channels reversibly change their conformation in response to changes in membrane potential
- At negative potential (during resting) stay closed
- At positive potentials (depolarization) open
- Voltage-gated Na⁺ channels respond faster and have *inactivation gates*

- Voltage-gated Na⁺ Channel inactivation gate
 - Blocks channel shortly after depolarization
 - Opens at repolarization state

- Positive feedback loop
 - Step 3, opening of voltage gated Na⁺ channels causes more Na⁺ to enter and more voltage gated Na⁺ channels to open
- Membrane depolarization comes close to but does not reach to E_{Na}
 - Na⁺ channels get inactivated and also voltage gated K⁺ channels open
- The threshold of most excitable membranes is about 15 mV less negative than the resting membrane potential (-55 mV)

- Cellular accumulation of Na^+ and loss of K^+ are prevented by the continuous action of the membrane Na^+/K^+ ATPase pumps

The Action Potential

- Graded changes in current cause graded changes in voltage.
- If voltage is depolarized beyond a threshold (about -50 mV), an action potential is triggered.

An Action Potential is “All-or-None”

- At a brief moment in time (~1 ms), an action potential either occurs or it does not
- The shape of an action potential is always the same
- The magnitude of the action potential does not change

- All or None
 - After passing the threshold, all the stimuli triggers same action potentials at the same amplitude
 - All voltage-gated Na⁺ channels open
- How do you differentiate between a weak and strong stimuli?
 - Number and patterns of action potentials transmitted per unit of time (frequency)

Firing Rate Depends on Current Magnitude

- The frequency of action potentials (“firing rate”) depends on the magnitude of depolarizing current

Refractory Periods

- Absolute refractory period
 - During the action potential a second stimulus can not produce another action potential
 - Voltage-gated Na⁺ channels are already open or in inactive state
- Relative refractory period
 - Coincides with the after hyperpolarization
 - A stimulus stronger than normal can produce action potential
 - Fewer Na⁺ channels available and some of the K⁺ channels are still open
- Limits the number of action potentials
- Helps separation of action potentials from each other
- Determines direction of action potential propagation

Action Potential Propagation

- Sequential opening and closing of voltage-gated Na^+ and K^+ channels along the membrane
 - The difference between the potentials causes current to flow, and depolarizes the adjacent membrane
 - The new action potential produces local currents of its own that depolarize the region adjacent to it, producing another action potential at the next site ...
- Because the membrane area behind is refractory, the direction of action potential propagation is away from a region of membrane that has recently been active

Velocity of Action Potential

- Fiber diameter ↑ Velocity ↑
 - Less internal resistance to local current
- Myelination ↑ Velocity ↑
 - Less charge flow between intracellular and extracellular fluid compartments (leakage)
 - Action potentials only at the nodes
 - More charge arrives at the node
 - Metabolically more efficient

Velocity of Action Potential

- 0.5 m/sec → 100 m/sec
 - small diameter, unmyelinated fiber = 0.5 m/sec
 - 4 sec from toe to brain
 - large diameter, myelinated fiber = 100 m/sec
 - 0.02 sec from toe to brain