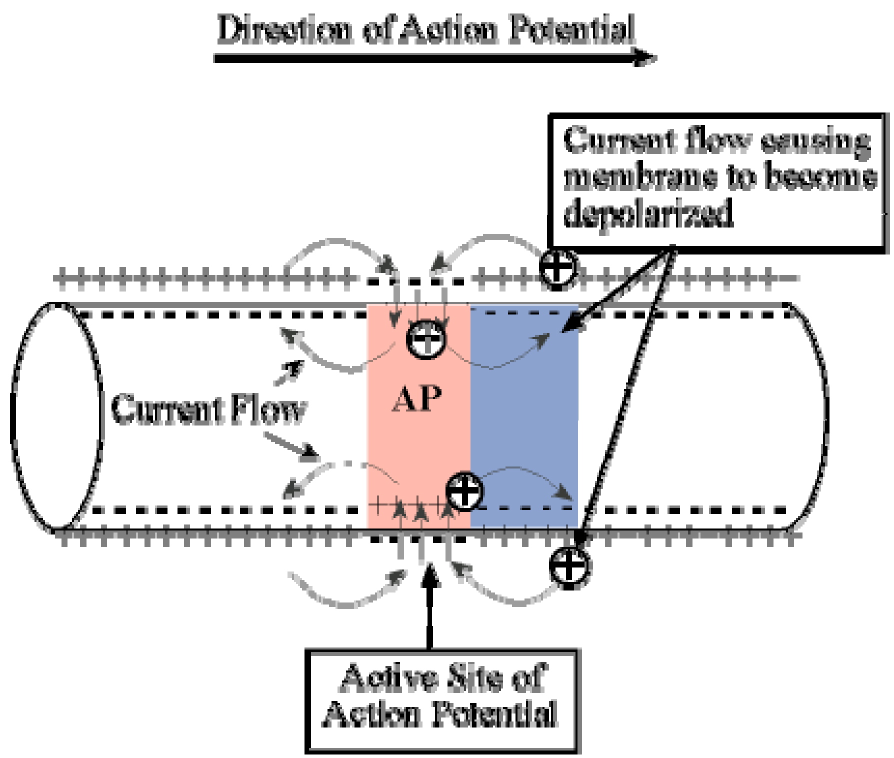
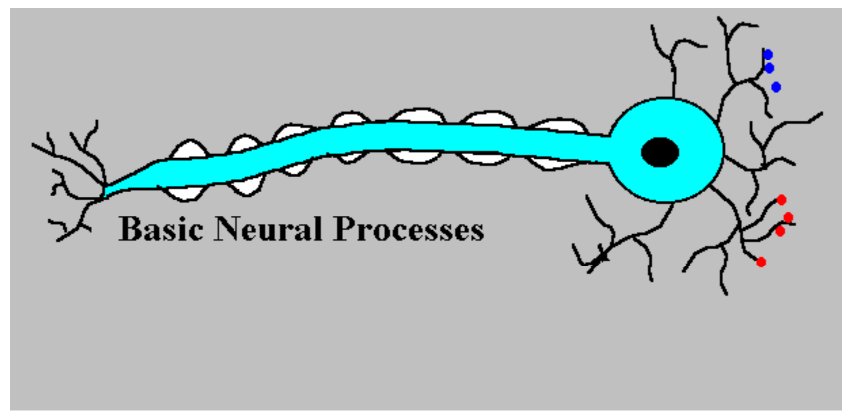
Lecture 22

Neuron Biophysics part 2

Action potential

- The action potential is an explosion of electrical activity that is created by a **depolarizing current**. This involves ions current through the membrane regulated by ions channels and ion pumps.
- That is how electrical signal propagates through neuron and is transmitted from neuron to neuron, from brain to all parts of the body

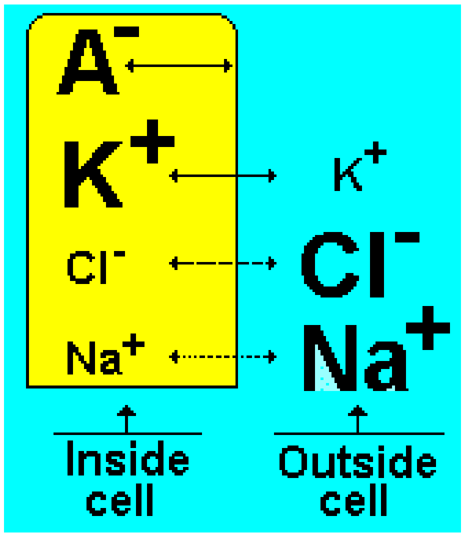




- Mechanisms involves 3 distinct features:

- Resting potential
- Generation of action potential
- Conduction of action potential along the fiber and synaptic transmission

Resting membrane potential

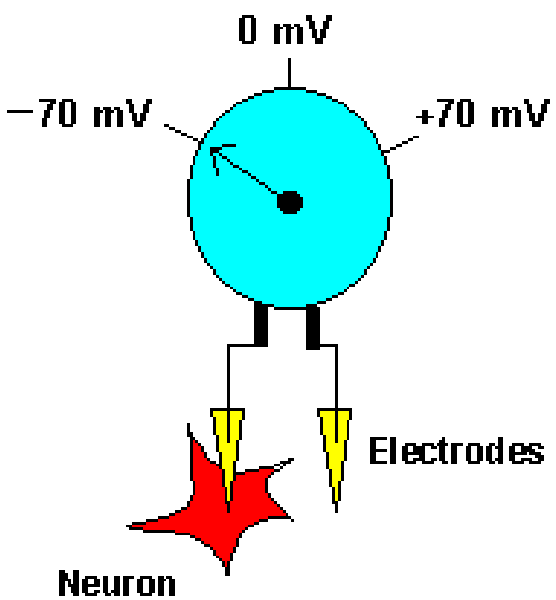


- When a neuron is not sending a signal, it is "at rest." When a neuron is at rest, the inside of the neuron is negative relative to the outside.
- Although the concentrations of the different ions attempt to balance out on both sides of the membrane, they cannot because the cell membrane allows only some ions to pass through channels (ion channels). At rest, potassium ions (K+) can cross through the membrane easily. Also at rest, chloride ions (Cl-)and sodium ions (Na+) have more difficult time crossing. The negatively charged protein molecules (A-) inside the neuron cannot cross the membrane.

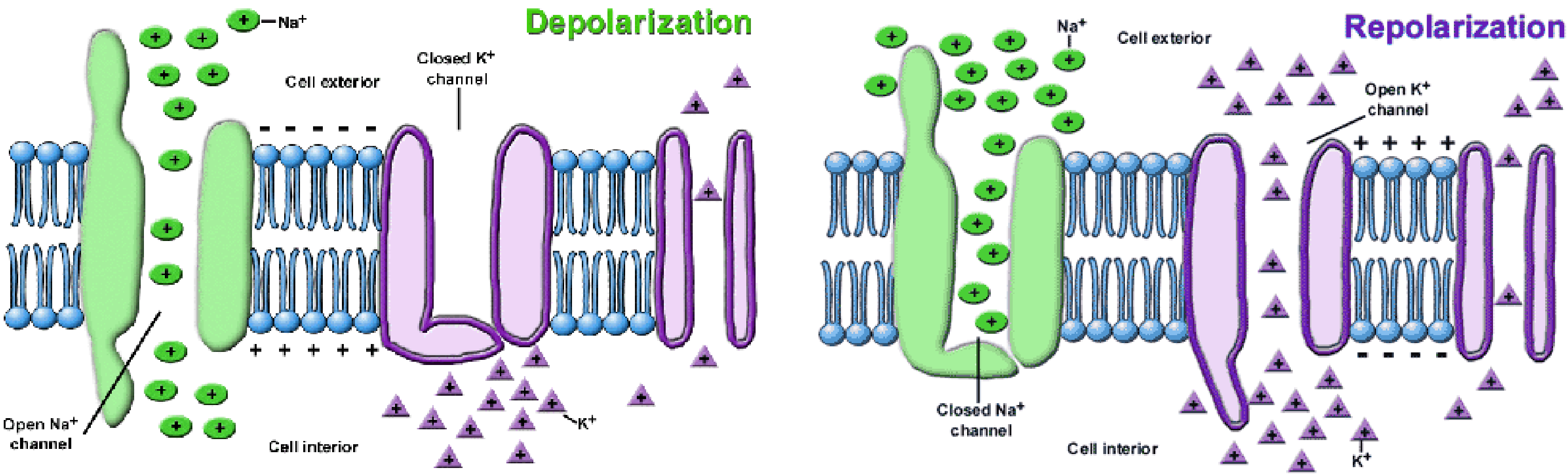
•In addition to these selective ion channels, there is a **Na/K pump** that uses energy to move three sodium ions out of the neuron for every two potassium ions it puts in.

resting potential

- When all these forces balance out, and the difference in the voltage between the inside and outside of the neuron is measured, you have the **resting potential**. The resting membrane potential of a neuron is about -70-80 mV - this means that the inside of the neuron is 70-80 mV less than the outside. At rest, there are relatively more sodium ions outside the neuron and more potassium ions inside that neuron.



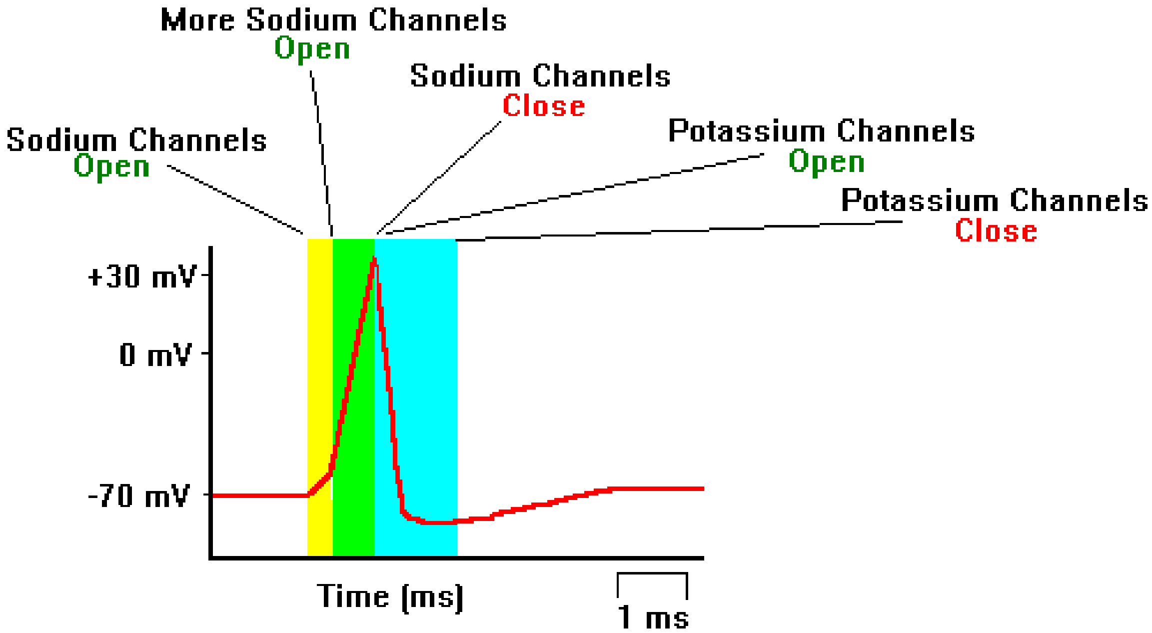
Action potential



The action potential is an explosion of electrical activity that is created by a **depolarizing current**. This means that some event (a stimulus) causes the resting potential to move toward 0 mV. When the depolarization reaches about -55 mV a neuron will fire an action potential. This is the **threshold**. If the neuron does not reach this critical threshold level, then no action potential will fire. when the threshold level is reached, an action potential of a fixed size will always fire

http://www.youtube.com/watch?v=U0NpTdge3aw&feature=related

Action potential



Neuroscientists use other words, such as a "spike" or an "impulse" for the action potential

when the threshold level is reached, an action potential of a fixed size will always fire for any given neuron, the size of the action potential is always the same. There are no big or small action potentials in one nerve cell - all action potentials are the same size. Therefore, the neuron either does not reach the threshold or a full action potential is fired - this is the "ALL OR NONE" principle

Propagation of action potential

- How does the action potential propagate along the axon?
- The sodium channels in the neuronal membrane are opened in response to a small depolarization of the membrane. So when an action potential depolarizes the membrane, the leading edge activates other adjacent sodium channels. This leads to another spike of depolarization of the leading edge of which activates more adjacent sodium channels ... etc. Thus a wave of depolarization spreads from the point of initiation.

- If this were all there was to it, then the action potential would propagate in all directions along an axon. But action potentials move in one direction. This is achieved because the sodium channels have a period following activation, during which they cannot open again. This ensures that the action potential is propagated in a specific direction along the axon.

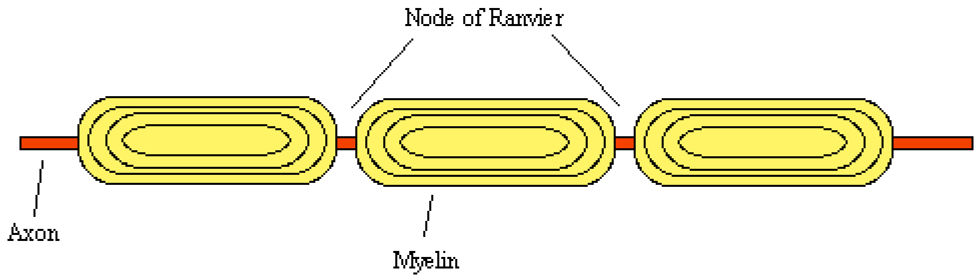
The speed of propagation

- **Conduction Velocity:**
- impulses typically travel along neurons at a speed of anywhere from 1 to 120 meters per second
- the speed of conduction can be influenced by:
  - the diameter of a fiber – the bigger – the faster
  - temperature
  - the presence or absence of myelin

- **The speed of propagation is related to the size of the axon.**
- The speed of action potential propagation is usually directly related to the size of the axon. Big axons result in fast transmission rates. For example, the squid has an axon nearly 1 mm in diameter that initiates a rapid escape reflex. Increasing the size of the axon retains more of the sodium ions that form the internal depolarization wave inside the axon.
- If we had to have axons the size of the squid giant axon in our brains, doorways would have to be substantially widened to accomodate our heads!!! We could only have a few muscles located at any great distance from our brains - so we'd all be extremely short with very large heads....not really feasible, is it? The answer is to insulate the axonal membrane to prevent the dissipation of the internal depolarization in small axons - myelin.

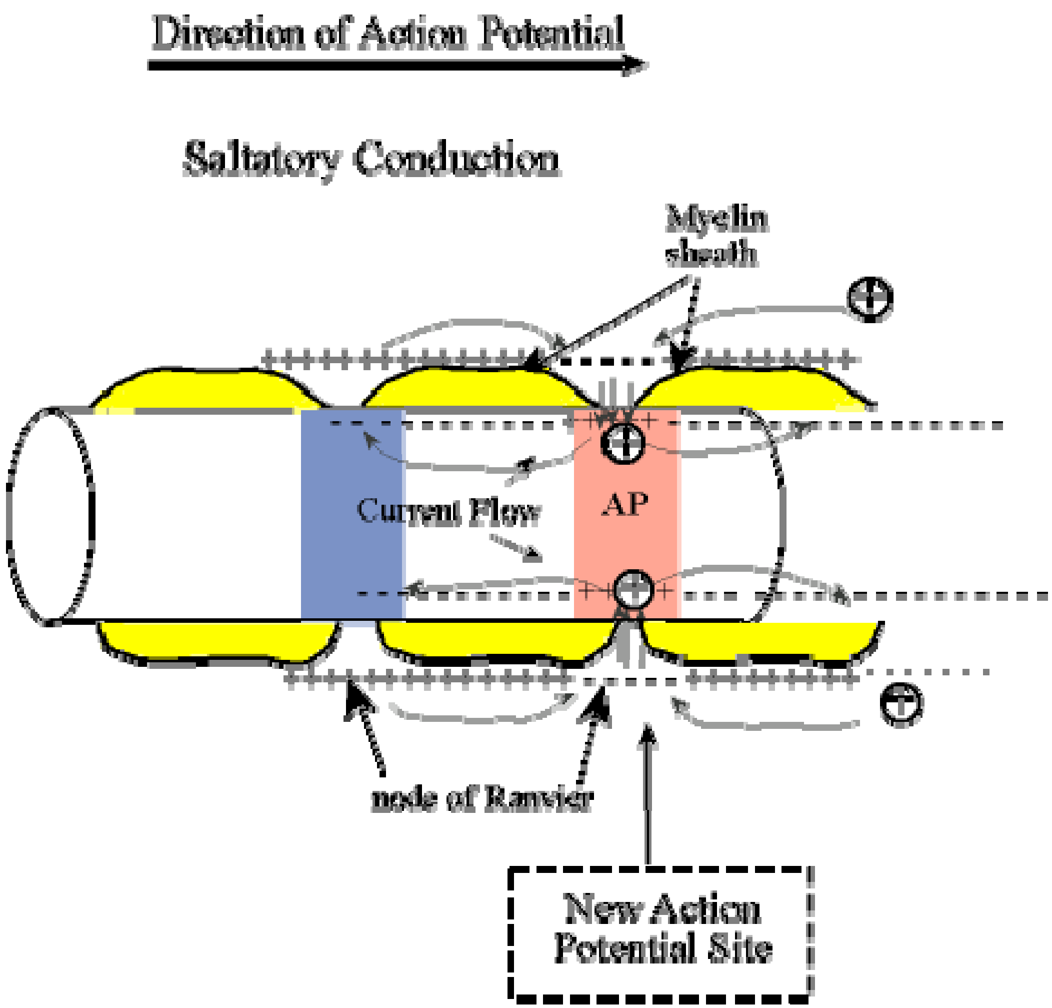
What does myelin do?

- a substance called myelin allows for rapid action potential propagation
- myelin is the fatty membranes of cells called Oligodendroglia (in the CNS) and Schwann Cells (in the PNS) that wraps around the axon and acts as an insulator, preventing the dissipation of the depolarisation wave.
- The sodium and potassium ion channels, and pumps associated with action potential propagation are concentrated at sites between blocks of myelin called the Nodes of Ranvier. This myelin sheath allows the action potential to jump from one node to another, greatly increasing the rate of transmission.



- Propagation and myelin:

- Without the myelin sheath, we cannot function. This is demonstrated by the devastating effects of Multiple Sclerosis, a demyelinating disease that affects bundles of axons in the brain, spinal cord and optic nerve, leading to lack of co-ordination and muscle control as well as difficulties with speech and vision.



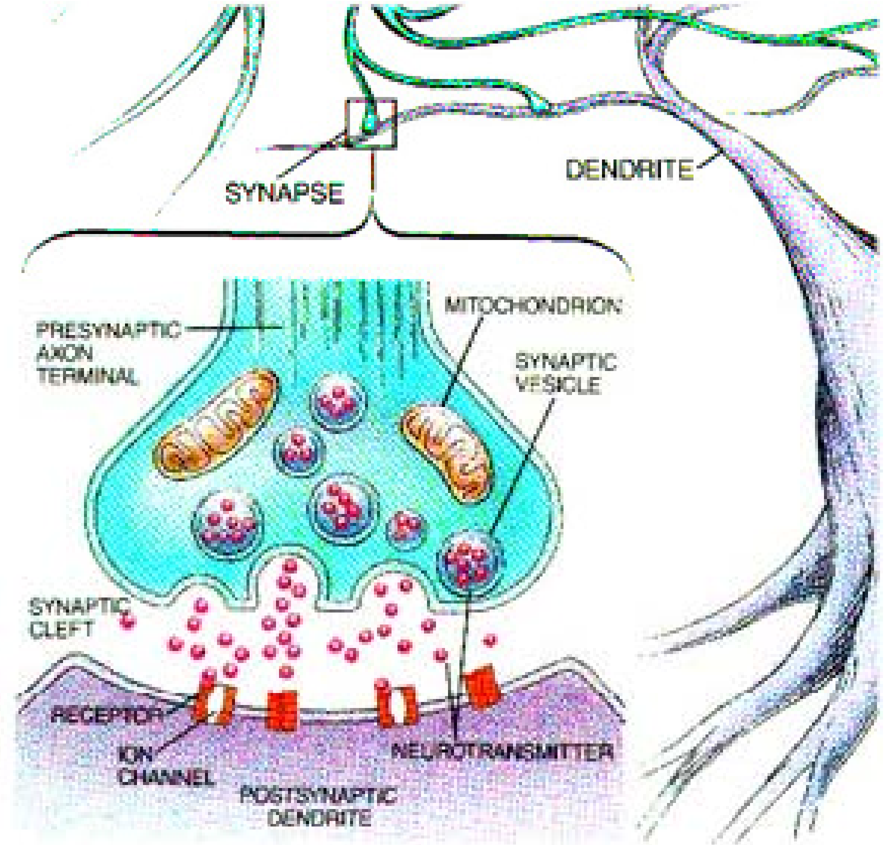
Because fat (myelin) acts as an insulator, membrane coated with myelin will not conduct an impulse. So, in a myelinated neuron, action potentials only occur along the nodes and, therefore, impulses 'jump' over the areas of myelin - going from node to node in a process called saltatory conduction (with the word saltatory meaning 'jumping'):

Because the impulse 'jumps' over areas of myelin, an impulse travels much faster along a myelinated neuron than along a non-myelinated neuron.

http://www.blackwellpublishing.com/matthews/actionp.html

synapse

- **Synapse = point of** impulse transmission between neurons; impulses are transmitted from pre-synaptic neurons to post-synaptic neurons
- synaptic cleft – small space in the junction of two neurons



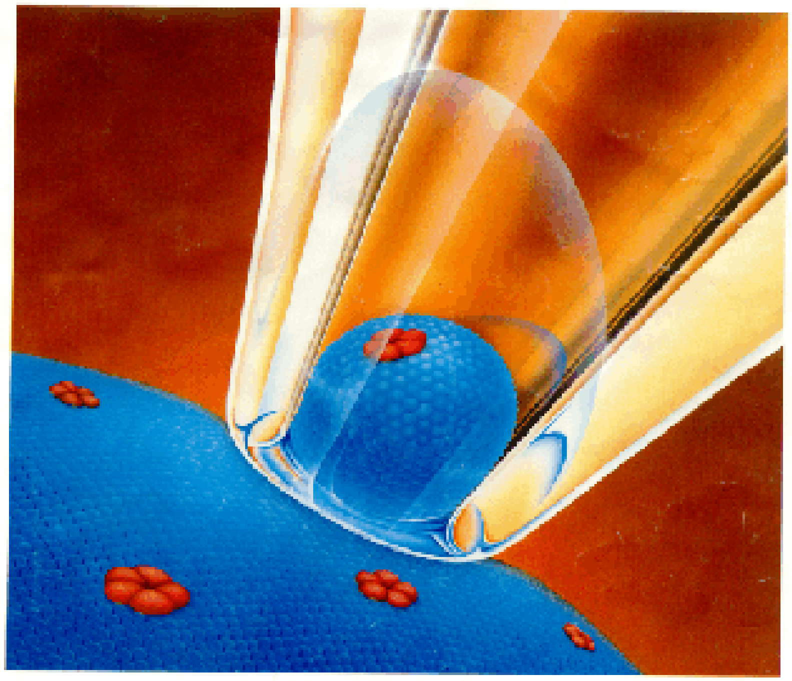
Synapse:
http://www.youtube.com/watch?v=HXx9qlJetSU
http://www.blackwellpublishing.com/matthews/default.html (reference to study)
http://www.blackwellpublishing.com/matthews/nmj.html (reference to study)

Synaptic transmission

- Neurons communicate at structures called **synapses** in a process called **synaptic transmission**. The synapse consists of the two neurons, one of which is sending information to the other. The sending neuron is known as the **pre-synaptic neuron** (i.e. before the synapse) while the receiving neuron is known as the **post-synaptic neuron** (i.e. after the synapse). Now, although the flow of information around the brain is achieved by electrical activity, communication between neurons is a chemical process. When an action potential reaches a synapse, pores in the cell membrane are opened allowing an influx of **calcium ions** (positively charged calcium atoms) into the pre-synaptic terminal. This causes a small 'packet' of a chemical **neurotransmitter** to be released into a small gap between the two cells, known as the **synaptic cleft**. The neurotransmitter diffuses across the synaptic cleft and interacts with specialized proteins called **receptors** that are embedded in the post-synaptic membrane. These receptors are ion channels that allow certain types of ions to pass through a pore within their structure. The pore is opened following interaction with the neurotransmitter allowing an influx of ions into the post-synaptic terminal, which is propagated along the dendrite towards the soma.

- http://www.bris.ac.uk/synaptic/public/basics_ch1_3.html (reference to study)

Patch Clamp



www-users.york.ac.uk/
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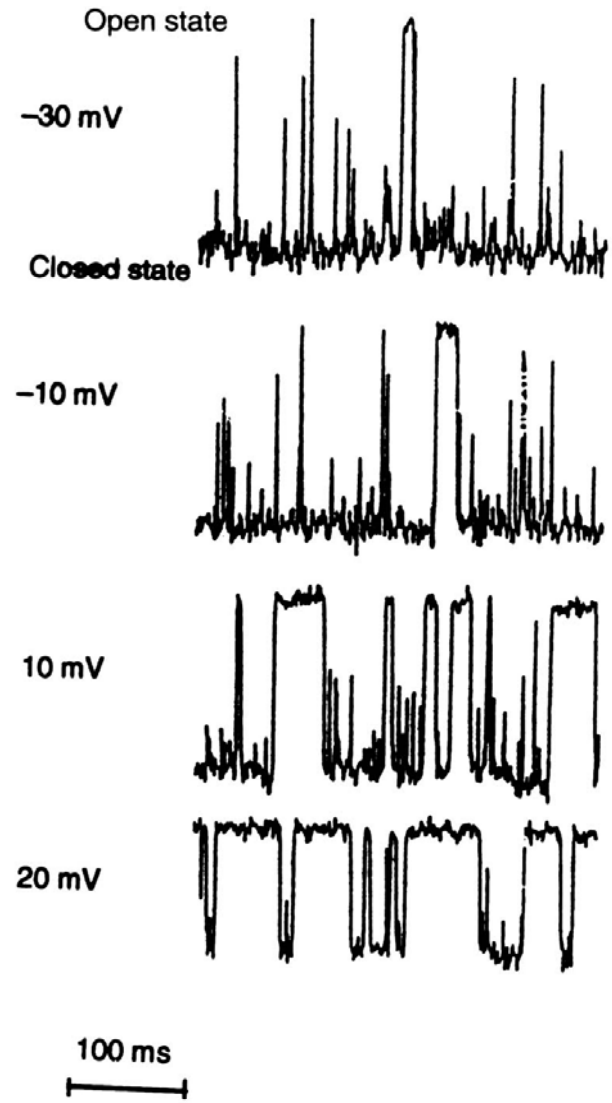
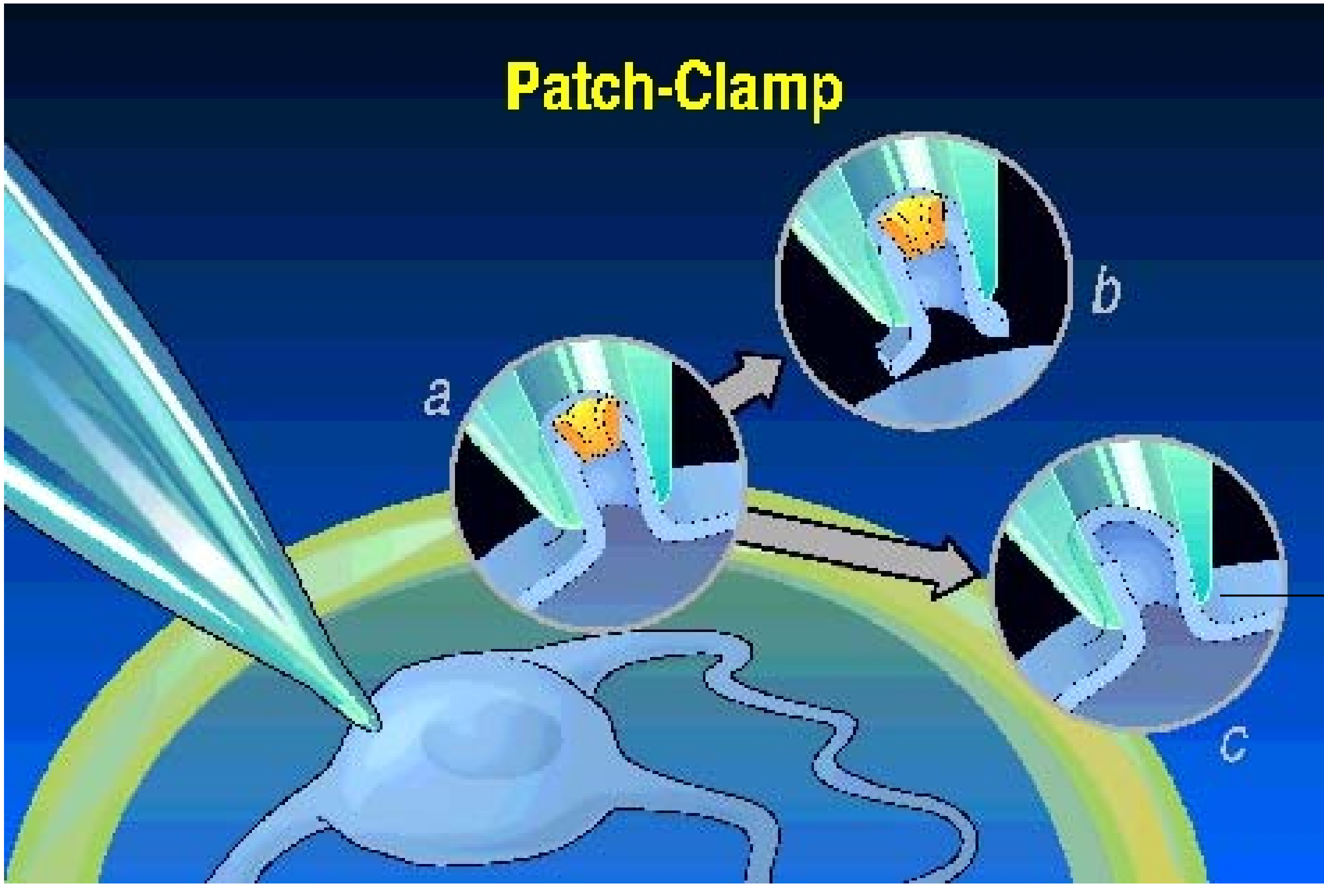
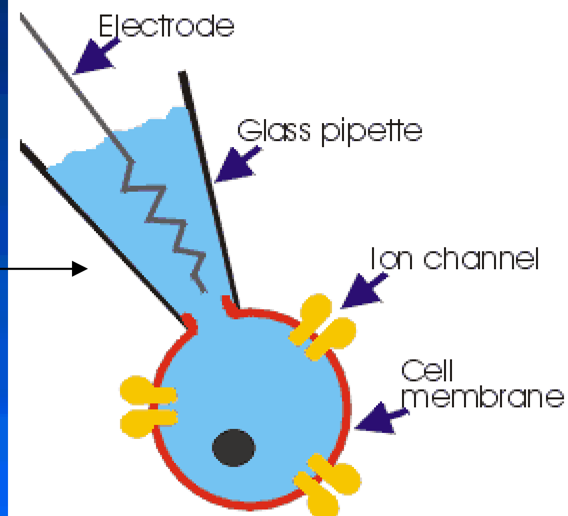


Methods to measure conductance of single ion channels

Patch-clamp: Glass pipette with tiny opening is used to measure membrane current



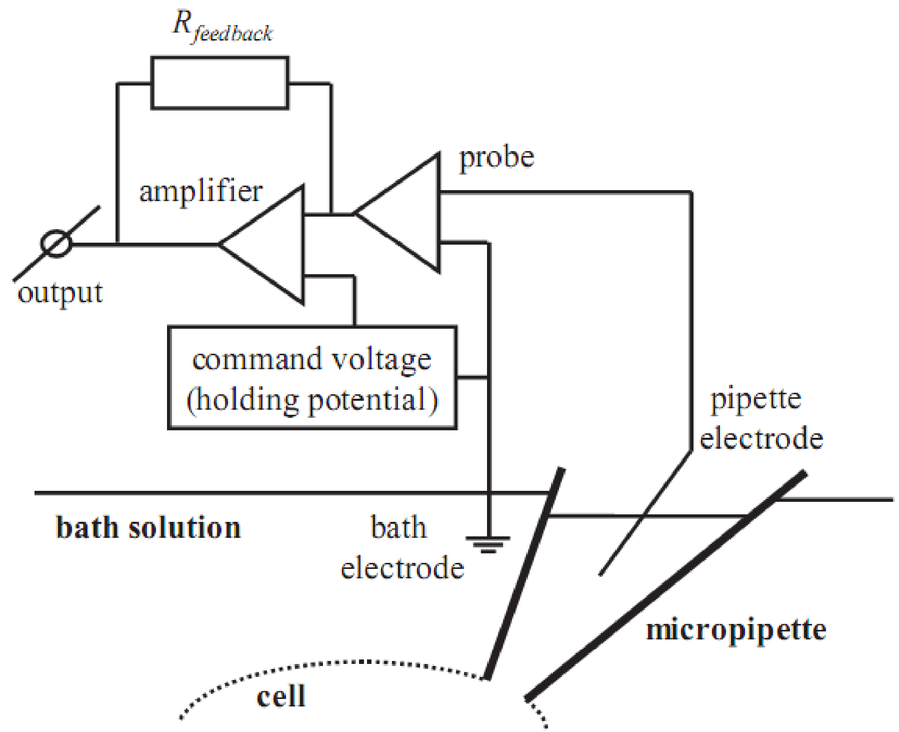


- Membrane potential studies began in 1940s using intracellular recording methods
- Neher and Sakmann pioneered the modern patch clamp in 1976, winning the Nobel Prize
- Patch clamp is an electrophysiology technique, which allows the study of single or multiple ion channels
- Particularly useful for the study of excitable tissues such as neuron cells

Recording Methods

- Voltage Clamp
  - Voltage is controlled and membrane current is recorded
  - Electronic feedback system
  - Measured potential is compared against the holding potential to determine current
    - ▫Ion channel current

- Current Clamp
  - ▫ Set up is the same
  - ▫ Current is fed through the electrode
  - ▫ Membrane voltage is recorded
  - ▫cell membrane potential



Summarizing Neurons and action potential

http://www.youtube.com/watch?v=MtJyHp_AZL8&feature=related

Transference equation

- Membrane potential is expressed through transference
- Transference – empirical parameter which plays same role as permeability coefficient, depends on interaction of ions with membrane

- we can consider membrane as an electric circuit in which ion current is a – current flowing through resistor with resistance R. According to Ohm's law current through the linear resistor:

$$J = \frac{\phi}{R} = G\phi$$

$$G = \frac{1}{R}$$ conductance

Electric potential

- Lets consider ionic current Na+, K+ and Cl-, total potential is given by Nernst and membrane potential
- Na+ current is driven by Na+ Nernst potential and membrane potential, which are opposite,
- If $\phi_r = \phi_{Na}$ no Na+ current will flow, the flux of Na ions:

$$J_{Na} = G_{Na}(\phi_r - \phi_{Na})$$

Similarly:

$$J_K = G_K(\phi_r - \phi_K)$$ K ions

$$J_{Cl} = G_{Cl}(\phi_r - \phi_{Cl})$$ Cl ions

In a steady state: $$J_{Na} + K_K + J_{Cl} = 0$$

Resting potential $$\phi_r = \frac{G_{Na}\phi_{Na} + G_K\phi_K - G_{Cl}\phi_{Cl}}{G_{Na} + G_K - G_{Cl}}$$

$$\boxed{T_{Na} = \frac{G_{Na}}{G_{Na} + G_K - G_{Cl}}}$$

The relative conductance of the ion is called ion transference T – analog of ion permeability

$$\boxed{\phi_r = T_{Na}\phi_{Na} + T_K\phi_K - T_{Cl}\phi_{Cl}}$$

Potential can be expressed through ion transference T

$$T_{Na} = \frac{1}{10+1} = 0.09$$

$$T_{K} = \frac{10}{10+1} = 0.91$$

In human nerve and muscle cells in resting state,

G, conductance of Na+ =1/10 of conductance of K+, other ions are negligible

$$\phi_r = (0.09)\times(+60) + (0.91)\times(-92) \approx -79mV$$

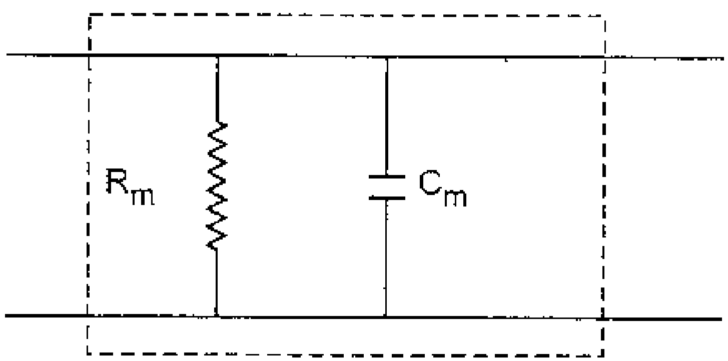
Close to experimentally observed -80 mV

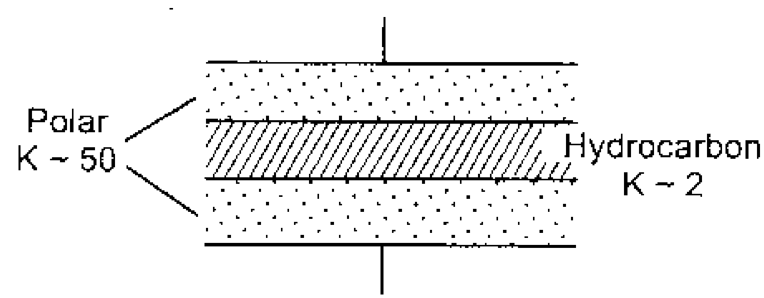
Electric analog of membrane

Element of membrane = parallel combination of capacitor Cm and resistor Rm

Two surfaces of membrane = two plates of a capacitor separated by the distance d =membrane thickness. Lipids = dielectric layer

Potential between plates = Nernst potential (for Na or K) and membrane potential



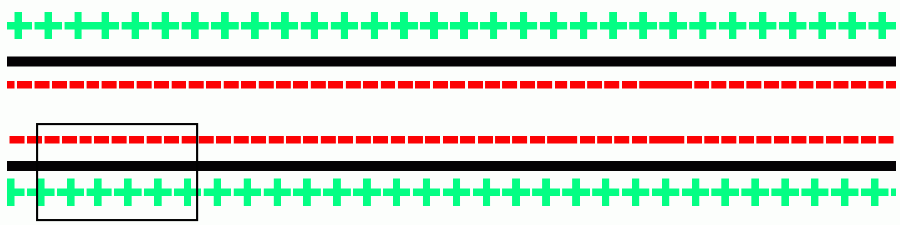


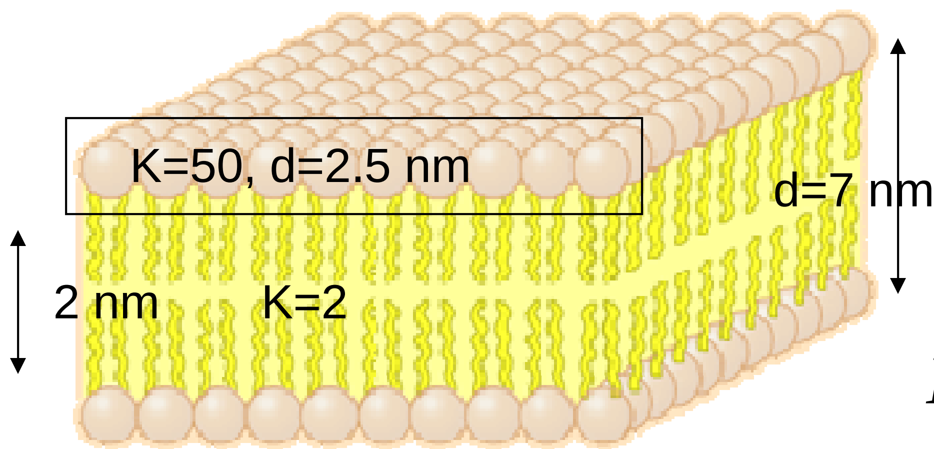
Capacitance → $C_m = 1\mu F/cm^2$

resistance → $R_m = 10\ \mu Ohm/cm^2$

dielectric constant → $K = 7$

$$\frac{d}{K} = \frac{d_1}{K_1} + \frac{d_2}{K_2}$$





Dielectric constant:

K=6.4

Capacitance:

$$C = \frac{K\varepsilon_0 A}{d} = 8.8\times10^{-3} F / m^2$$

Electric field:

Surface charge density

$$E = \frac{\sigma}{\varepsilon_0} = \frac{\phi}{d}$$

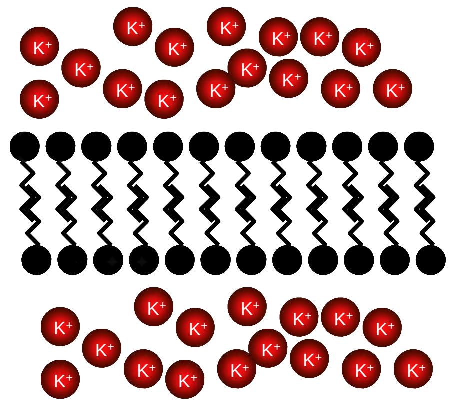
$$E = \frac{\phi}{d} = \frac{80mV}{7nm} = 1.2\times10^{7} V / m$$

Surface charge density:

$$\sigma = E\varepsilon_0 = (1.2\times10^{7}\,V/m)\times(8.85\times10^{-12}\,F/m)\approx 10^{-4}\,C/m^2$$

If the charge comes from ions in contact with membrane,

total number of charged atoms with contact in membrane is:



$$\frac{total\_charge\_per\_m^2}{charge\_of\_an\_electron} = \frac{10^{-4}\,C/m^2}{1.6\times10^{-19}\,C} \approx 10^{15}\,atoms/m^2$$

- **Resistance:** $$R_m = 7 \times 10^{-2} Ohm / m^2$$
- **Conductance:** $$G_m = 10 \quad Ohm^{-1} per \quad m^2$$

When membrane potential changes, the charge on the capacitor also changes according to:

$$Q = C_m \phi$$

$$\frac{\Delta Q}{\Delta t} = C_m \frac{\Delta \phi}{\Delta t}$$

The charge of capacitor leaks – ionic current

$$\frac{\Delta Q}{\Delta t} = J_{ion}$$

- ionic current through membrane

$$C_m \frac{\Delta \phi}{\Delta t} = \frac{\phi}{R_m}$$

Time dependence

$$\phi(t) = \phi(0)e^{-t/\tau}$$

$$\tau = R_m C_m$$

Time constant of
equivalent RC-circuit

Resistance X Capacitance

Specific
resistance
of the
membrane

$$\tau = R_m C_m = \frac{p_m d}{A} \times \frac{K\varepsilon_0 A}{d} = K\varepsilon_0 p_m = 10^{-3}\,\mathrm{sec}$$

Time constant is independent on Area or thickness

Membrane capacitor charges or discharges up to 60% of the peak within a millisec