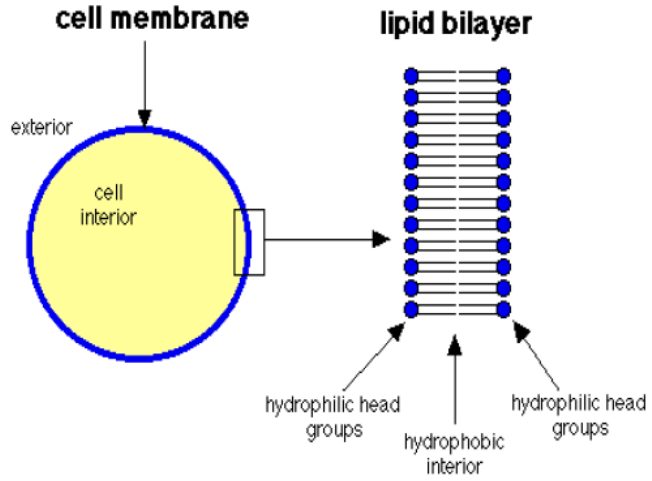
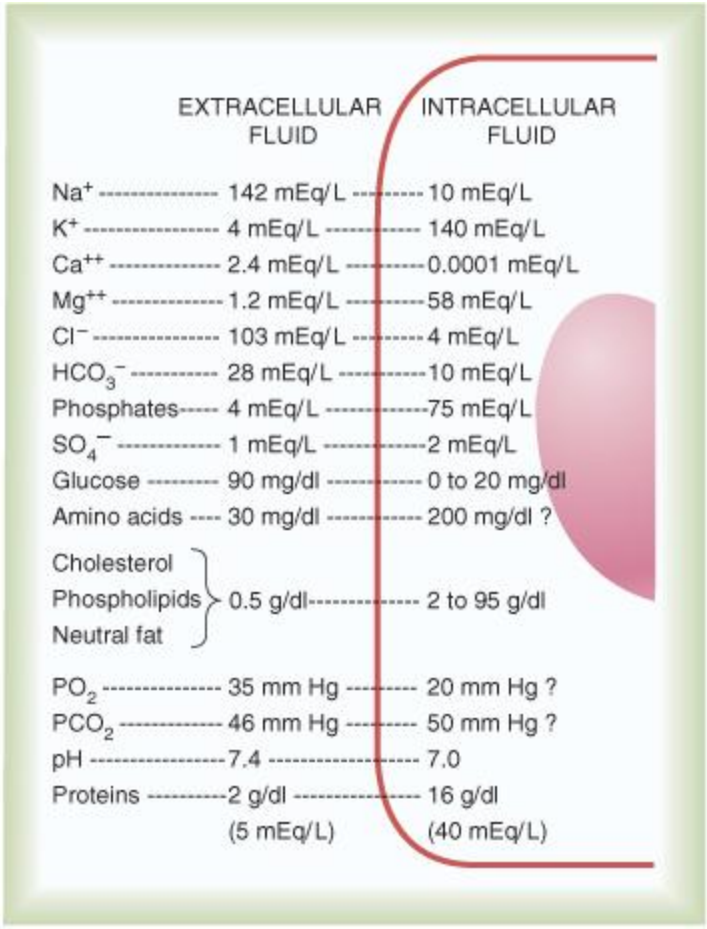
BIEN500: Lecture 04
– Chapters 04 & 05
To be covered:
- Membrane as barrier
- Passive (diffusion) vs. Active transport (pump)
- Simple vs. facilitated diffusion
- Gated channels
- 3 Factors affecting net rate of diffusion
- Primary active transport
- Secondary active transports

***Some content Adapted from Dr. Alan Chiu*

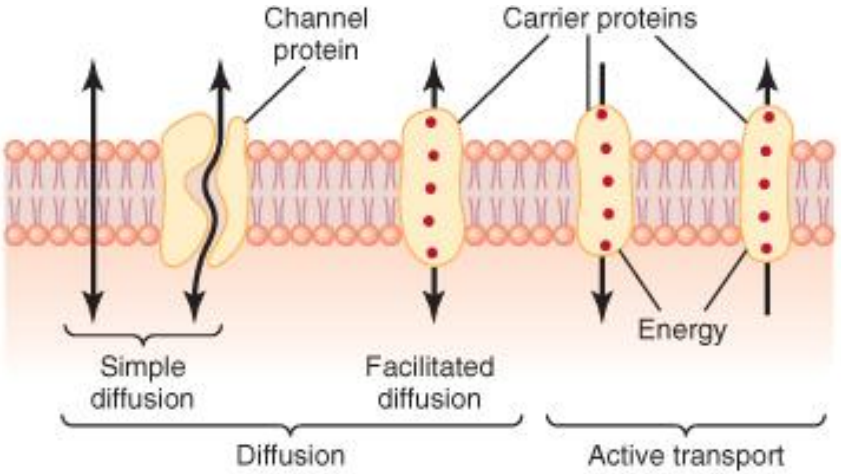
Membrane as barrier



- Barrier against movement of water molecules and water-soluble substances.
- Concentrations of important electrolytes and other substance are different in the extracellular (outside the cell) and intracellul (inside the cell) medium.



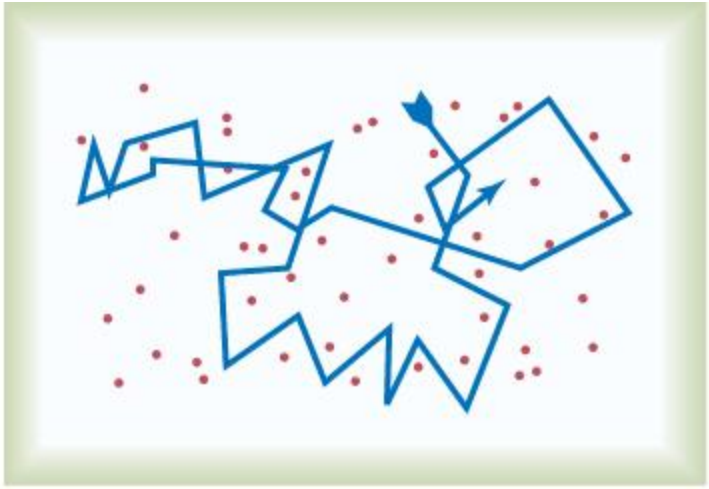
Transport mechanisms



- Diffusion:
  - phenomenon of free energy as a result of random movement of molecules (Brownian motion).
  - Move from high to low concentration until equally distributed.
- Active transport:
  - Move against energy gradient (from low to high concentration)
  - Requires energy input

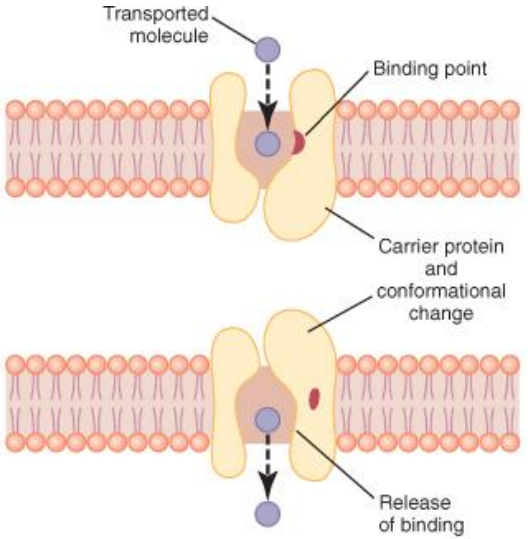
Diffusion – Simple diffusion

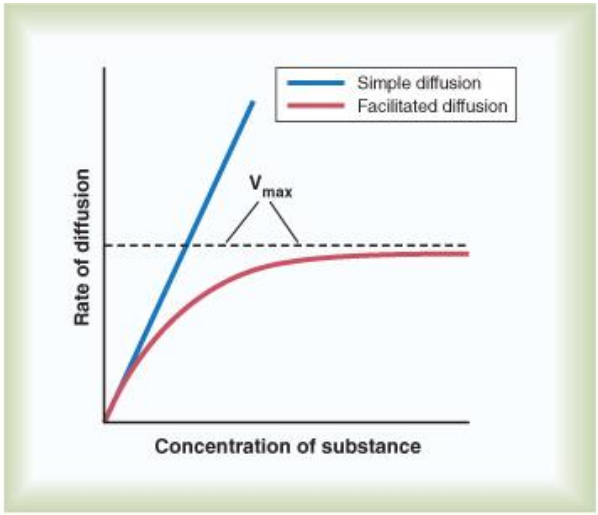
- Kinetic movement of molecules through membrane opening or inter-molecular spaces (protein channels).
- Without any interaction with protein channels.
- Depended on amount of substance available, kinetic energy, number and size of openings.



Diffusion – Facilitated diffusion

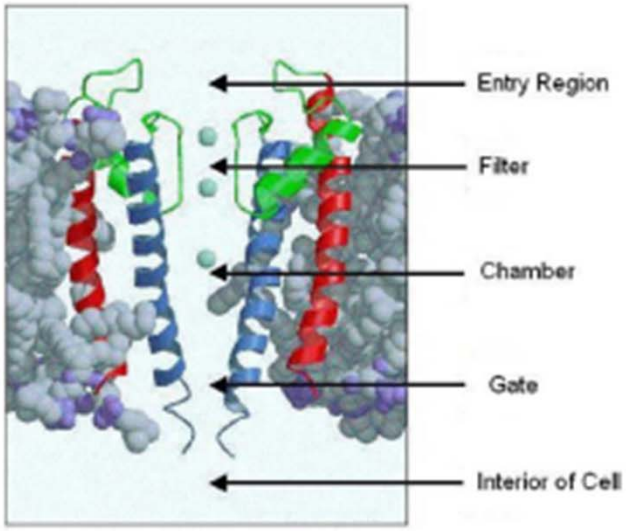
- Proteins act as carriers/pores to bind to the substance and shuttle them through the membrane.
- Related substance can compete for the same carrier.
- Maximum rate of transport exists and is limited by the rate at which the carrier can undergo changes back and forth between the binding and release states.



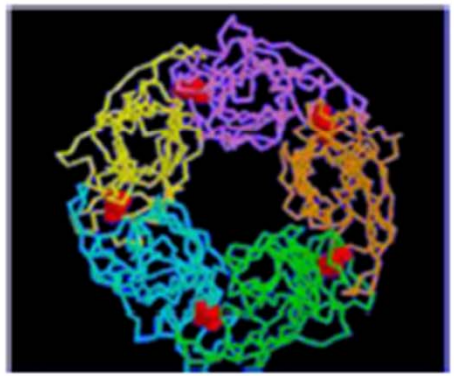


Permeability of channels

- Voltage-gated
- – Molecular conformation
- responds to electrical potential
- across the cell membrane:
- Important in excitable cells such as neurons
- And muscle



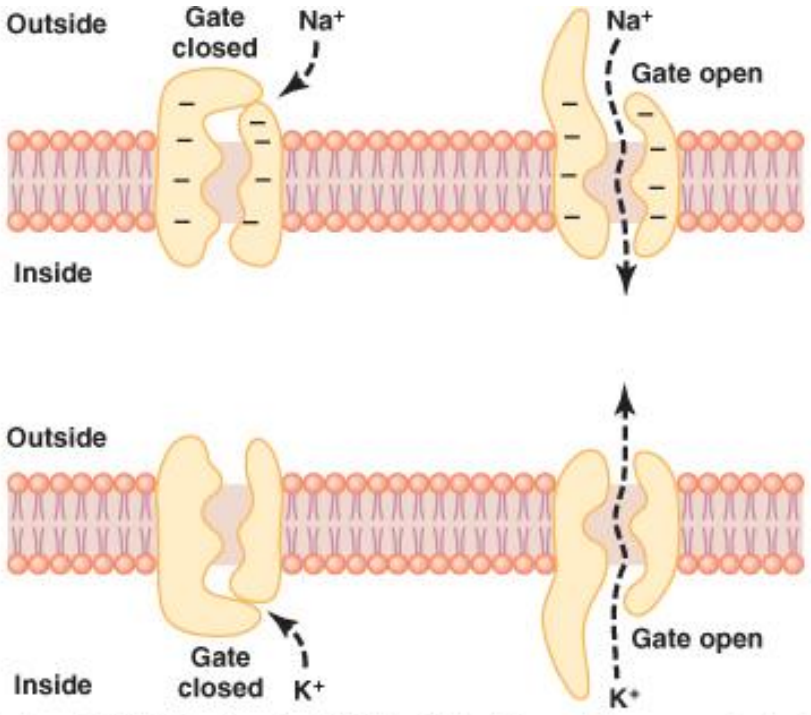
- Ligand-gated:
- – Channels are opened by
- binding of chemical substance
- (ligand) with the protein.
- – Conformational changes that
- open / close the gate



-Remember, the channels are proteins, so they are complex and can change shape

Permeability of channels

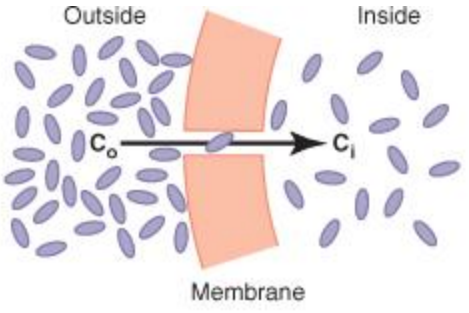
- Selectively permeable based on protein structure



Negatively charged channel
Pulled hydrated Na close by
Strip Na of water molecule

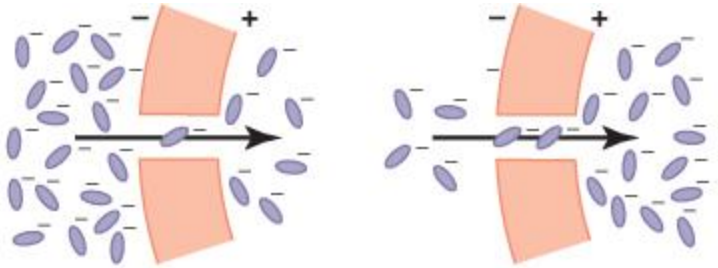
Hydrated K is smaller than hydrated Na
Smaller hydrated K can pass

Three factors affecting diffusion



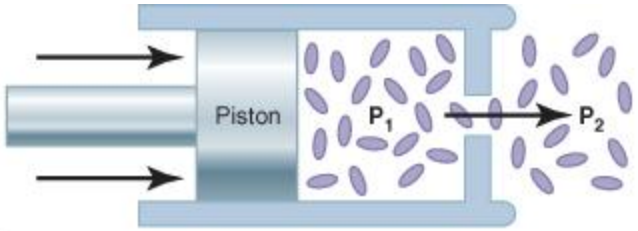
A

Concentration gradient



B

Electrical potential



C

Pressure

Osmosis

- Special term used for the diffusion of water through cell
- membranes
- • Although water is polar, it is still able to pass through
- the lipid bilayer
- • Water passes by diffusion from a region of higher to a
- region of lower concentration (of water).
- • Water is never transported actively

- ***So, if you put a cell in pure water, what would tend to happen? Why?***

Water movement in/out of cell: aquaporins

However, the aquaporins discovered by Peter Agre (Nobel Prize, 2003), demonstrating channels for water to pass into the cell by single file.

So: some water can passively move in and out of the cell thru the cell membrane,
But:
Aquaporins allow faster movement of this water in and out of the cell as well

The channels are integral membrane proteins, so they span the full lipid bilayer.

Many human cell types express aquaporins, as do certain bacteria and many other organisms such as plants, for which water transport is essential.

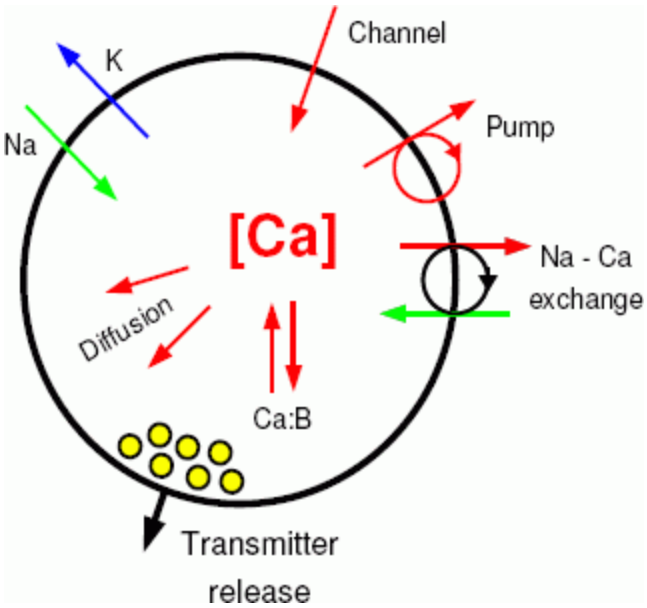
Animation:
www.nobelprize.org/nobel_prizes/chemistry/laureates/2003/chemanim1.mpg

Primary and Secondary Active Transport: Compare and contrast

- 1. In primary active transport, the energy is derived directly from breakdown of ATP or some other high-energy phosphate compound.
- 2. in secondary active transport, energy is derived secondarily from energy that has been stored in to form of ionic concentration differences of secondary molecular or ionic substances between the two sides of a cell membrane, created originally by primary active transport.

Active transport - Primary

- Example, Ca-Na pump (triggers muscle contraction)



- Example, H-K pump (secrete gastric juice)

Primary Active Transport of Calcium Ions

Another important primary active transport mechanism is the calcium pump.

Calcium ions (Ca^{2+}) are normally maintained at an extremely low concentration in the intracellular cytosol of virtually all cells of the body.

This level of maintenance is achieved mainly by to primary active transport calcium pumps:

1) One is in the cell membrane, and pumps calcium to the outside of the cell.
2) The other pumps Ca^{2+} ions into one or more of the intracellular vesicular organelles of the cell, such as the sarcoplasmic reticulum of muscle cells and the mitochondria in all cells.

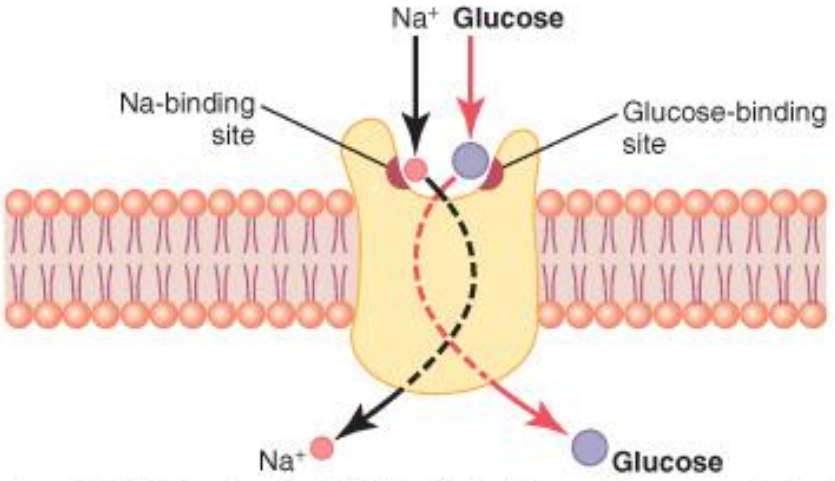
In each of these cases, the carrier protein penetrates the membrane and functions as an enzyme ATPase, using ATP as energy to carry out the pump functions.

Secondary Active transport details

- Also known as: co-transport and counter-transport.
- Example: co-transport of glucose and amino acids along with sodium ions
- Details: glucose and many amino acids are transported into most cells against large concentration gradients; this is a co-transport mechanism.
- The transport carrier protein has two binding sites on its exterior side, one for sodium and one for glucose.
- Sodium is high on the outside and low inside, which provides energy for the transport.
- Movement of molecules is not allowed until both sodium and glucose attach, and then a conformational change takes place. Thus, this is a sodium-glucose co-transport mechanism.
- This system is important in transport across renal and intestinal epithelial cells, for example.
- Sodium co-transport of amino acids occurs in a similar fashion, using a different set of transport proteins.

Active transport – Secondary

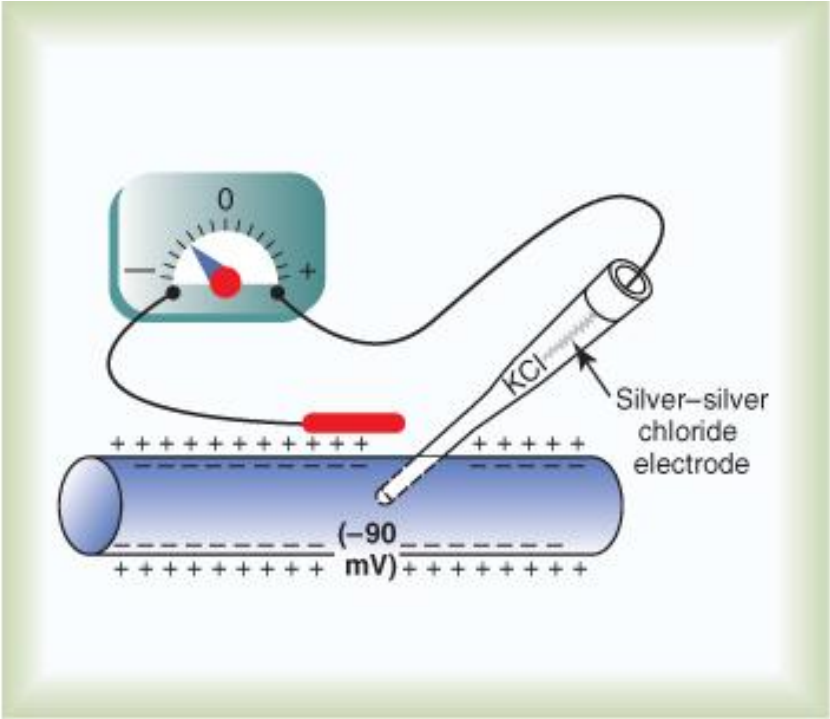
- Energy derived mainly from the energy that has been stored in the form of ionic concentration difference between two sides of a membrane (created by the primary active transport)
- Co-transport (same direction): Example, Na/Glucose transport (epithelial cells of intestinal tract, renal tubules of kidenys)



BIEN500 – Chapter 05

- Nernst potential
- Resting membrane potential
- Generation of action potential
- Propagation of action potential
- Rhythmicity
- Refractoriness
- Myelinated vs unmyelinated nerve fibers

Membrane Potential



~3M KCl conductive solution.

- Potential across the cell membrane is measured inside the cell with extracellular medium as reference.
- (outside the cell as reference)

Nernst potential

- Diffusion potential – the potential to diffuse across the
- membrane because of concentration difference.
- • Nernst potential – the potential exactly opposes the net
- diffusion of a particular ion through the membrane.

$$EMF = \pm 61 \log \frac{[inside]}{[outside]}$$

- EMF= electromotive force
- • The greater the ratio, the greater the tendency for the ion
- to diffuse outward.
- • The sign of EMF depends on whether the ion is
- positively or negatively charged

Nernst potential-2

$$EMF = \pm 61 \log \frac{[inside]}{[outside]}$$

Sign of EMF= (+) if the ion is negative
Sign of EMF= (-) if the ion is positive

Log ratio also determines the sign:

>1; <1= concentration gradient inside/outside

Nernst potential-3

Nernst potential example

- Sodium
- (+ ion, wants to go into cell)
- Expect Nernst potential +'ve

Why?

- Potassium
- (+ ion, wants to go out of cell)
- Expect Nernst potential –'ve

Why?

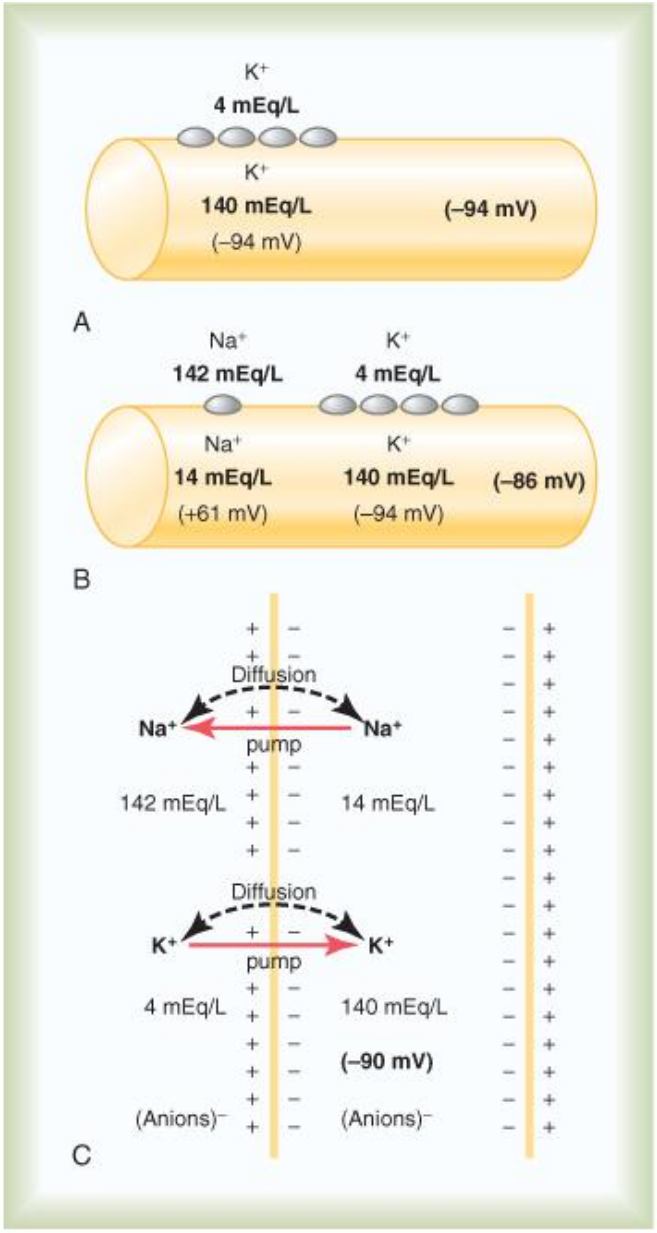
$$EMF = \pm 61 \log \frac{[inside]}{[outside]}$$

Do the math!

Resting membrane potential

- When a membrane is permeable to multiple ions
- The overall membrane potential is some combination of individual ionic concentrations
- Goldman-Hodgkin-Katz (GHK) equation
- Na, K and Cl are most important ions involved in development of membrane potentials in nerve and muscle fibers.

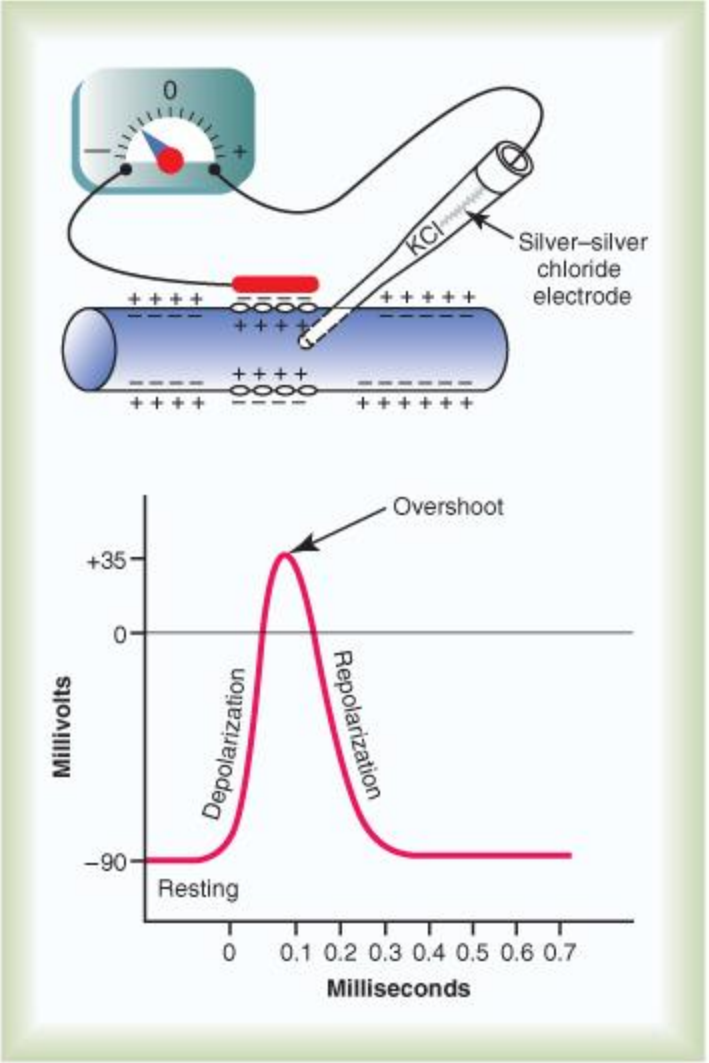
$$EMF = -61\log\frac{[Na]_i P_{Na} + [K]_i P_K + [Cl]_o P_{Cl}}{[Na]_o P_{Na} + [K]_o P_K + [Cl]_i P_{Cl}}$$

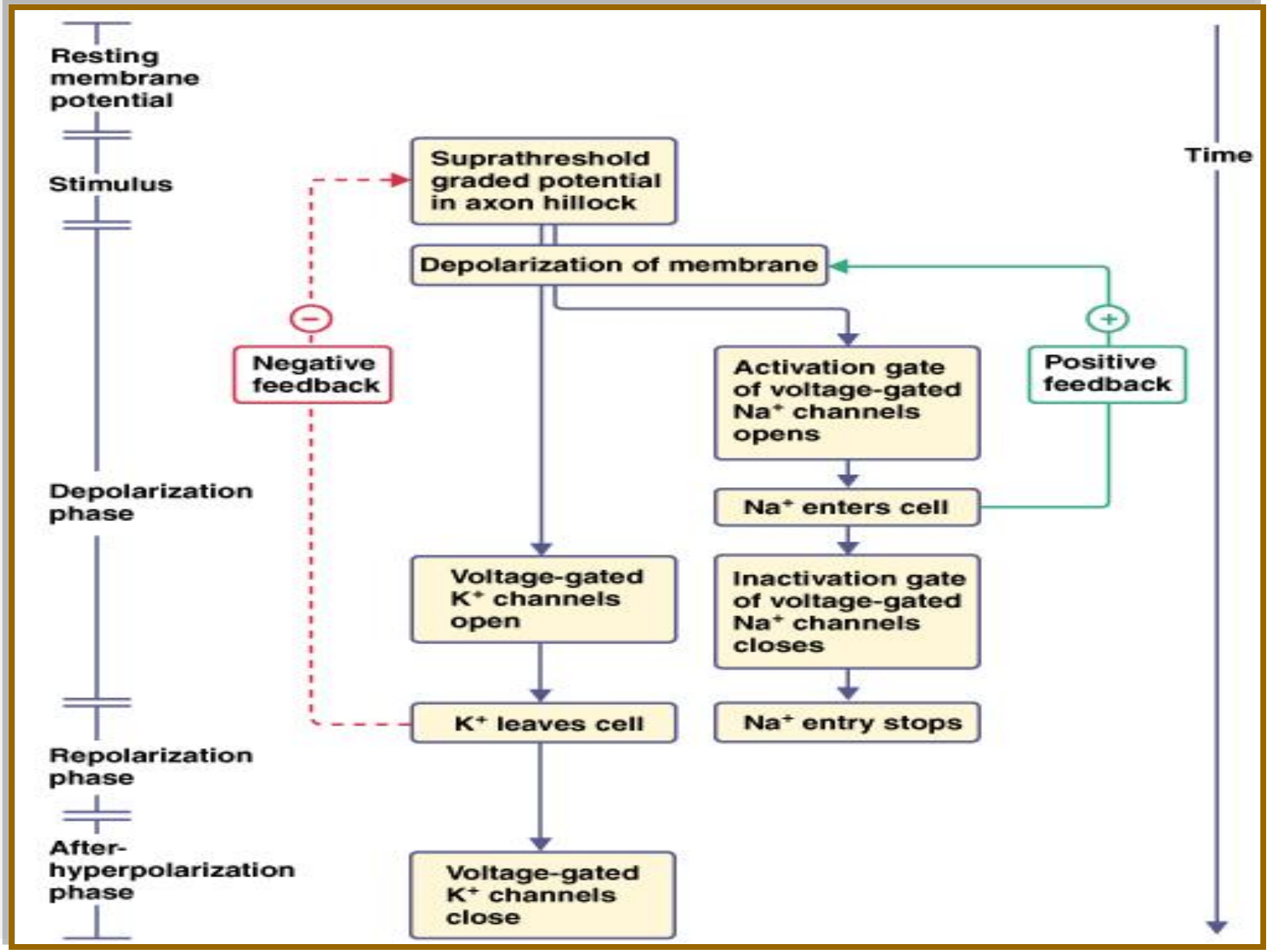


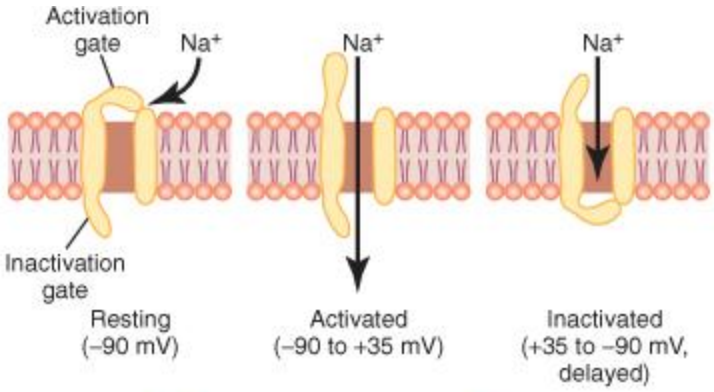
- A – If membrane is only permeable to potassium.
- B – If membrane is permeable to potassium and sodium.
- C – If Na-K pump is also active.
- The actual membrane potential is the weighted average of the Nernst potentials of individual ions. (~-90 to -60mV)

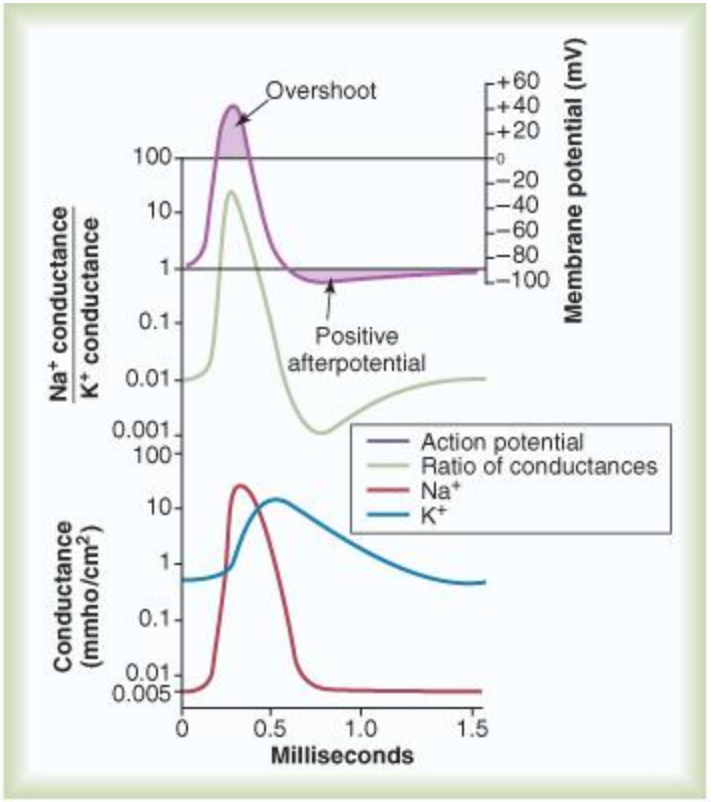
Action potential

- Nerve signal are transmitted by action potentials – rapid changes in the membrane potential.
- Onset of action potential is rapid (1/10000 second)




Resting membrane potential
Stimulus
Depolarization phase
Repolarization phase
After-hyperpolarization phase
Suprathreshold graded potential in axon hillock
Depolarization of membrane
Negative feedback
Activation gate of voltage-gated Na+ channels opens
Positive feedback
Na+ enters cell
Voltage-gated K+ channels open
Inactivation gate of voltage-gated Na+ channels closes
K+ leaves cell
Na+ entry stops
Voltage-gated K+ channels close
Time





- Leakage of K is larger than Na at resting
- Note K is slightly slower than Na
- Na channels close before K

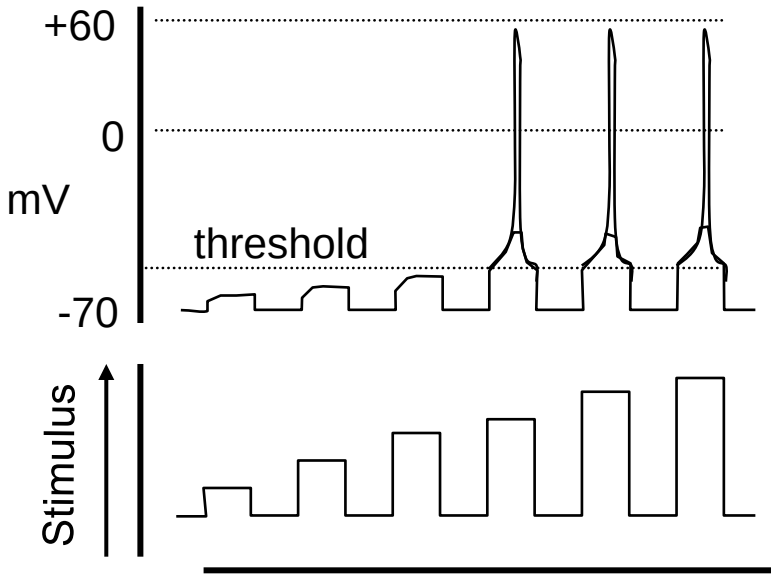
The role of Na-K pump

- It is necessary to re-establish the Na and K concentration difference by Na-K pump.
- Action potential cannot be elicited at the same location until the Na and K concentration difference is sufficiently established.

- Absolute refractory period: The amount of time after an action potential in which no other action potentials can be elicited regardless of the strength of the stimulation.
- Relative refractory period: The threshold necessary to elicit other action potentials is greater than is necessary at resting.

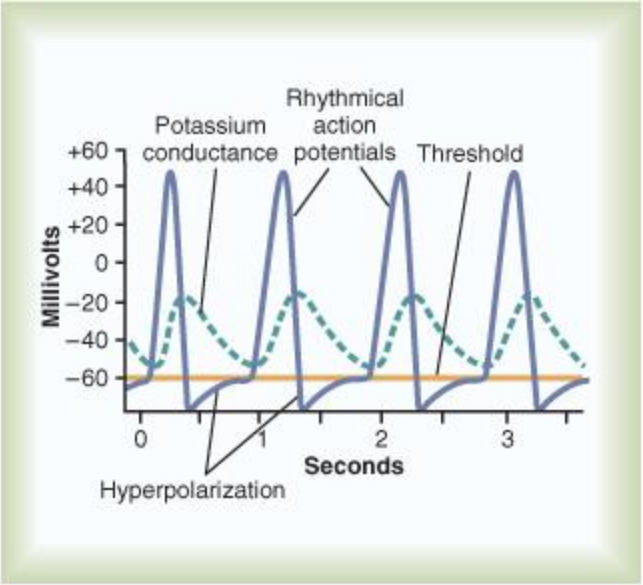
Properties of APs

- are all-or-none events
  - threshold voltage (usually 15 mV positive to resting potential)
- are initiated by depolarization
  - action potentials can be induced in nerve and muscle by extrinsic (percutaneous) stimulation
- have constant amplitude
  - APs do not summate - information is coded by frequency not amplitude.
- have constant conduction velocity
  - True for given fibre. Fibres with large diameter conduct faster than small fibres.



Rhythmicity

- Rhythmic action potentials can be elicited by a DC stimulation.
- Spontaneous rhythmicity can occur when the natural state of the membrane is permeable enough to Na ions.



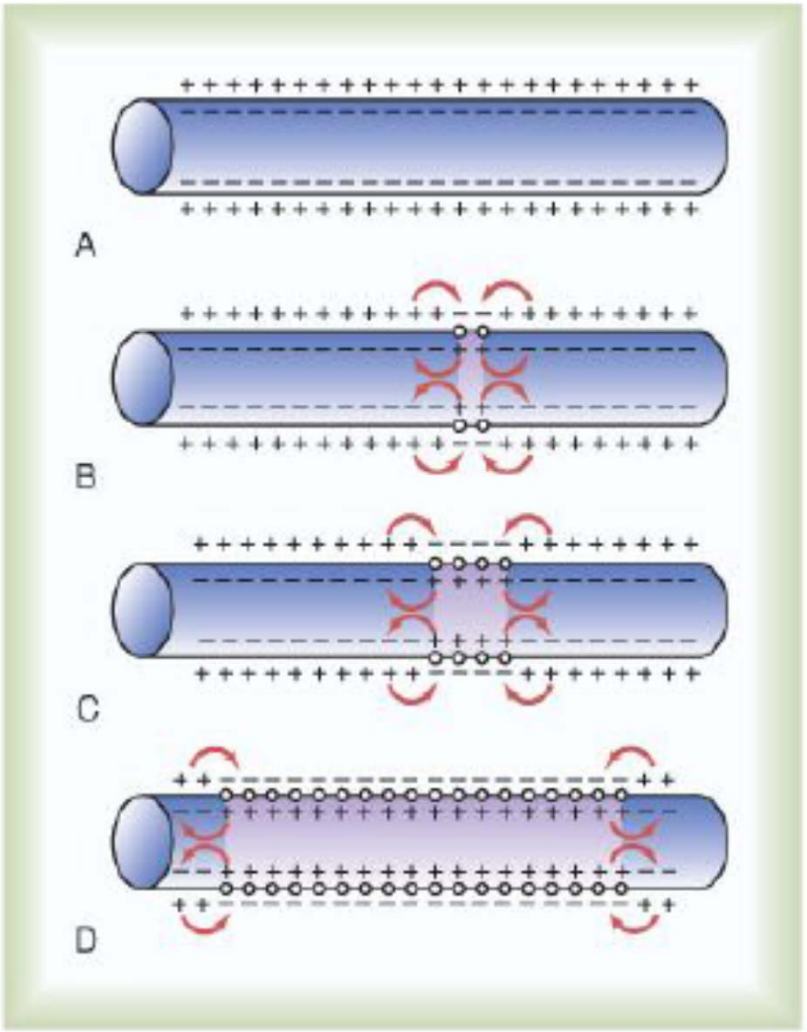
Propagation

Action potential elicited at one point will excite adjacent portions of the membrane.

• Action potential produces local circuit current

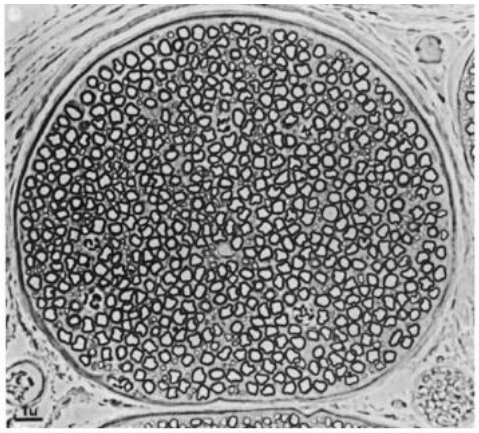
• No single direction of propagation, but action potential travels in all direction away from site of stimulation.

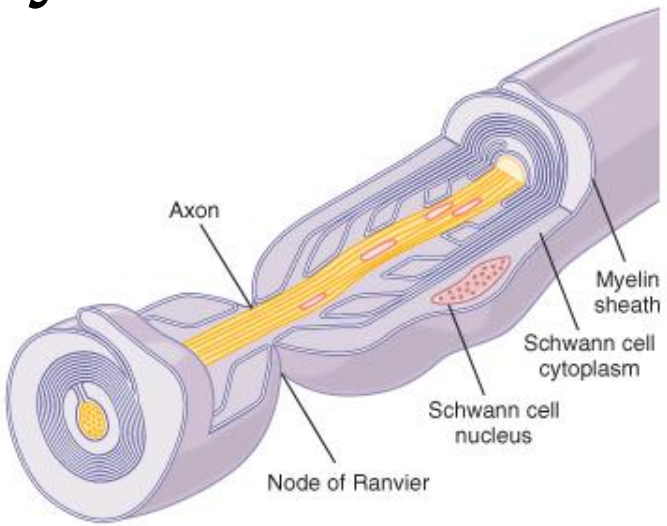
Chemical signalling, the release of Neurotransmitters, then helps to give it directionality.



Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - www.studentconsult.com

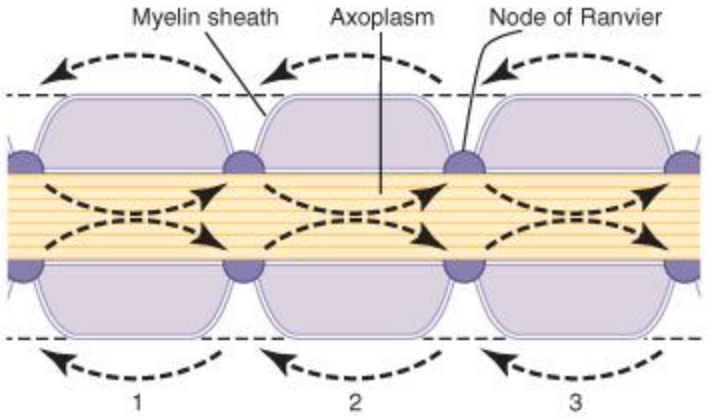
Myelinated vs Unmyelinated fibers



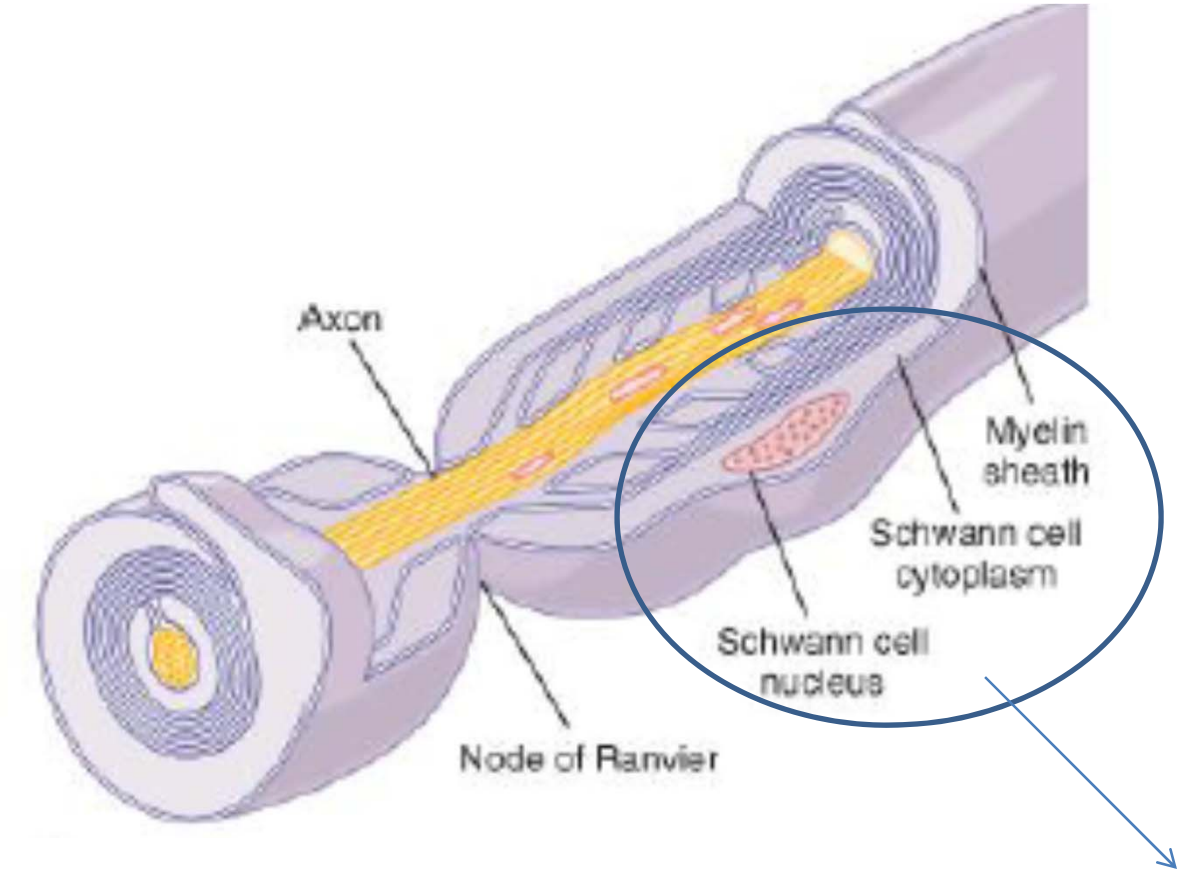


A

- Above is a nerve trunk
- Action potentials can only occur in saltatory conducting nodes.
- Propagation of electrical activity is faster in the myelinated region.



Myelination-2



In the CNS, the oligodendrocyte
Is the myelinating cell

End!