Chapter 3: Neurophysiology: Conduction, Transmission, and the Integration of Neural Signals

- **Communication Within a Neuron**
- **Communication Between Neurons**

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Communication Within a Neuron

- **Electricity:**

negative pole = greater number of electrons, greater negative charge

positive pole = fewer electrons, less negative charge

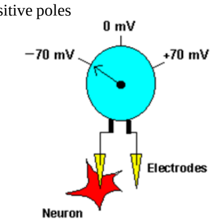
current = flow of electrons from negative to positive pole (measured in amperes)

electrical potential = difference in electrical charge (measured in volts) between negative and positive poles

- **Recording the Membrane Potential of a Neuron:**

Resting Potential = -70mV

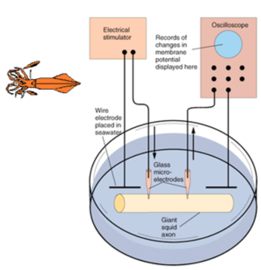
(varies from one neuron to another)

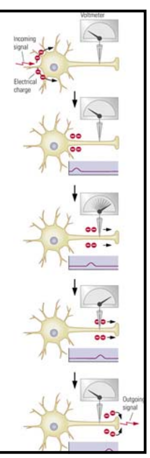


Communication Within a Neuron

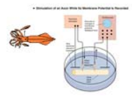
- **Stimulating the Neuronal Membrane with a Microelectrode:**

► Stimulation of an Axon While Its Membrane Potential Is Recorded



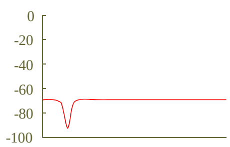


Communication Within a Neuron

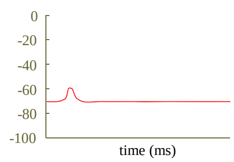


- Stimulate with microelectrode
- Record with second microelectrode

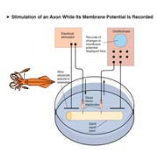
- **Hyperpolarization:**
  Apply small negative current to increase negative membrane potential



- **Depolarization**
  Apply depolarizing current to decrease membrane potential toward neutrality

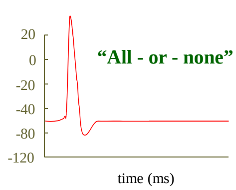


Communication Within a Neuron



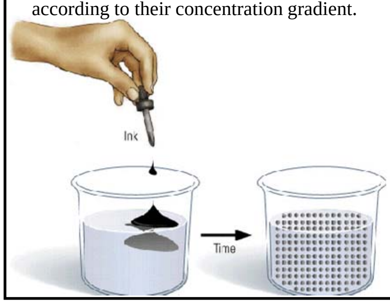
- **Depolarization:**
  Apply a slightly larger depolarizing current to reach -55mV threshold

- **Action Potential:**
  A disproportionately large response, constant regardless of magnitude of stimulation above -55mV



Communication Within a Neuron

- **Concentration Gradient:**
  - Molecules are in constant motion.
  - In the absence of external forces or barriers, molecules diffuse according to their concentration gradient.



Communication Within a Neuron

- **Voltage Gradient / Electrostatic Potential:**
  - Electrolytes dissociate into ions in solution.
  - e.g., NaCl dissociates into Na^+ (a cation) and Cl^- (an anion).

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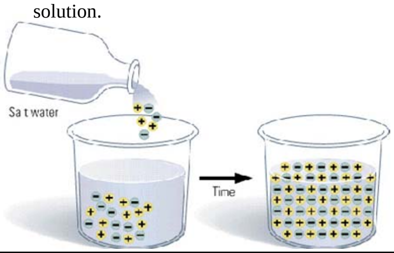
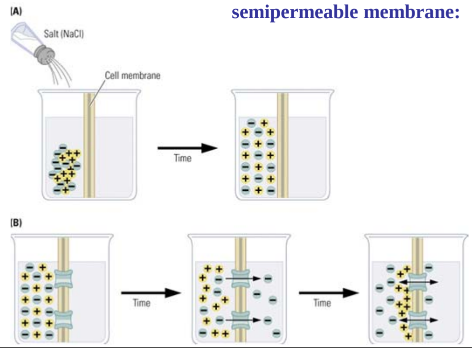
  - Like ions (i.e. those with the same charge) will repel each other in solution.



Communication Within a Neuron

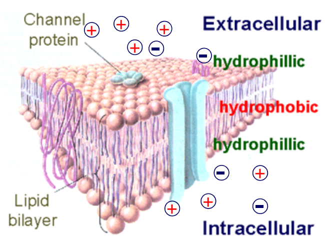
- **Dispersion of charged particles with an impermeable and a semipermeable membrane:**



Communication Within a Neuron

Ion Exchange

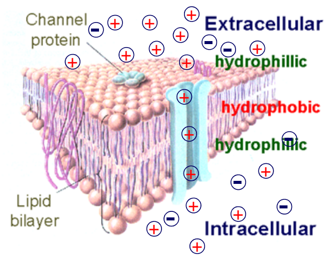
- **Positive ions (cations):** sodium (Na^+), potassium (K^+)
- **Negative ions (anions):** chloride (Cl^-), proteins



Communication Within a Neuron

Ion Exchange

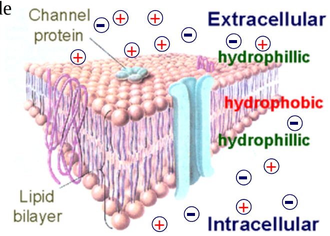
- **Channel proteins:** Cylindrical proteins that permit controlled exchange of ions across the membrane.



Communication Within a Neuron

Ion Exchange

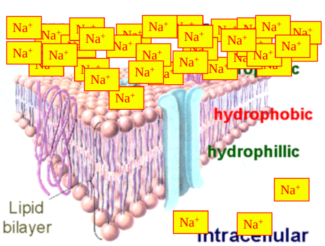
- **Resting potential:** In the absence of disturbance the membrane maintains a slightly negative electrical potential (i.e.balance of ionic charges) inside the neuron, with respect to the outside.



Communication Within a Neuron

Ion Exchange

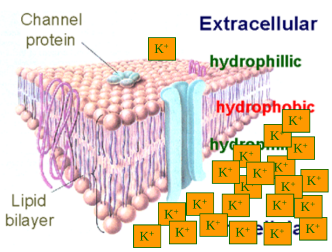
- **Sodium (Na^+):** More than ten times more concentrated outside the cell (extracellular) than inside the cell (intracellular)



Communication Within a Neuron

Ion Exchange

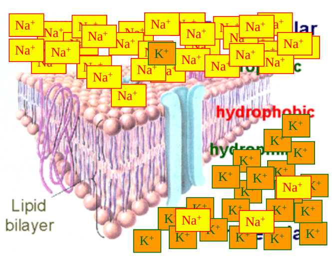
- **Potassium (K^+):** More than twenty times more concentrated inside the cell (intracellular) than outside the cell (extracellular)



Communication Within a Neuron

Ion Exchange

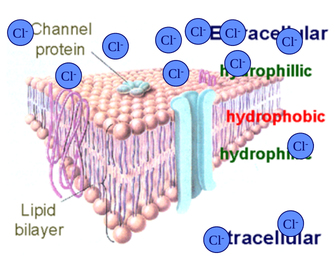
- **[Na^+] > [K+]:** There are many more sodium ions than potassium ions, providing a net positive extracellular potential.



Communication Within a Neuron

Ion Exchange

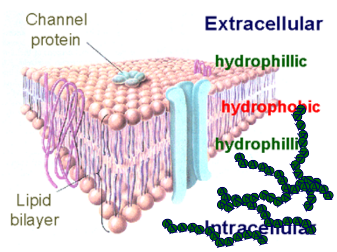
- **Chloride (Cl^-):** More concentrated in the extracellular space than the intracellular space



Communication Within a Neuron

Ion Exchange

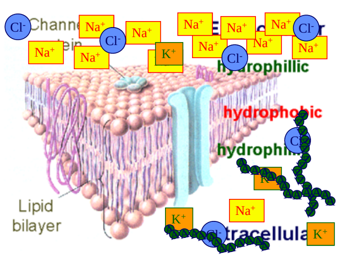
- **Proteins:** Virtually absent from extracellular space and concentrated in the intracellular space (negatively charged)



Communication Within a Neuron

Ion Exchange

- **Resting Potential:** Difference between the net charge (considering all the positive and negative charges) inside the cell, relative to the net charge outside the cell (approx. -70mV in the giant squid axon).



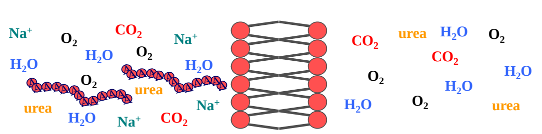
Communication Within a Neuron

Ion Exchange

- **Selective Permeability:** Some molecules can freely cross the cell membrane (e.g. O_2, CO_2, urea, water).

  Most larger molecules (e.g. negatively charged proteins) and ions (e.g. Na^+) are prevented from freely crossing the membrane.

intracellular extracellular

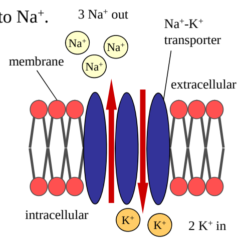


Communication Within a Neuron

Ion Exchange

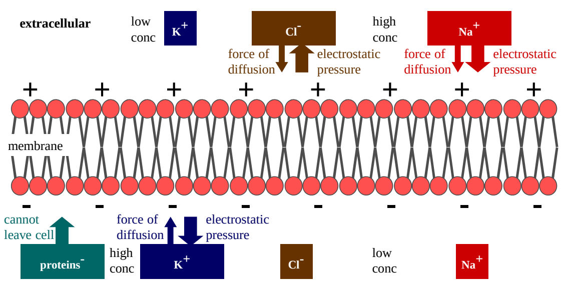
Sodium-Potassium Pump: Na^+ and K^+ are actively transported across the membrane by specific Na^+/K^+ transport proteins

- **Na^+:** Na^+/K^+ pump actively transports 3 Na^+ out of the cell.
  Na^+ concentration gradient would push Na^+ back in.
  Electrical gradient would push Na^+ back in.
  BUT the membrane is almost impermeable to Na^+.
- **K^+:** Na^+/K^+ pump actively transports 2 K^+ into the cell.
  K^+ concentration gradient would push K^+ back out.
  The membrane is semipermeable to K^+, so K^+ could leak back out.
  BUT the electrical gradient keeps K^+ inside the cell.



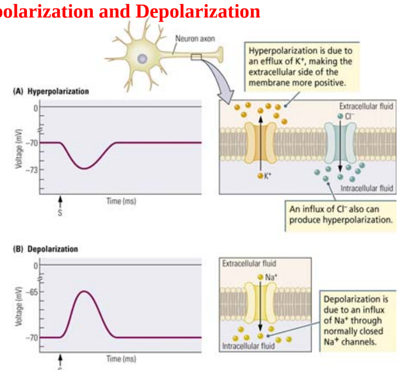
Communication Within a Neuron

Summary of Forces on Charged Particles



Communication Within a Neuron

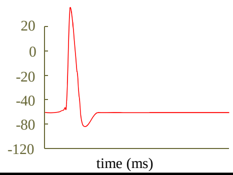
Hyperpolarization and Depolarization



Communication Within a Neuron

Why a Resting Potential?

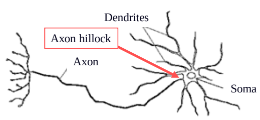
- **Extremely high energy expenditure:** Very energy expensive, approximately 40% of neuron's energy resources
- **Extremely rapid, strong response:** By maintaining a high concentration gradient and electrostatic potential, the neuron is prepared to exert a very rapid and powerful response when called upon - THE ACTION POTENTIAL!!

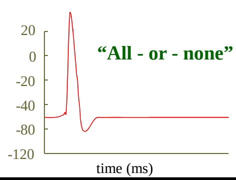


Communication Within a Neuron

The Action Potential and the Axon Hillock

- **Axon Hillock:**
  Electrochemical input from soma arrives at axon hillock. If above threshold, action potential is initiated.

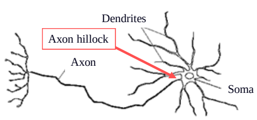


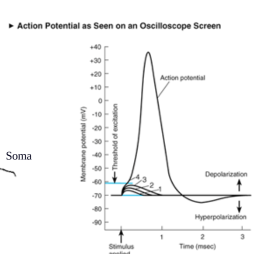


Communication Within a Neuron

The "All-Or-None-Law"

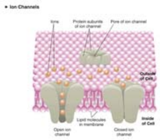
For all stimuli that exceed threshold –
The size and shape of the action potential are independent of the intensity of the stimulus that initiated it.





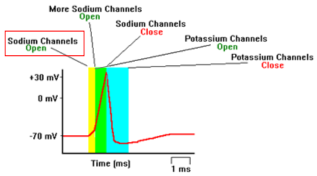
Communication Within a Neuron

The Action Potential



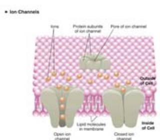
- **Voltage-Gated Ion Channels:**
  Respond by opening or closing according to the value of the membrane potential

- **At -70 to -55mV**
  Some Na^+ channels open
  Small Na^+ influx
  Some K^+ channels open
  Small K^+ efflux
  Driven by conc. gradient & electrostatic pressure.



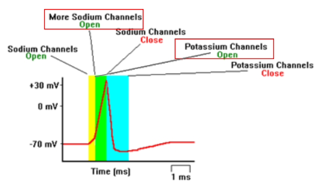
Communication Within a Neuron

The Action Potential



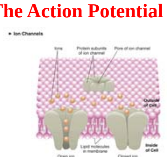
- **Voltage-Gated Ion Channels:**
  Respond by opening or closing according to the value of the membrane potential

- **At -55mV**
  Na^+ channels open
  Na^+ rushes in
  K^+ channels open
  K^+ exits
  Driven by conc. gradient & electrostatic pressure.



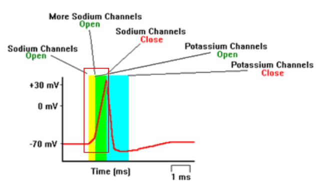
Communication Within a Neuron

The Action Potential



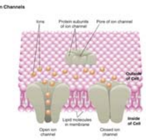
- **Voltage-Gated Ion Channels:**
  Respond by opening or closing according to the value of the membrane potential

- **Depolarization & Reverse Polarization**
  Rapid change in membrane potential from -70mV to +40mV



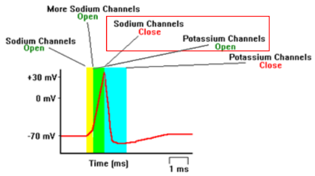
Communication Within a Neuron

The Action Potential



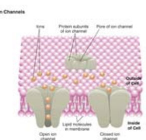
- **Voltage-Gated Ion Channels:** Respond by opening or closing according to the value of the membrane potential

- **Reverse polarization**
  - Na^+ channels become refractory
  - Cannot open again until resting potential is re-established



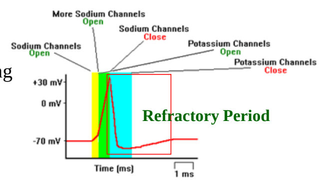
Communication Within a Neuron

The Action Potential



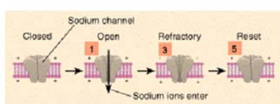
- **Voltage-Gated Ion Channels:** Respond by opening or closing according to the value of the membrane potential

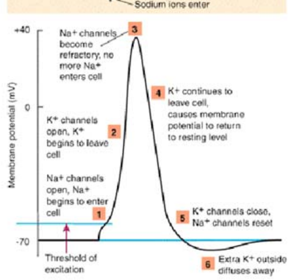
- **After-hyperpolarization**
  - Neuron overshoots resting potential.
  - External K^+diffuses, restoring resting potential
  - Na^+/K^+ pump restores ion balance



Communication Within a Neuron

The Action Potential



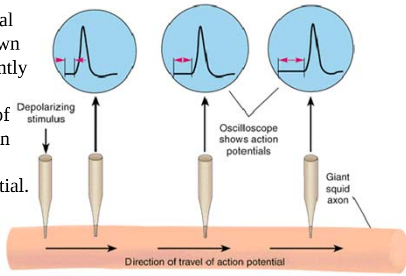


Communication Within a Neuron

Propagation of The Action Potential

> **Propagated signal retains intensity**

As action potential is transmitted down axon, it is constantly renewed
- depolarization of area around action potential creates new action potential.

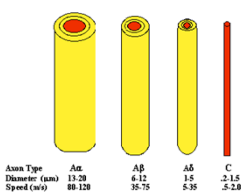


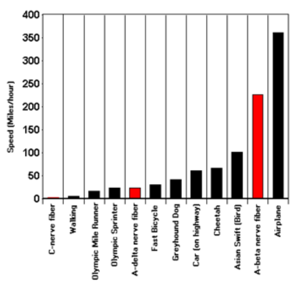
Communication Within a Neuron

Propagation of The Action Potential

> **Speed of conduction varies:**

Thin unmyelinated -> less than1 m/s
Thick unmyelinated -> 10m/s
Thick myelinated -> 100 m/s
Electricity -> 300,000,000 m/s





Communication Within a Neuron

Saltatory Conduction

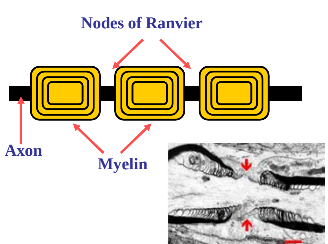
> **Action Potential "jumps" from one node to the next:**

AP cannot regenerate at myelin due to
1- insulation
2- Na^+ channels mostly at nodes

Positive charges repel to next node

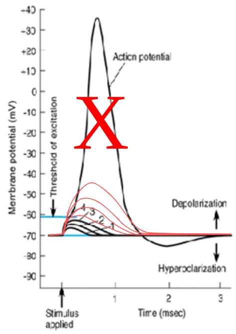
AP re-established

Saltatory conduction = fast propagation of AP



Communication Within a Neuron

Graded Potentials



Interneurons:

Lack axon or short axon.

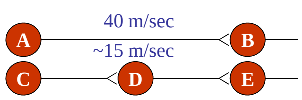
Depolarize or hyperpolarize in proportion to the intensity of the stimulus.

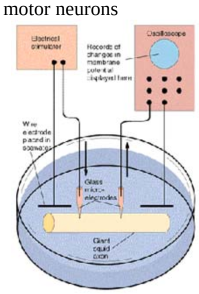
Alterations in membrane potential decay rapidly as they are conducted.

Communication Between Neurons

- **Charles Scott Sherrington – Discovery of the Synapse**

- (1906) demonstrated gaps between neurons, behaviorally
- studied the leg flexion reflex in a dog
- measured conduction velocity in sensory & motor neurons
- measured distance of input to spinal cord
- measured distance of output to muscle
- pinched foot, measured delay until flexion
- found delay longer than expected
- reasoned gaps between neurons
- called gaps "synapses" (after Cajal)





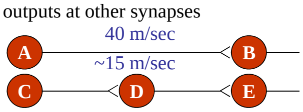
Communication Between Neurons

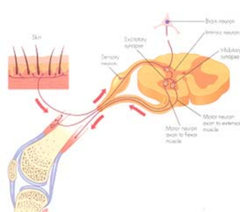
- **Charles Scott Sherrington – Discovery of the Synapse**

1) Reflexes are slower than conduction along an axon. Consequently, there must be some delay at synapses

2) Several weak stimuli presented at slightly different times or slightly different locations produce a stronger reflex than a single stimulus does. Therefore, the synapses must be able to *summate* stimuli

3) When one set of muscles is excited, another set is relaxed. Accordingly, the input can simultaneously excite outputs at some synapses while inhibiting outputs at other synapses

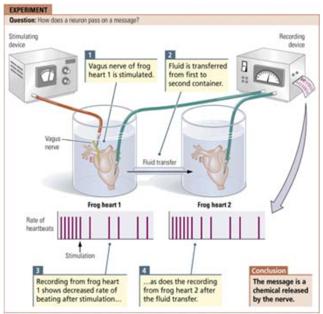




Communication Between Neurons

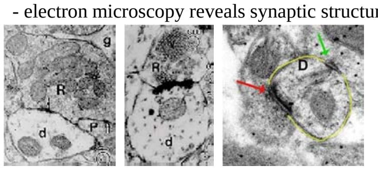
- **Otto Leowi – Discovery of Chemical Neurotransmission**
  - (1921) demonstrated neurons transmit using a chemical messenger
  - stimulated frog vagus nerve
  - transferred bath from stimulated heart to second heart
  - both hearts decreased rate of beating


Otto Loewi
(1873–1961)



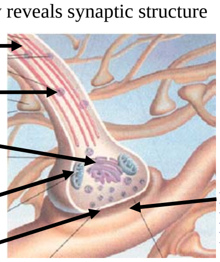
Communication Between Neurons

- **The Structure of Synapses**
  - electron microscopy reveals synaptic structure



Communication Between Neurons

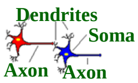
- **The Structure of Synapses**
  - electron microscopy reveals synaptic structure



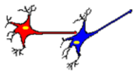
Synaptic cleft is approx. 200 Å.
Neurons have an average of 1000 synapses each.

Communication Between Neurons

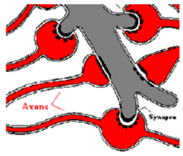
- **Most common types of synapses**



Axodendritic



Axosomatic

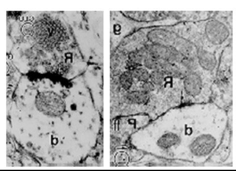


- Synapses are junctions between axon terminals and cell membranes of other neurons

Communication Between Neurons

- **Excitatory and Inhibitory Messages**
  - Specific synapses provide excitatory (depolarizing) input
  - Other synapses provide inhibitory (hyperpolarizing) input
  - Type I synapses = located primarily on shafts or spines of dendrites, round vesicles, thick presynaptic density, wide synaptic cleft, large active zone, excitatory input
  - Type II synapses = located primarily on soma, flattened vesicles, thin presynaptic density, narrow synaptic cleft, small active zone, inhibitory input

Type I **Type II**



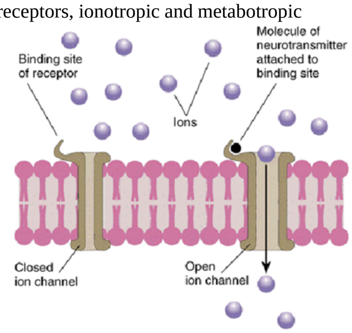
Communication Between Neurons

- **The Types of Receptors for Neurotransmitters**
  - two main classes of receptors, ionotropic and metabotropic

Ionotropic receptors:

Open a neurotransmitter-dependent ion channel when a molecule of neurotransmitter binds

This changes the local postsynaptic membrane potential.



Communication Between Neurons

- **The Types of Receptors for Neurotransmitters**

Different receptors are coupled to different ion channels

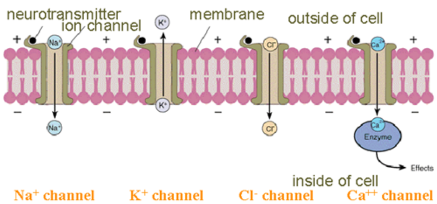
The type of ion channel determines whether input is excitatory or inhibitory

Na^+ channels:

Most important excitatory input (EPSP)

K^+ channels:

Inhibitory input (IPSP)



Communication Between Neurons

- **The Types of Receptors for Neurotransmitters**

Different receptors are coupled to different ion channels

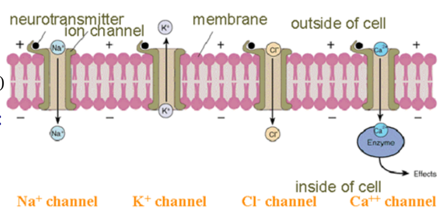
The type of ion channel determines whether input is excitatory or inhibitory

Cl^- channels:

Decrease the depolarization of excited neurons (neutralize EPSP)

Ca^{2+} channels:

Excitatory input (EPSP)



Communication Between Neurons

- **The Types of Receptors for Neurotransmitters**

Neurons exhibit a basal rate of firing of action potentials:

basal or spontaneous firing rate

excitatory input

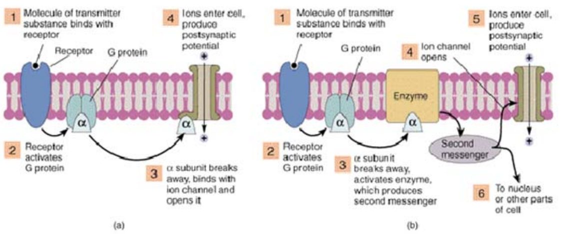
inhibitory input

Communication Between Neurons

- **The Types of Receptors for Neurotransmitters**

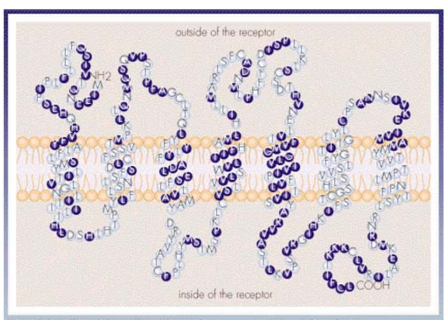
Metabotropic receptors: activate an associated protein (G protein) which triggers the opening of an ion channel.

This changes the local postsynaptic membrane potential or changes chemical activities within the cell.



Communication Between Neurons

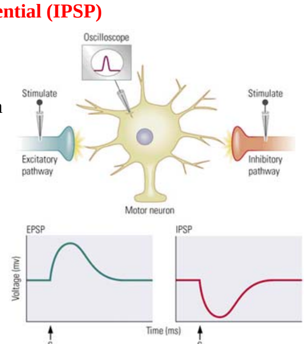
- **The Types of Receptors for Neurotransmitters**



Communication Between Neurons

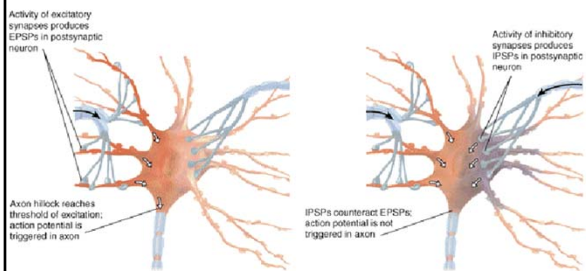
Excitatory Postsynaptic Potential (EPSP) and Inhibitory Postsynaptic Potential (IPSP)

- **EPSP:**
  Depolarizing input to the soma or a dendrite produces a local graded EPSP
- **IPSP:**
  Hyperpolarizing input to the soma or a dendrite produces a local graded IPSP



Communication Between Neurons

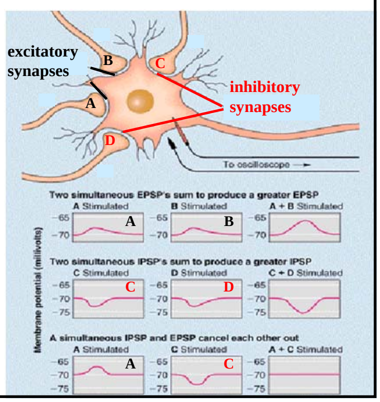
Summation of EPSPs and IPSPs



- EPSPs summate to produce an Action Potential
- IPSPs counteract the effects of EPSPs to block the Action Potential

Communication Between Neurons

Spatial Summation



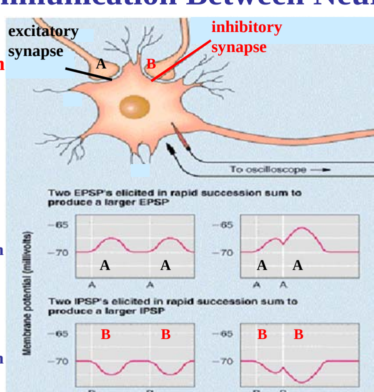
Summation

Summation

Cancellation

Communication Between Neurons

Temporal Summation



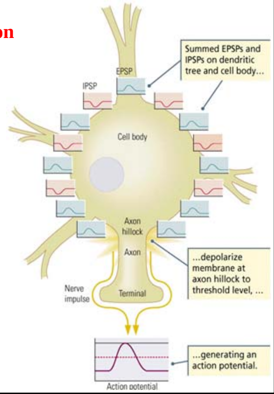
No Summation — Summation

No Summation — Summation

Communication Between Neurons

Temporal and Spatial Summation

- **EPSPs and IPSPs:**
  Excitatory and inhibitory inputs diffuse along the interior surface of the cell membrane, summate (or cancel) and the net potential registered at the axon hillock may initiate an action potential.

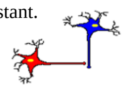


Communication Between Neurons

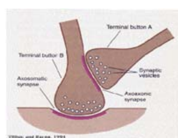
Other Types of Synapses

- **Axoaxonic synapses – A Special Case:**
  Axoaxonic synapses do not contribute directly to neural integration. Rather, they modulate the amount of neurotransmitter release from the terminal boutons of the postsynaptic neuron.

  Ordinarily the number of quanta of neurotransmitter release per action potential is constant.



Axoaxonic



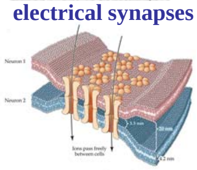
presynaptic inhibition: decrease in neurotransmitter release
presynaptic facilitation: increase in neurotransmitter release
due to actions of axoaxonic synapses

Communication Between Neurons

Other Types of Synapses

varicosities

electrical synapses



Dendrodendritic synapses :
Occur on some very small interneurons.
May participate in regulatory functions
- e.g. organization of groups of neurons
small size, difficult to study, function unknown

Varicosities:
Not really synapses, beadlike swellings along axon where neurotransmitter is released

Gap Junctions (Electrical Synapses) :
narrow gap
ion channels communicate directly between cells
common in invertebrates, less common in vertebrates.
functions largely unknown in vertebrates
- may participate in neuroplastic processes such as sensitization.

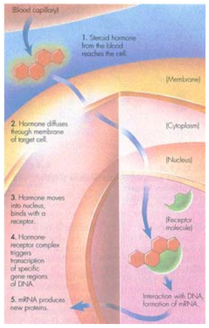
Communication Between Neurons

Other Types of Synapses

- **Nonsynaptic Chemical Communication:** Neurons have membrane-bound receptors all over their membranes. Neurons also have cytosolic and nuclear receptors.

  These non-synaptic receptors bind a variety of specific neurotransmitters, neuromodulators, and hormones.

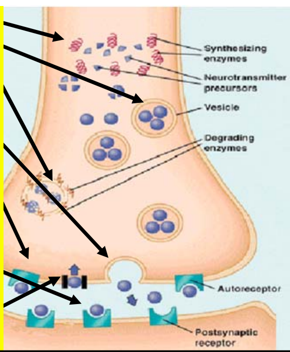
  Most non-synaptic membrane-bound receptors are metabotropic. Some are ionotropic. All known cytosolic and nuclear receptors are metabotropic.



Communication Between Neurons

- **Seven Stages in Neurotransmitter Function**

1. Neurotransmitters are synthesized.
2. Neurotransmitters are stored in vesicles.
3. Neurotransmitters that leak from vesicles are destroyed by enzymes.
4. Action potentials cause vesicles to fuse with membrane and release neurotransmitters into the synapse.
5. Released neurotransmitters bind to autoreceptors and inhibit further synthesis and release.
6. Released neurotransmitters bind to postsynaptic receptors.
7. Released neurotransmitters are removed by reuptake or enzymatic degradation.



Communication Between Neurons

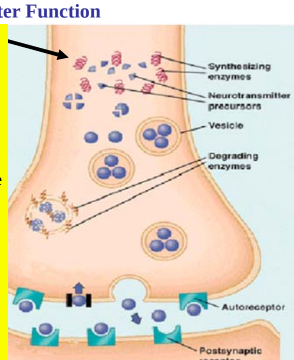
- **Seven Stages in Neurotransmitter Function**

1. Neurotransmitters are synthesized.

Protein and peptide neurotransmitters are synthesized from DNA template in the soma. These proteins/peptides may be altered after synthesis

Other neurotransmitters are synthesized by modification of ingested substances. These may be manufactured right in the axon terminal.

Energy for these actions is provided by chemical reactions in the mitochondria.



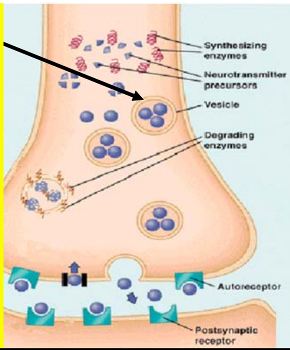
Communication Between Neurons

> Seven Stages in Neurotransmitter Function

2. Neurotransmitters are stored in vesicles.

Vesicular packaging occurs in the golgi apparatus in the cell body or in the axon terminal.

Some vesicles are further packaged into storage granules that hold many vesicles.

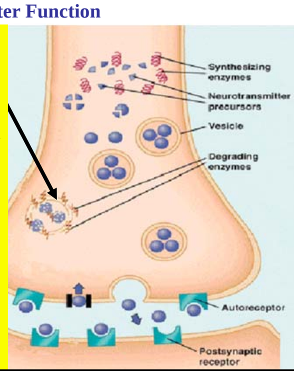


Communication Between Neurons

> Seven Stages in Neurotransmitter Function

3. Neurotransmitters that leak from vesicles are destroyed by enzymes.

Catabolizing enzymes (proteins) digest any neurotransmitter molecules that leak out of vesicles.

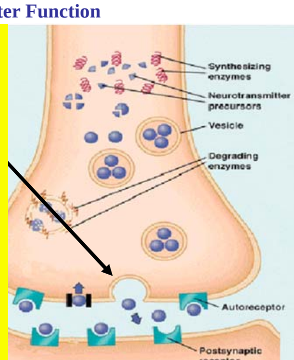


Communication Between Neurons

> Seven Stages in Neurotransmitter Function

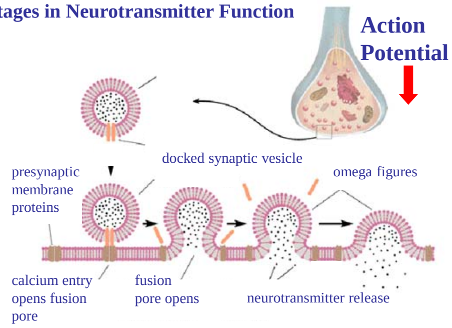
4. Action potentials cause vesicles to fuse with membrane and release neurotransmitters into the synapse.

Action potentials actually cause vesicles to migrate toward the presynaptic membrane and to fuse to the membrane.



Communication Between Neurons

- Seven Stages in Neurotransmitter Function



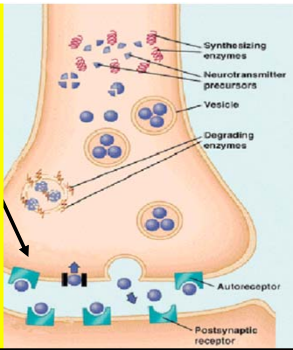
Released neurotransmitters diffuse passively across the synapse.

Communication Between Neurons

- Seven Stages in Neurotransmitter Function

5. Released neurotransmitters bind to autoreceptors and inhibit further synthesis and release.

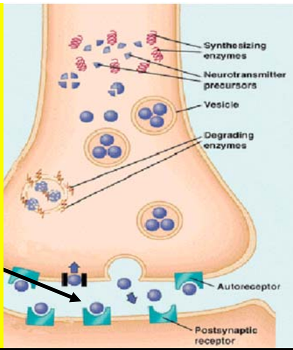
Autoreceptors are located on the presynaptic neuron that releases the neurotransmitter. They activate mechanisms in the neuron that inhibit further synthesis and release.



Communication Between Neurons

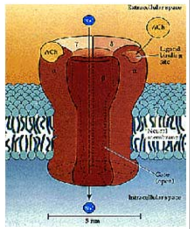
- Seven Stages in Neurotransmitter Function

6. Released neurotransmitters bind to postsynaptic receptors.



Communication Between Neurons

- **Seven Stages in Neurotransmitter Function**
  - The released neurotransmitter binds to a specific site on a postsynaptic receptor protein.
  - Depending upon which type of receptor the neurotransmitter binds to, it will either:
    1) cause excitation (depolarization) of the postsynaptic neuron, or
    2) cause inhibition (hyperpolarization) of the postsynaptic neuron, or
    3) produce changes in chemical activities inside of the postsynaptic neuron

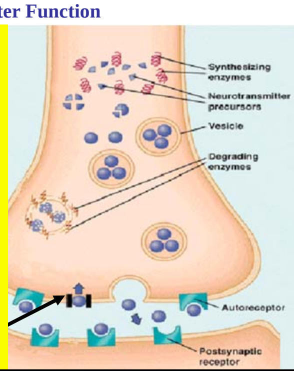


  - The effect from releasing one vesicle full of neurotransmitter on the postsynaptic neuron is very small – a quantum effect. Many quanta are required to significantly alter the activity of the postsynaptic neuron.

Communication Between Neurons

- **Seven Stages in Neurotransmitter Function**

7. Released neurotransmitters are removed by reuptake or enzymatic degradation.

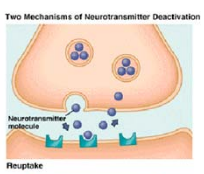


Communication Between Neurons

- **Seven Stages in Neurotransmitter Function**

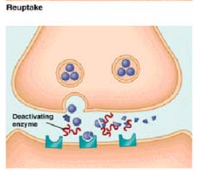
2 Mechanisms of deactivation:

- **Reuptake**



- **transporters**

- **Enzymatic Degradation**

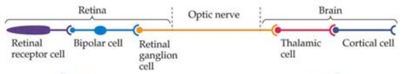


- **AChE**
- **MAO**

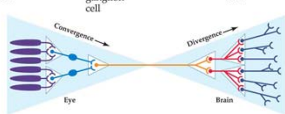
Communication Between Neurons

Types of Circuits

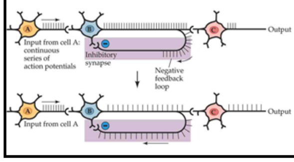
simple neural chain



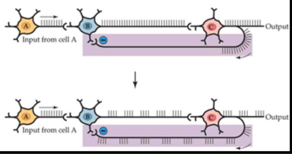
convergence and divergence



axon collateral



oscillator circuit



Reading Assignment

Before next class

Chapter 4: The Chemical Basis of Behavior: Neurotransmitters and Neuropharmacology
Breedlove, Rosenzweig, & Watson