Ionic basis of excitability

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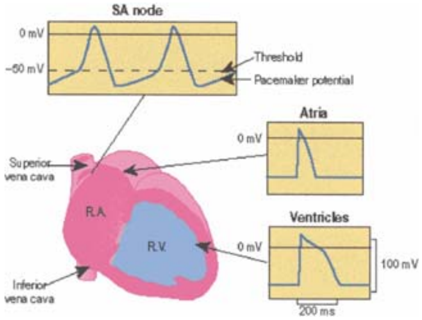
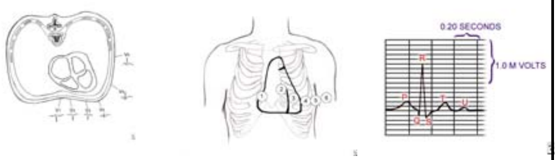
- Living cells have the ability to generate electricity.
- Electrical currents generated by cells result from the movement of **<u>ions</u>** across the plasma membrane.
- The simultaneous electrical activity of a large number of cells generate an electrical field that extend far beyond its locus of origin.

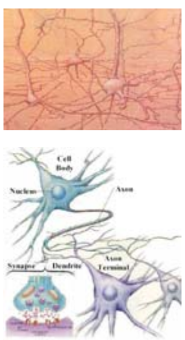
ELECTROCARDIOGRAPHY



The ECG (electrocardiogram) is generated by a flow of current through the body due to current source generated by the spreading action potential.

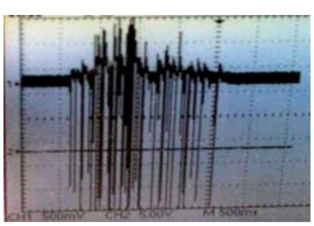


ELECTROENCEPHALOGRAPHY



ELECTROMYOGRAPHIE

Extracellular recording of the the electrical activity of contracting skeletal muscle cells

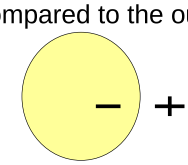


Excitable cells

-Resting Membrane Potential-

The cytoplasm contains **negatively charged** organic ions that can not leave the cell.

As a result, in ALL cells, the electrical potential in and outside the cell are different. The inside having a potential negative compared to the outside.



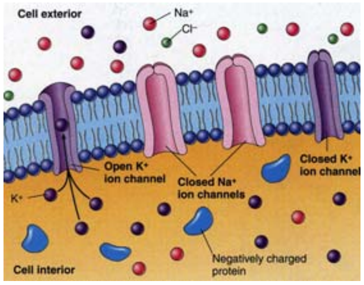
The plasma membrane

The core lipid bilayer of the plasma membrane is not permeable to charged particles. Thus:

- It can not conduct electricity.
- Ions (Na^+, K^+, Ca^{2+}…) are unevenly distributed between the intracellular and extracellular space.

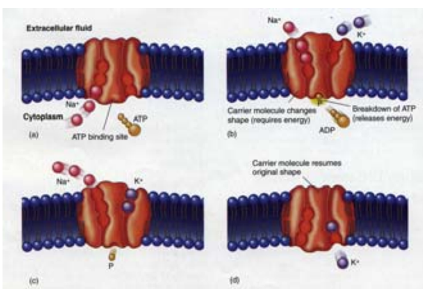
Ions CAN however permeate the plasma membrane. In order to do so, ionic gates or channels must open in the lipid bilayer.

There are many such protein channels imbedded in the membrane. These channels are ion selective and their gating tightly regulated.



ions	in	out
Na^+	10	142
K^+	148	5
Ca^{2+}	low	1.5

-The Na^+/K^+ pump-



Movement of ions across the membrane

If an ionic channel in the membrane opens, ions will use this water filled pore to move across the plasma membrane.

Where do they move to ?

They move in the direction of the largest driving force acting on them.

There are 2 driving forces that move ions across the membrane:

- The concentration gradient.
- The electrical gradient.

Driving force from concentration gradient

If movement is allowed (open channel), ions distribution will tend to **equilibrate** across the membrane.

Thus <u>net</u> movement of ions will proceed from the compartment of **high concentration** to the compartment of **low concentration**.

Example: Na^+ ions

the concentration gradient for sodium is from outside to inside the cell. If sodium channels open, this driving force will tend to move sodium ions to the intracellular space until concentration in both compartments is equal (equilibrium)

Driving force from electrical gradient

Electrical charge of the same sign (+ or -) REPPEL each other.

Electrical charges of opposite sign ATTRACT each other.

Thus, the net charge sign of an ion's environment will affect the random movement of this ion.

Example: Na^+ ions

The intracellular space is negatively charged compared to the extracellular space. This generate an electrical driving force which ATTRACT Na^+ ions inside the cell.

If sodium channels open, this force will drive the movement of sodium from the outside to the inside.

Net movement of ions across the membrane

The net movement of ions across the membrane will result from the influence of these 2 forces.

- For sodium ions these 2 forces are in the same direction.
- For potassium ions these 2 forces oppose each other.

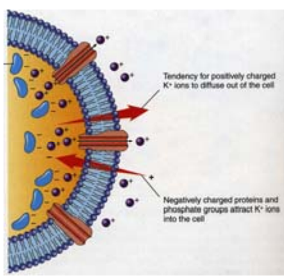
The equilibrium potential for an ion

- Electrical potential across the membrane or MEMBRANE POTENTIAL will affect the net driving force that moves ions.
- For example, if the intracellular space becomes more negative (hyperpolarization), the driving force for sodium ions will increase while the driving force for potassium ions will decrease.

- For any ions there will be a value of membrane potential at which there will be no net movement of this ion because the electrical driving force exactly oppose the concentration gradient driving force.

- This value of membrane potential is called the EQUILIBRIUM POTENTIAL for that particular ion.

-Equilibrium Potential-



K^+ equilibrium potential

$$E_k = 60 \ln \frac{[K^+]_o}{[K^+]_i}$$

-Membrane Potential-

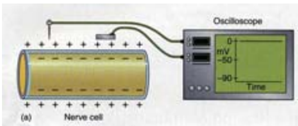
$$V_m = 60 \ln \left\{ P_{Na} \frac{[Na^+]_o}{[Na^+]_i} + P_k \frac{[K^+]_o}{[K^+]_i} + P_{Cl} \frac{[Cl^-]_i}{[Cl^-]_o} \right\}$$

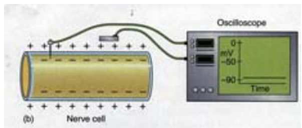
The most direct way of investigating ion channel function is to record the current which flows through the open channel or to measure the changes in membrane potential that this produces.

Potential measurements

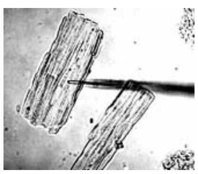
The potential across the cell membrane can be measured by inserting a glass microelectrode with a very fine tip into the cell and measuring the difference between the potential it records and that registered by a second electrode (the reference electrode) in the bath solution outside the cell.

Recording a cell membrane potential



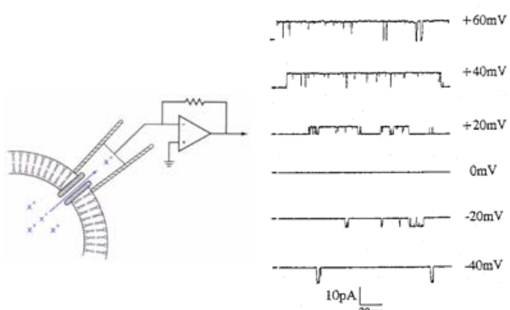


Voltage Clamp / patch clamp



This technique allows the membrane potential to be held (clamped) at a constant value.

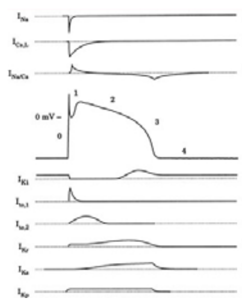
The current that flows through the membrane at any particular potential can then be measured.

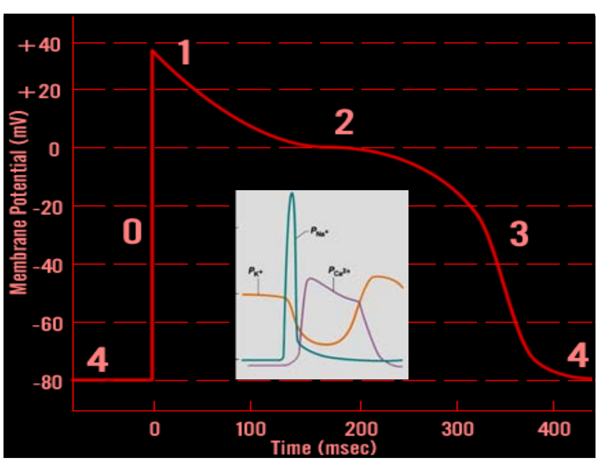


-The Action Potential-

action potential and ionic currents

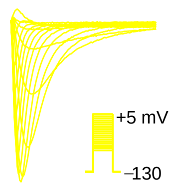
The action potential results from activation of voltage-dependent ion channels in the plasma membrane



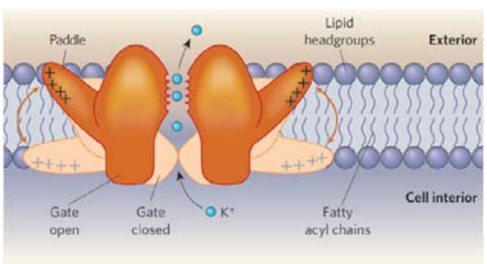


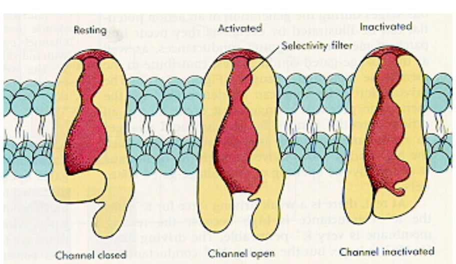
Voltage-Dependant Channels

- Opening and closing of ionic channels in excitable cells is controlled by voltage.

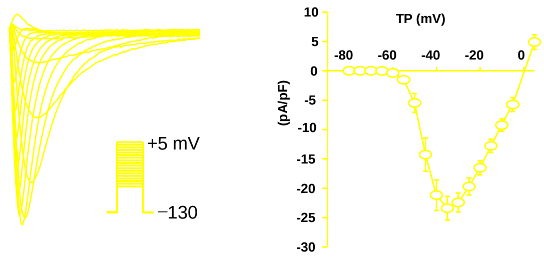


Protein channels have voltage sensors, and the conformation of the protein will change with membrane potential.

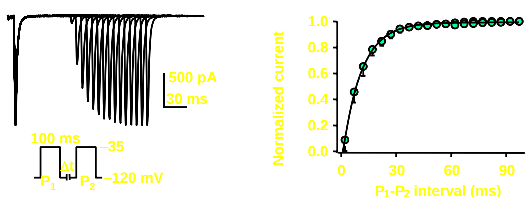


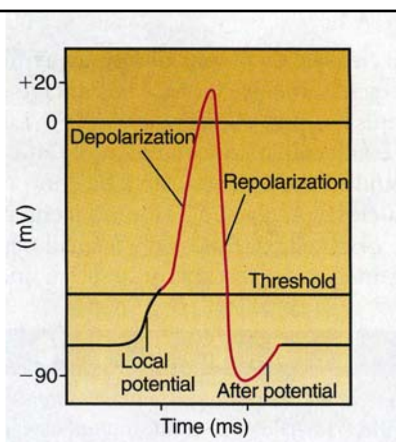


Na^+ current (I_{Na}) in guinea pig ventricular myocytes

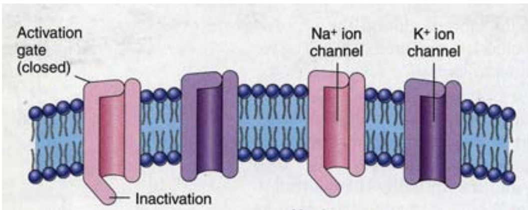


I_{Na} recovery from inactivation

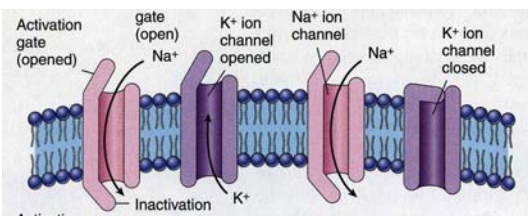




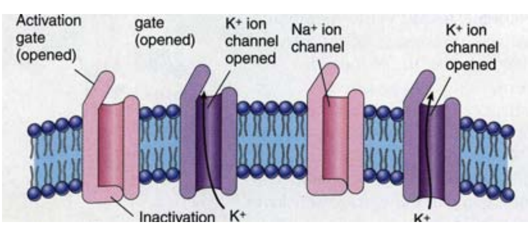
At Rest…..



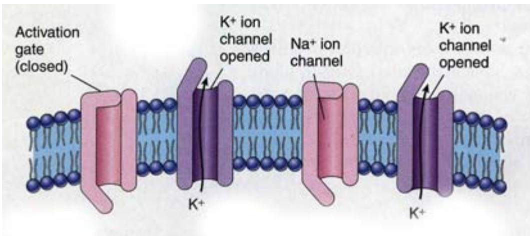
Upstroke phase….



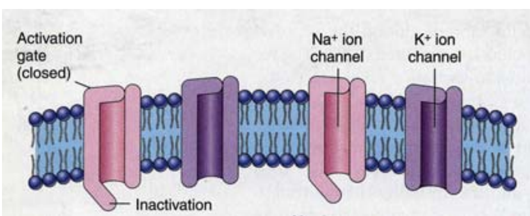
Repolarization phase……



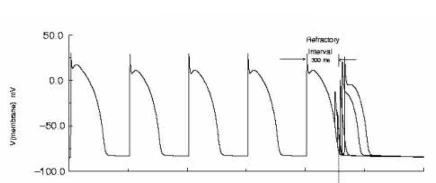
Sodium channels recover from inactivation……



Back to rest……..



-Refractory Period-



Characteristics of an action potential

1. Action potentials are produced when a local potential reaches threshold.
2. Action potentials are all-or-none.
3. Depolarization is a result of increased membrane permeability to Na^+ ions and movement of Na^+ ions into the cell. Activation gates of the voltage-gated Na^+ ion channels open.
4. Repolarization is a result of decreased membrane permeability to Na^+ ions and increased membrane permeability to K^+ ions, which stops Na^+ ion movement into the cell and increased K^+ ion movement out of the cell. The inactivation gates of the voltage-gated Na^+ ion channels close, and the voltage-gated K^+ ion channels open.
5. No action potential is produced by a stimulus, no matter how strong, during the absolute refractory period. During the relative refractory period a stronger-than-threshold stimulus can produce an action potential.
6. Action potentials are propagated, and for a given axon or muscle fiber the magnitude of the action potential is constant.
7. Stimulus strength determines the frequency of action potentials. Unless accommodation occurs, stimulus duration determines how long action potentials are produced.