

M U N I

M E D

Introduction to neurophysiology

Cellular base of nervous system

Synapse

Contact

Kamil Ďuriš

Department of Pathological Physiology (A18)

kduris@med.muni.cz

Why and how to **STUDY** neuroscience

Philosophy : Mind behind Mind



Neuroscience: Brain

Psychology : Mind



PS Deb

<http://www.slideshare.net/drpsdeb/presentations>

What is nervous system good for?

The role of nervous system

Unicellular organism

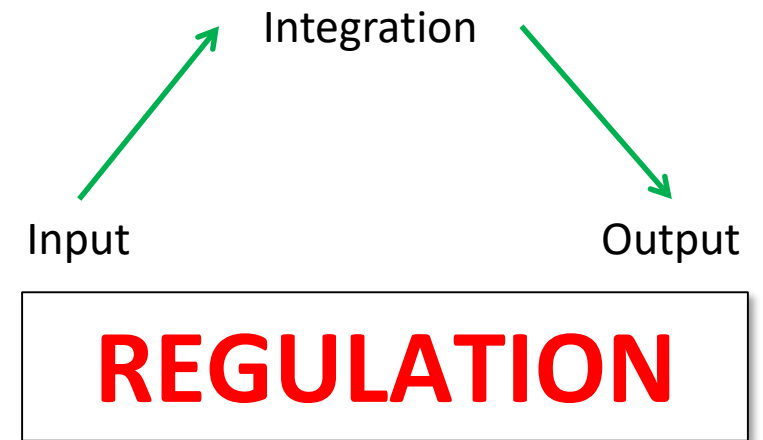
- One cell has to do everything- lower effectivity
- Total dependence on environment
- High level of stress
- Short life time

Multicellular organism

- Functional specialization of particular cells – higher effectivity
- Inner environment – homeostasis
- Lower level of stress
- Longer life time

The role of nervous system

- Essentials for survival of multicellular organism
- Maintaining homeostasis
 - The composition of inner environment
 - The integrity of organ/ bodily barriers
- Coordination of bodily functions
 - To receive signals from outer and inner environment
 - To process this information
 - To respond in a coordinate manner to these stimuli

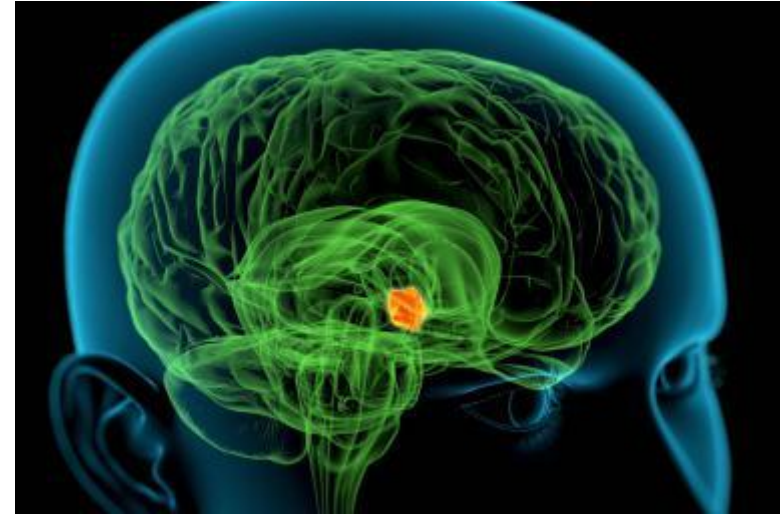


The role of nervous system

- Regulation
 - Nervous
 - Humoral

The role of nervous system

- Regulation
 - Nervous
 - Humoral



<http://biology.about.com/od/anatomy/p/Hypothalamus.htm>

Central nervous system controls both types of regulations

The role of nervous system

Humoral regulations

- Hormone
- Non-specific channel of conduction (blood stream)
- Target site defined by specific receptor

Nervous regulations

- Neurtransmitters
- Specific channel of conduction
- Target site defined by infrastructure

The role of nervous system

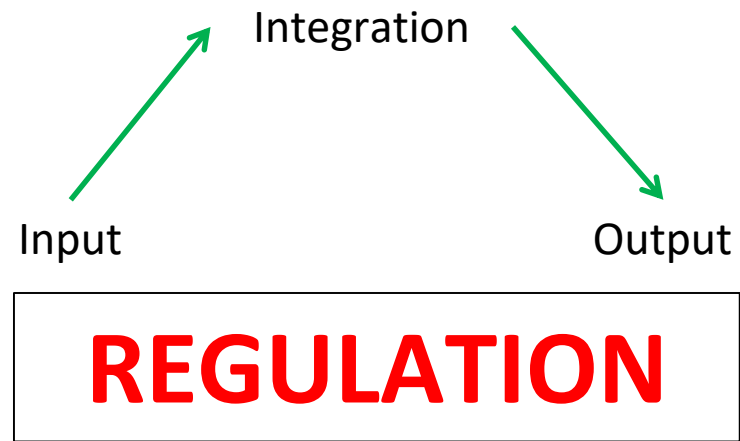
Humoral regulations

- Hormone
- Non-specific channel of conduction (blood stream)
- Target site defined by specific receptor
- Low energetical demands
 - Slow
- Long duration

Nervous regulations

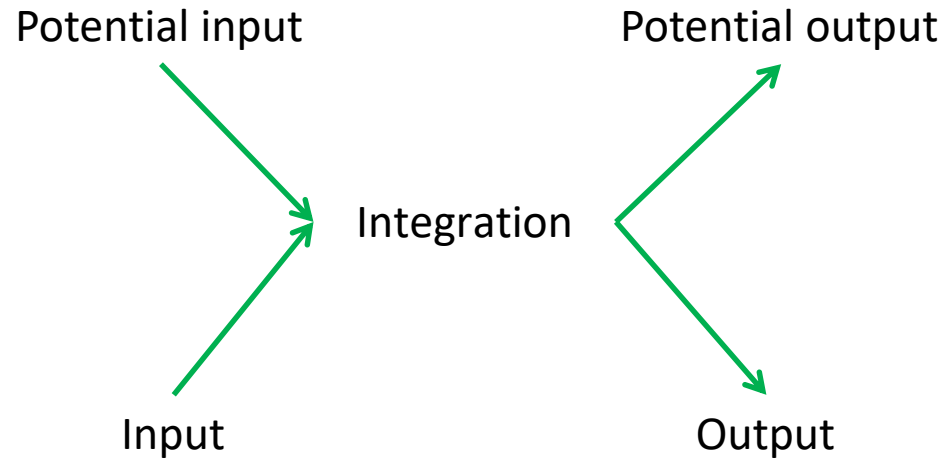
- Neurtransmitters
- Specific channel of conduction
 - Target site defined by infrastructure
- High energetical demands
 - Fast
- Short duration

The role of nervous system



The role of nervous system

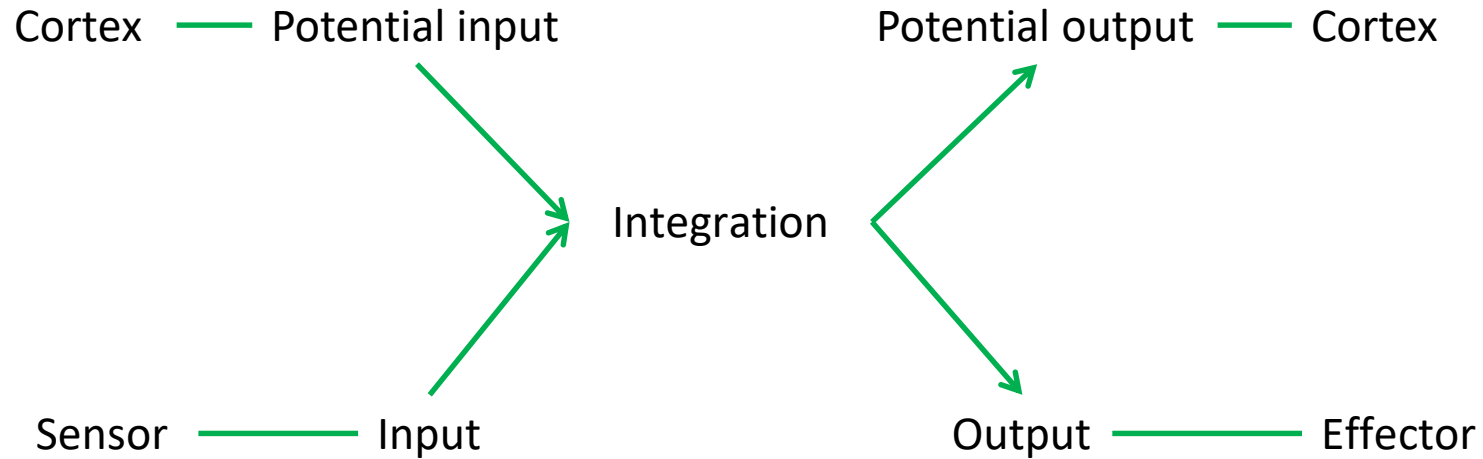
ANTICIPATION



REGULATION

The role of nervous system

ANTICIPATION



REGULATION

Evolutionary approach

- Evolutionary old structures have not been replaced by new ones during evolution, but the old has been kept and the new added

Evolutionary approach

- Evolutionary old structures have not been replaced by new ones during evolution, but the old has been kept and the new added
- Evolutionary younger structures were associated with new functions or with the improvement in existing functions

Evolutionary approach

- Evolutionary old structures have not been replaced by new ones during evolution, but the old has been kept and the new added
- Evolutionary younger structures were associated with new functions or with the improvement in existing functions
- It is important to ask what is any particular function good for and how it has been improved in course of evolution

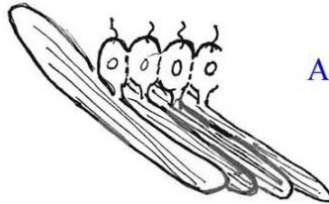
Evolutionary approach

Evolution is not revolution



Evolution of the nervous system

Input → Integration → Output



A. Myoepithelium:
contractile epithelial cells
responding to stimulation and
interconnected by electrical
synapses (gap junctions)

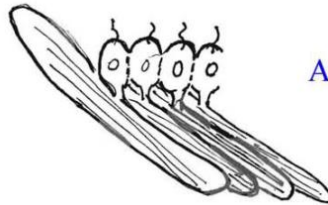
Gerald Schneider. *9.14 Brain Structure and Its Origins, Spring 2014*. (Massachusetts Institute of Technology: MIT OpenCourseWare), <http://ocw.mit.edu> (Accessed). License:Creative Commons BY-NC-SA

Four basic types of tissue

- ✓ Epithelial
- ✓ Connective
- ✓ Muscular
- ✓ Nervous

Evolution of the nervous system

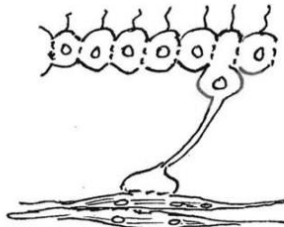
Input → Integration → Output



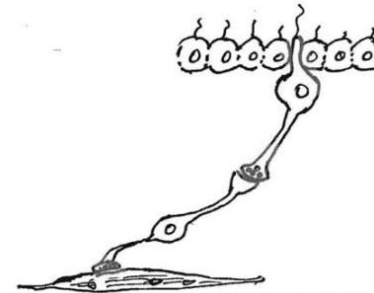
A. Myoepithelium:
contractile epithelial cells
responding to stimulation and
interconnected by electrical
synapses (gap junctions)



B. Protomyocytes separate
from sensory epithelium,
all connected by electrical
synapses



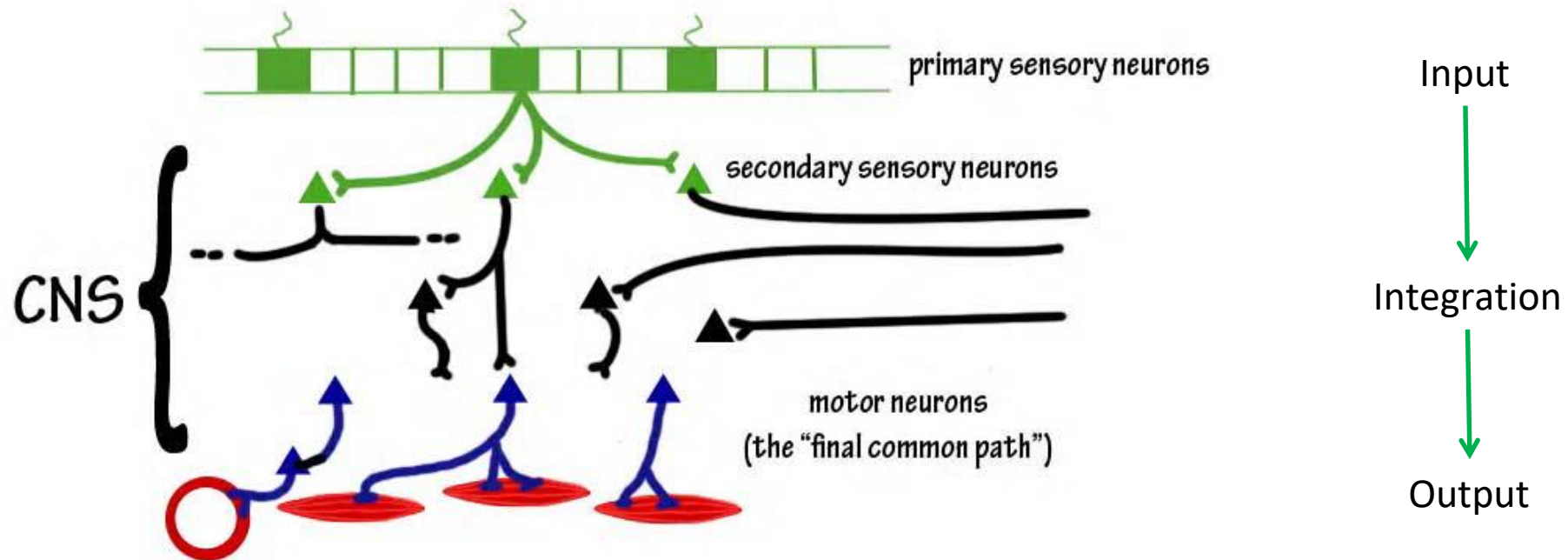
C. Protoneurons appear,
sensory and connected to
separate contractile cells



D. Neurons appear, separate
from both neurosensory cells
and contractile cells.
Chemical synapses appear.

Gerald Schneider. *9.14 Brain Structure and Its Origins, Spring 2014*. (Massachusetts Institute of Technology: MIT OpenCourseWare), <http://ocw.mit.edu> (Accessed). License:Creative Commons BY-NC-SA

Evolution of the nervous system



Gerald Schneider. *9.14 Brain Structure and Its Origins, Spring 2014*. (Massachusetts Institute of Technology: MIT OpenCourseWare), <http://ocw.mit.edu> (Accessed). License:Creative Commons BY-NC-SA

Compartmentalization

- Cellular specialization leads to compartmentalization on several levels
 - Tissue level
 - Organ level
 - Organ system level
- There are barriers in between compartments
- Properties/content may vary among different compartments

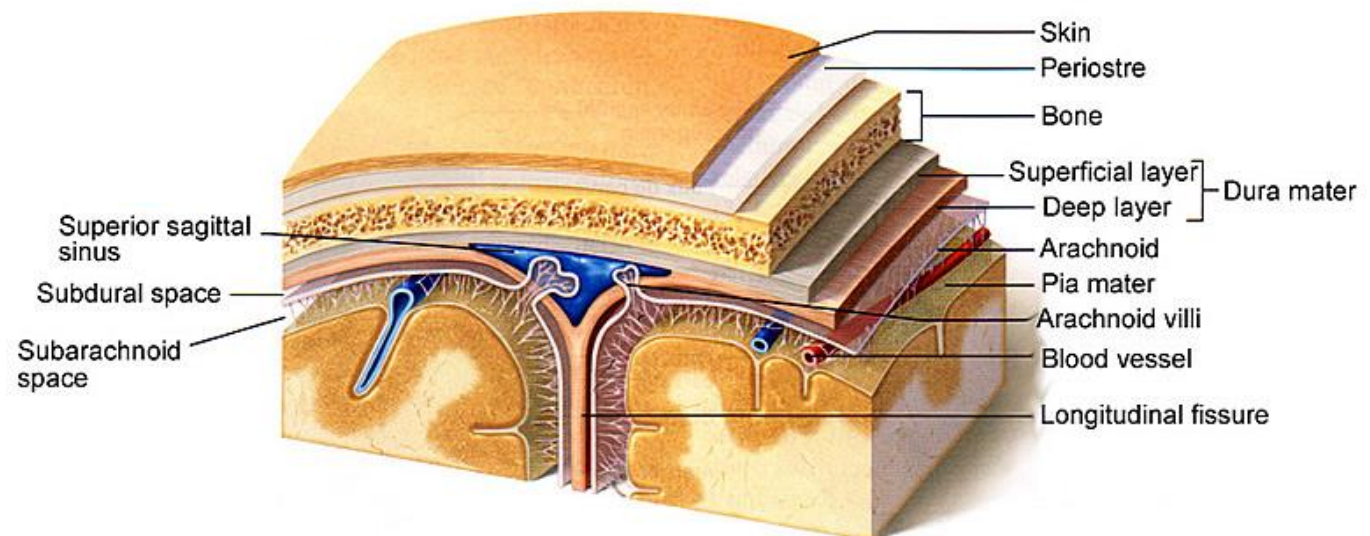
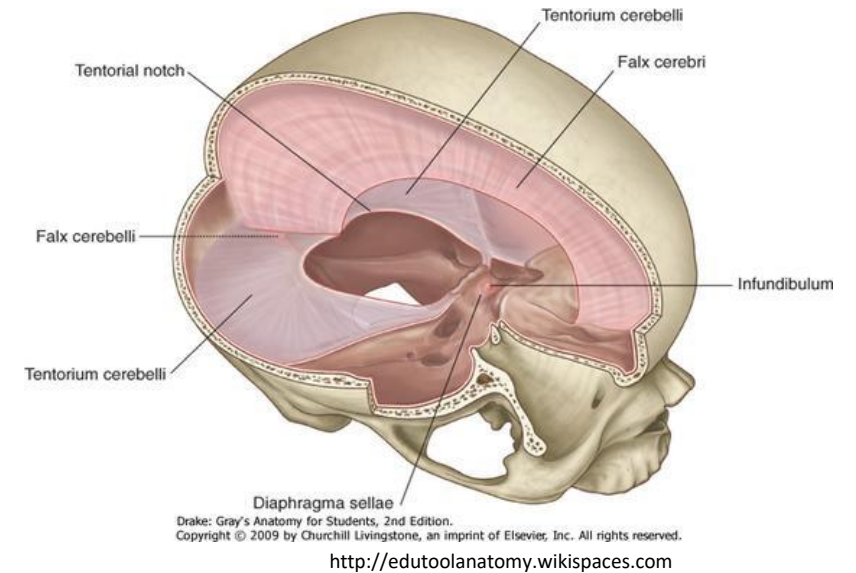
Compartmentalization

- Cellular specialization leads to compartmentalization
 - Tissue level
 - Organ level
 - Organism level
- There are barriers between compartments
- Properties/capabilities vary among different compartments

The brain homeostasis is maintained within a narrow range thanks to hematoencephalic barrier and astrocyte activity
This allows neuronal cells to live for the entire life of the individual

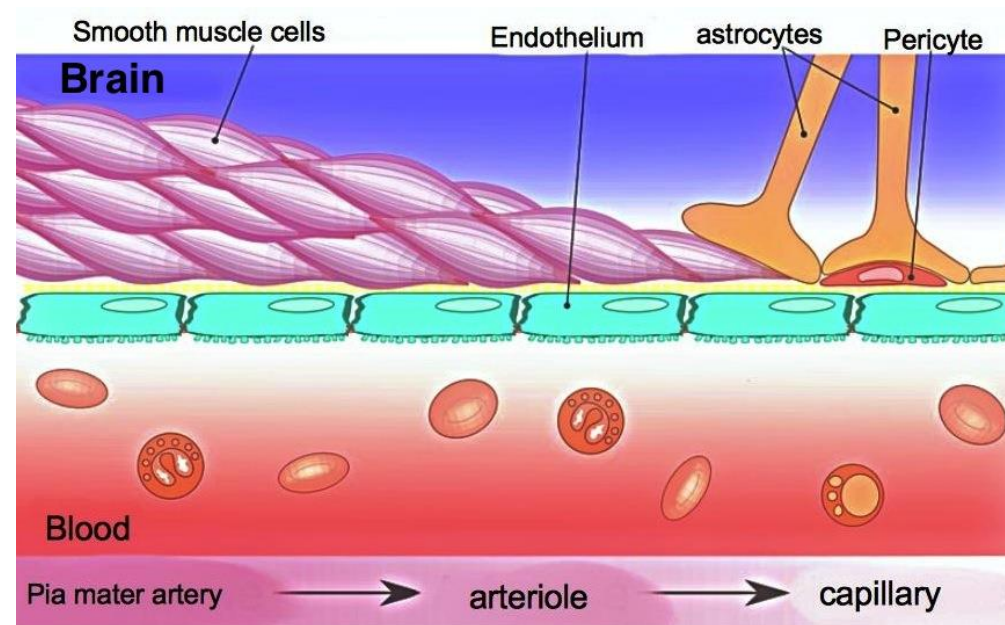
Intracranial compartment

- ✓ „Very specific region“
- ✓ Brain
- ✓ Cerebrospinal fluid
- ✓ Blood (intravascular)
- ✓ Barriers
 - Meningeal
 - Hematoliquor
 - Hematoencephalic



Hematoencephalic barrier

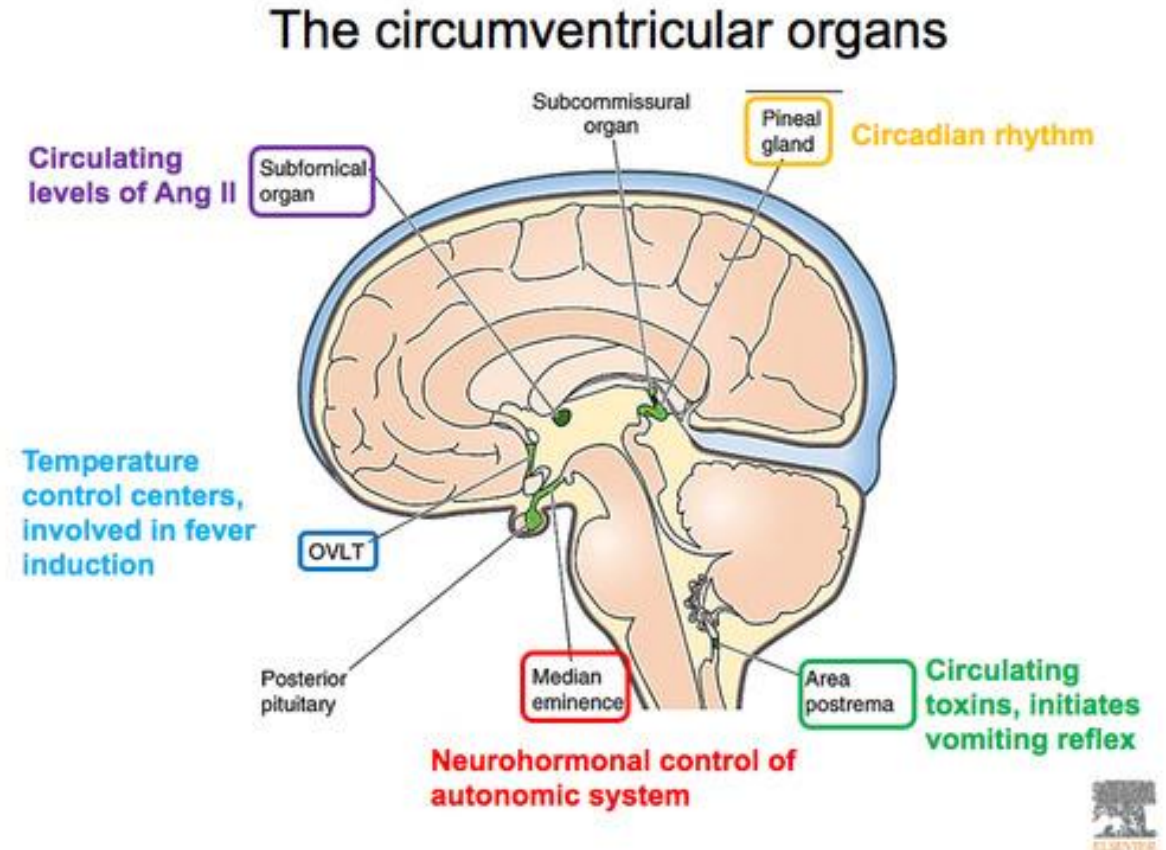
- Highly organised structure
 - Endothelial cells (low permeability thanks to zonula occludens)
 - Basal membrane
 - Astrocytes
 - Pericytes



https://upload.wikimedia.org/wikipedia/commons/1/12/Blood_vessels_brain_english.jpg

Circumventricular organs

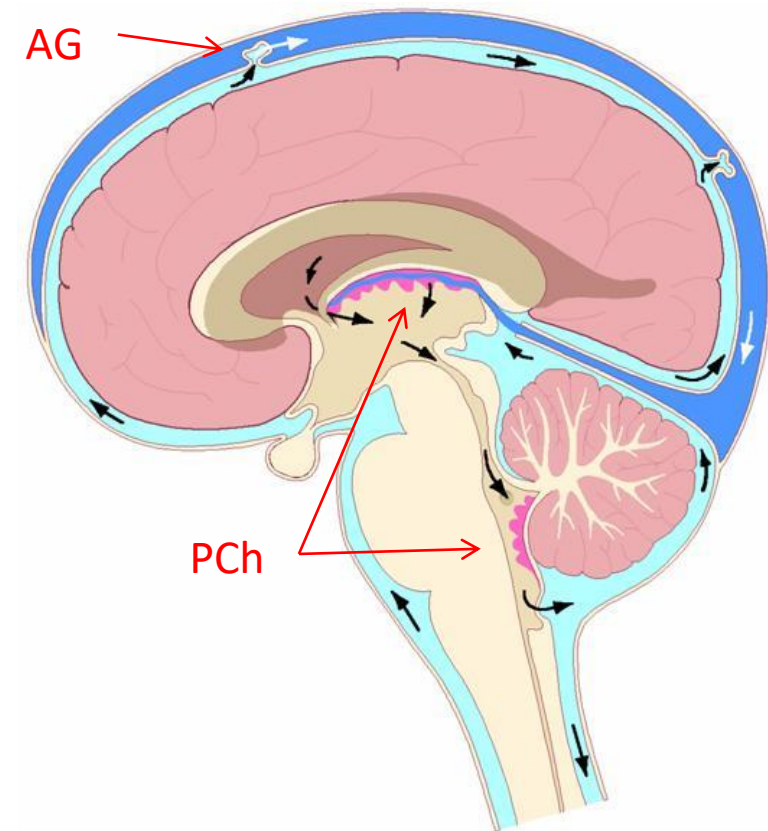
- Rich vascularisation
- Modified hematoencephalic barrier
- Sensors
- Secretion



http://www.neuros.org/index.php?option=com_photos&view=photos&oid=hafizbilal

Cerebrospinal fluid

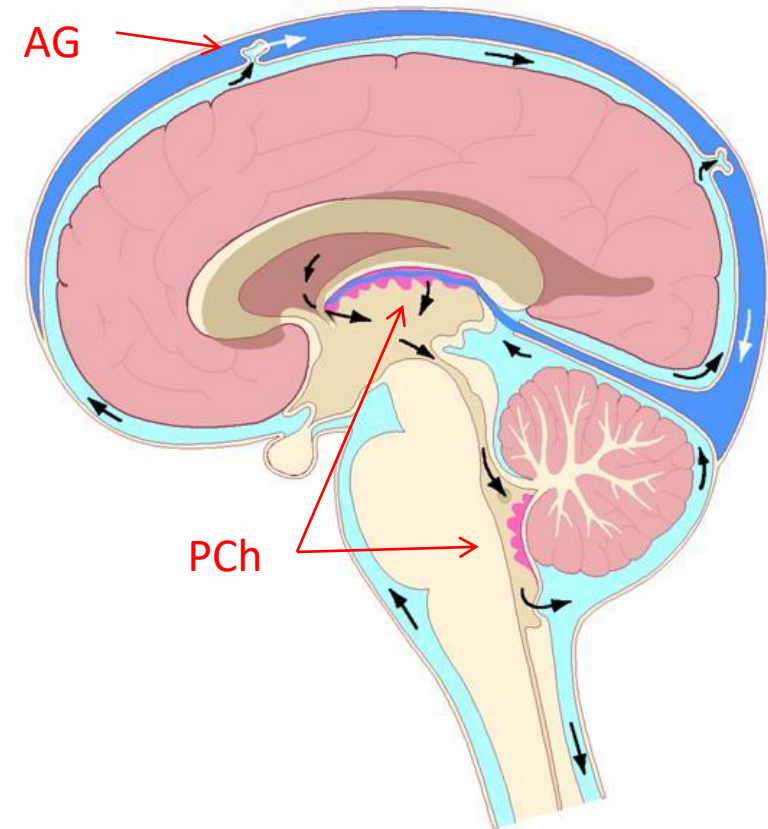
- Content
 - ✓ High levels of Mg^{+} and Na^{+}
 - ✓ Low levels of K^{+} and Ca^{2+}
 - ✓ Almost no cells (max 5/ml)
- Function
 - ✓ Protection
 - ✓ Microenvironment of neurons and glia
 - Metabolic function
 - Immunologic function
 - Transport function and so on



<http://www.control.tfe.umu.se>

Cerebrospinal fluid

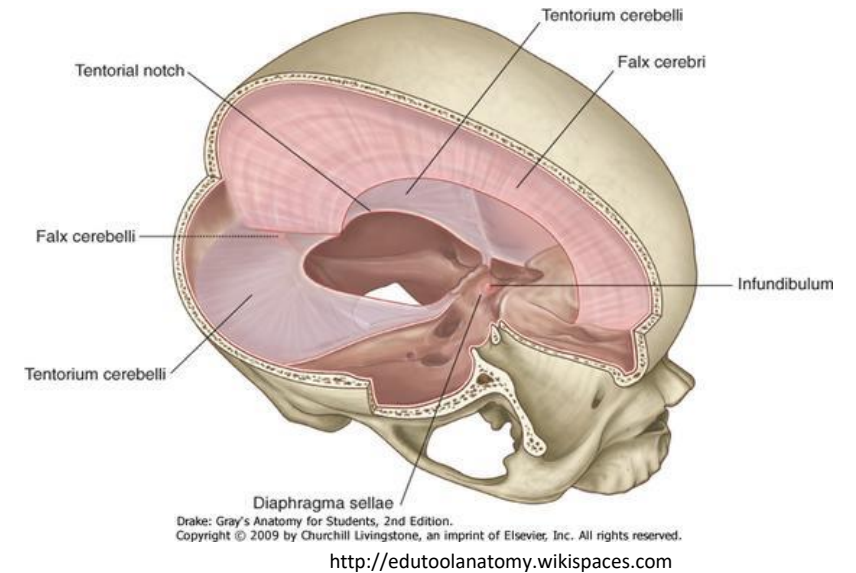
- Clear fluid produced by active secretion
- Liquor space
 - lined by ependymal cells
 - 150-250 ml
- Production
 - ✓ Plexus choroideus (PCh) -70%
 - ✓ Cell metabolism
 - ✓ Capillary filtration
 - 450-750 ml/day
- Resorption
 - ✓ Archnoid granulations (AG)



<http://www.control.tfe.umu.se>

Intracranial compartment

- Brain
- Cerebrospinal fluid
- Blood (intravascular)
- Intracranial pressure (ICP)
 - Critical determinant of cerebral perfusion
- Cerebral perfusion pressure (CPP)
pressure gradient driving blood
flow intracranially



$$!!! \text{ CPP } = \text{ MAP } - \text{ ICP } !!!$$

Cerebral perfusion pressure | Intracranial pressure
Mean arterial pressure

Cellular base of nervous system

Synapse

Cellular base of nervous system

- Neuronal cells
 - Reception, integration and propagation of information
 - Unique, irreplaceable
- Neuroglial cells
 - Support for neuronal cells
 - Easily replaceable
- The total amount of neuronal cells - 100 billions (10^{11})
- Neuron/glia ratio
 - 1/10 - 50 (Principles of Neural Science, 4th ed., 2012)
 - 1/2 – 10 (Principles of Neural Science, 5th ed., 2012)
 - 1/1 (Nolte's Human Brain, 7th ed., 2015)

Neuroglial cells

Central nervous system

- Astrocytes
 - Hematoencephalic b.
 - Homeostasis maintaining
 - Metabolism of neurotransmitters
 - Important during brain development
- Oligodendrocytes
 - Myelin sheat
- Microglia
 - Immune funtion
- Ependymal cells
 - Choroid plexus
 - (hemato-liquor barrier)
 - Ventricular lining
(liquoro-encephalic barrier)

Peripheral nervous system

- Satelite cells
 - Support functions in PNS

- Schwan cells
 - Myelin sheat

Background Activity

The inside of the cell

- ✓ ...
- ✓ Synthesis
- ✓ Transport
- ✓ ...

Neuron

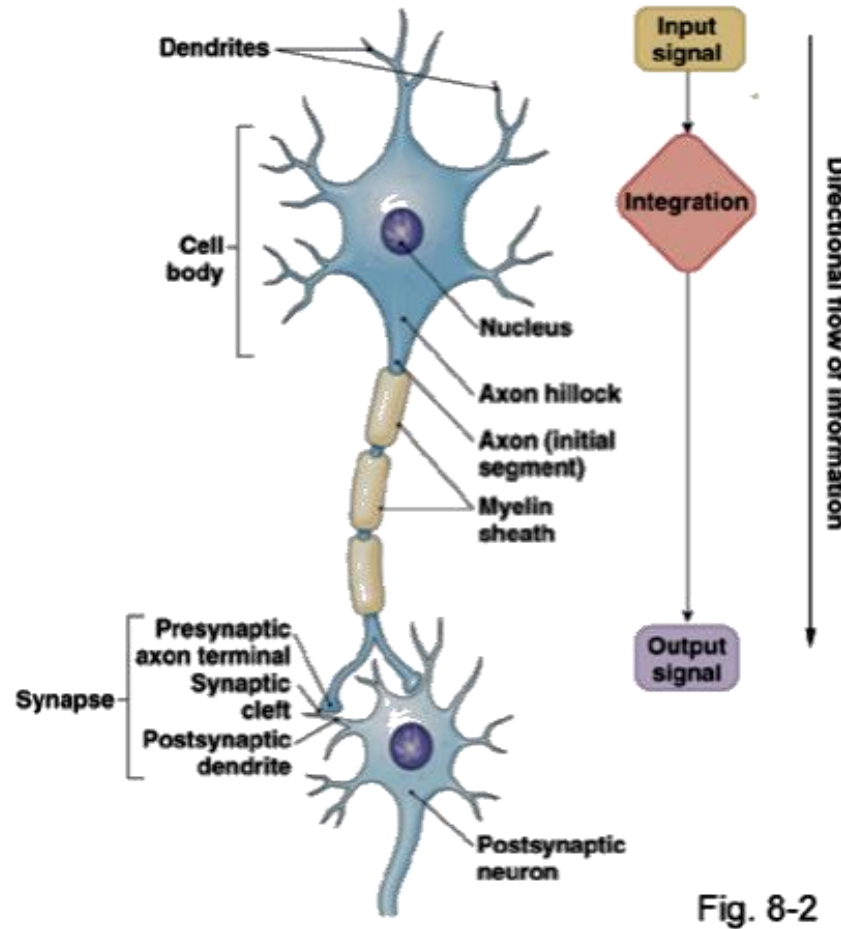


Fig. 8-2

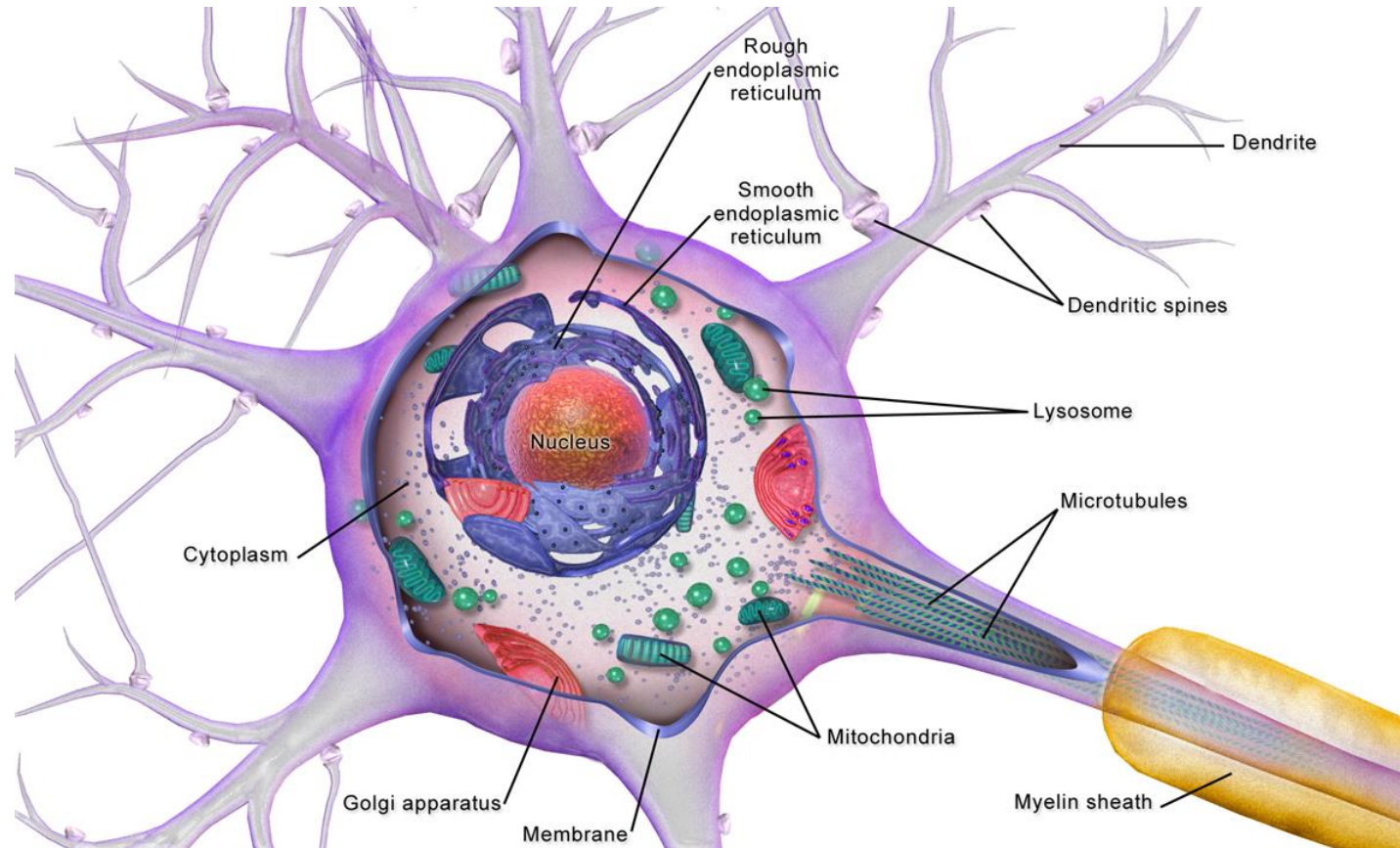
Information processing and transmission

The membrane

- ✓ Signal reception
- ✓ Signal integration
- ✓ AP generation
- ✓ AP propagation
- ✓ Signal transmission

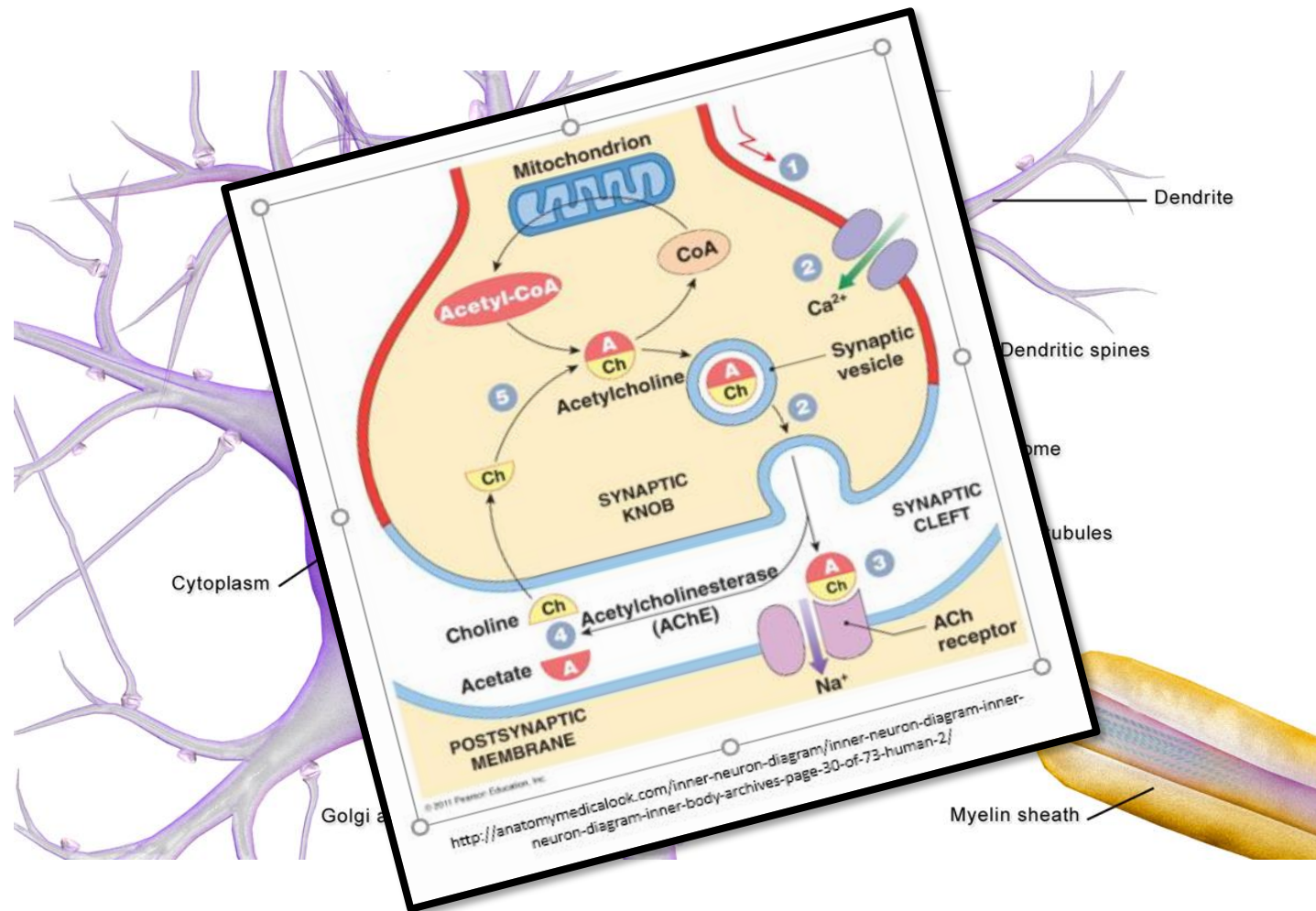
<http://www.slideshare.net/drpsdeb/presentations>

Background Activity



https://upload.wikimedia.org/wikipedia/commons/e/ed/Neuron_Cell_Body.png

Background Activity



https://upload.wikimedia.org/wikipedia/commons/e/ed/Neuron_Cell_Body.png

Background Activity

Fast axonal transport

- bidirectional
- ATP dependant
- associated with microtubules: dynein and kinesin

Fast axonal transport

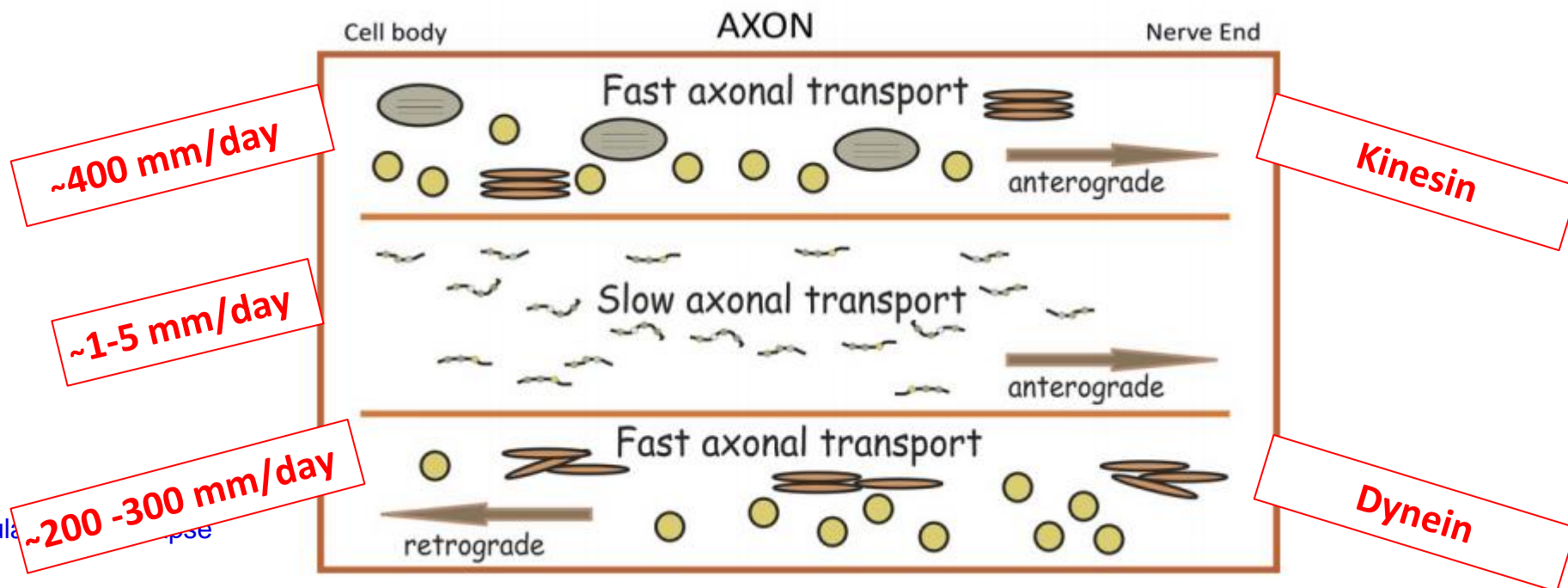
Golgi derived vesicles
lysosomes, mitochondria
structural elements of
endoplasmic reticulum

Slow axonal transport

- unidirectional,
- ATP independant
- conducted by sliding, polymerizing and protein interacting

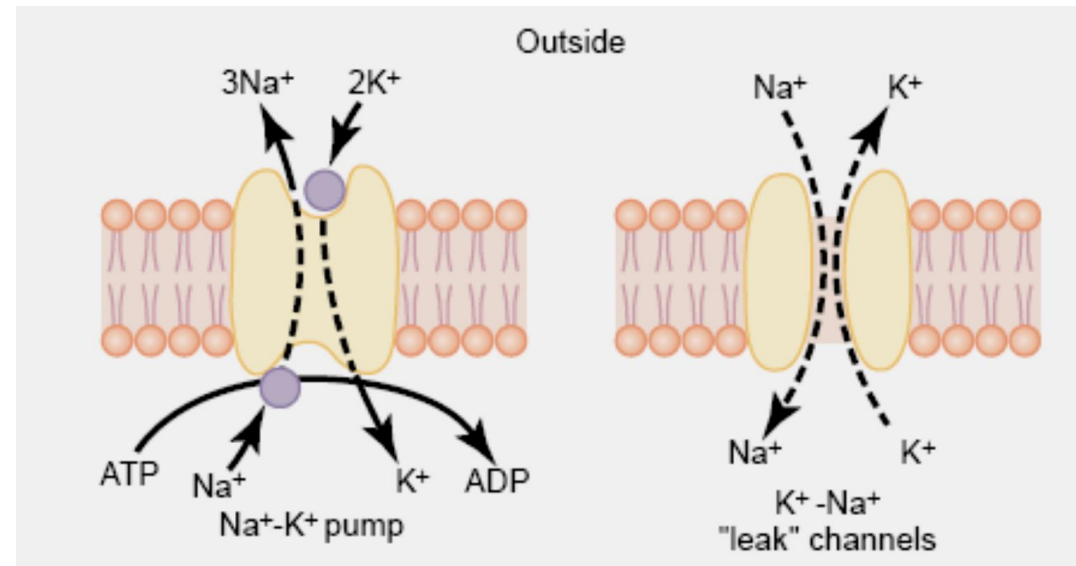
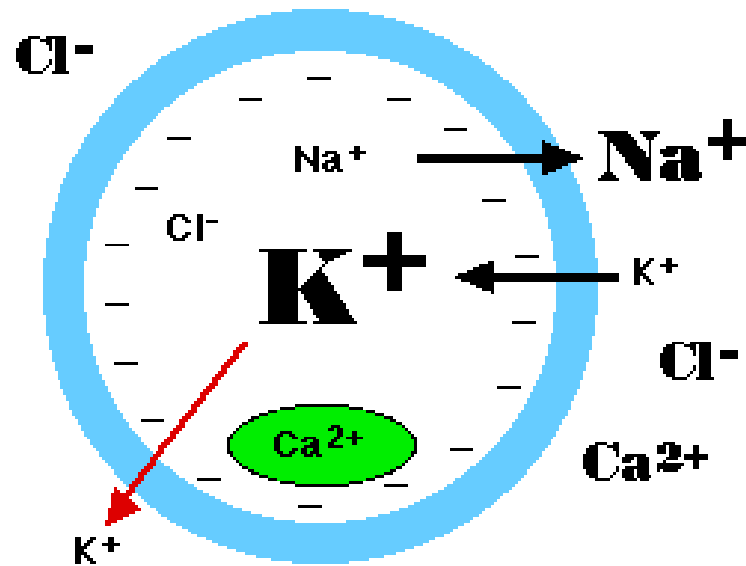
Slow axonal transport

microfilaments, microtubules
neurofilaments
cytosolic protein complexes



Membrane potential

- Due to differences in the concentrations of ions on opposite sides of a cellular membrane



<http://www.slideshare.net/drpsdeb/presentations>

Resting membrane potential of a neuron



<http://assassinscreed.ubi.com>

Resting potential
around -70 mV

- Highly instable state of membrane
- Why? – Speed!
- High energetical demands
 - ✓ Oxygen - 20% of total body consumption
 - ✓ Glucose – 25% of total body consumption

Action potential

- Quick voltage change on the membrane
- Spreads along the axon
- All or nothing principle

Resting potential
around -70 mV

Threshold potential
around -55 mV

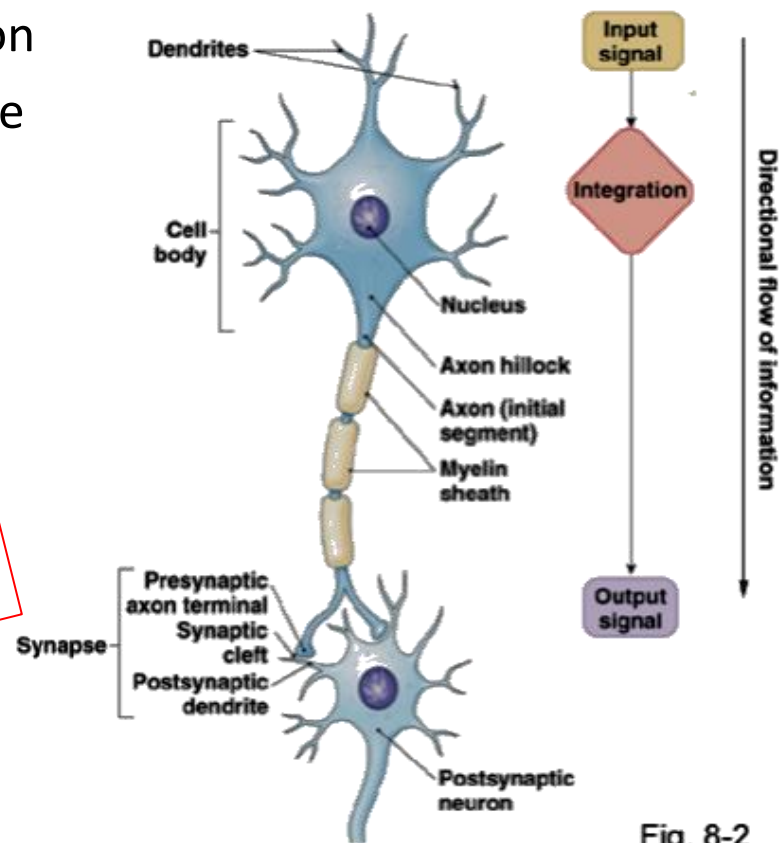
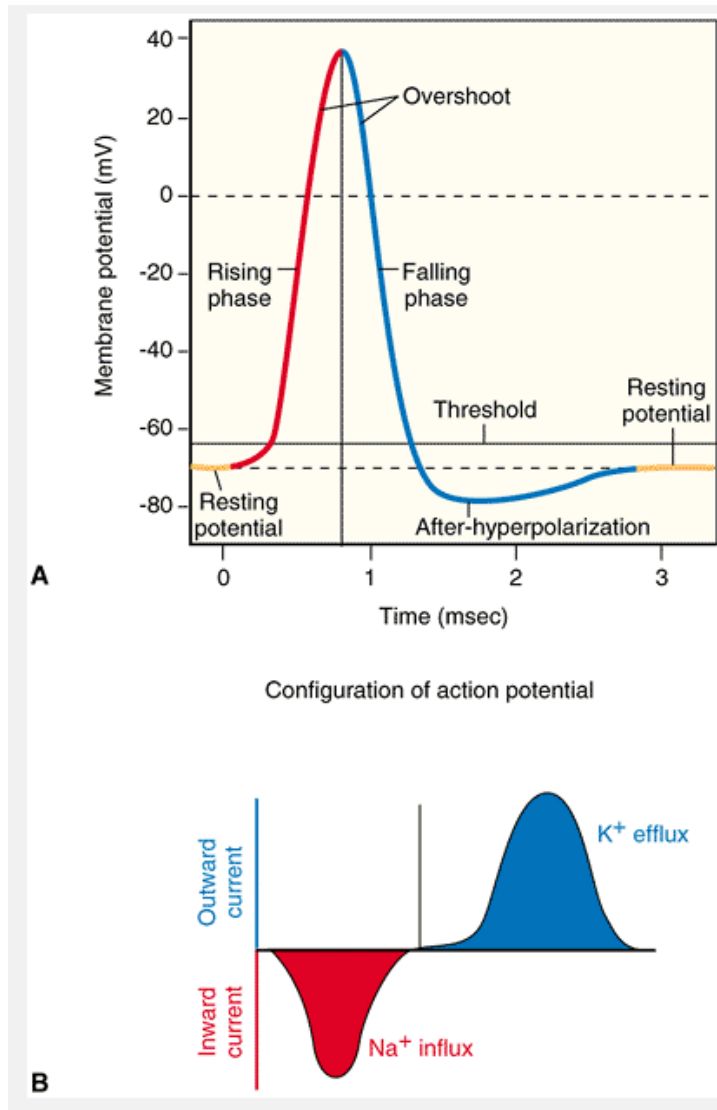
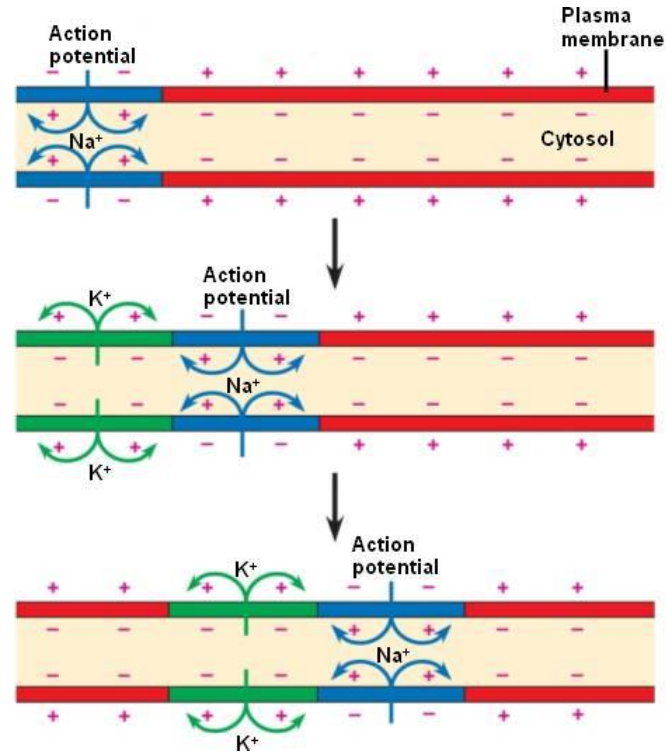
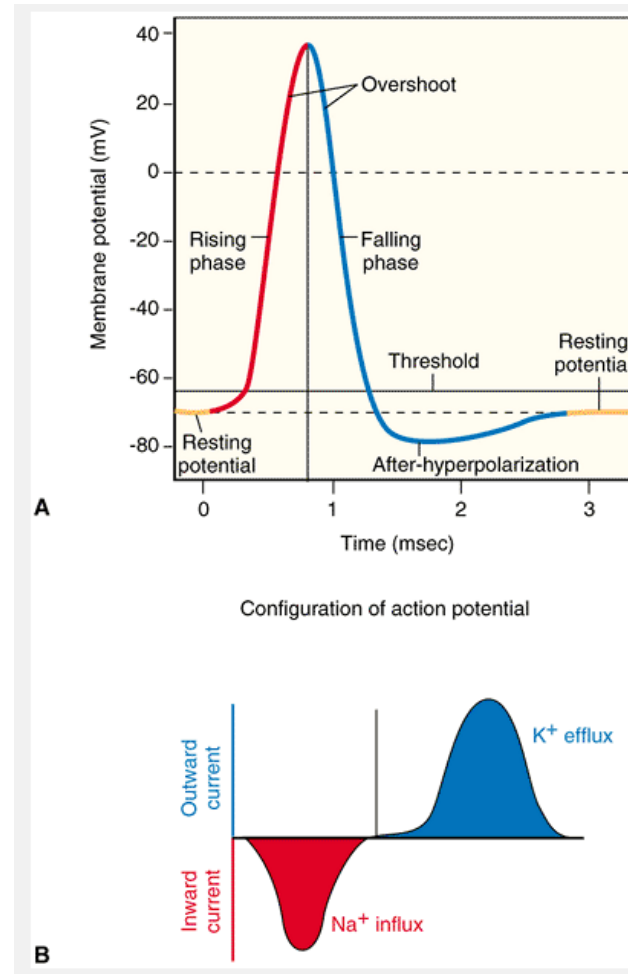


Fig. 8-2



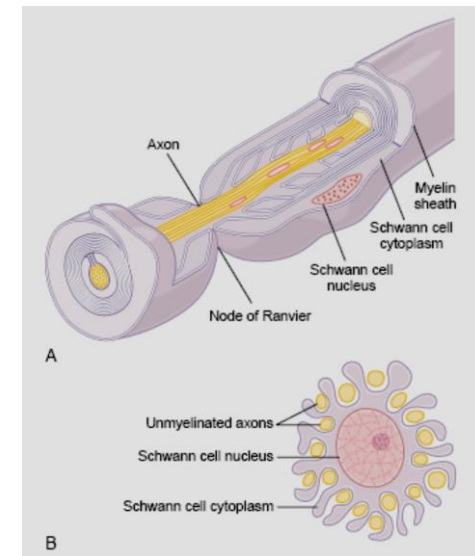
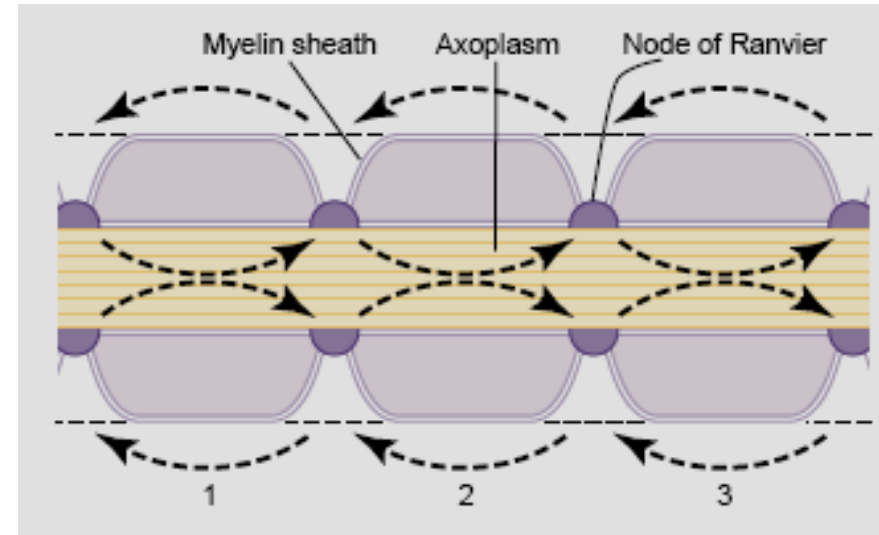
Action potential spreading



- Local currents
- Anterograde

Saltatory conduction

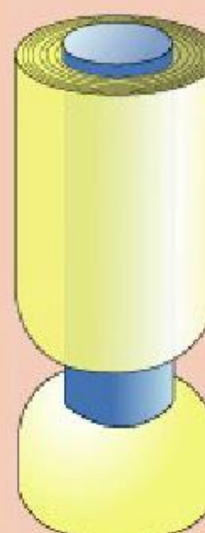
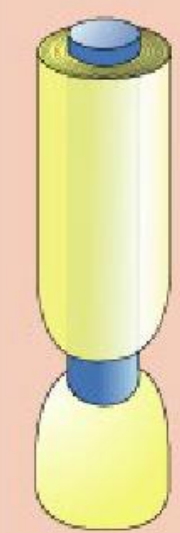


- Myelin sheath
- Nodes of Ranvier
- Economy
- Speed of conduction
- Speed of conduction also dependent of nerve fibre diameter
 - the electrical resistance is inversly proportional to area of cross-section



<http://www.slideshare.net/drpsdeb/presentations>

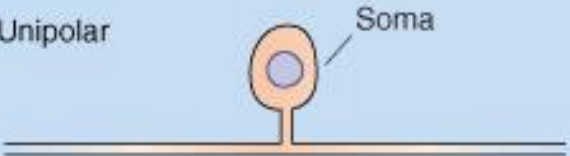

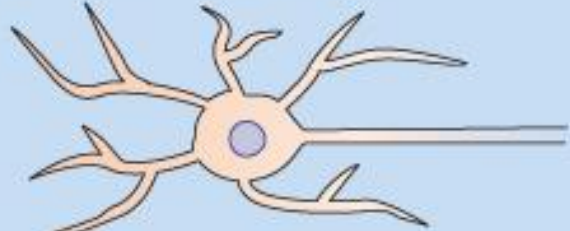
Classification of nerve fibers

- In humans mostly myelinated
- All fibers are myelinated in CNS
- Non-myelinated are evolutionary old ones

	A α	A β	A δ	C
1 ^o Axon to skin				
1 ^o Axon to muscle				
	Group I	Group II	Group III	Group IV
				
Diameter (um)	12-20	6-12	1-6	0.2-1.5
Speed(m/sec)	70-170	30-70	5-30	0.5-2
Sensory receptors	Proprioceptors of skeletal muscle	Mechanoreceptors of skin	Pain, temperature	Temp, pain, itch

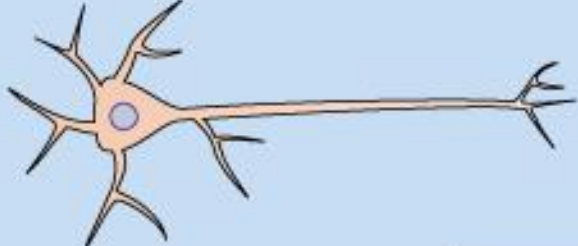
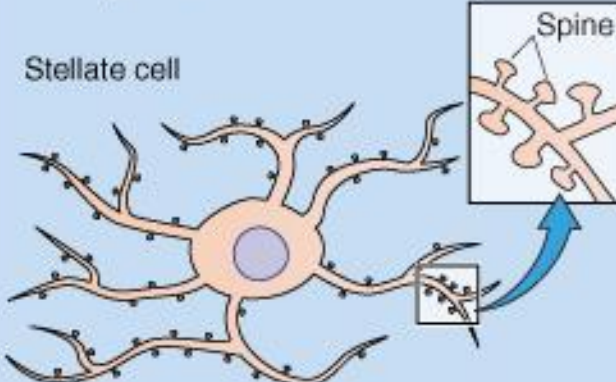
<http://neuroscience.uth.tmc.edu/s2/chapter04.html>

Neuronal classification

Basis for classification	Example	Functional implication	Structure
<p>3. Number of processes</p> <p>One process exits the cell body</p>	<p>Unipolar neuron (dorsal root ganglion cell)</p>	<p>Small area for receiving synaptic input: highly specialized function</p>	<p>Unipolar</p>  <p>Soma</p>
<p>Two processes exit the cell body</p>	<p>Bipolar neuron (retinal bipolar cell)</p>	<p>Small area for receiving synaptic input: highly specialized function</p>	<p>Bipolar</p> 
<p>Many processes exit the cell body</p>	<p>Multipolar neuron (spinal motor neuron)</p>	<p>Large area for receiving synaptic input; determines the pattern of incoming axons that can interact with the cell</p>	<p>Multipolar</p> 

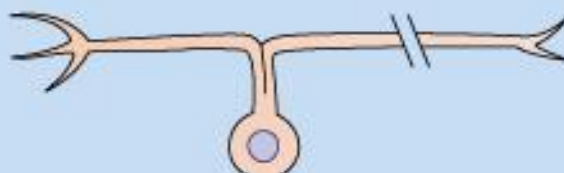

<http://www.slideshare.net/CsillaEgri/presentations>

Neuronal classification

Basis for classification	Example	Functional implication	Structure
2. Dendritic pattern Pyramid-shaped spread of dendrites	Pyramidal cell (hippocampal pyramidal neuron)	Large area for receiving synaptic input; determines the pattern of incoming axons that can interact with the cell (i.e., pyramid-shaped)	Pyramidal cell 
Radial-shaped spread of dendrites	Stellate cell (cortical stellate cell)	Large area for receiving synaptic input; determines pattern of incoming axons that can interact with the cell (i.e., star-shaped)	Stellate cell 

<http://www.slideshare.net/CsillaEgri/presentations>

Neuronal classification

Basis for classification	Example	Functional implication	Structure
<p>1. Axonal projection</p> <p>Goes to a distant brain area</p>	<p>Projection neuron or Principal neuron or Golgi type I cell (cortical motor neuron)</p>	<p>Affects different brain areas</p>	<p>Dorsal root ganglion cell</p> 
<p>Stays in a local brain area</p>	<p>Intrinsic neuron or Interneuron or Golgi type II cell (cortical inhibitory neuron)</p>	<p>Affects only nearby neurons</p>	<p>Retinal bipolar cell</p> 

<http://www.slideshare.net/CsillaEgri/presentations>

Synapse

- Communication between neurons
- Electrical
- Chemical

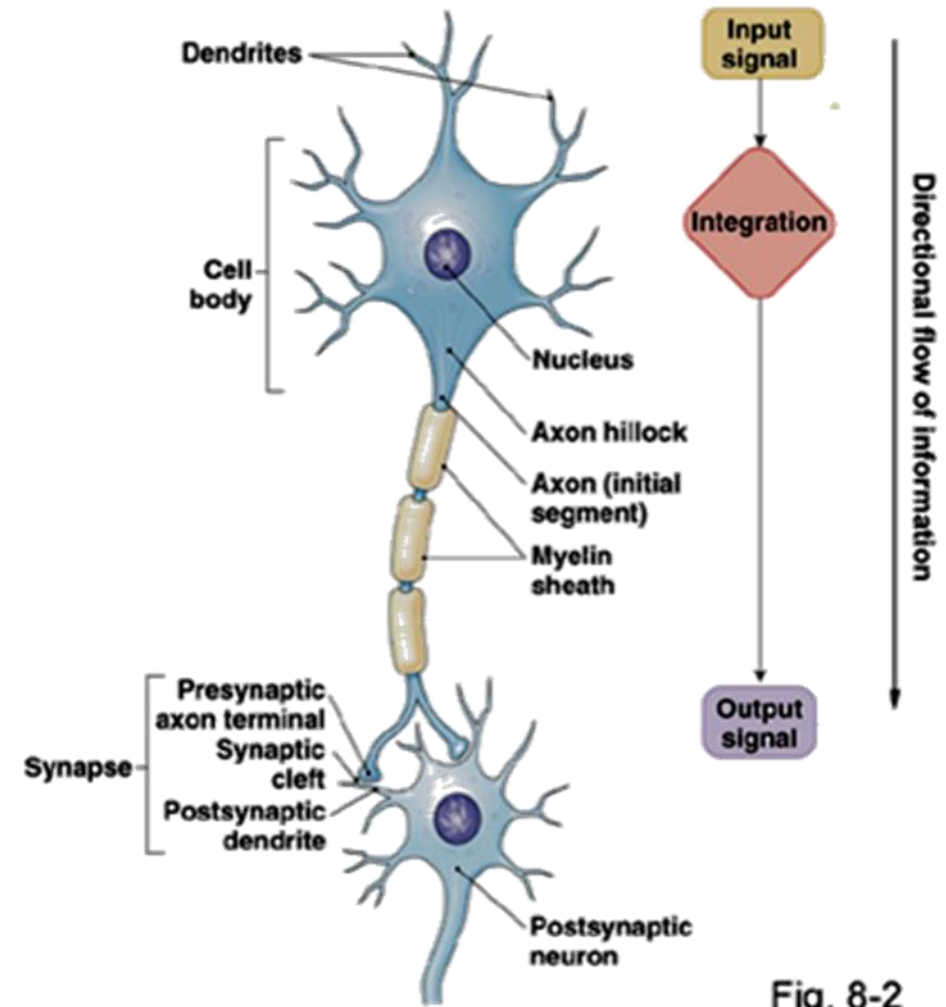
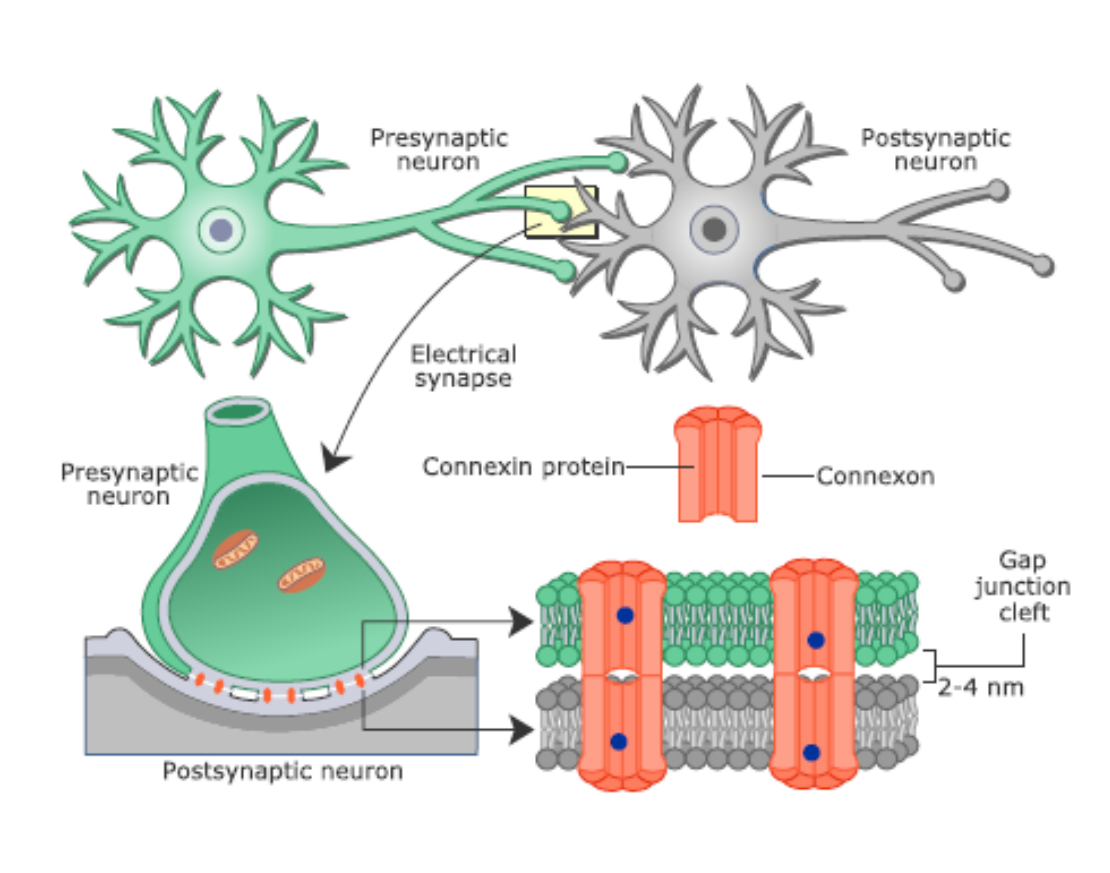


Fig. 8-2

<http://www.slideshare.net/CsillaEgri/presentations>

Electrical synapse

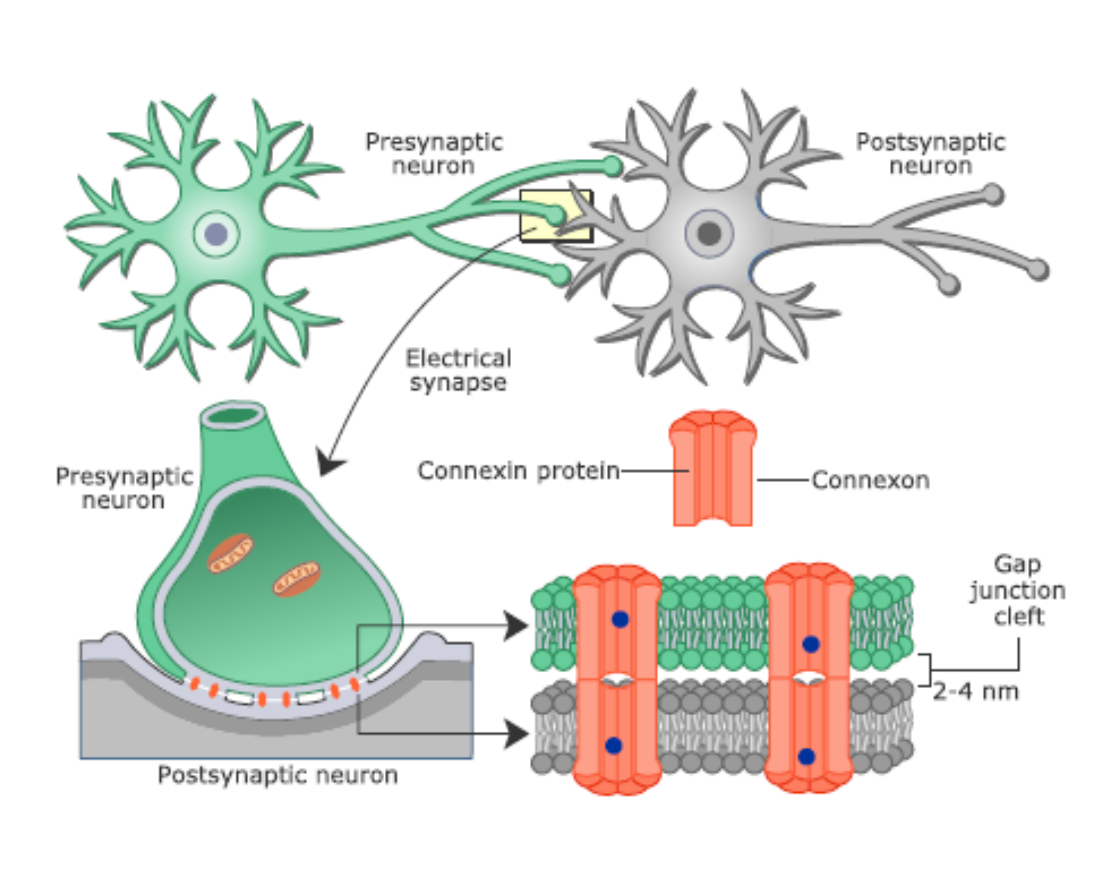
- Evolutionary old
- Less frequent than ch.
- Ubiquitous



<http://www.slideshare.net/CsillaEgri/presentations>

Electrical synapse

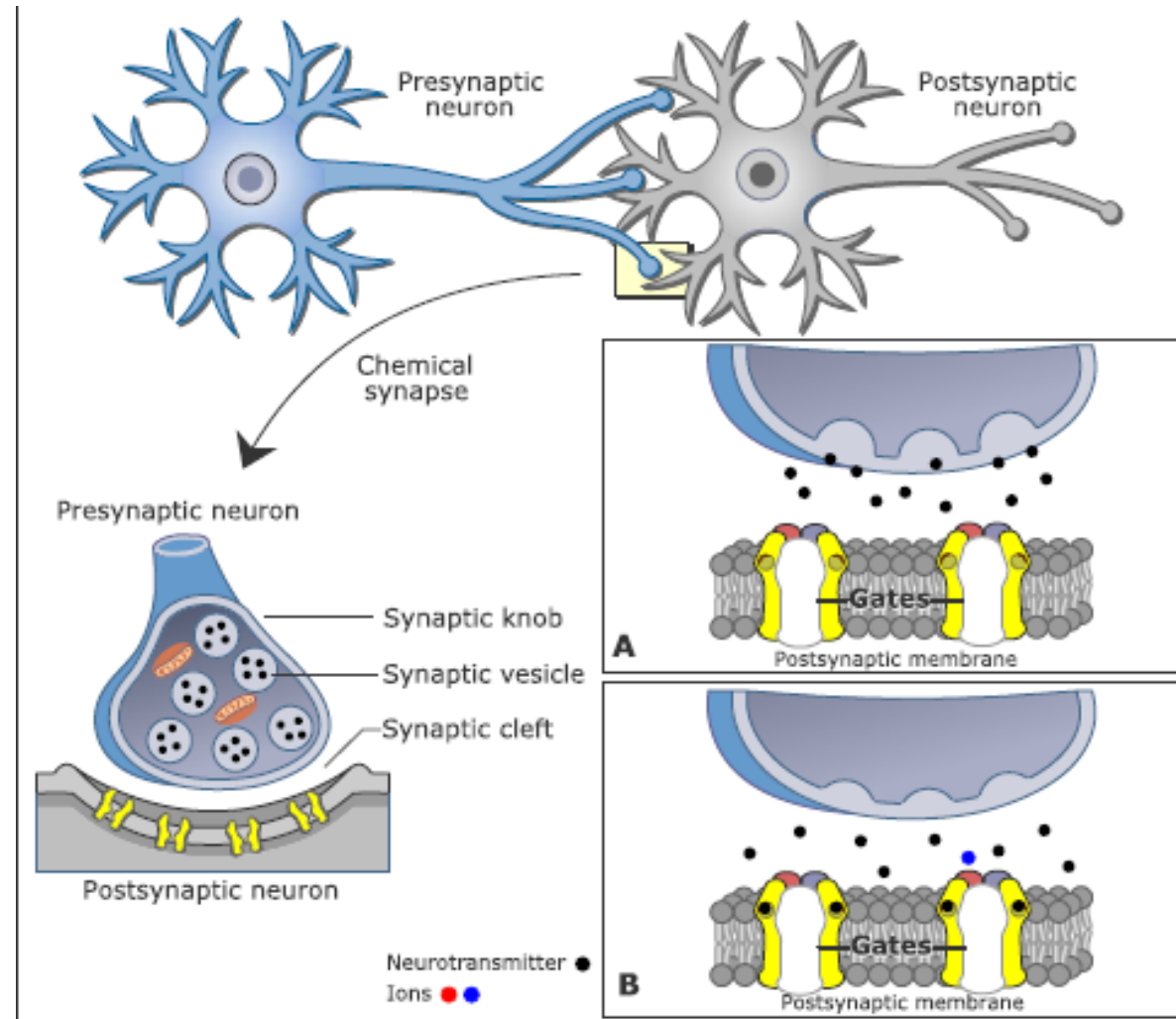
- Evolutionary old
- Less frequent than ch.
- Ubiquitous
- Gap junctions
- Bidirectional transmission
- Fast
- Strength of signal may decrease



<http://www.slideshare.net/CsillaEgri/presentations>

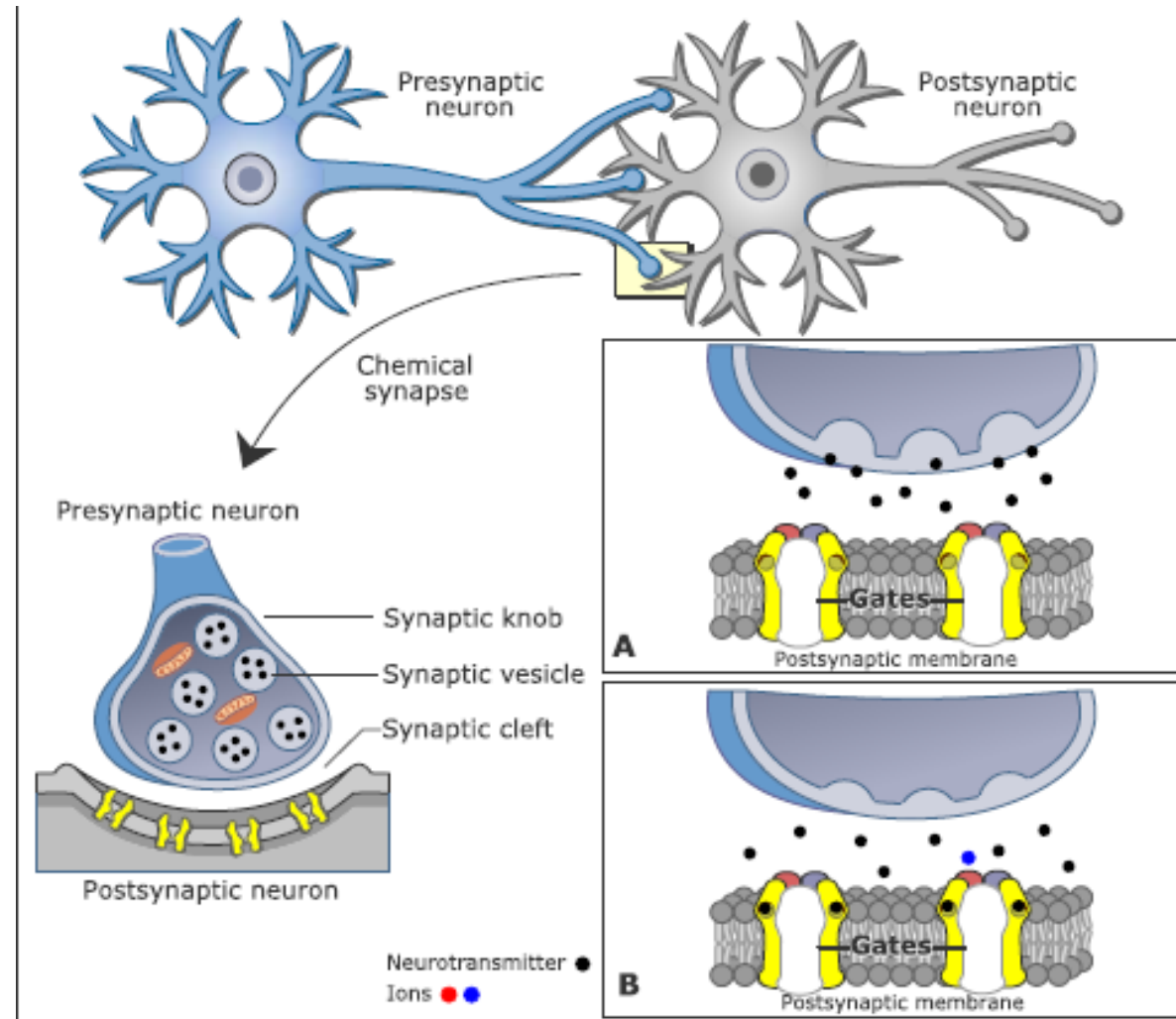
Chemical synapse

- Evolutionary young
- Majority type of s.

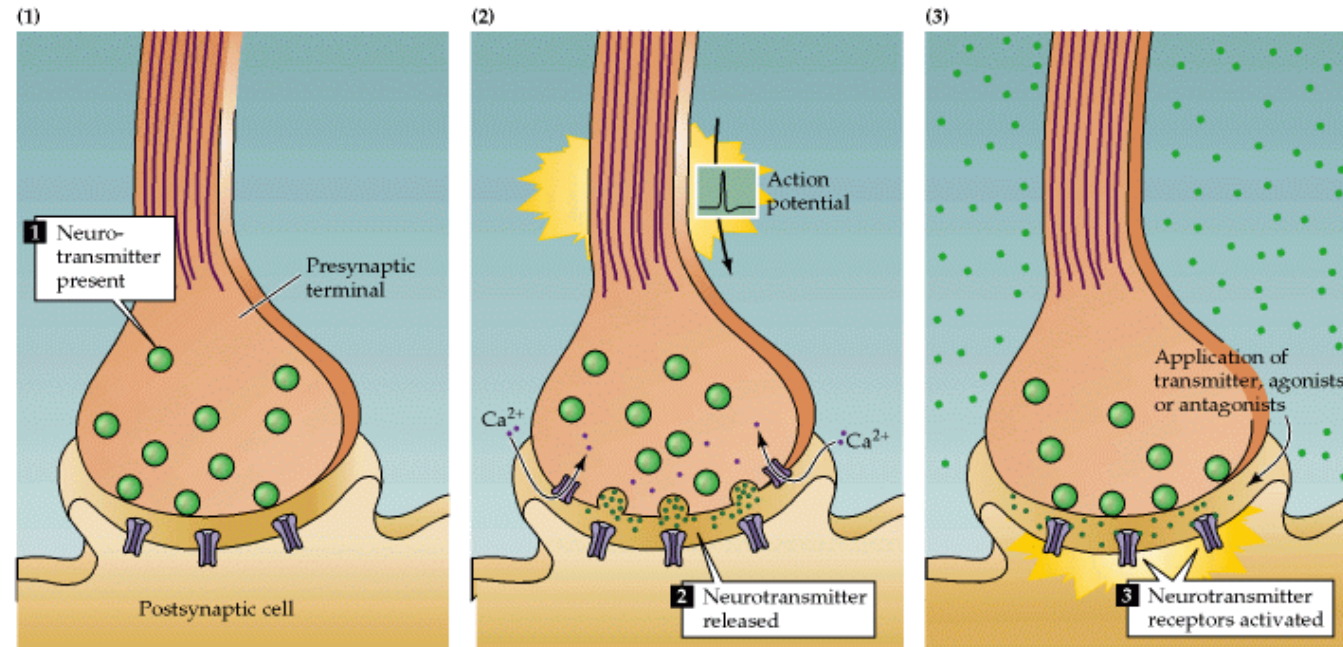


Chemical synapse

- Evolutionary young
- Majority type of s.
- Unidirectional
- Synaptic cleft
- Neurotransmitter
- Constant signal strength



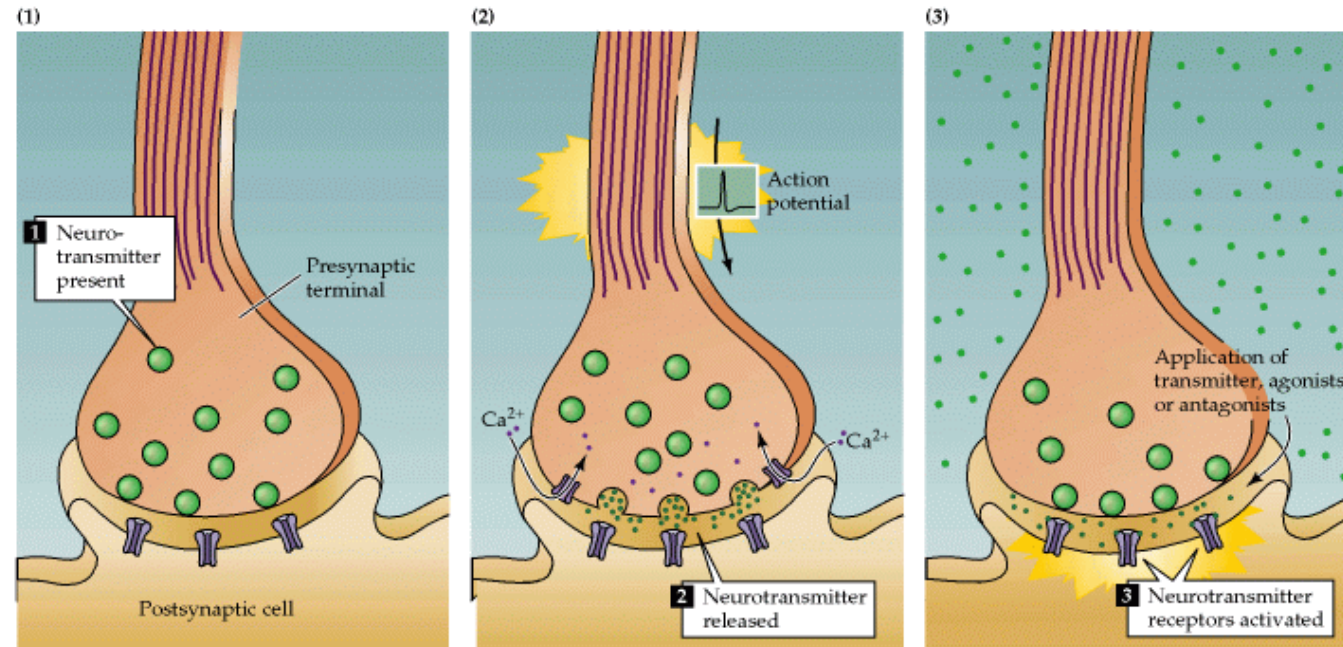
Neurotransmitter



<http://www.slideshare.net/CsillaEgri/presentations>

- Present in presynaptic neuron

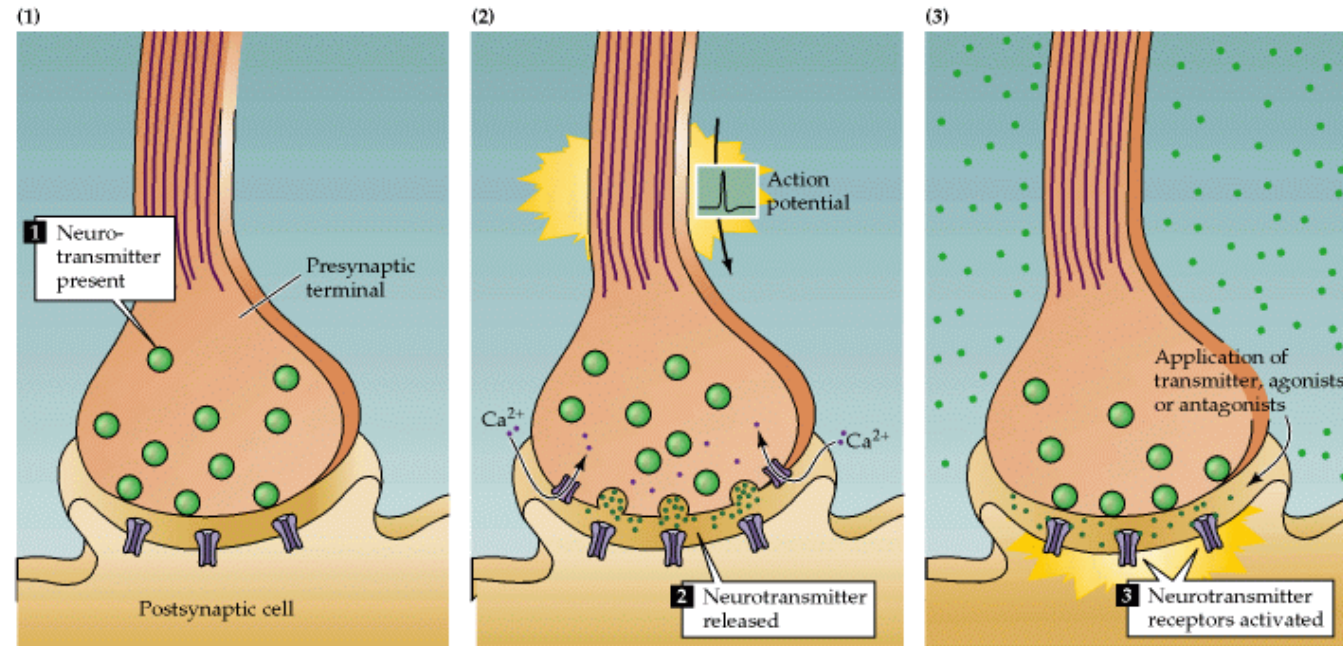
Neurotransmitter



<http://www.slideshare.net/CsillaEgri/presentations>

- Present in presynaptic neuron
- Released into the synaptic cleft due to depolarization of presynaptic neuron (Ca^{2+} dependent mechanism)

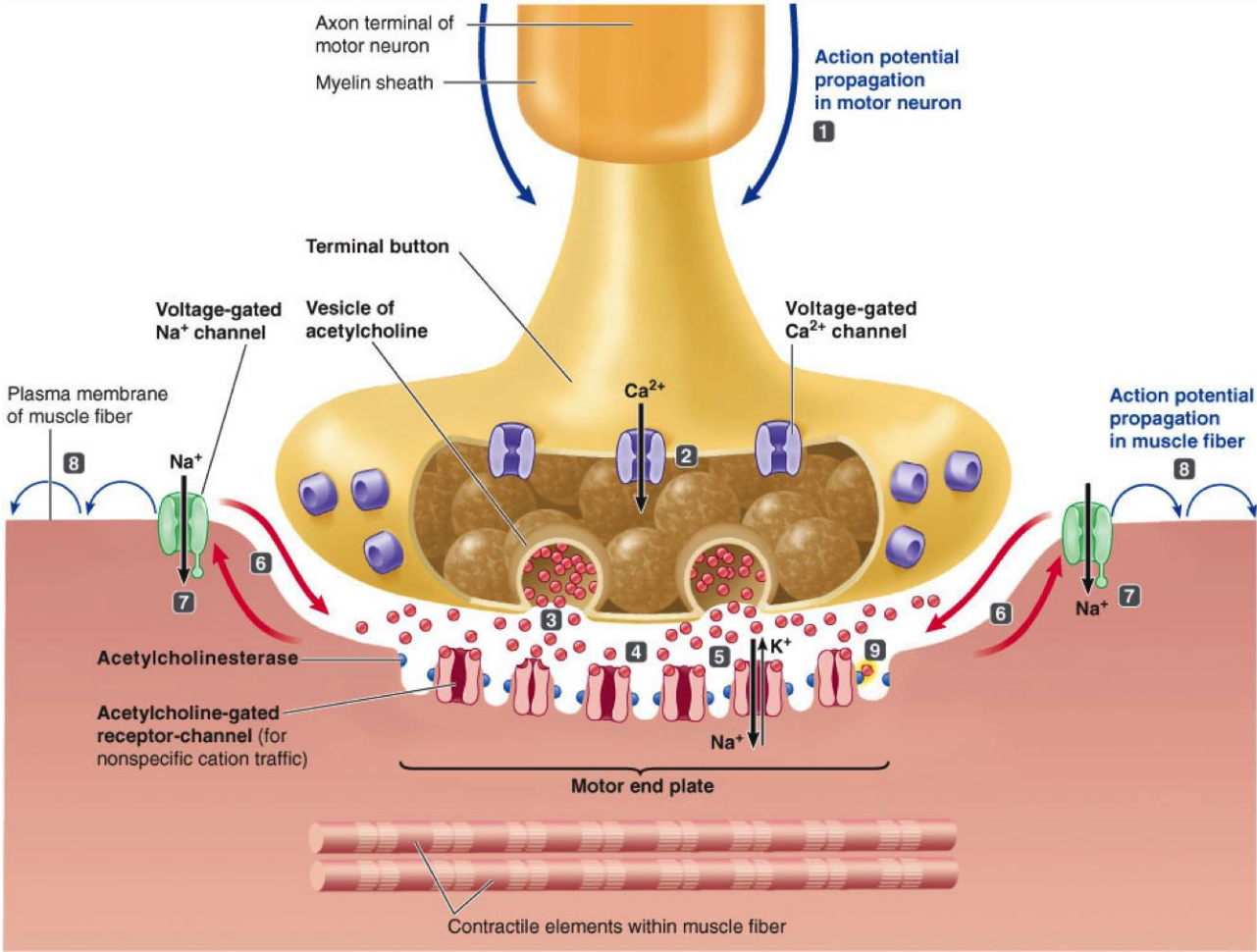
Neurotransmitter



<http://www.slideshare.net/CsillaEgri/presentations>

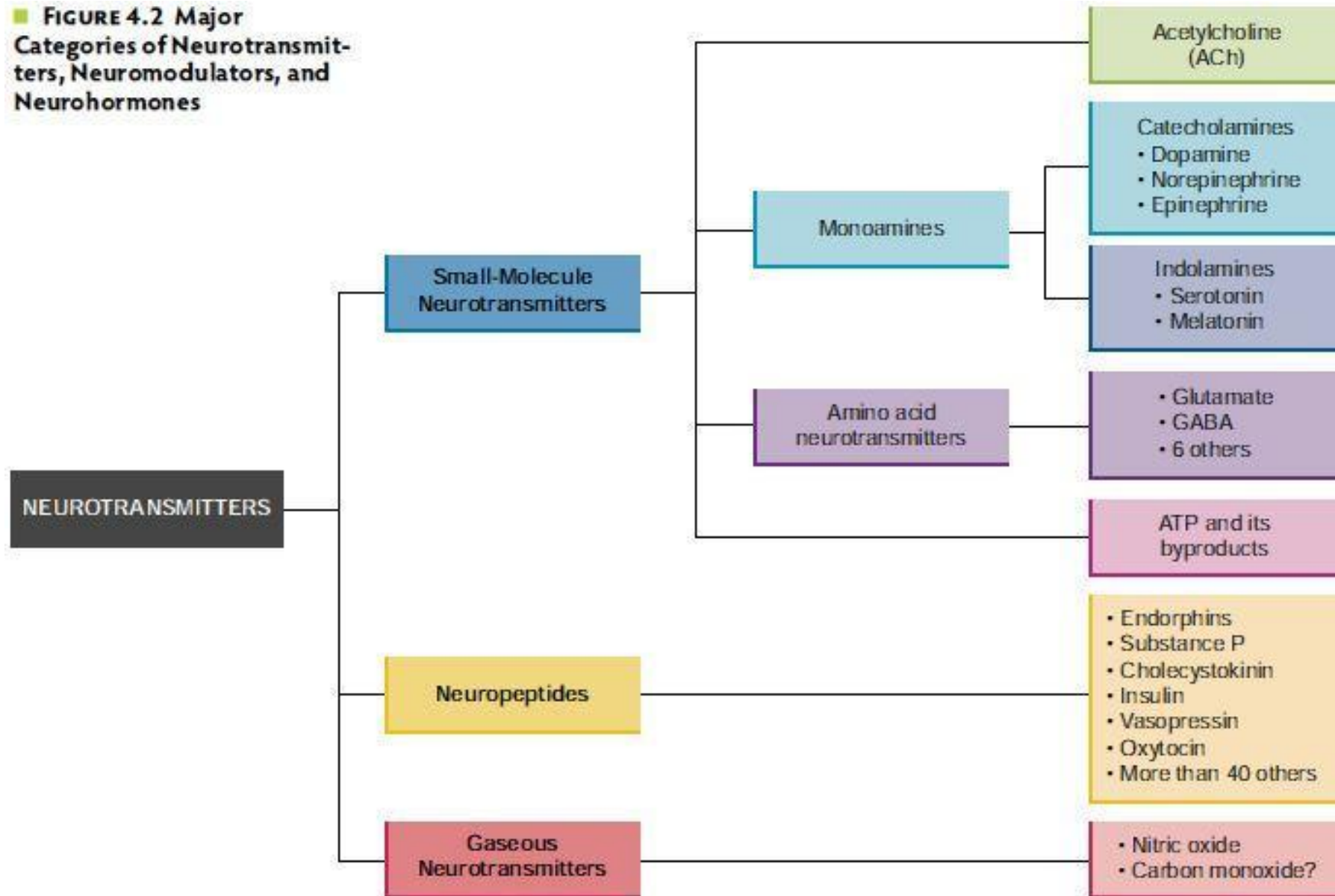
- Present in presynaptic neuron
- Released into the synaptic cleft due to depolarization of presynaptic neuron (Ca^{2+} dependent mechanism)
- Specific receptor has to be present in postsynaptic membrane

Neuromuscular junction



https://classconnection.s3.amazonaws.com/754/flashcards/2034754/png/ch_7_pic_41349381290275.png

■ **FIGURE 4.2 Major Categories of Neurotransmitters, Neuromodulators, and Neurohormones**



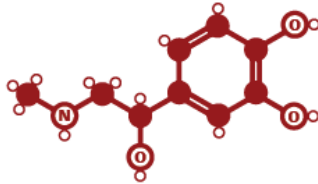
<https://classconnection.s3.amazonaws.com/108/flashcards/956108/jpg/bookpic421333407057201.jpg>

THE STRUCTURES OF NEUROTRANSMITTERS

STRUCTURE KEY: ● Carbon atom ○ Hydrogen atom ○ Oxygen atom (N) Nitrogen atom (R) Rest of molecule

ADRENALINE

Fight or flight neurotransmitter



Produced in stressful or exciting situations. Increases heart rate & blood flow, leading to a physical boost & heightened awareness.

NORADRENALINE

Concentration neurotransmitter



Affects attention & responding actions in the brain, & involved in fight or flight response. Contracts blood vessels, increasing blood flow.

DOPAMINE

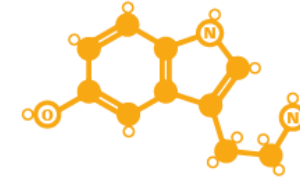
Pleasure neurotransmitter



Feelings of pleasure, and also addiction, movement, and motivation. People repeat behaviours that lead to dopamine release.

SEROTONIN

Mood neurotransmitter



Contributes to well-being & happiness; helps sleep cycle & digestive system regulation. Affected by exercise & light exposure.

GABA

Calming neurotransmitter



Calms firing nerves in CNS. High levels improve focus; low levels cause anxiety. Also contributes to motor control & vision.

ACETYLCHOLINE

Learning neurotransmitter



Involved in thought, learning, & memory. Activates muscle action in the body. Also associated with attention and awakening.

GLUTAMATE

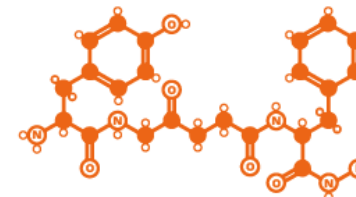
Memory neurotransmitter



Most common brain neurotransmitter. Involved in learning & memory, regulates development & creation of nerve contacts.

ENDORPHINS

Euphoria neurotransmitters



Released during exercise, excitement, & sex, producing well-being & euphoria, reducing pain. Biologically active section shown.



© COMPOUND INTEREST 2015 - WWW.COMPOUNDCHEM.COM | Twitter: @compoundchem | Facebook: www.facebook.com/compoundchem
This graphic is shared under a Creative Commons Attribution-NonCommercial-NoDerivatives licence.

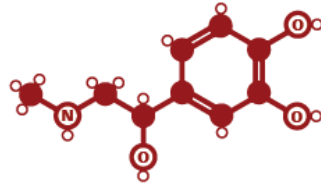


THE STRUCTURES OF NEUROTRANSMITTERS

STRUCTURE KEY: ● Carbon atom ○ Hydrogen atom ⊙ Oxygen atom ⊙ Nitrogen atom ⊙ Rest of molecule

ADRENALINE

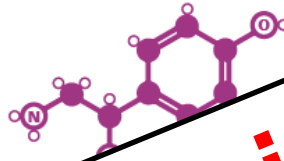
Fight or flight neurotransmitter



Produced in stressful or exciting situations. Increases heart rate & blood flow, leading to a physical boost & heightened awareness.

NORADRENALINE

Concentration neurotransmitter



Excitatory
(Glutamate, acetylcholin)

x
Inhibitory
(GABA)

GABA

Calming neurotransmitter



Calms firing nerves in CNS. High levels improve focus; low levels cause anxiety. Also contributes to motor control & vision.

DOPAMINE

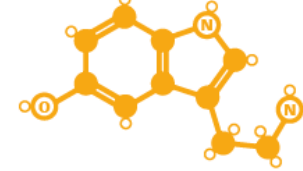
Pleasure neurotransmitter



Most common brain neurotransmitter. Involved in learning & memory, regulates development & creation of nerve contacts.

SEROTONIN

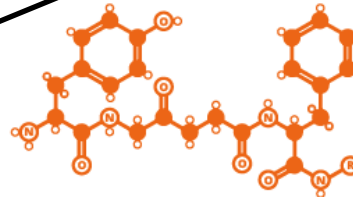
Mood neurotransmitter



Contributes to well-being & happiness; helps sleep cycle & digestive system regulation. Affected by exercise & light exposure.

ENDORPHINS

Euphoria neurotransmitters



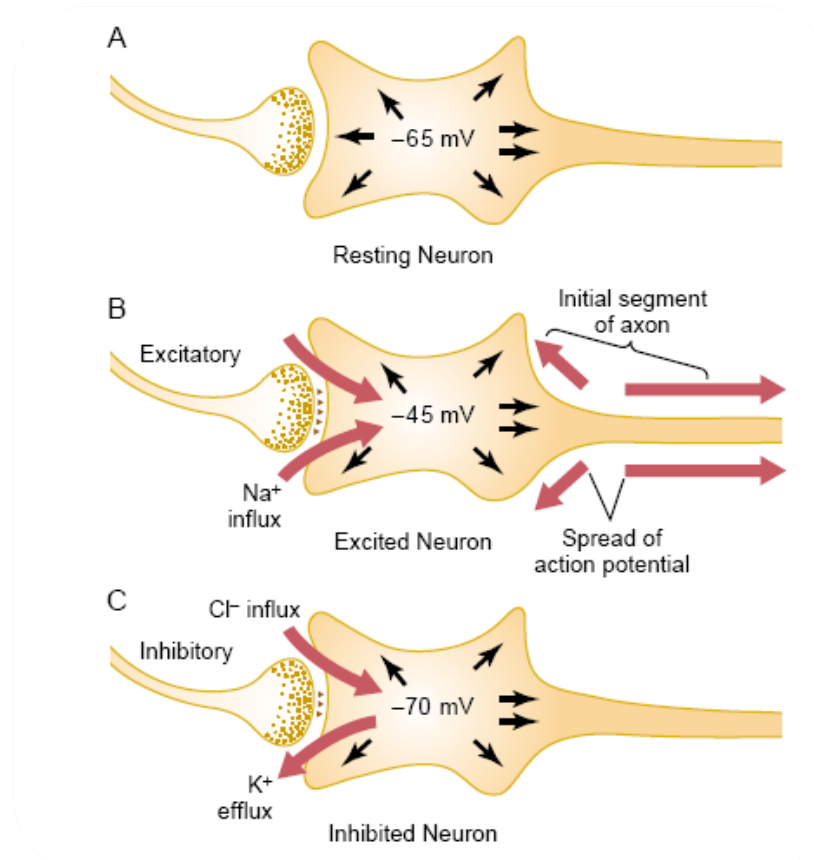
Released during exercise, excitement, & sex, producing well-being & euphoria, reducing pain. Biologically active section shown.



© COMPOUND INTEREST 2015 - WWW.COMPOUNDCHEM.COM | Twitter: @compoundchem | Facebook: www.facebook.com/compoundchem
This graphic is shared under a Creative Commons Attribution-NonCommercial-NoDerivatives licence.



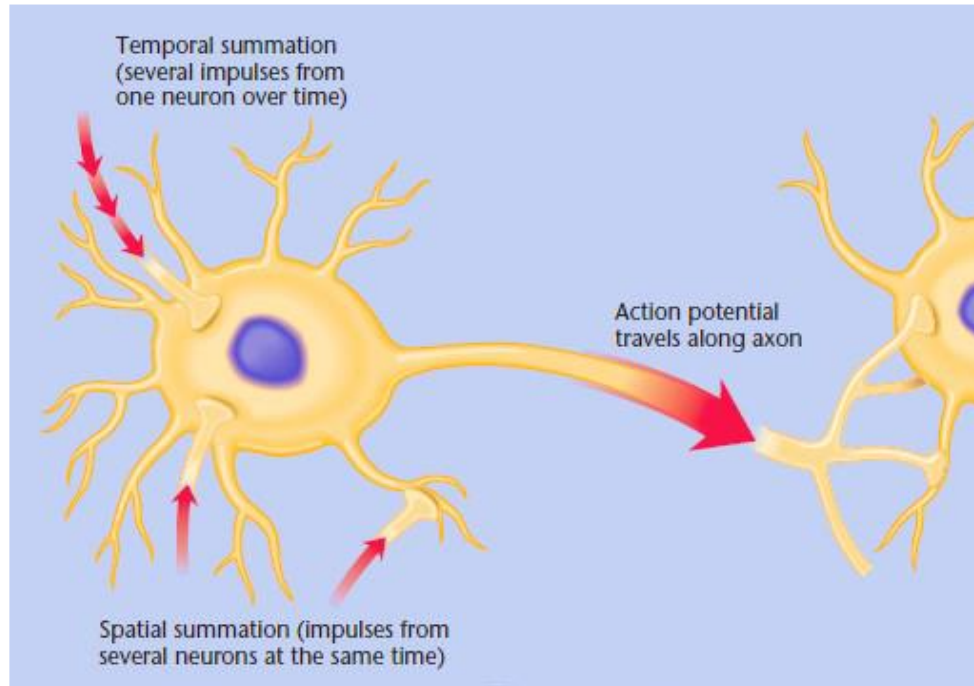
Excitatory/inhibitory postsynaptic potential



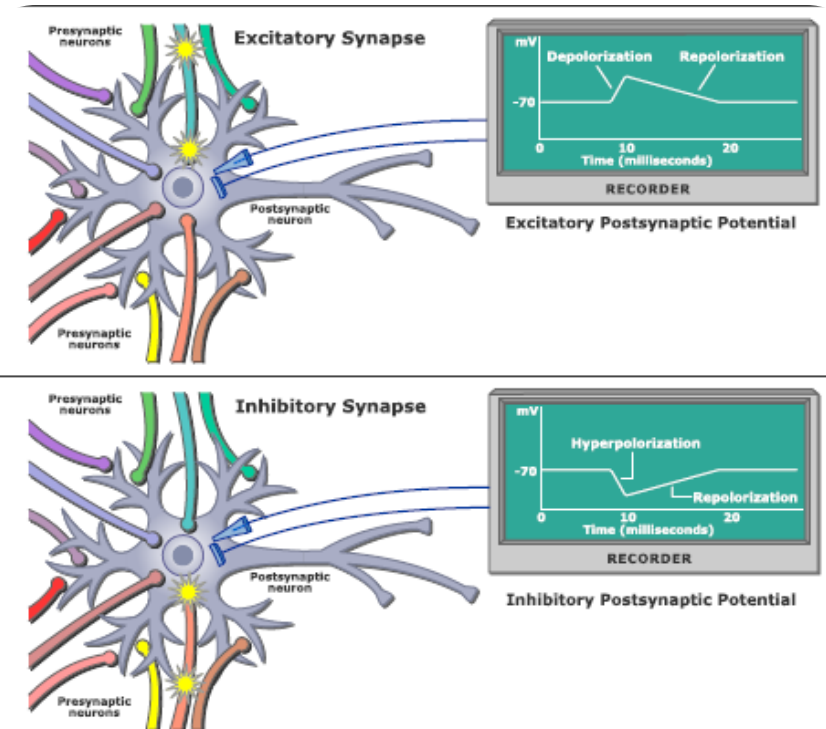
<http://www.slideshare.net/drpsdeb/presentations>

Signal summation

- Temporal
- Spatial

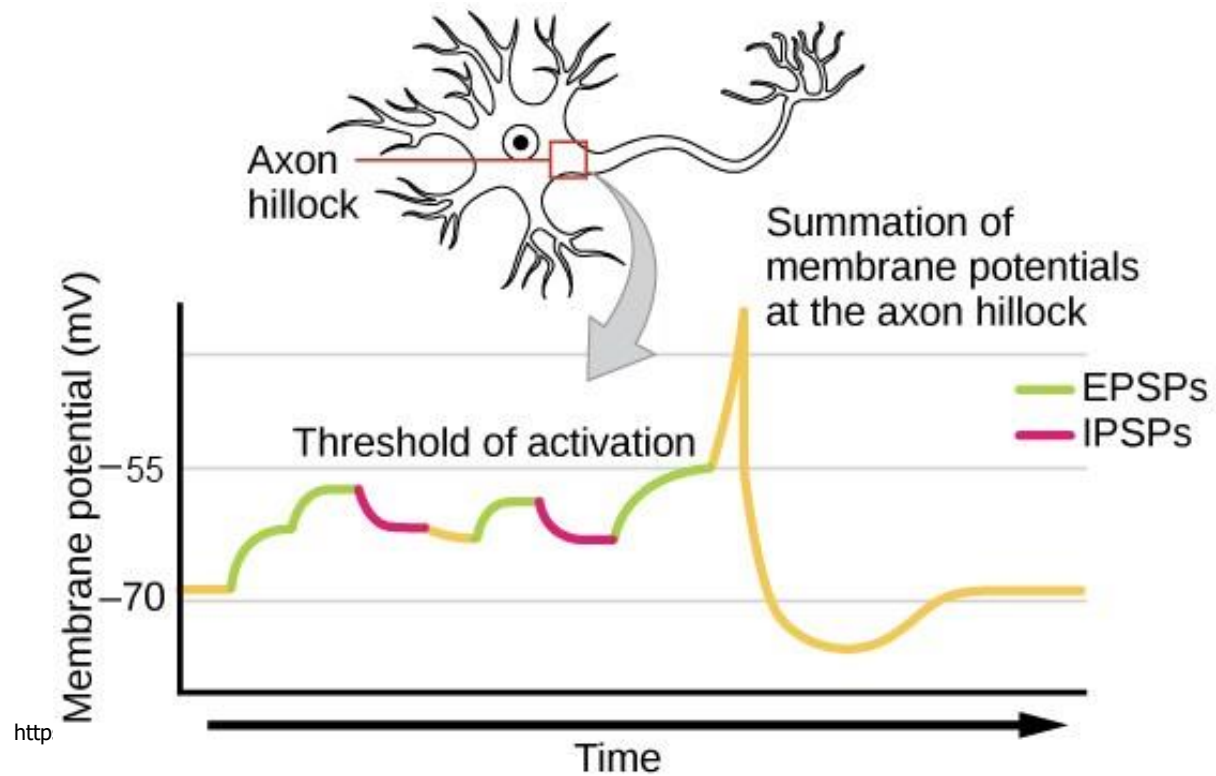


https://www.slideshare.net/drgabe/biological-psychology-synapses?from_action=save



<http://www.slideshare.net/drpsdeb/presentations>

Signal summation



http

<http://www.geon.us/Memory/images/Summation.jpg>

Synaptic convergence

Average number of synapses in one neuronal cell in primates

- ✓ Primary visual cortex (area17)
– aprox. 4 000
- ✓ Primary motor cortex (area4)
– aprox. 60 000

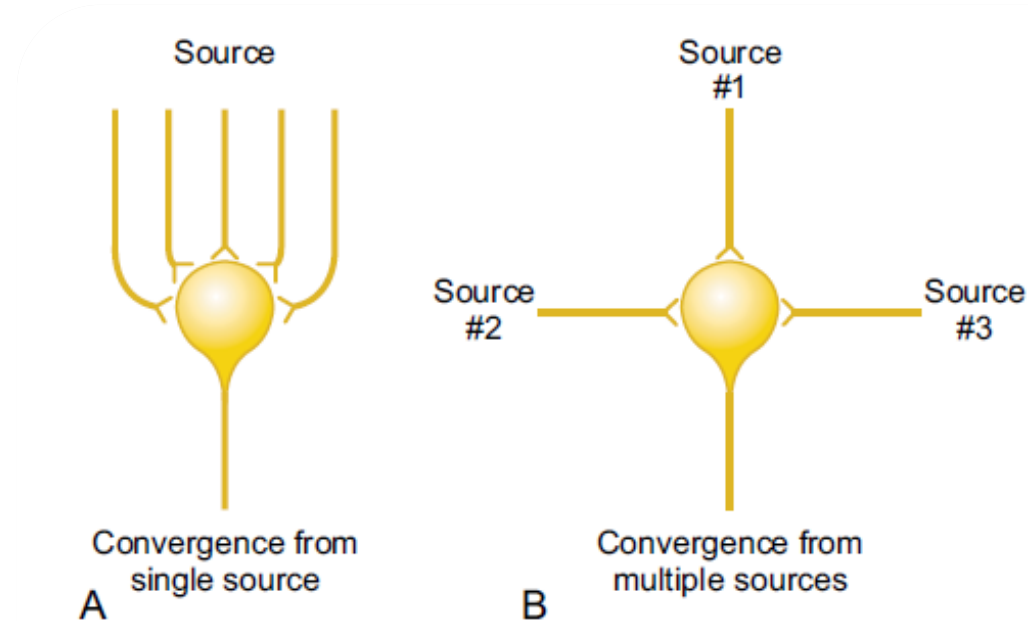


Figure 46-12

"Convergence" of multiple input fibers onto a single neuron. *A*, Multiple input fibers from a single source. *B*, Input fibers from multiple separate sources.

<http://www.slideshare.net/drpsdeb/presentations>

Synaptic divergence

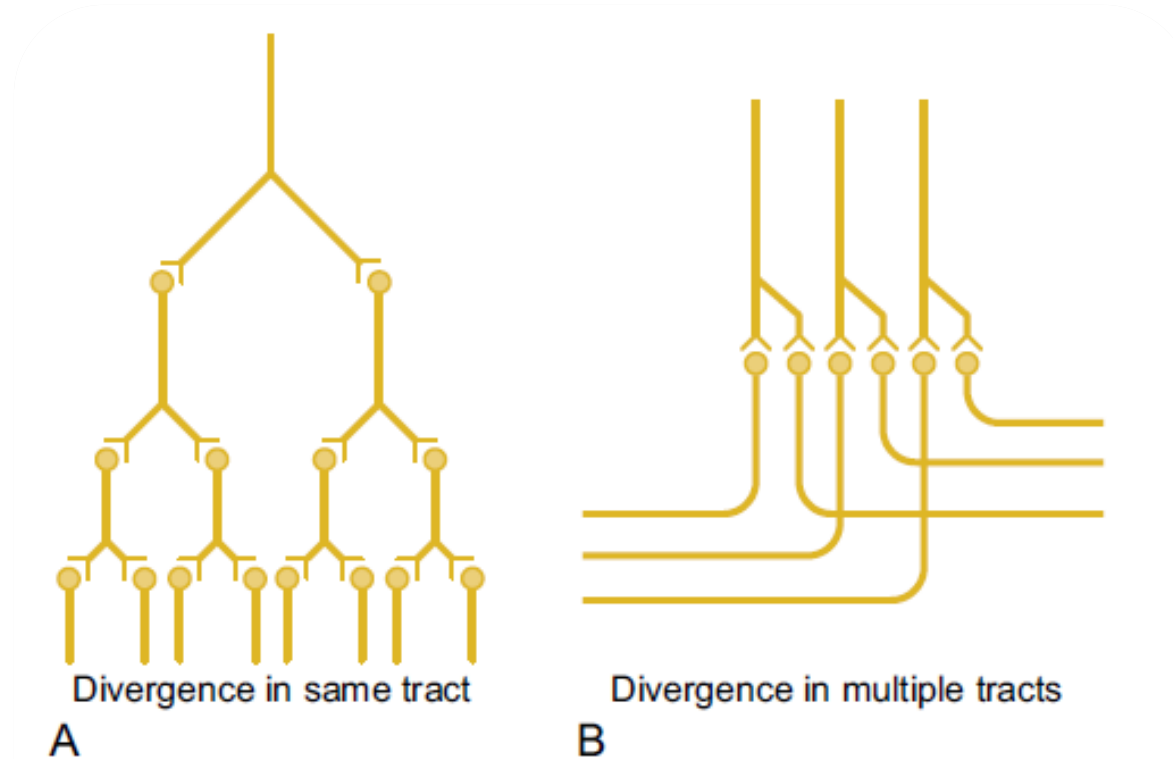
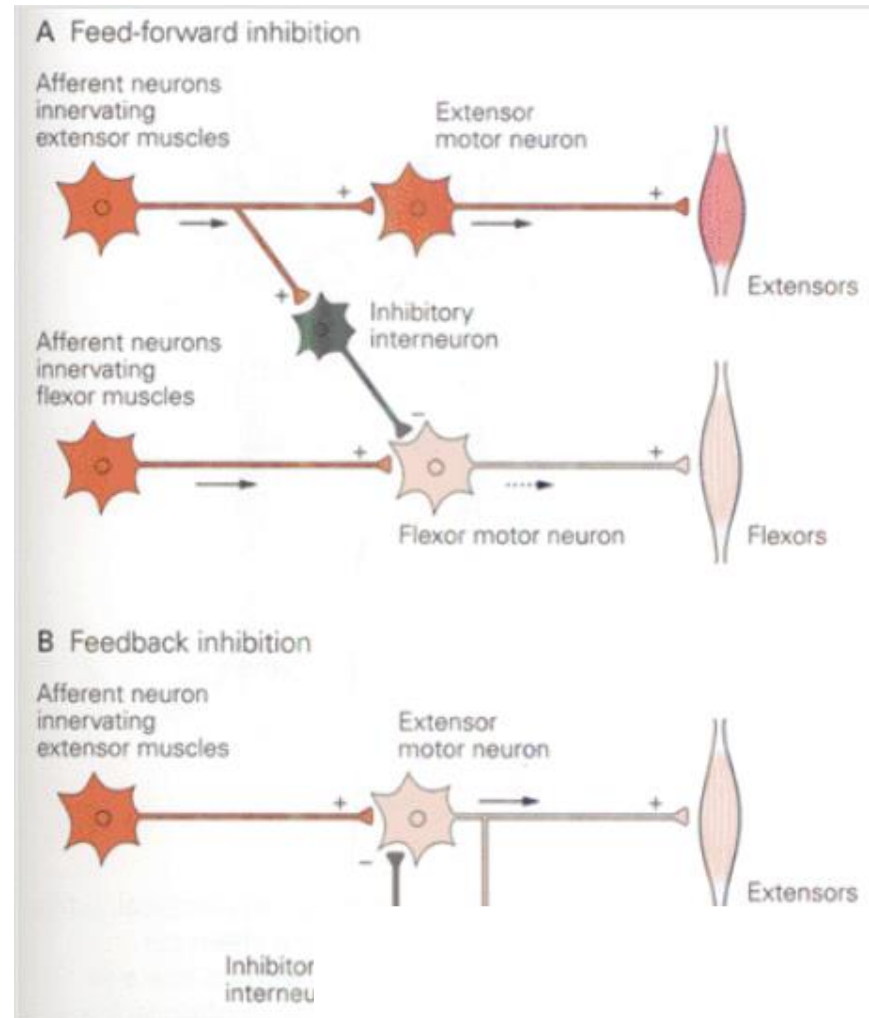


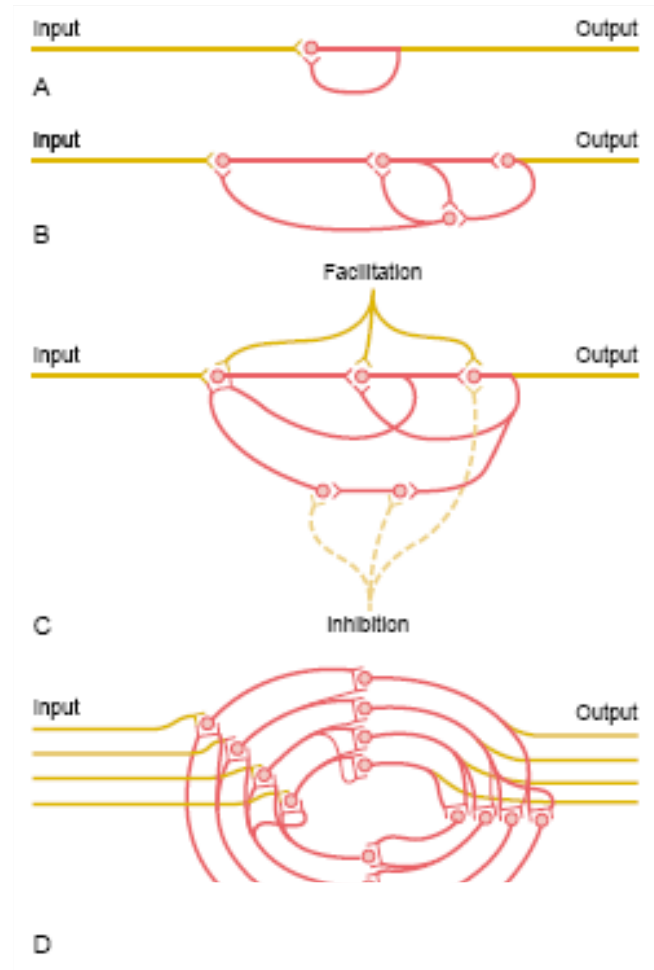
Figure 46-11

“Divergence” in neuronal pathways. *A*, Divergence within a pathway to cause “amplification” of the signal. *B*, Divergence into multiple tracts to transmit the signal to separate areas.

Networking



Networking



Neurotransmission

vs. Neuromodulation

- Information transmission

- Regulation of NS activity

Neurotransmission

- Information transmission
- Specific

vs. Neuromodulation

- Regulation of NS activity
- Diffuse (volume transmission)

Neurotransmission

- Information transmission
- Specific
- Receptors – ion channels

vs. Neuromodulation

- Regulation of NS activity
- Diffuse (volume transmission)
- Receptors – G-proteins

Neurotransmission

- Information transmission
- Specific
- Receptors – ion channels
- Short duration
 - membrane potential changes

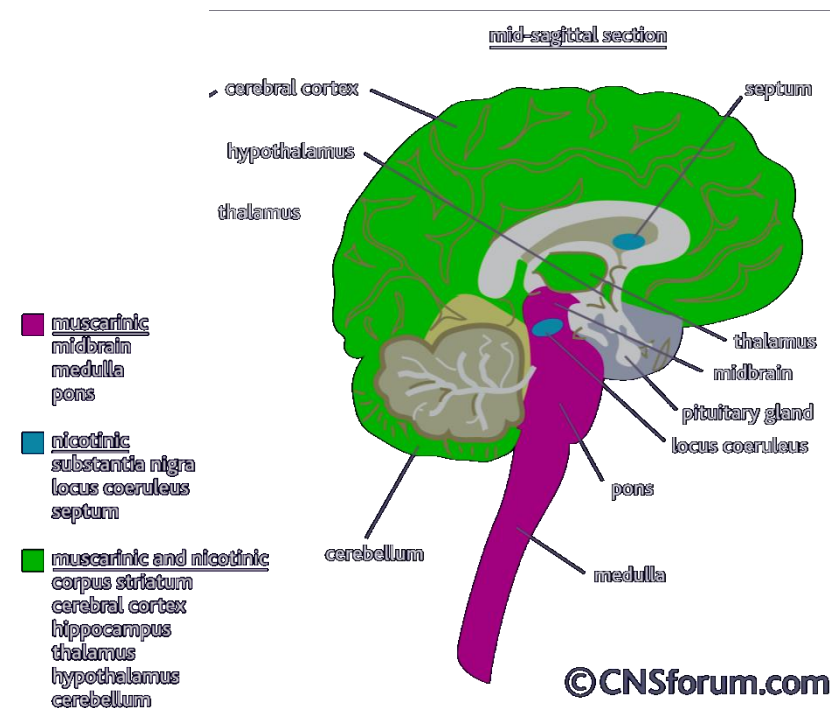
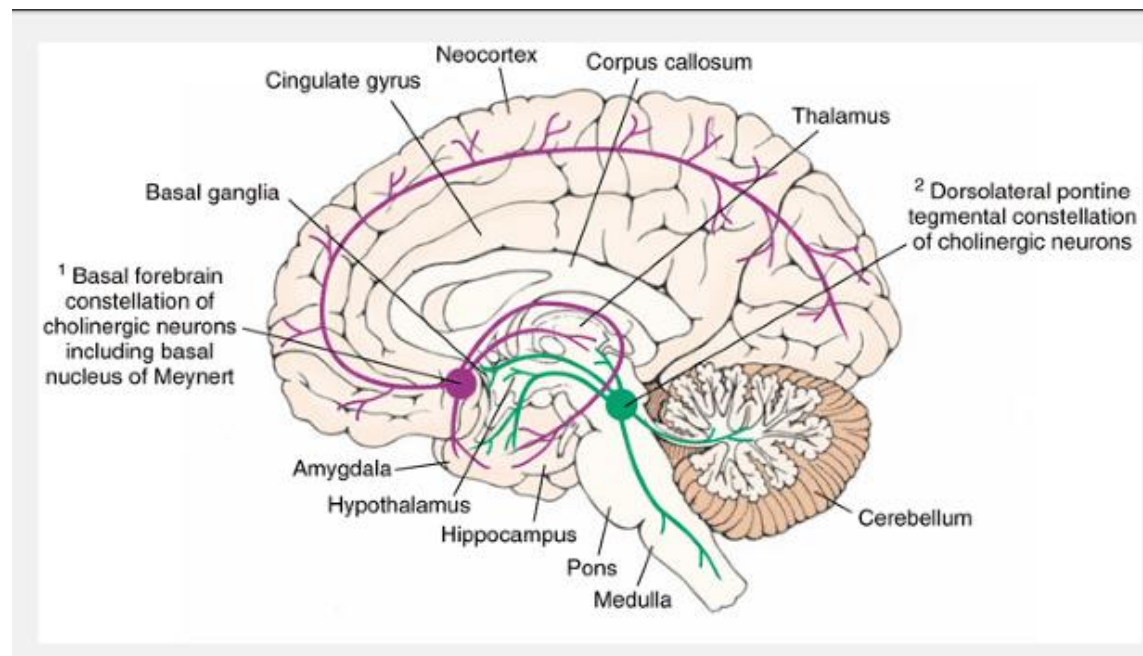
vs. Neuromodulation

- Regulation of NS activity
- Diffuse (volume transmission)
- Receptors – G-proteins
- Longer duration
 - changes in synaptic properties

Acetylcholine

- Nucleus basalis (Meynerti) and other nuclei
- Nicotin receptors
- Muscarin receptors

- Sleep/wake regulation
- Cognitive functions
- Behavior
- Emotions

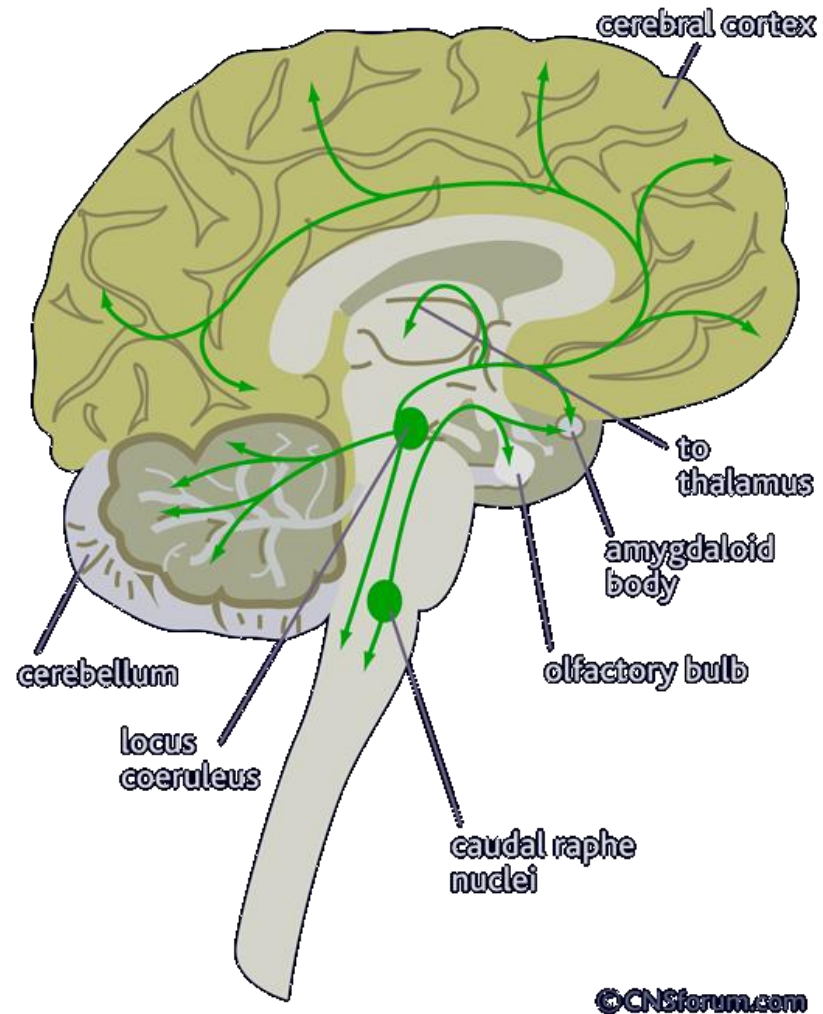


<http://www.slideshare.net/drpsdeb/presentations>

Noradrenalin

- Locus coeruleus
- Nuclei raphe caudalis

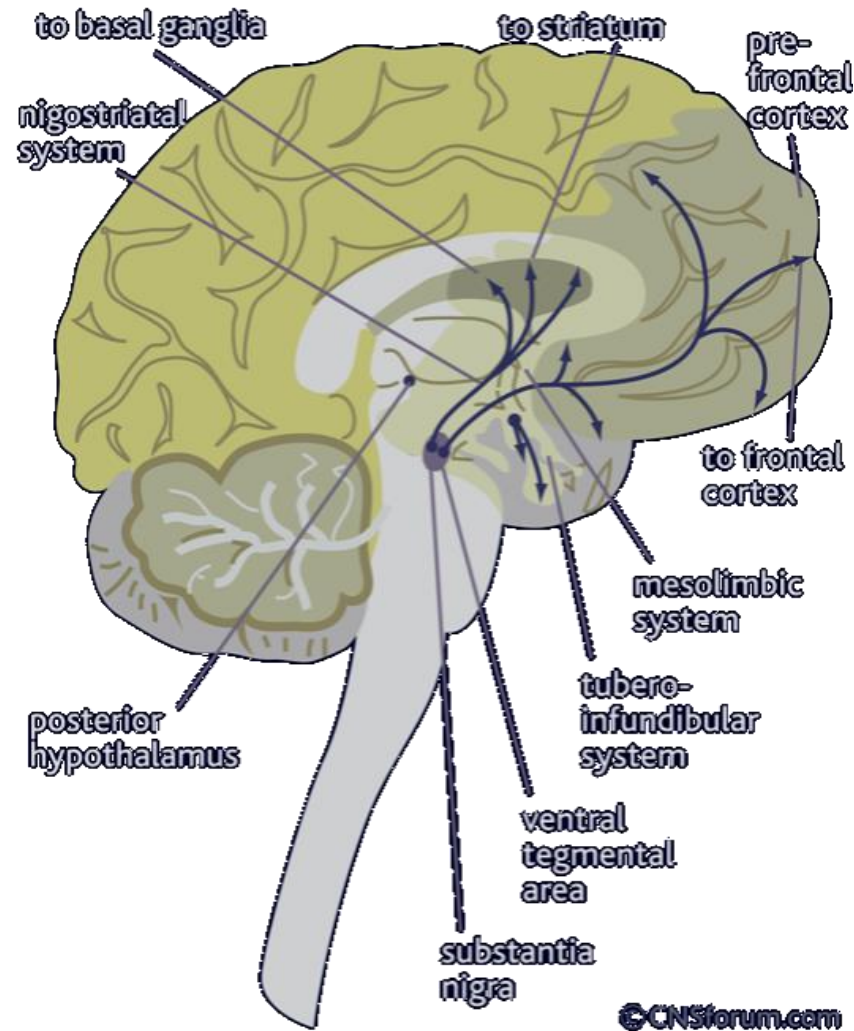
- Vigilance
- Responsiveness to unexpected stimuli
- Memory
- Learning



<http://www.slideshare.net/drpsdeb/presentations>

Dopamin

- Nigrostriatal system
 - Movement
 - Sensory stimuli
- Ventro- tegmentno-mesolimbic-frontal system
 - Reward
 - Cognitive function
 - Emotional behavior
- Tubero-infundibular system
 - Hypothalamic-pituitary regulation
- D1 receptors – excitatory
- D2 receptors - inhibitory

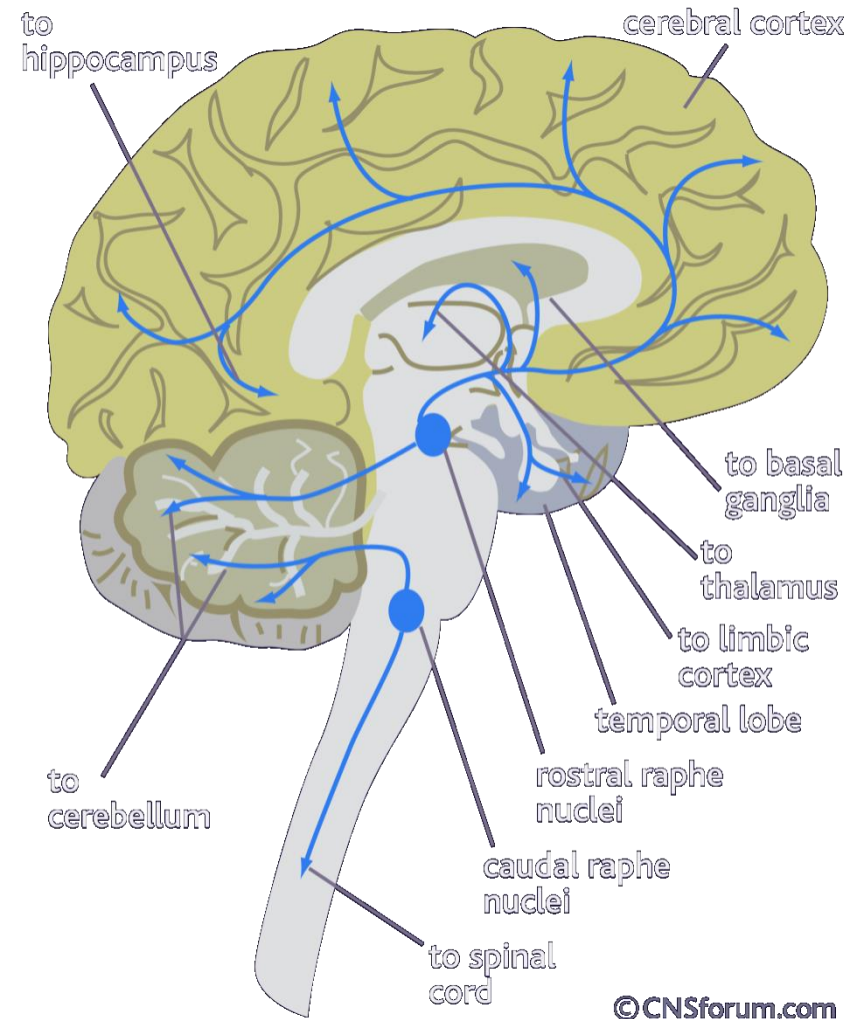


<http://www.slideshare.net/drpsdeb/presentations>

Serotonin

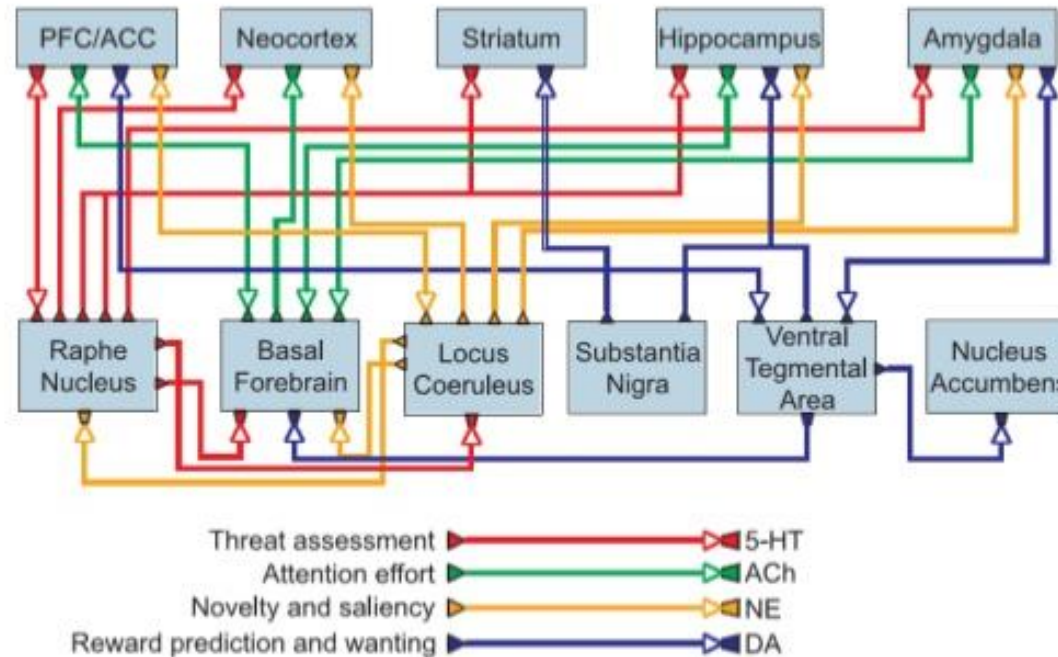
- Nuclei raphe rostralis
- Nuclei raphe caudalis

- Anxiety/relaxation
- Impulsive behavior
- Sleep



<http://www.slideshare.net/drpsdeb/presentations>

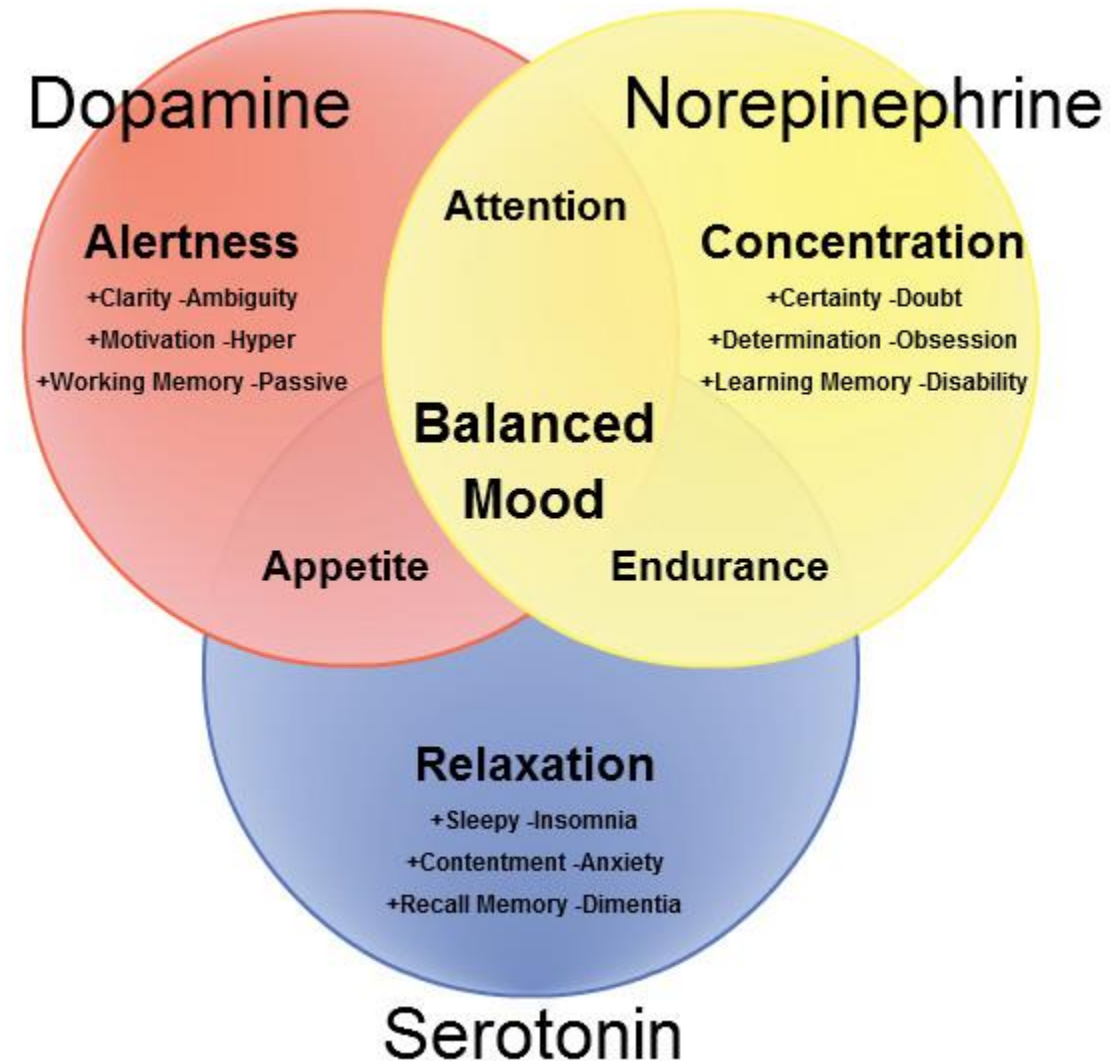
Neuromodulatory systems



Jeffrey L. Krichmar, Adaptive Behavior 2008; 16; 385

<http://image.slidesharecdn.com/neuromodulationincognition-140119031056-phpapp02/95/neuromodulation-in-cognition-5-638.jpg?cb=1419657931>

Neuromodulatory systems



M U N I

M E D