Lecture 21

Neuron Biophysics

Regulatory systems in multicellular organisms

- Endocrine system :
- Controls and coordinates activities by secreting hormones through blood and fluid circulation (slow, chemical signals)
- Nervous system:
- Controls and coordinates activities by generating and transmitting electrical signals (fast)

Neurobiophysics

- Studies mechanisms of sensing, monitoring of external excitations, coding and transmitting information
- which occur in nervous system through electric signal propagation,

Nervous systems

- 3 parts:
- Receptors
- Neurons
- Effectors

Receptors

- Receptors - cells which are sensitive to certain stimulus:

Exteroceptors – sensitive to outside stimuli:

Rods and cones - light receptors in eye -

Hair cells – sound receptors in ear

Taste buds – chemoreceptors in tongue

Enteroceptors – sensitive to inside stimuli:

baroreceptors – blood pressure changes

Chemoreceptors for ex – concentration changes of carbon dioxide in the blood

Neurons and glial cells

- The brain and spinal cord are made up of many cells, including neurons and glial cells. Neurons are cells that send and receive electro-chemical signals to and from the brain and nervous system. They vary in size from 4 microns to 100 microns in diameter. Their length varies from a fraction of an inch to several feet.

- Unlike most other cells, neurons cannot re-grow after damage (except neurons from the hippocampus). Fortunately, there are about 100 billion neurons in the brain.

  Glial cells - provide support functions for the neurons, make up 90 percent of the brain's cells. Glial cells are nerve cells that don't carry nerve impulses.
- The various glial (meaning "glue") cells perform many important functions, including: digestion of parts of dead neurons, manufacturing myelin for neurons, providing physical and nutritional support for neurons, and more.

- Types of glial cells include Schwann's Cells, Satellite Cells, Microglia, Oligodendroglia, and Astroglia.
- Neuroglia (meaning "nerve glue") cells guide neurons during fetal development.

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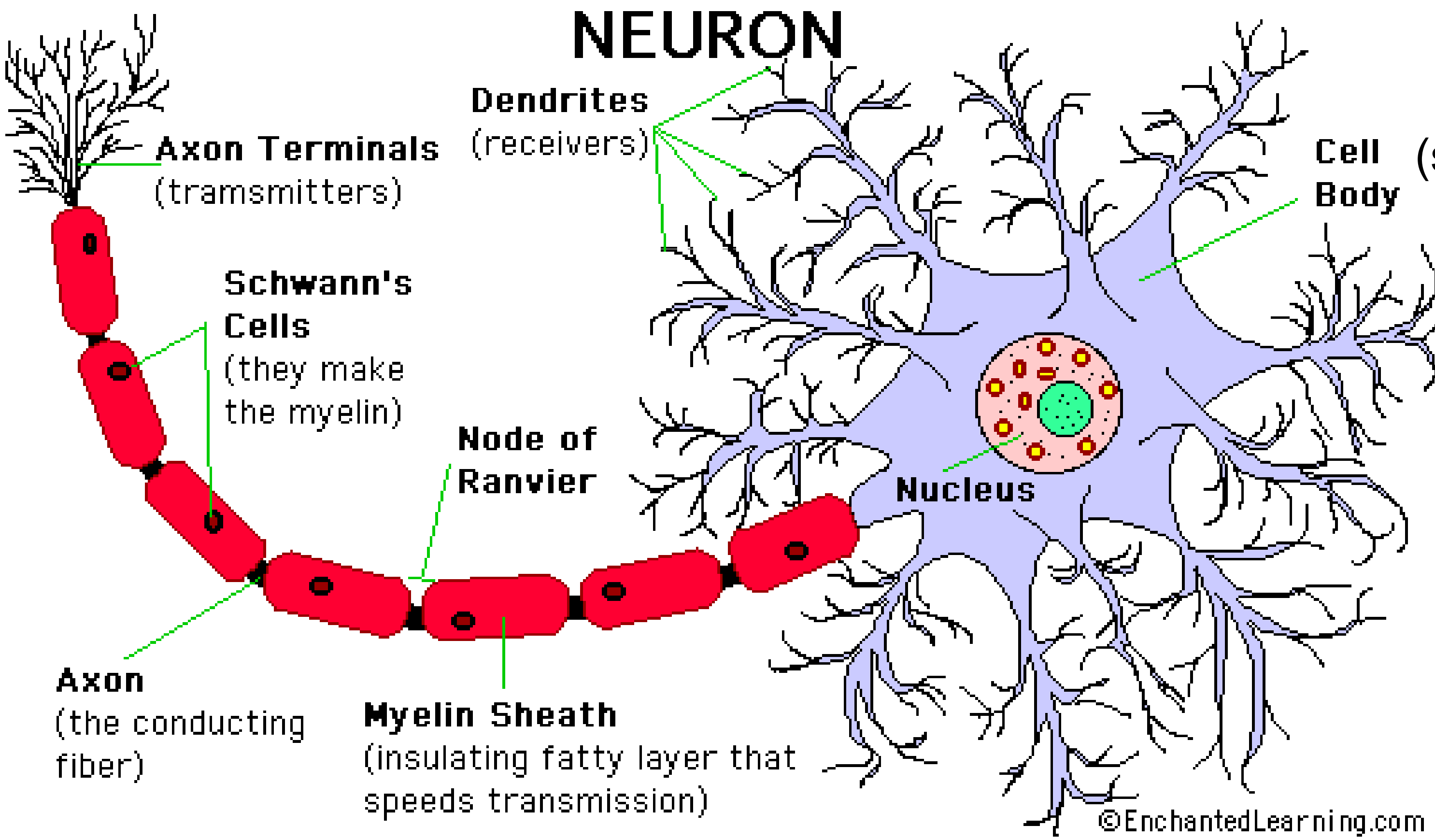
Neuron anatomy



(soma)

http://www.enchantedlearning.com/subjects/anatomy/brain/Neuron.shtml

Neuron anatomy

- **Neurons** are single nerve cells that transmit nerve signals to and from the brain. The neuron consists of a **cell body (or soma)** with branching **dendrites** (signal receivers) and a projection called an **axon**, which conduct the nerve signal. At the other end of the axon, the **axon terminals** transmit the electro-chemical signal across a **synapse** (the gap between the axon terminal and the receiving cell).

- The word "neuron" was introduced by the German scientist Heinrich Wilhelm Gottfried von Waldeyer-Hartz in 1891 (he also introduced the term "chromosome").

- The **axon**, a long extension of a nerve cell, transfers information from the cell body. Bundles of axons are known as nerves. Dendrites bring information to the cell body.

- **Myelin** coats and insulates the axon (except for periodic breaks called nodes of Ranvier), increasing transmission speed along the axon. Myelin is manufactured by Schwann's cells, and consists of 70-80% lipids (fat) and 20-30% protein.

- The **cell body (soma)** contains the neuron's nucleus (with DNA and typical nuclear organelles). Dendrites branch from the cell body and receive messages.
- A typical neuron has about 1,000 to 10,000 synapses (junction contacts to communicate with other neurons, muscle cells, glands).

Neuron types

Depending on their functions there are two groups of neurons:

- Sensory neurons:
- Collect and transmit signals from receptors to central nervous system (CNS)

- Motor neurons
- Carry signals from central nervous system (CNS) to effectors

Effectors:

are cells that respond to signals from motor neurons

These are muscle cells and glands in animals

- Neurons send messages **electrochemically**. This means that chemicals cause an electrical signal. Chemicals that have an electrical charge, - **ions.**
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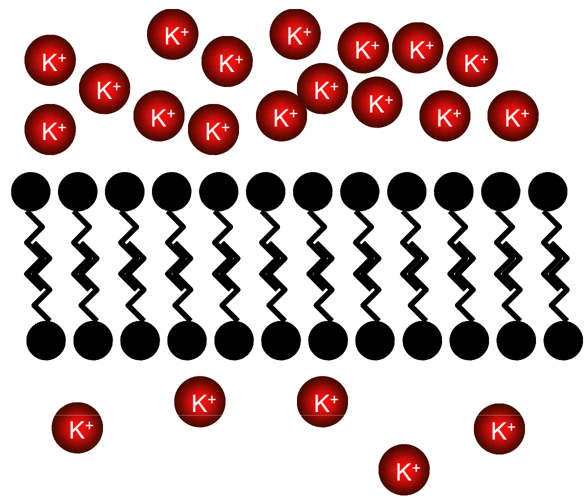
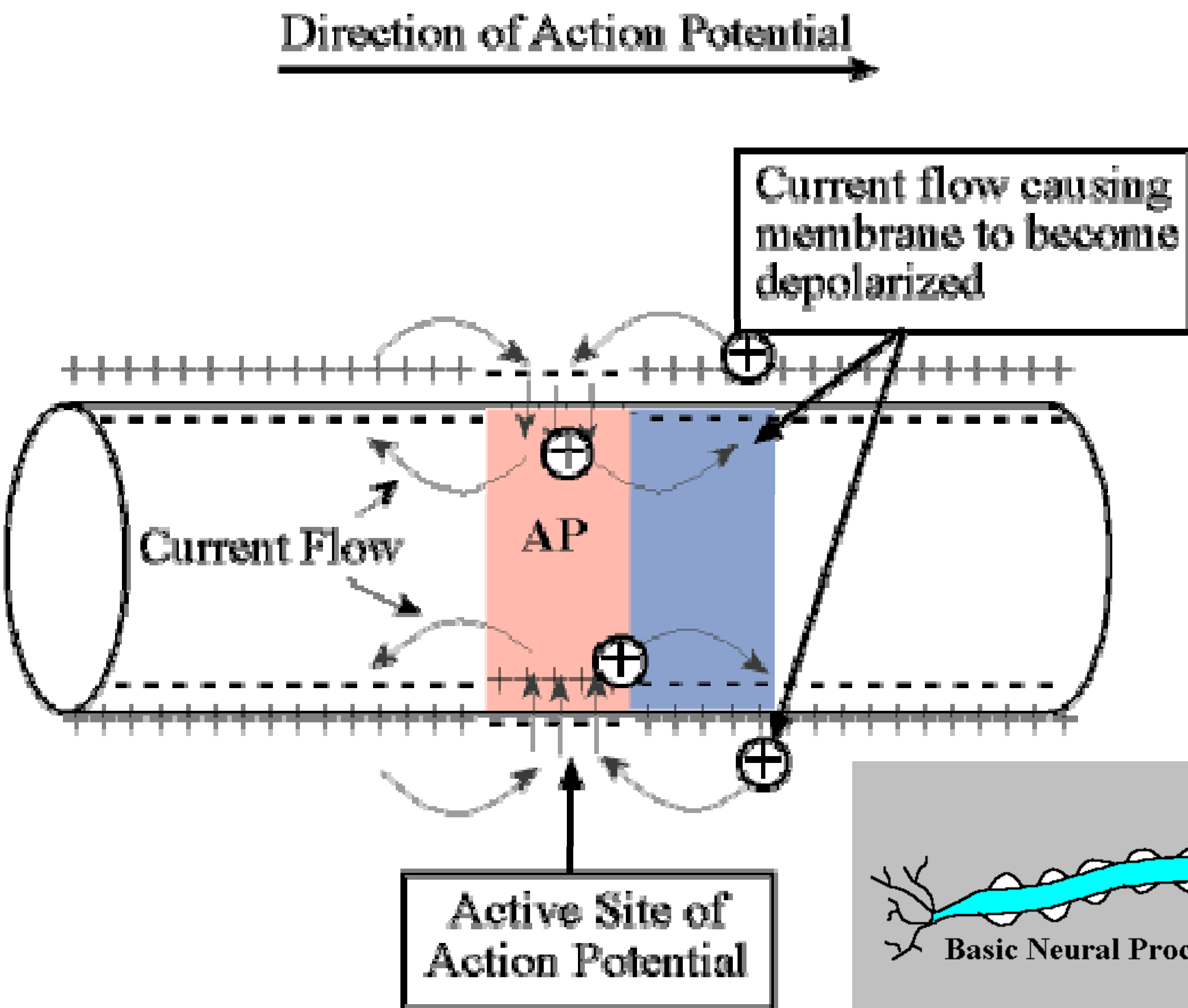
- The important ions in the nervous system are sodium and potassium (both have 1 positive charge, +), calcium (has 2 positive charges, ++) and chloride (has a negative charge, -).
- There are also some negatively charged protein molecules.
- It is also important to remember that nerve cells are surrounded by a semi-permeable membrane that allows some ions to pass through and blocks the passage of other ions.
- Membrane is asymmetrical and can have different concentrations of charged ions. Membrane is also asymmetrical due to the different lipids present on one side versus another – these are reasons why different charge is present on one side of the membrane versus another side and why a **membrane potential is created**.

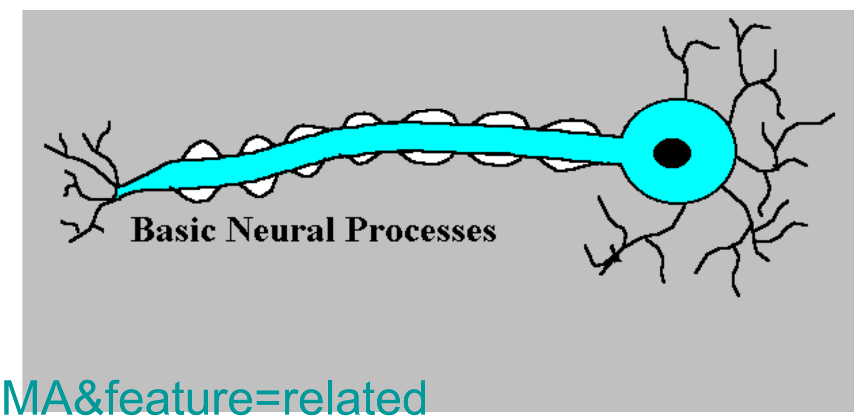
Mechanism of neuron excitation and nerve impulse propagation

- Nerve conduction/stimulation is based on ion exchange and the potential change across the membrane:
- Resting potential ~ 70mV
- Change in ion concentration or electric field as a response to stimulus leads to membrane depolarization and nerve impulses



Action potential → **Resting potential** → **Depolarization** → **Action potential** →





http://www.youtube.com/watch?v=mEsF7ezvWMA&feature=related

http://www.youtube.com/watch?v=nrTDY-SzQ7E&NR=1

Physico-chemical nature of membrane potential

- Membrane potential is created
- 1. by diffusion of ions (Nernst potential) due the differences in ion concentrations at outer and inner surfaces of plasma membrane, and due to the structural differences in lipid membrane
- 2. Donnan potential – due to different membrane permeability to different substances
- 3. Active pumping of ions by Na/K ion pumps with the help of ATP

Nernst potential

Diffusion or Nernst potential develops due to diffusion of a particular ion type across cell membrane, if ionic concentrations inside and outside are different. In equilibrium ion current =0, and concentration gradient is balanced by diffusion potential:

Nernst equation

$$\varphi = -\frac{RT}{ZF} \ln \frac{Ci}{Co}$$

inside

outside

If concentrations of ions outside and inside are different – potential develops , and in opposite if there is a potential, then ions will be at different concentrations outside and inside in equilibrium

because the electrical charge, or potential, depends on the *concentration* of ions in solution, using the **Nernst equation** the electrical potential across the neuron's membrane can be calculated from the ion concentrations.

- The Nernst equation states that potential across the membrane is predicted by five relationships:
- 1. *Potential* is related to the "ideal gas constant," R, because the motion of ions is involved.
- 2. *Potential* is also proportional to the absolute temperature, T, because ions move faster at higher temperatures.
- 3. Ions will diffuse from a region of higher concentration across the membrane to a region of lower concentration along their concentration gradient. In the Nernst equation, this diffusion along concentration gradients means that the potential across the membrane will depend on the logarithm of the concentrations of each ion inside (*i*) and outside (*o*) the membrane).
- 4. Potential is inversely proportional to the charge, *z*, on the ion in question because one needs fewer ions to yield the same difference in charge if each ion has a greater charge.
- 5. Potential is inversely proportional to *F*, the Faraday constant, a unit of electrical charge.

Using concentrations of ions calculate Nernst potential

Ions	Concentration mM/L		Nernst potential
	in	out	
Na^+	15	140	?
K^+	13.5	4	?
CL^-	4	120	?
HCO_3^-	10	24	?

Example

- Calculate Nernst Potential

$$\varphi = -\frac{RT}{ZF} ln \frac{Ci}{Co}$$

Using concentrations of ions calculate Nernst potential

Ions	Concentration mM/L		Nernst potential
	in	out	
Na^+ K^+ CL^-	149 13.5 4	15 4 120	+58 -92 -89

Actual membrane potential is -80 mV, therefore we need to consider ions together not separately

Hodkin-Katz-Goldman Potential

- 1. equilibrium (resting) state of the membrane is in fact (non-equilibrium) steady state. This implies that individual ionic currents independently exist across membrane, but the total current =0, this means that net positive flux = net negative charge flux, in steady state. Fluid on both sides is electrically neutral.

- Steady state HKG condition: $$J_K + J_{Na} - J_{Cl} = 0$$

- Nernst equilibrium condition: $$J_K = J_{Na} = J_{Cl} = ... = 0$$

HKG

- 2. HKG assumes that each of the ionic currents is caused by respective ionic concentration gradients and common electric potential gradient across membrane
- Individual current: $$J_i = -D_i \left[\frac{\Delta C_i}{\Delta x} + \frac{z_i F}{RT} C_i \frac{\Delta \phi}{\Delta x} \right]$$
- 3. Interaction between diffusing ions and between ions and membrane are accounted through permeability coefficients P=Dβ/δ. Potential:

$$V = -\frac{RT}{F} \ln \frac{P_K[K^+]_{in} + P_{Na}[Na^+]_{in} + P_{Cl}[Cl^-]_{out}}{P_K[K^+]_{out} + P_{Na}[Na^+]_{out} + P_{Cl}[Cl^-]_{in}}$$

- steady state membrane potential due to simultaneous diffusion of several ions under both electric and concentration gradients

Example, HKG potential:

- In plasma membrane: $$P_K : P_{Na} : P_{Cl} = 1 : 0.01 : 0.5$$
- using concentration table, at 20C, we can estimate HKG potential:
- -84 mV

Donnan potential

- Large molecular ions which can not move through the membrane concentrate inside the cell and contribute to membrane electric potential - this contribution is called Donnan potential

- In Equilibrium:

Electrical neutrality :

$A^+_{inside} + B^-_{inside} + Q^-_{inside} = 0$
$B^-_{outside} + A^+_{outside} = 0$

Thermal equilibrium:

$$A^+{}_i \cdot B^-{}_i = A^+{}_o \cdot B^-{}_o$$

Conservation of ions

$A^+_{inside} + A^+_{outside} = \text{constant}$
$B^-_{inside} + B^-_{outside} = \text{constant}$

Example. Donnan potential

- A membrane which is permeable to Na+ and Cl- separates two solutions, one of which contains a large anion Q-, to which the membrane is impermeable. The initial concentrations are (using i and o subscripts to designate the inside and outside compartments):

- $[Na+]_0 = [Cl-]_0 = 0.09\ mol.dm^{-3}$
- $[Na+]_i = 0.15\ mol.dm^{-3}$
- $[Cl-]_i = 0.09\ mol.dm^{-3}$
- $[Q-]_i = 0.08 mol.dm^{-3}$

- If the temperature is 20 ºC, what Donnan potential difference develops across the membrane?

Solution

Calculate final C using:

1) Thermal equilibrium:

$$\frac{[Na^+]_i}{[Na^+]_o} = \frac{[Cl^-]_o}{[Cl^-]_i}$$

2) Electrical neutrality :

$[Na]_i + [Cl]_i + Q_i = 0$
$[Cl]_o + [Na]_o = 0$

3) Conservation of ions

$[Na]_i + [Na]_o = \text{constant}$
$[Cl]_i + [Cl]_o = \text{constant}$

$$\varphi = -\frac{RT}{ZF} ln \frac{Ci}{Co}$$

Calculate Na potential using final C inside and outside – for this calculate final concentrations

Answer membrane potential = -9 mV

F=96,500 C/mol, T=293, R=8.32 J /(mol K)

Solution