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Introduction to neurophysiology
Cellular base of nervous system
Synapse
Somatosenstivity and pain

Contact

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Why and how to STUDY neuroscience

Philosophy : Mind behind Mind

PS Deb

FACTS

THEORIES

Neuroscience: Brain

Psychology : Mind

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

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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

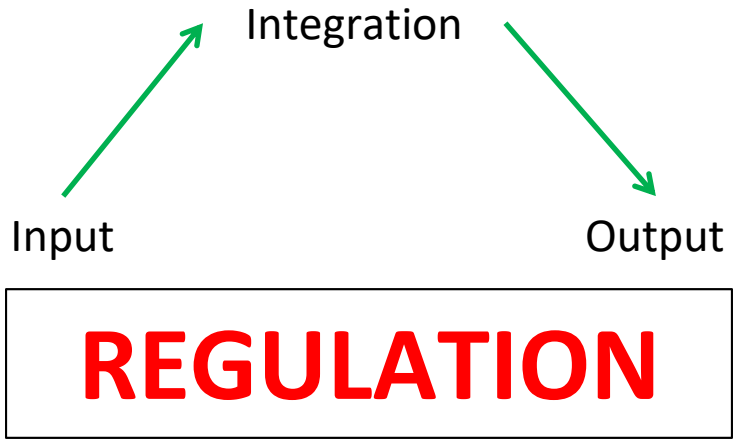
- Functional specialization of particular cells – higher effectivity
- Inner environment – homeostasis
- Lower level of stress
- Longer life time

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



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The role of nervous system

- Regulation
  - Nervous
  - Humoral

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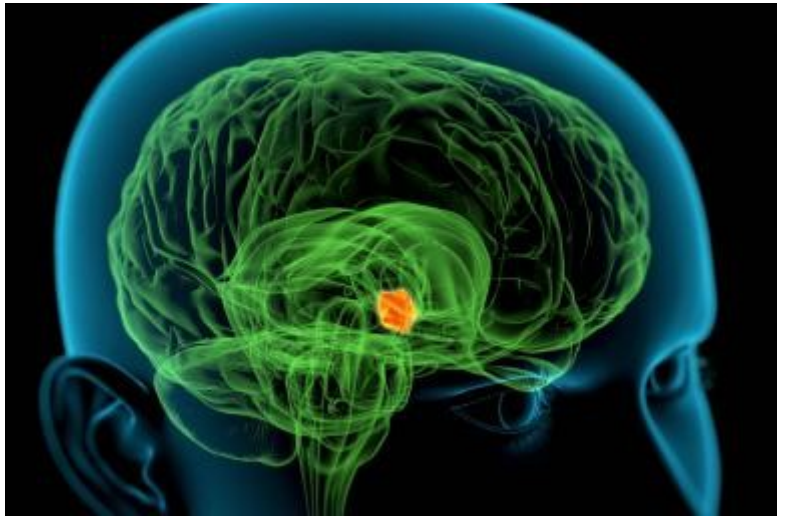
The role of nervous system

- Regulation
  - Nervous
  - Humoral



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

Central nervous system controls both types of regulations

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The role of nervous system

Humoral regulations

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

Nervous regylations

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

The role of nervous system

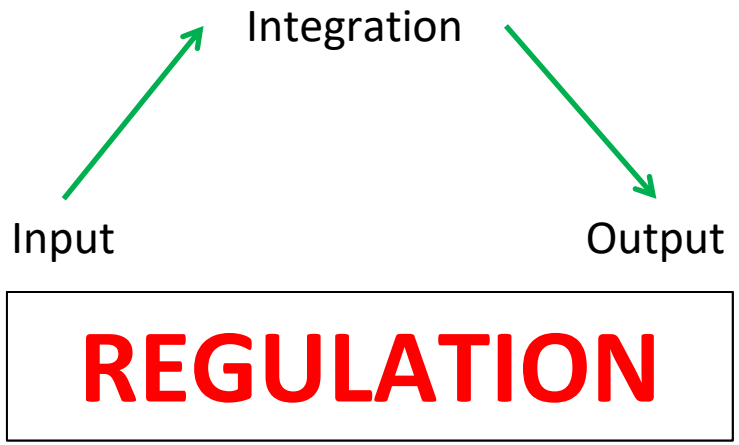
Humoral regulations

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

Nervous regylations

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

The role of nervous system



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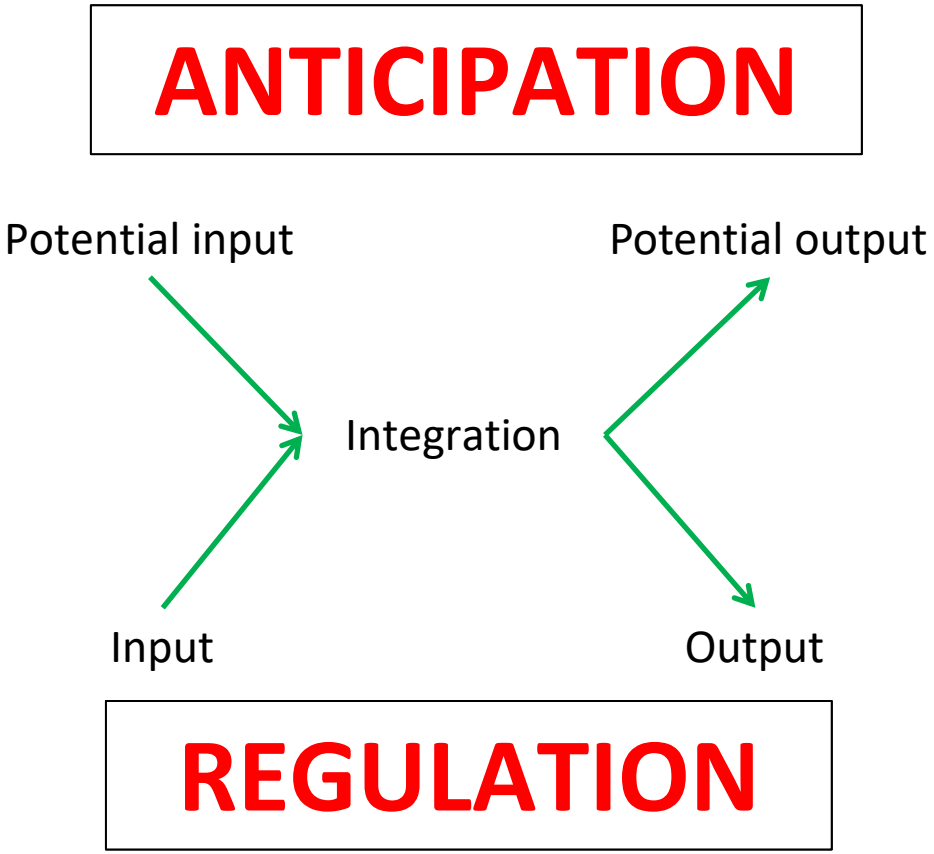
The role of nervous system



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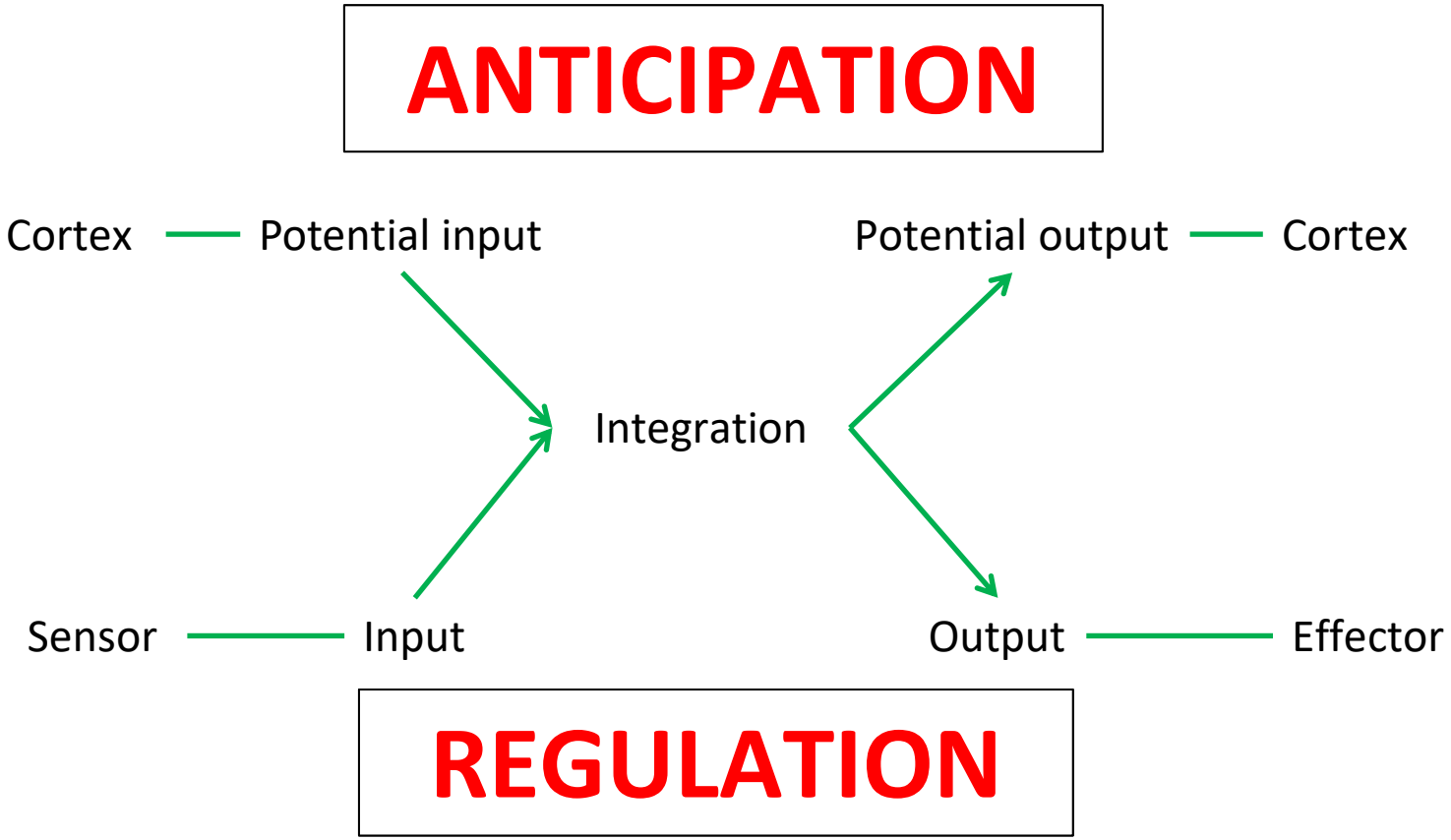
The role of nervous system



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Evolutionary approach

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

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- 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

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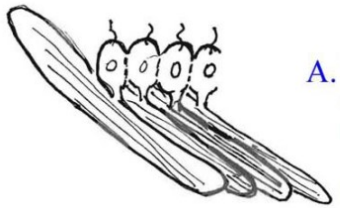
Evolution of the nervous system

Input → Integration → Output



Four basic types of tissue

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

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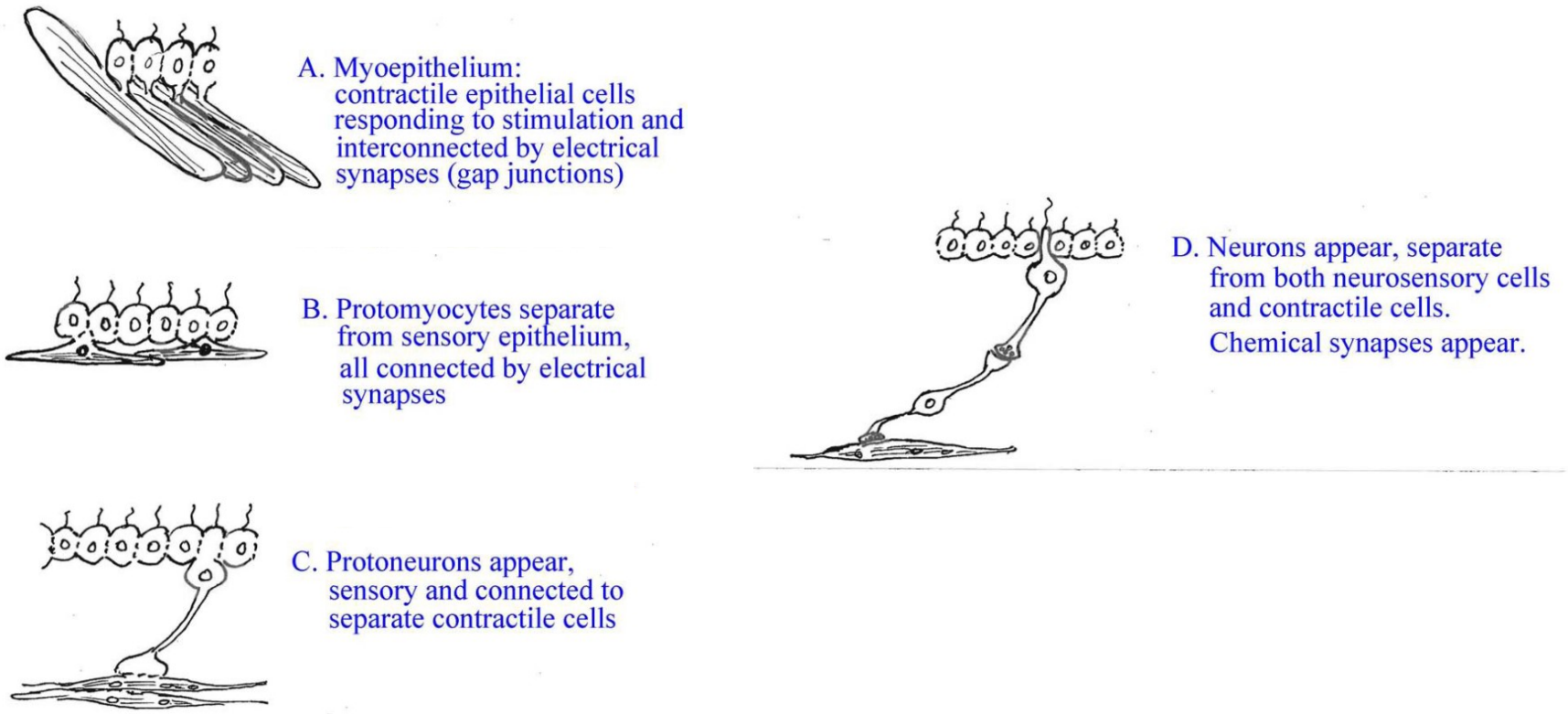
Evolution of the nervous system

Input → Integration → Output



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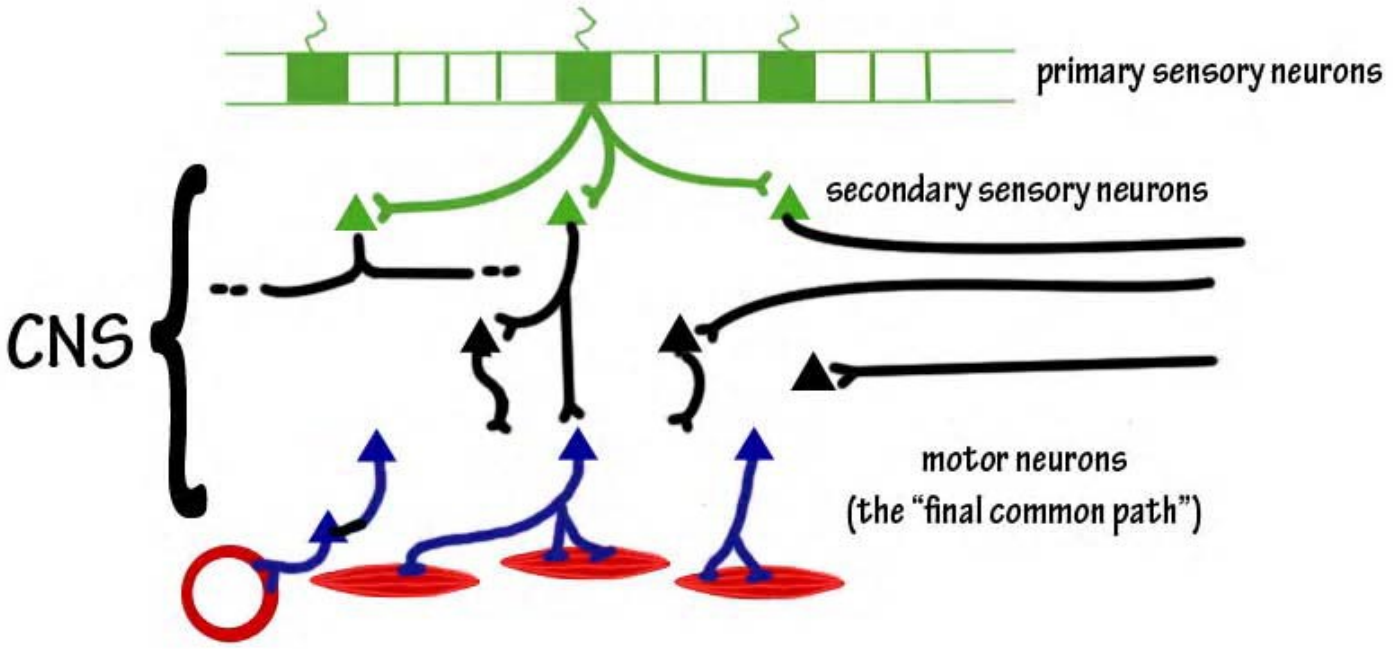
Evolution of the nervous system



Input

Integration

Output

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

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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

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Compartmentalization

- Cellular specialization leads to compartmentalizatio vels
  - Tissue level
  - Organ level
  - Organ
- There are
- Properties/c 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

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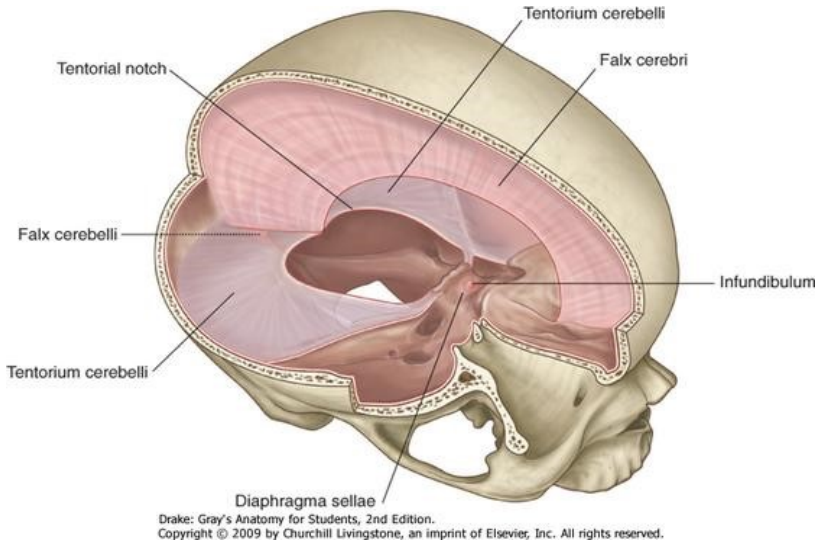
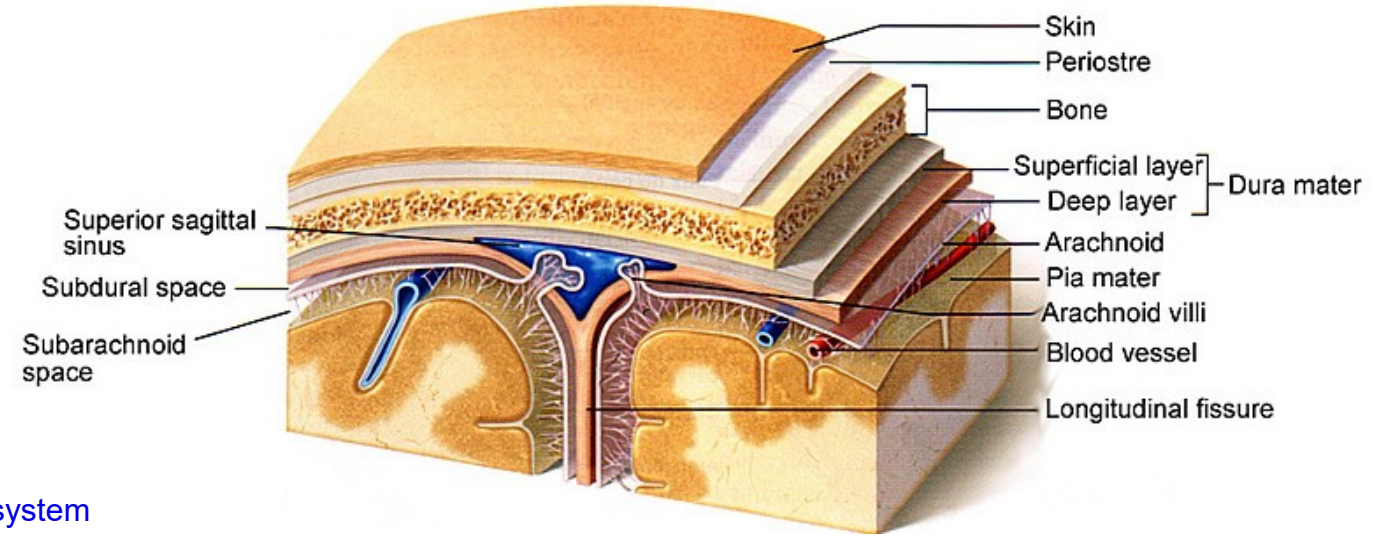
Intracranial compartment

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



http://edutoolanatomy.wikispaces.com



http://www.corpshumain.ca/en/Cerveau3_en.php

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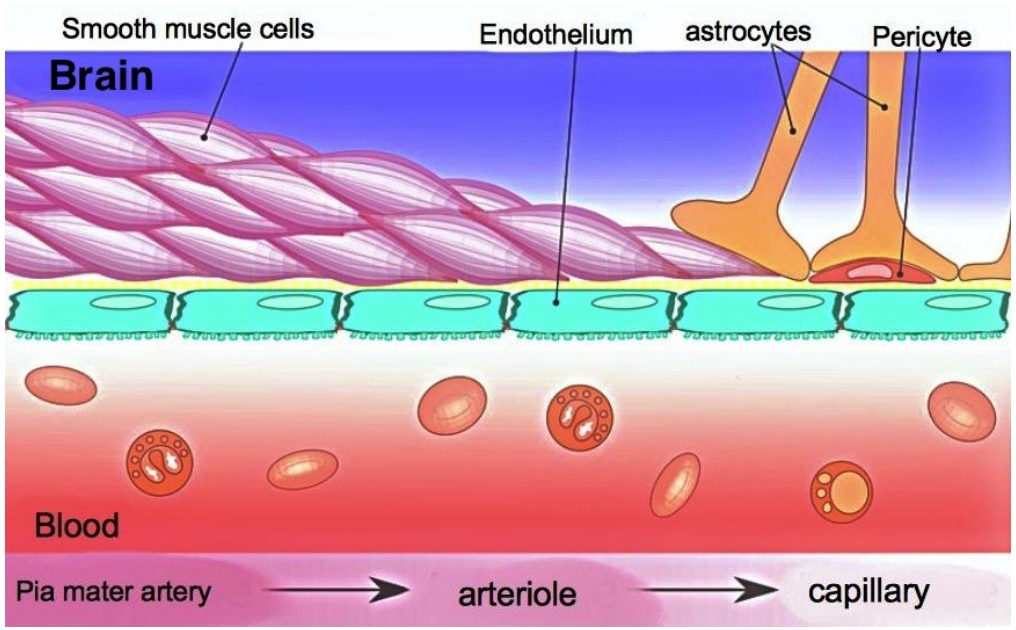
Hematoencephalic barrier

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



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

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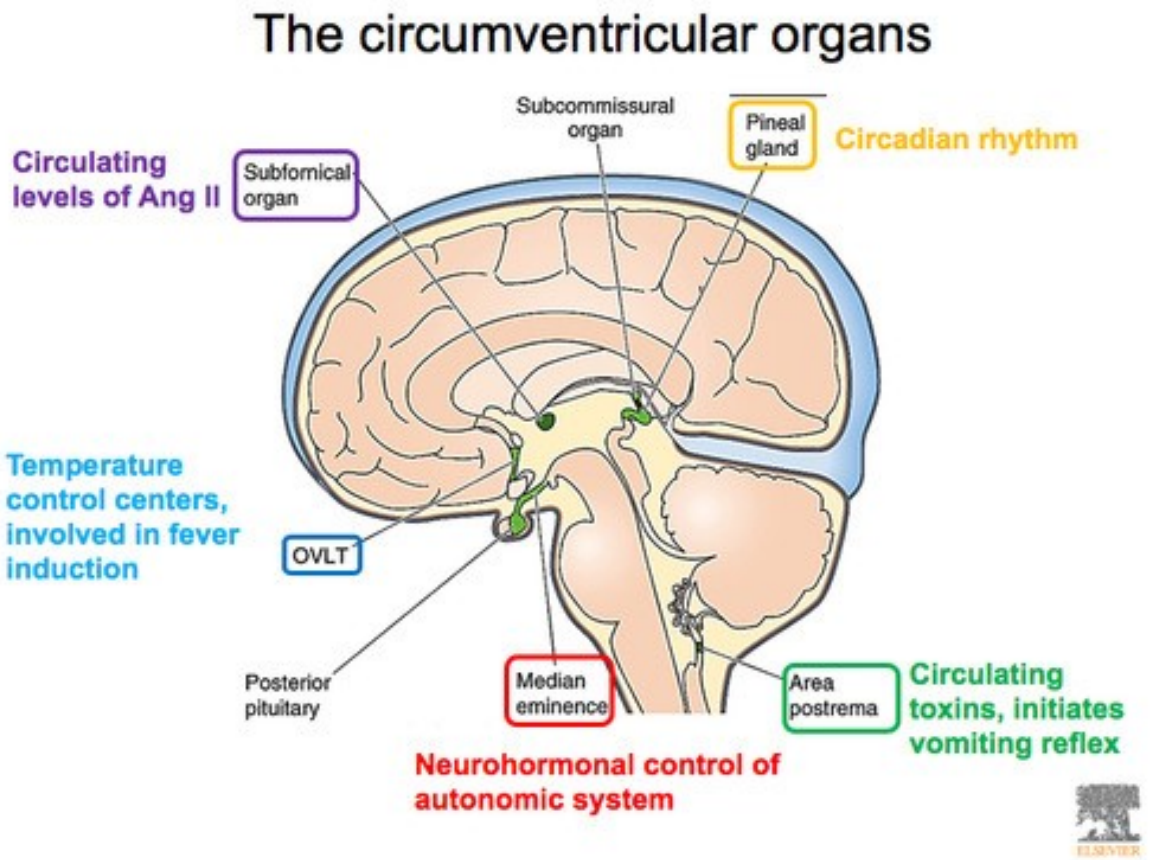
Circumventricular organs

- Rich vascularisation
- Modified hematoencephalic barrier
- Sensors
- Secretion



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

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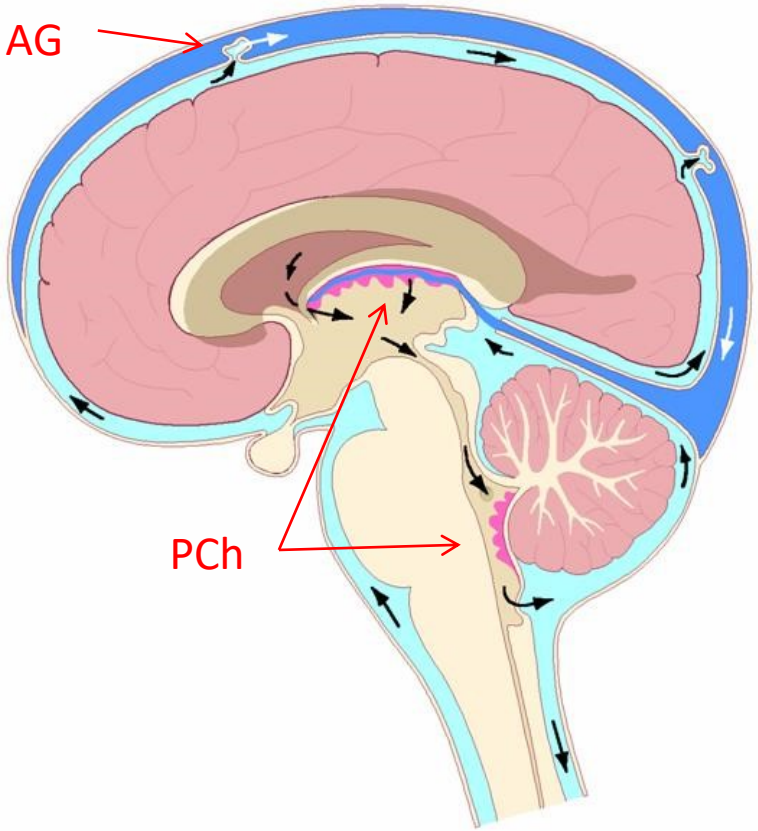
Cerebrospinal fluid

- 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

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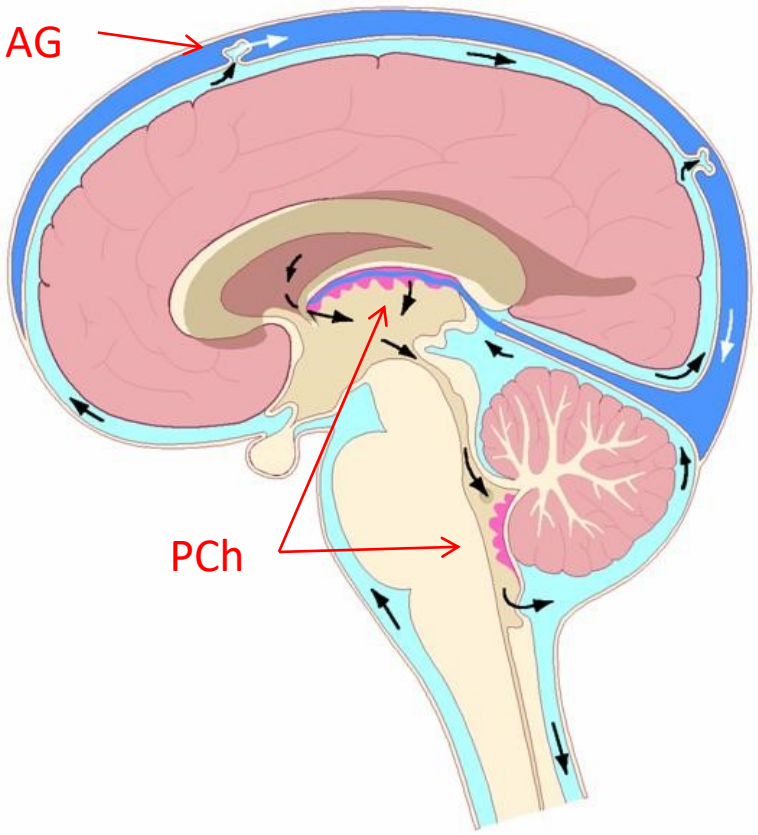
Cerebrospinal fluid

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



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

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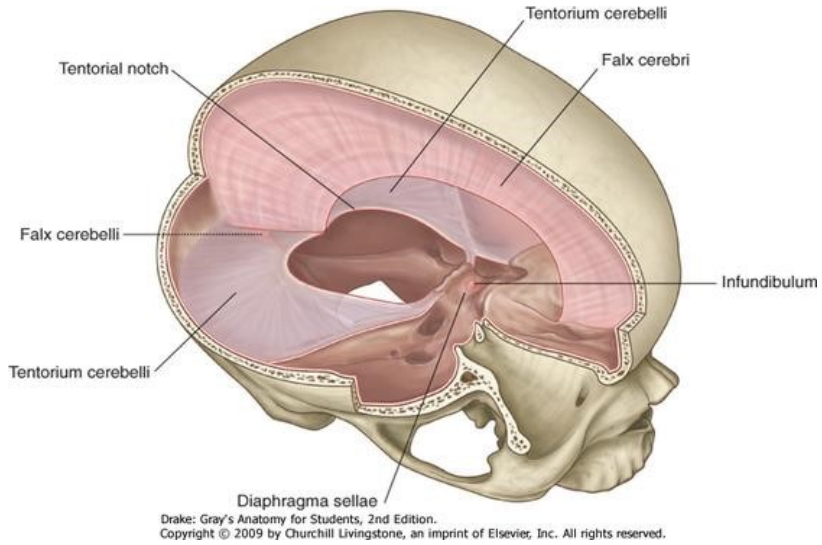
Intracranial compartment

- Brain
- Cerebrospinal fluid
- Blood (intravascular)

- Intracranial pressure (ICP)
  - Critical determinant of cerebral perfusion

- Cerebral perfusion pressure (CPP) pressure gradient driving blood flow intracranialy



http://edutoolanatomy.wikispaces.com

!!! CPP = MAP – ICP !!!

Cerebral perfusion pressure | Mean arterial pressure | Intracranial pressure

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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 replacable
- The total amount of neuronal cells - 100 billions (10^{11})
- Neruon/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

    (liquro-encephalic barrier)

Peripheral nervous system

- Satelite cells
  - Support functions in PNS
- Schwan cells
  - Myelin sheat

Neuron

Background Activity

The inside of the cell

- ✓ …
- ✓ Synthesis
- ✓ Transport
- ✓ …

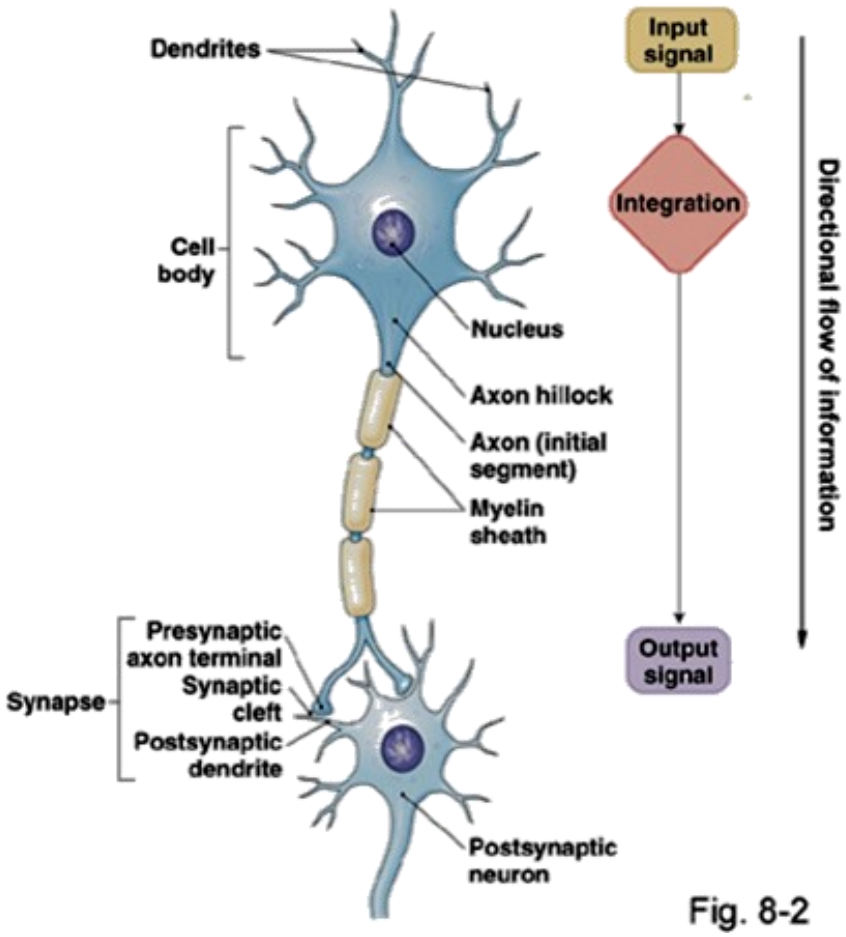

Fig. 8-2

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Information processing and transmission

The membrane

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

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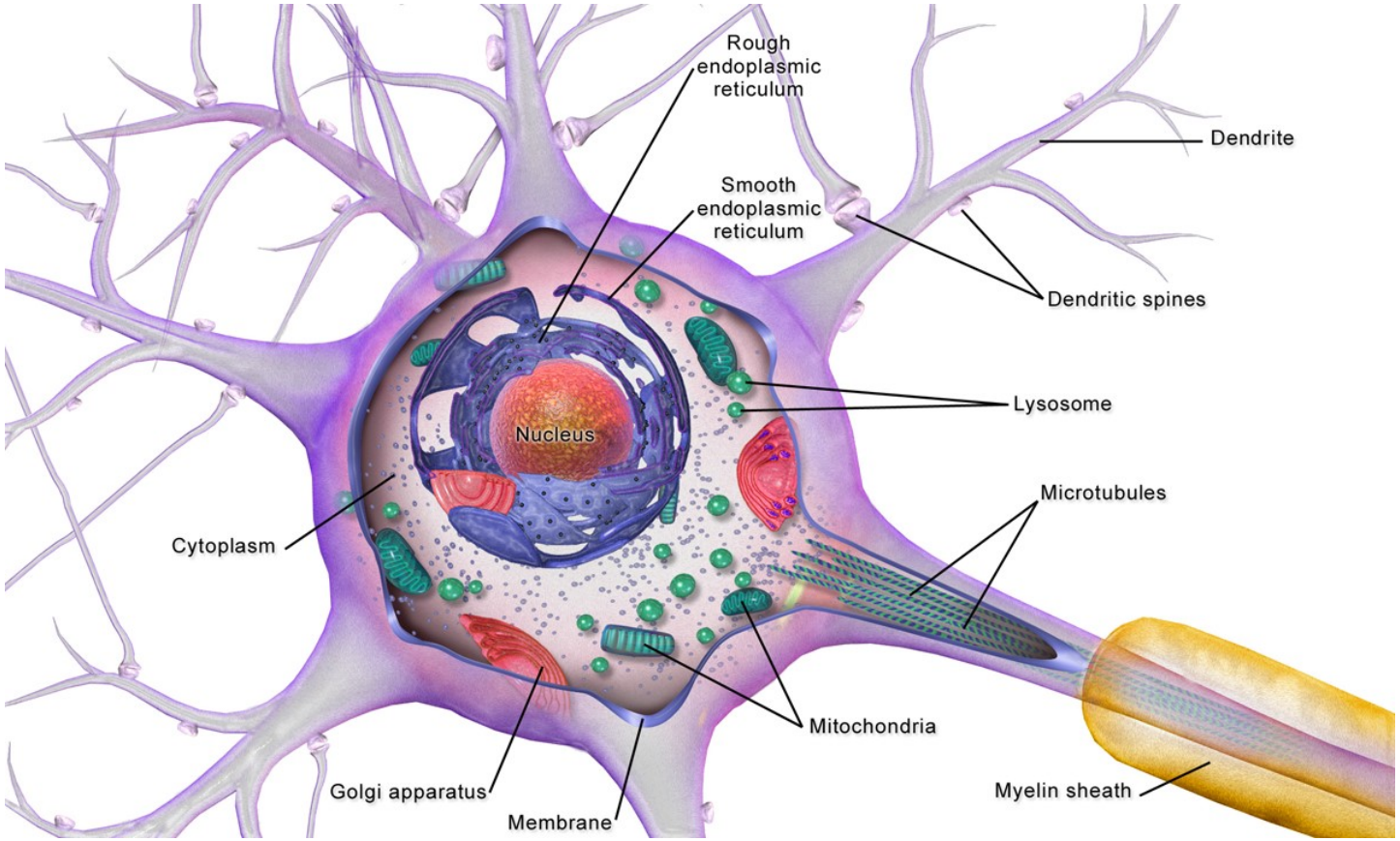
Background Activity



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

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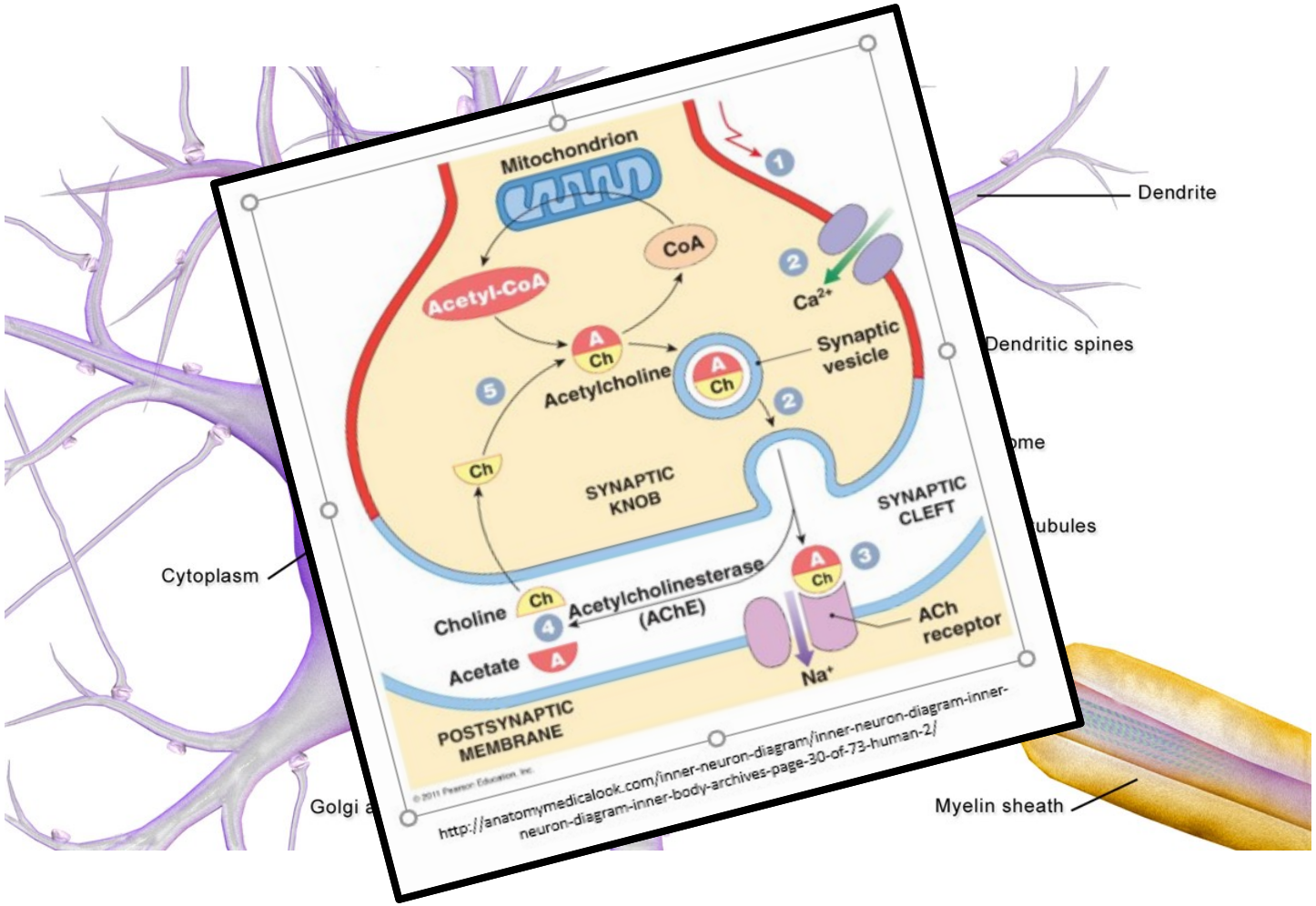
Background Activity



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

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Background Activity

Fast axonal transport

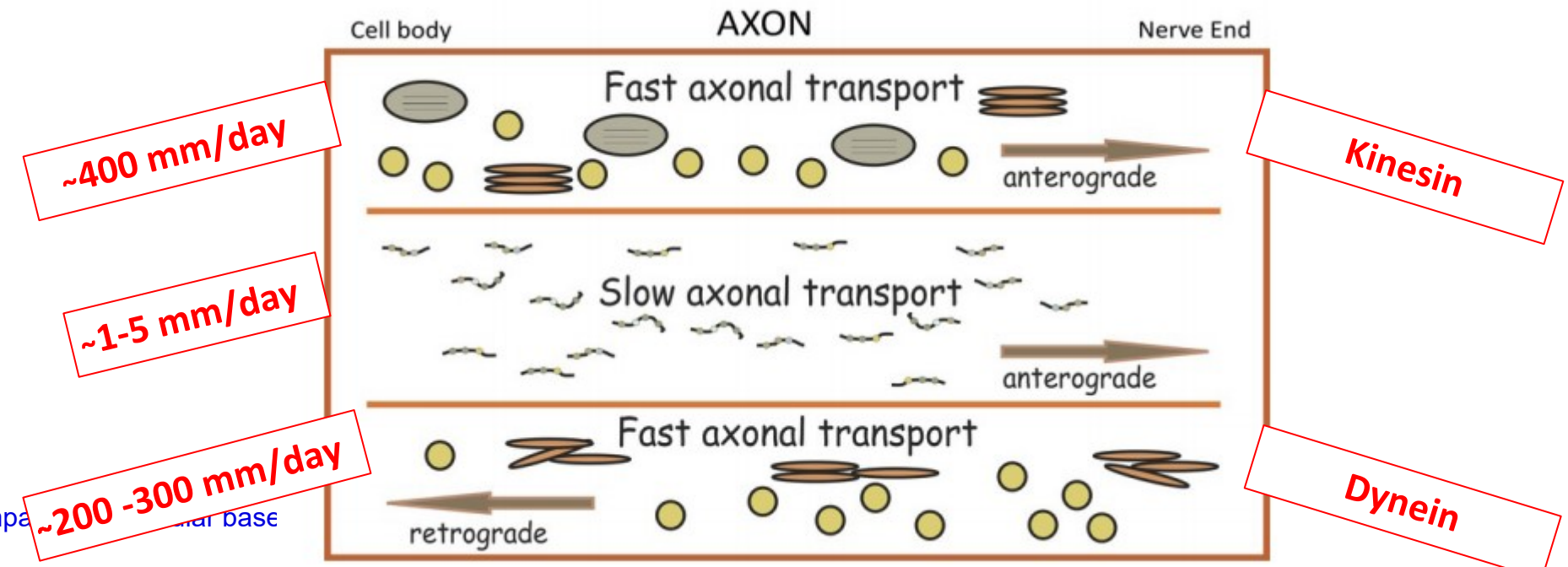
- bidirectional
- ATP dependant
- associated with microtubules: dynein and kinesin

Slow axonal transport

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

Fast axonal transport
Golgi derived vesicles
lysosmes, mitochondria
structural elements of
endoplasmic reticulum

Slow axonal transport
microfilaments, microtubules
neurofilaments
cytosolic protein complexes



http://www.oapublishinglondon.com/images/article/pdf/1397255957.pdf

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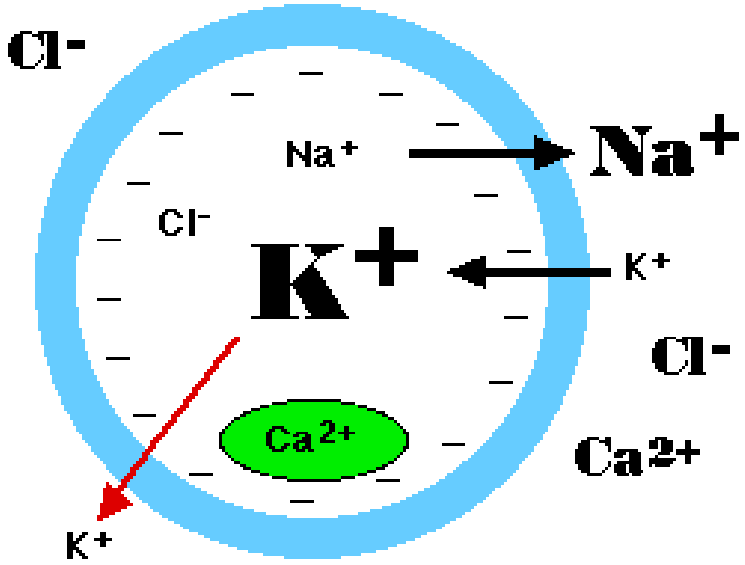
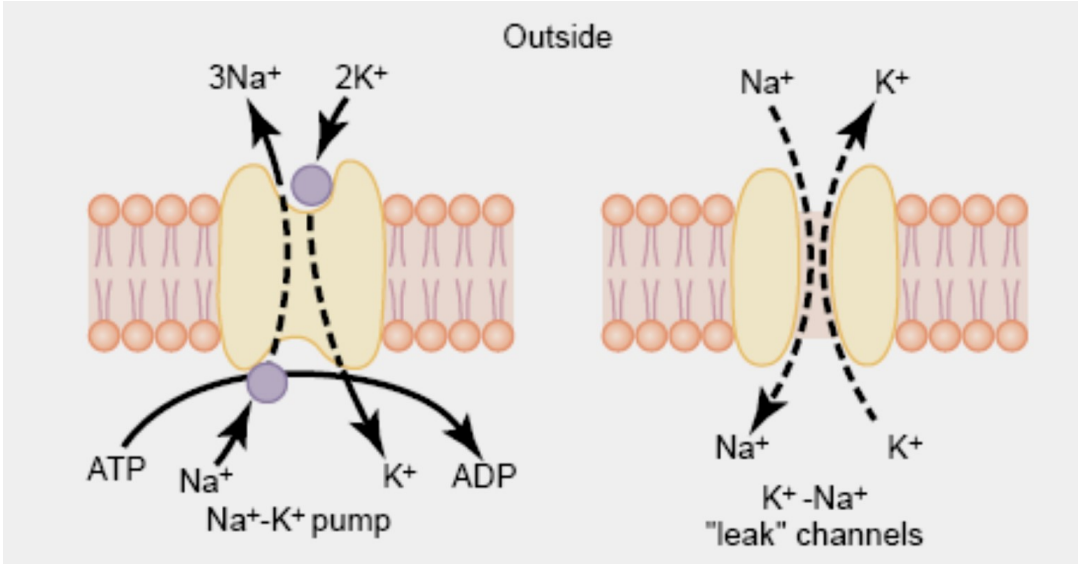
Membrane potential

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





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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

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Action potential

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

Resting potential around -70 mV

Treshold potential around -55 mV

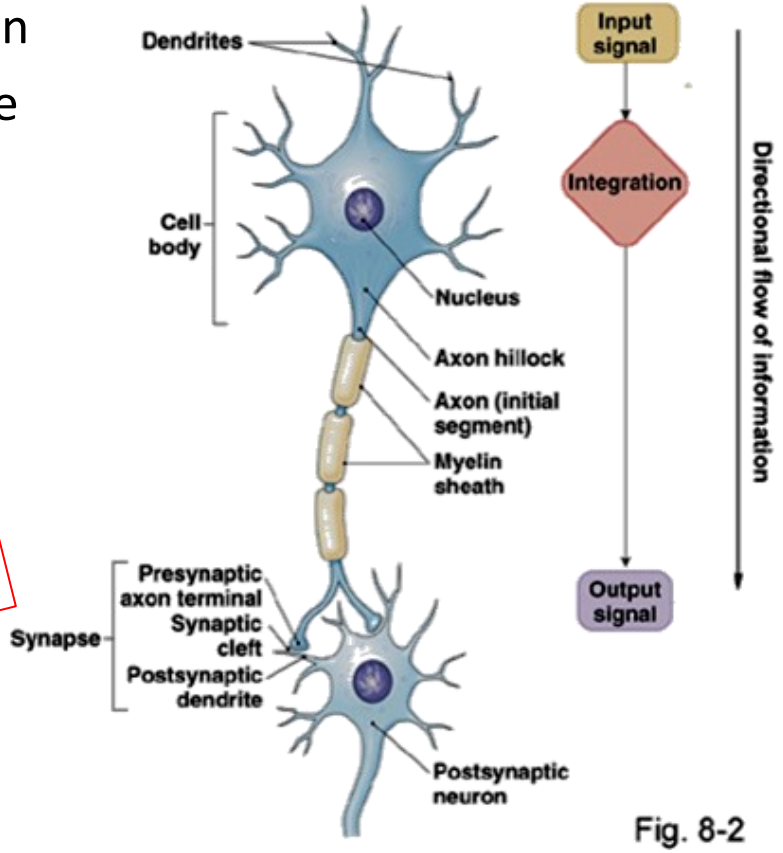
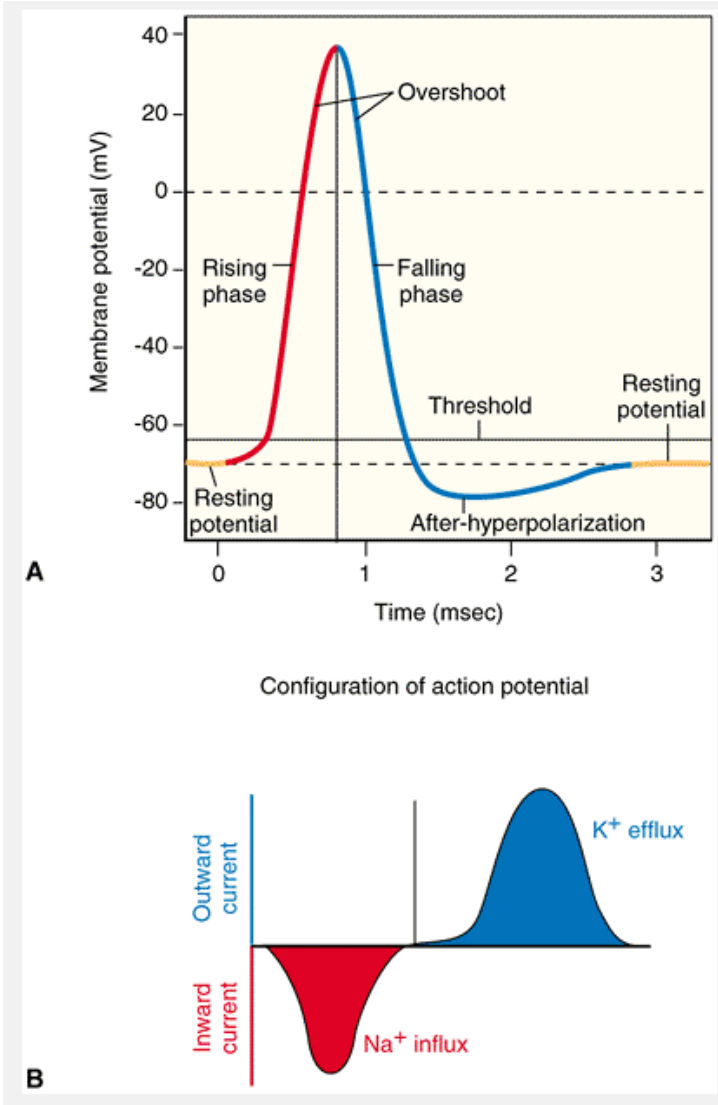


Fig. 8-2



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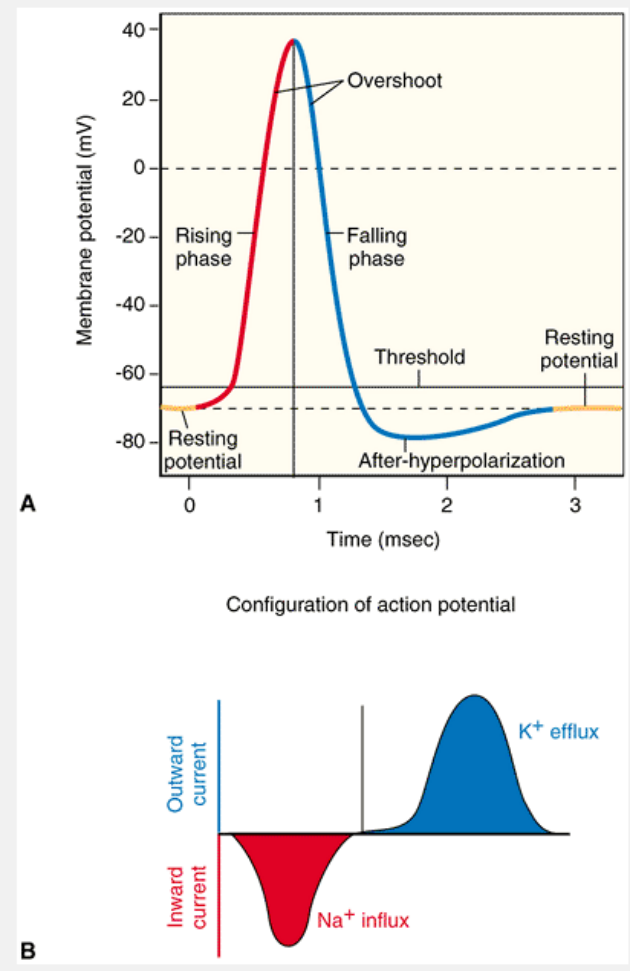
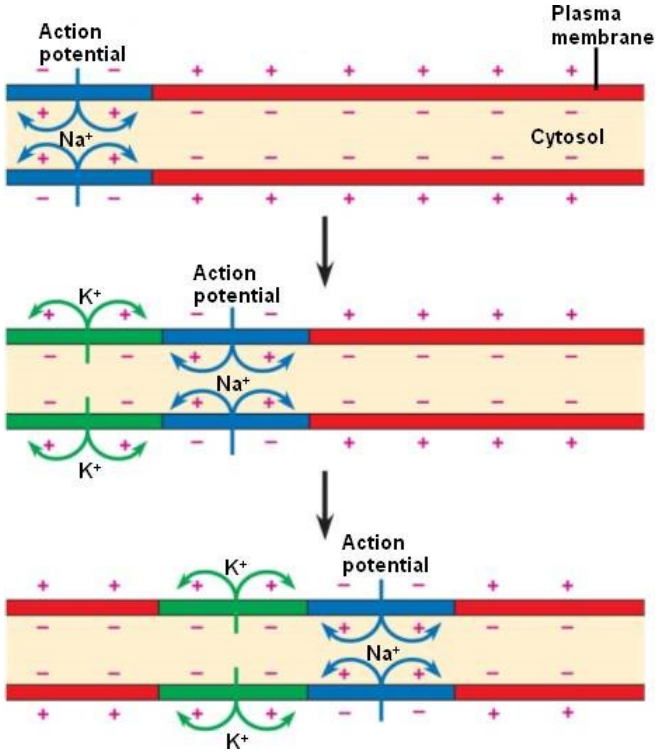
Action potential spreading





- Local currents
- Anterograde

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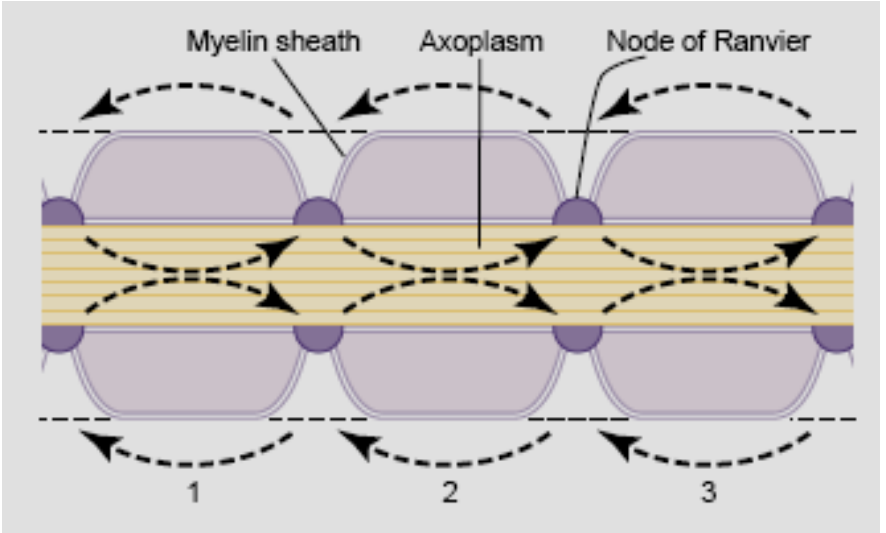
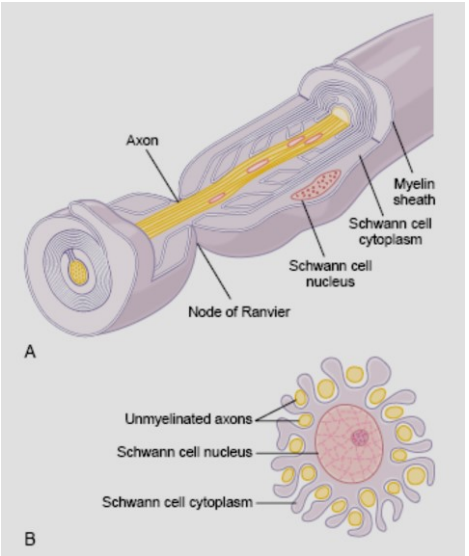
Saltatory conduction

- Myelin sheat
- 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





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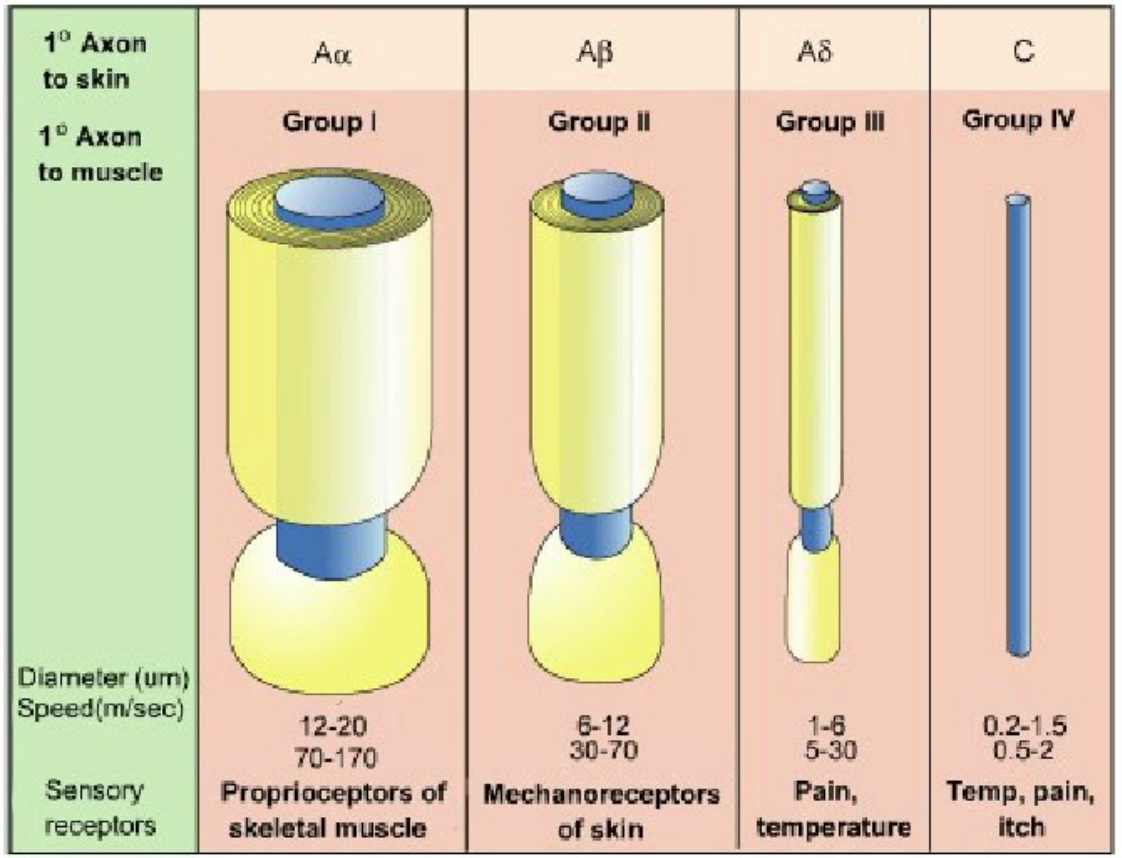
Classification of nerve fibers

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



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

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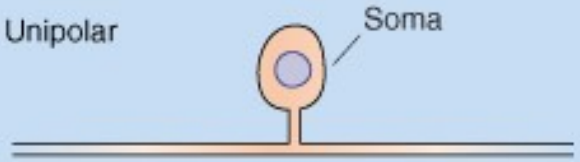
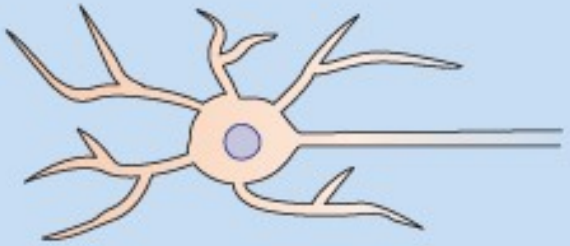
Neuronal classification

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

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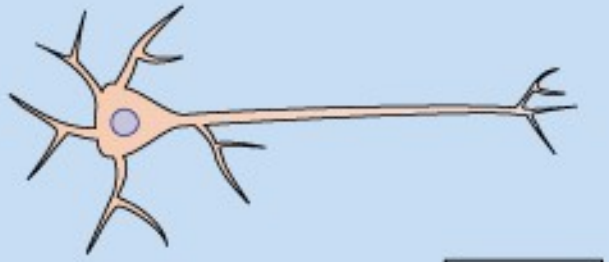
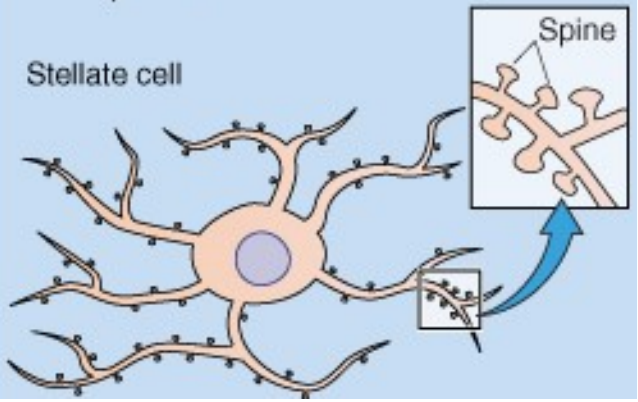
Neuronal classification

Basis for classification	Example	Functional implication	Structure
2. Dendritic pattern			Pyramidal cell
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)	
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 

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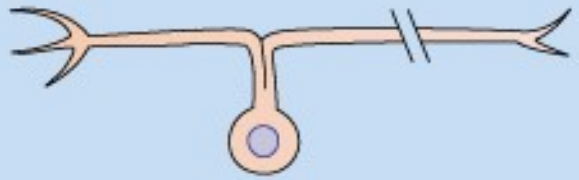
Neuronal classification

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

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Synapse

- Communication between neurons

- Electrical
- Chemical

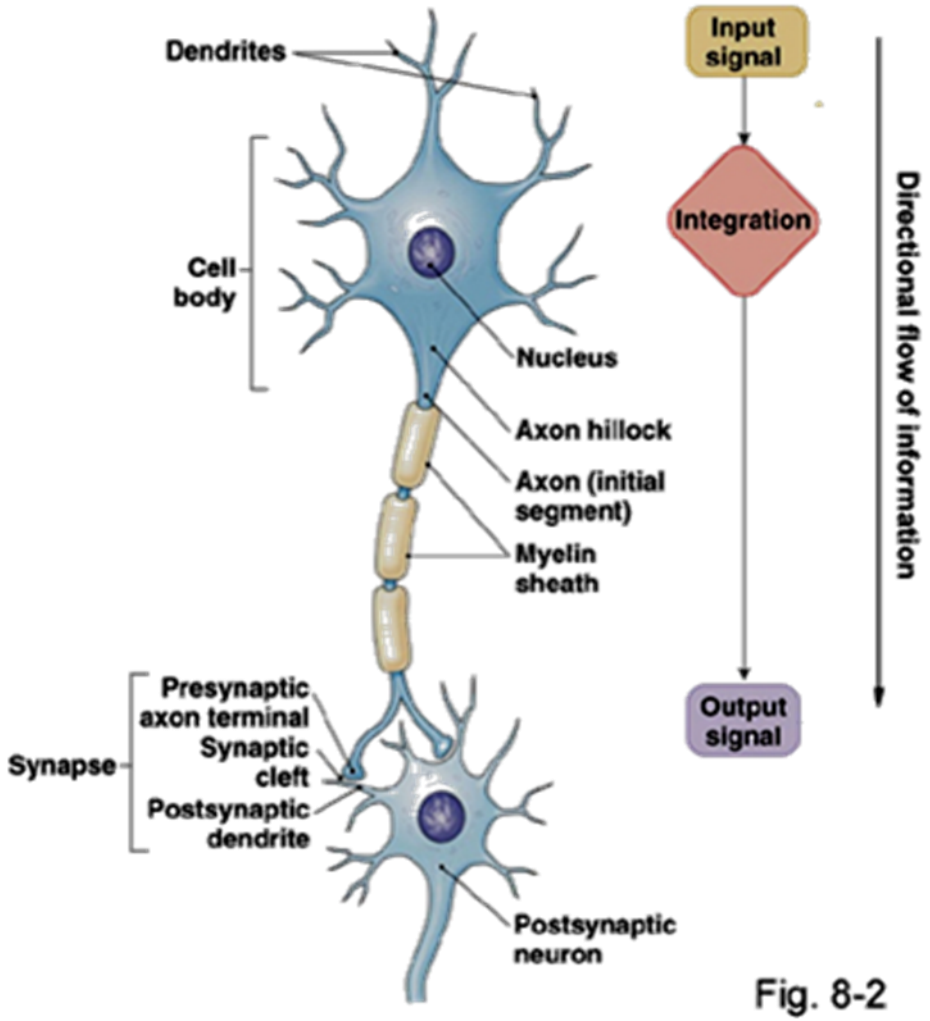

Fig. 8-2

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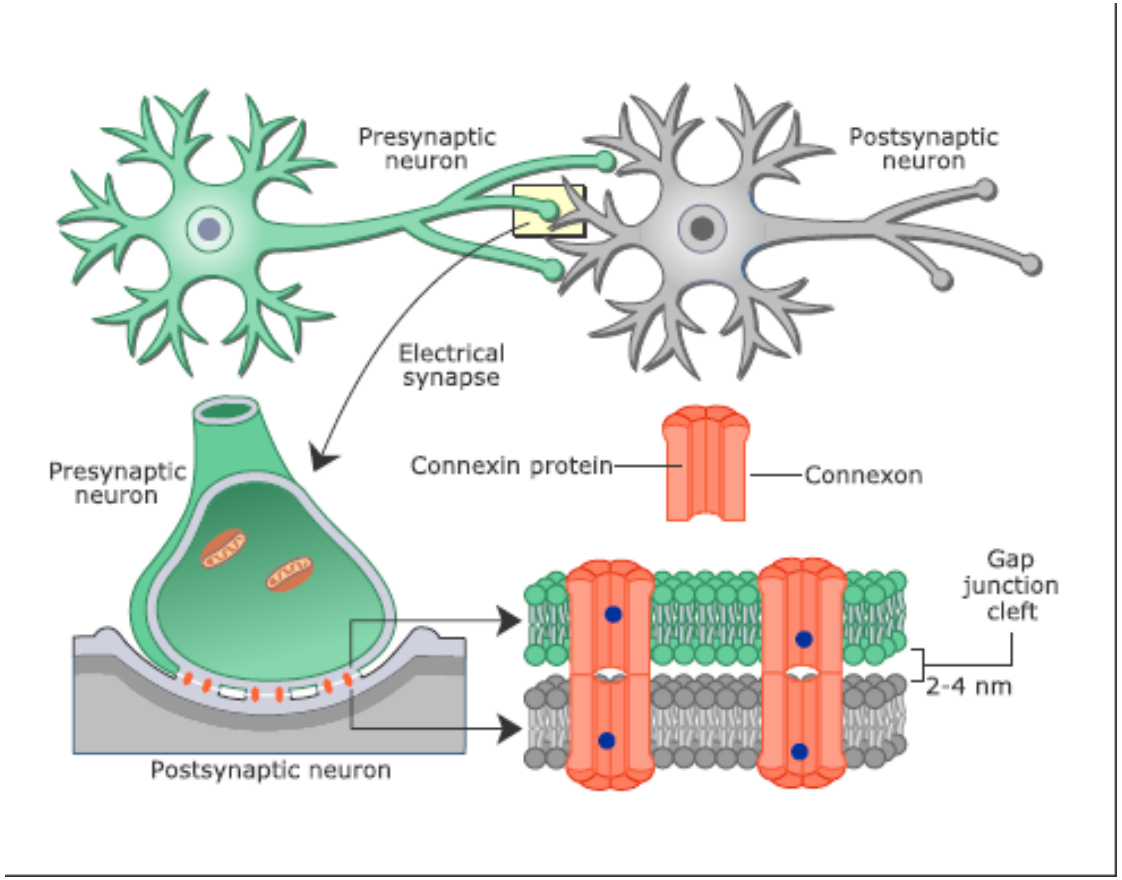
Electrical synapse

- Evolutionary old
- Less frequent than ch.
- Ubiquitous



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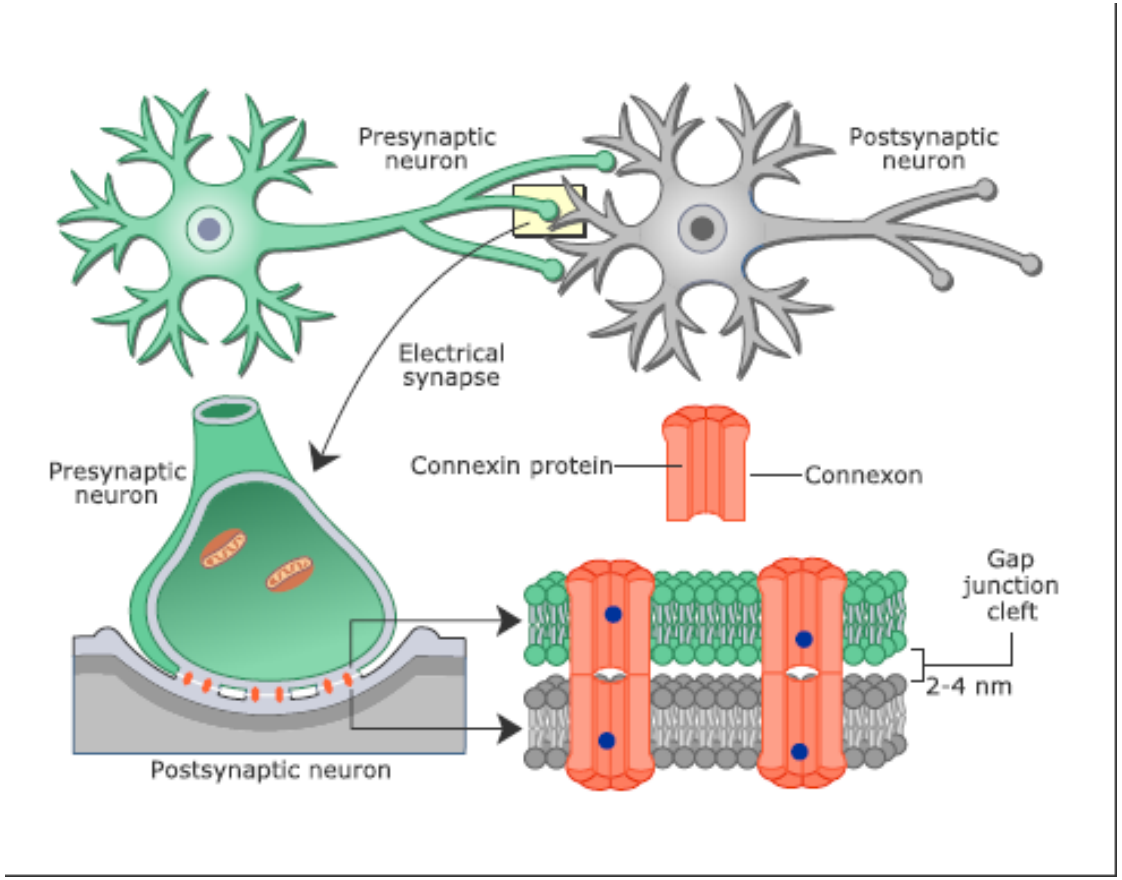
Electrical synapse

- Evolutionary old
- Less frequent than ch.
- Ubiquitous

- Gap junctions
- Bidirectional tranmission
- Fast
- Strength of signal may decrease



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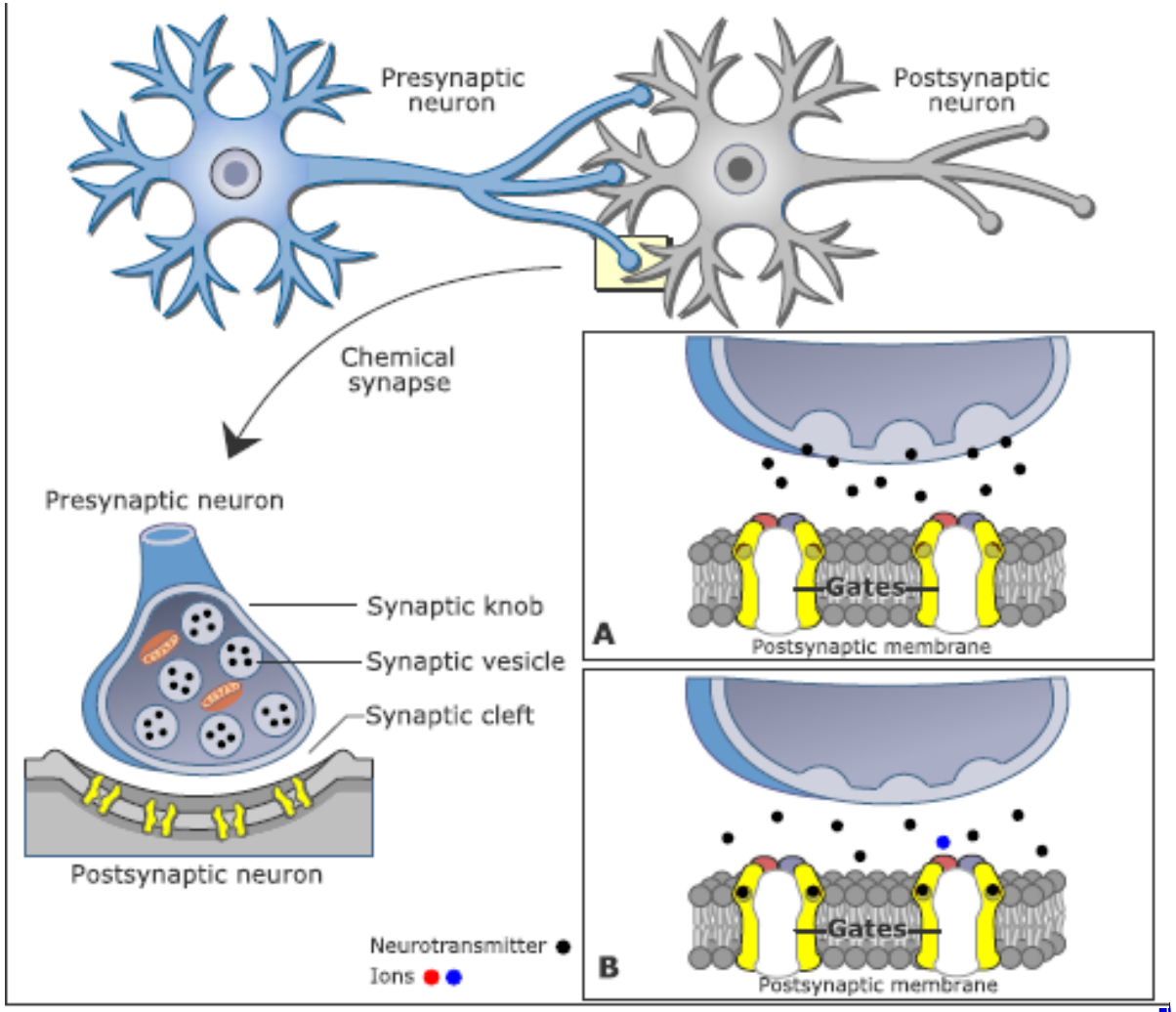
Chemical synapse

- Evolutionary young
- Majority type of s.



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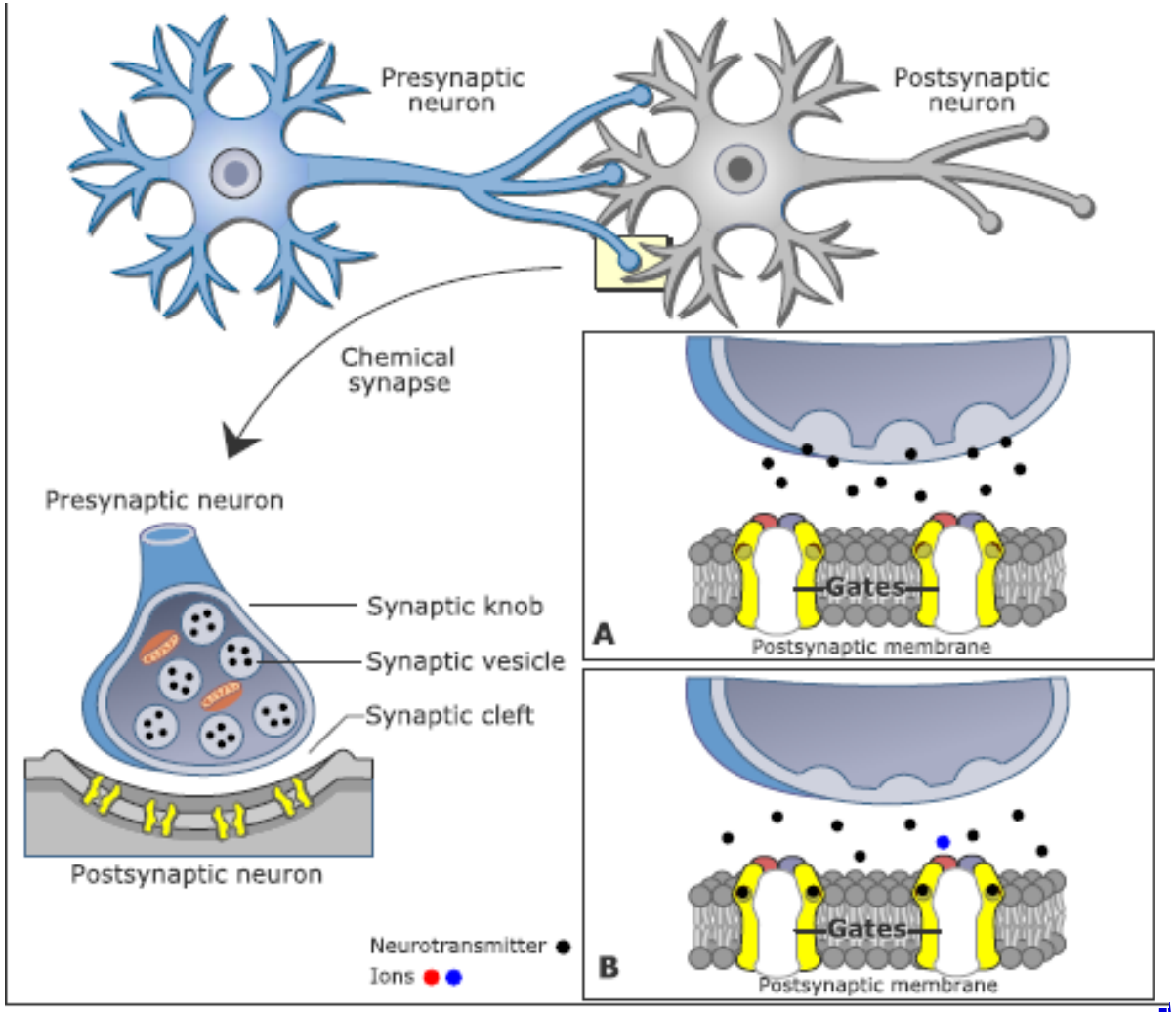
Chemical synapse

- Evolutionary young
- Majority type of s.

- Unidirectional
- Synaptic cleft
- Neurotransmitter
- Constant signal strength



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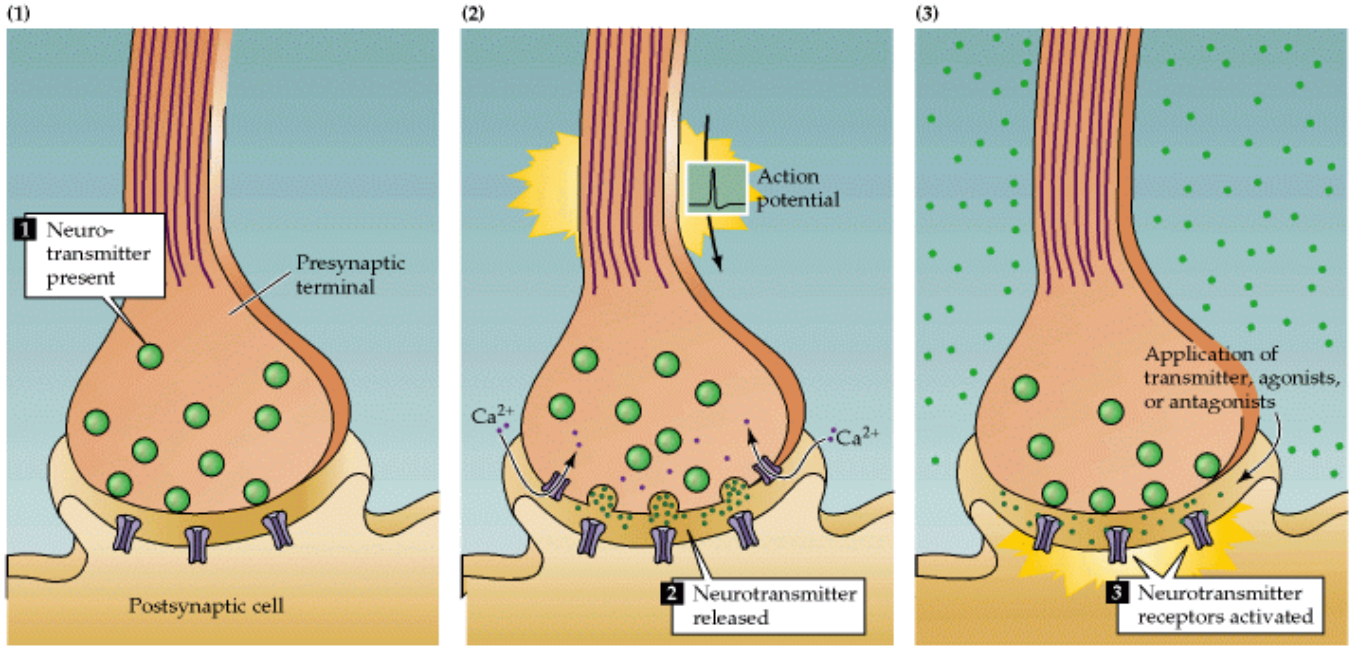
Neurotrasnsmiter



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- Present in presinaptic neuron

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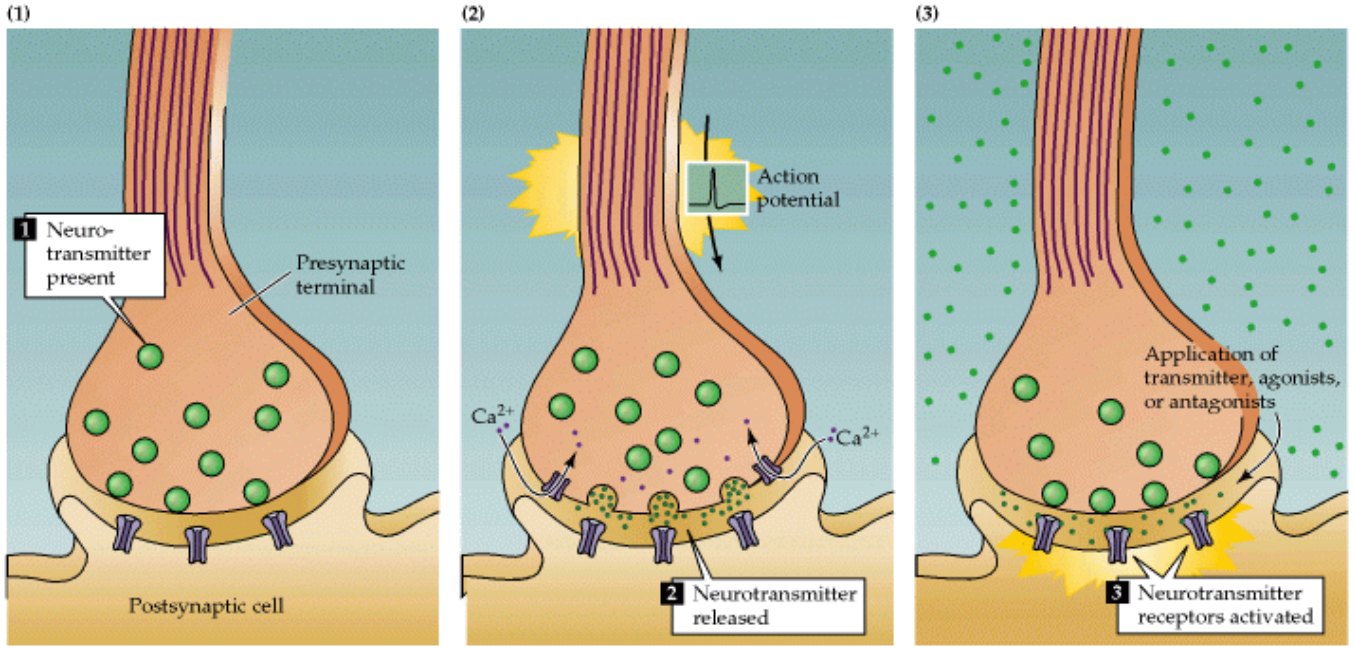
Neurotrasnsmiter



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

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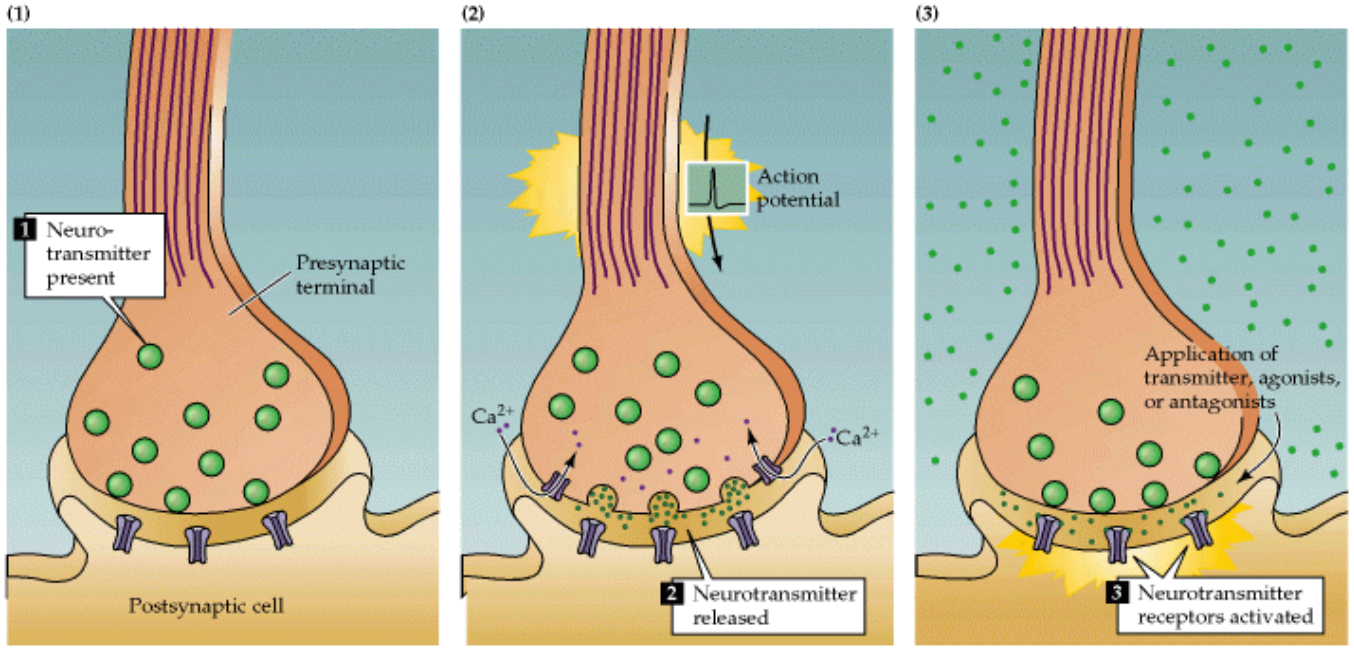
Neurotrasnsmiter



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

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Neuromuscular junction

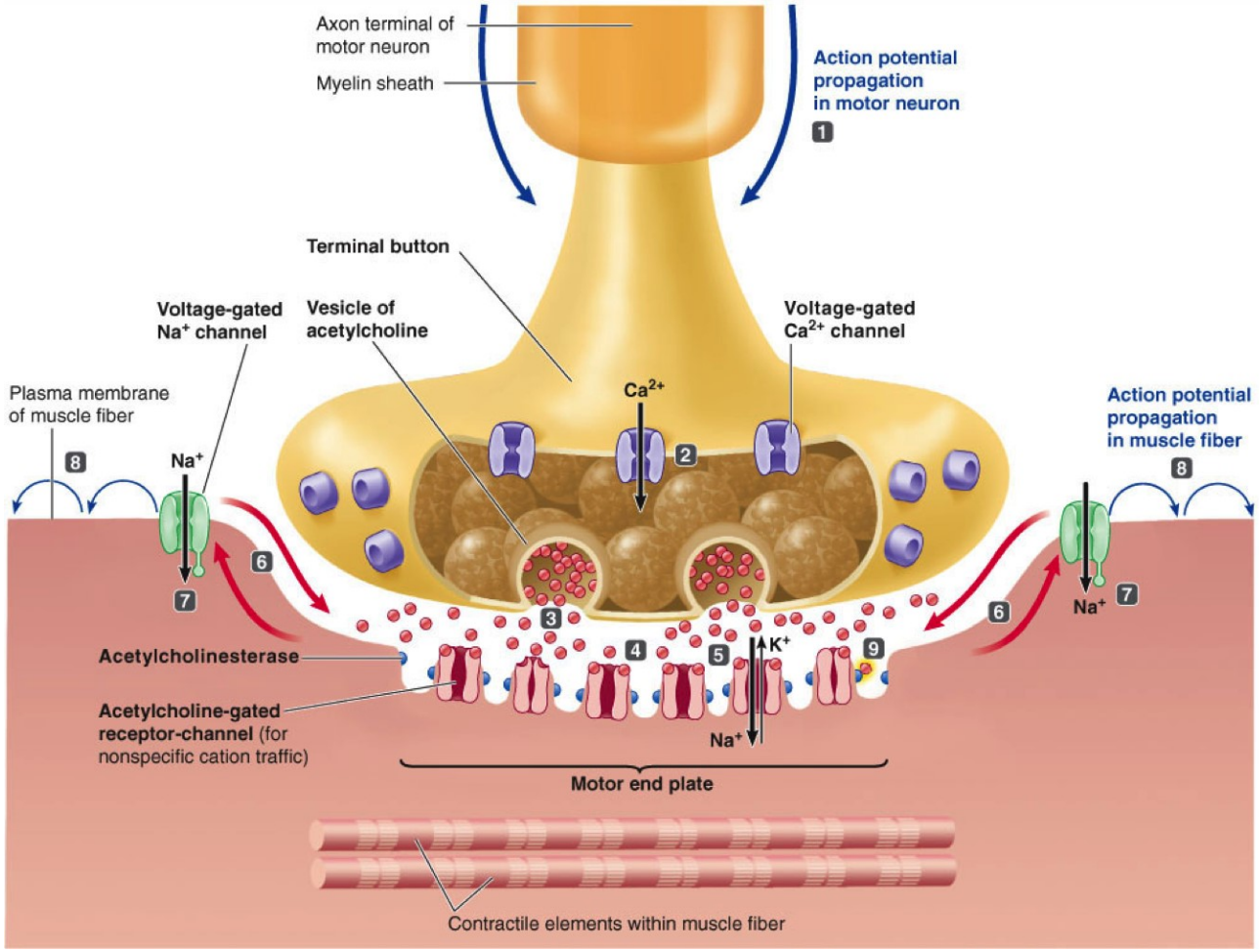

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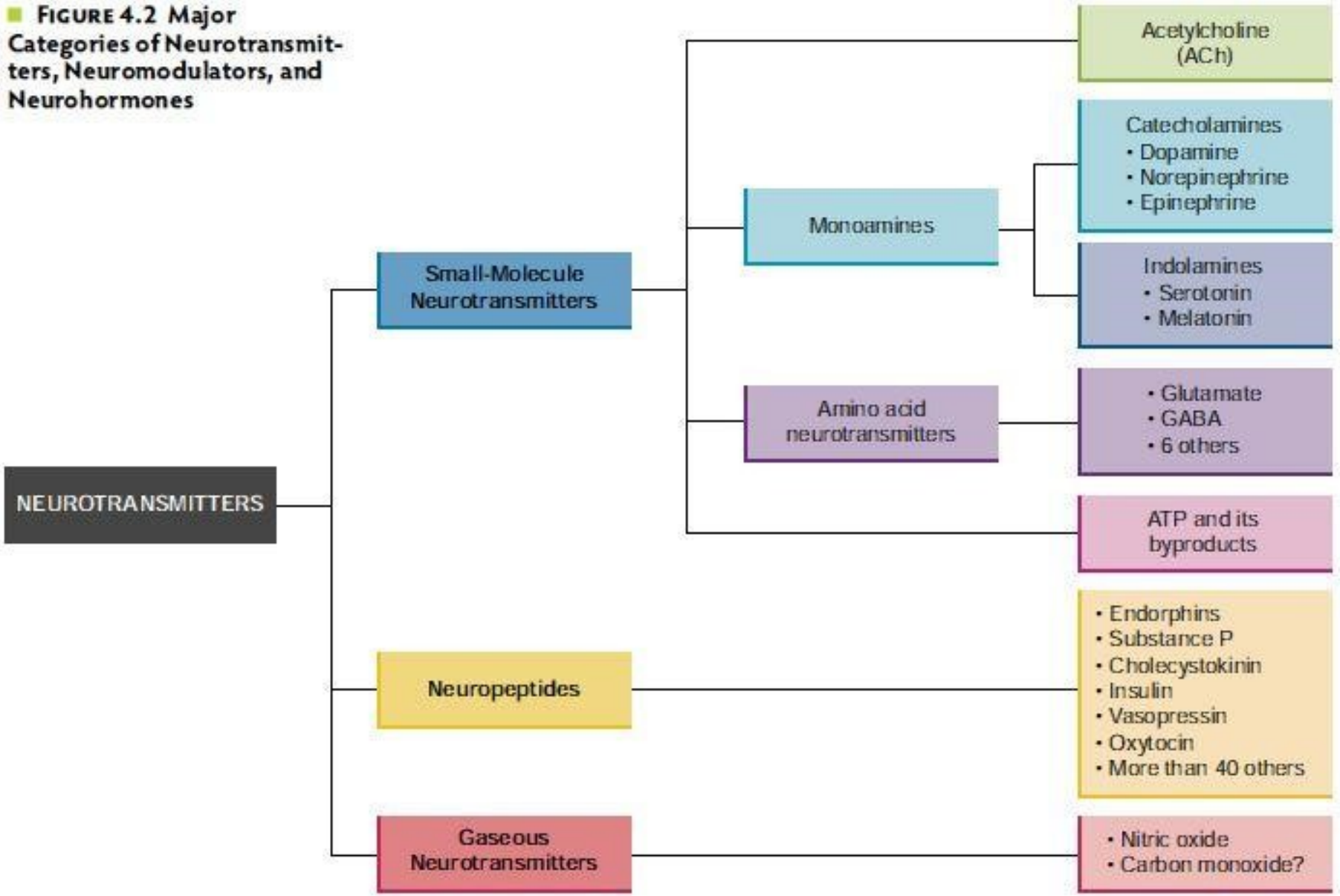
FIGURE 4.2 Major Categories of Neurotransmitters, Neuromodulators, and Neurohormones



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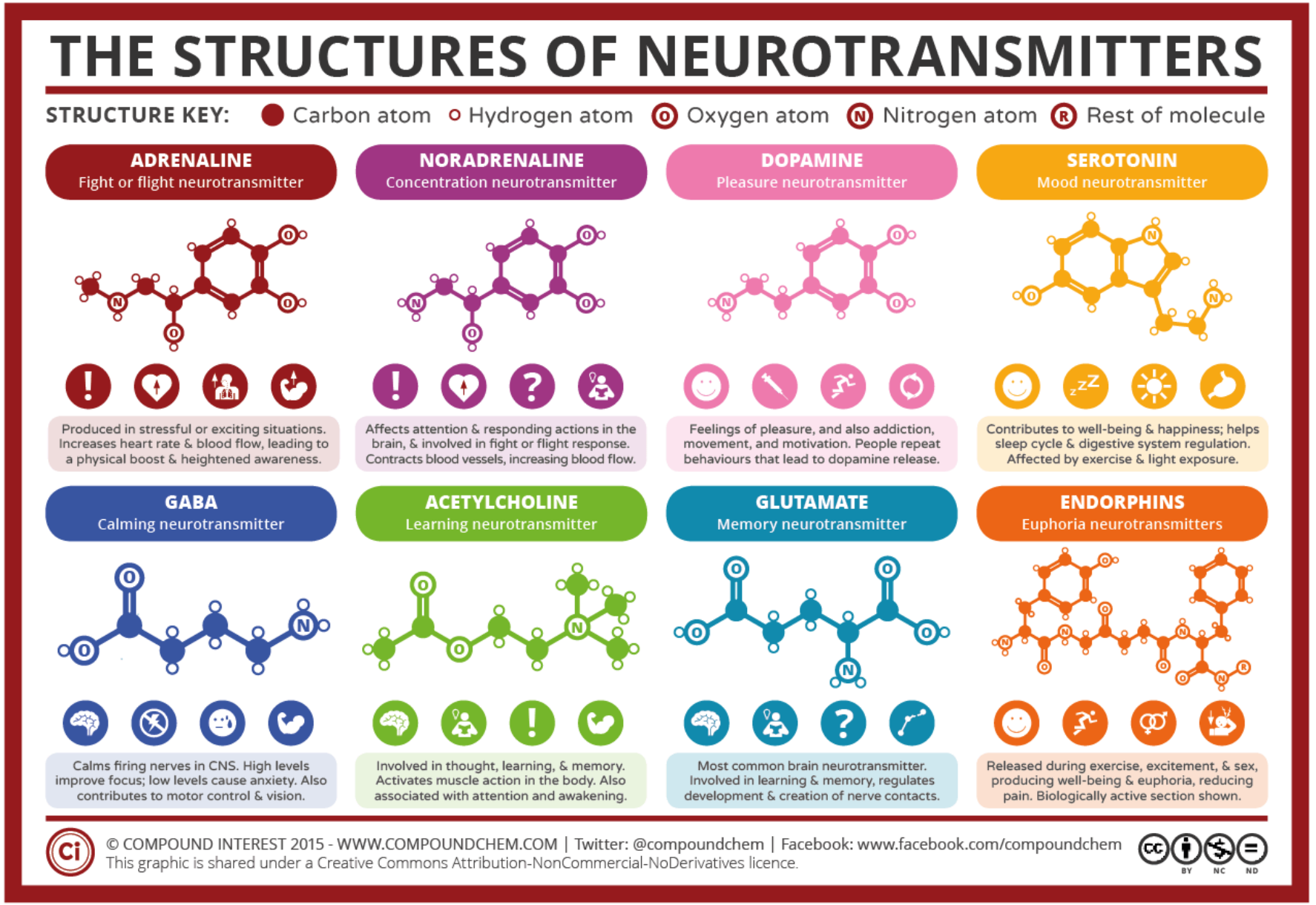

http://www.compoundchem.com/2015/07/30/neurotransmitters/

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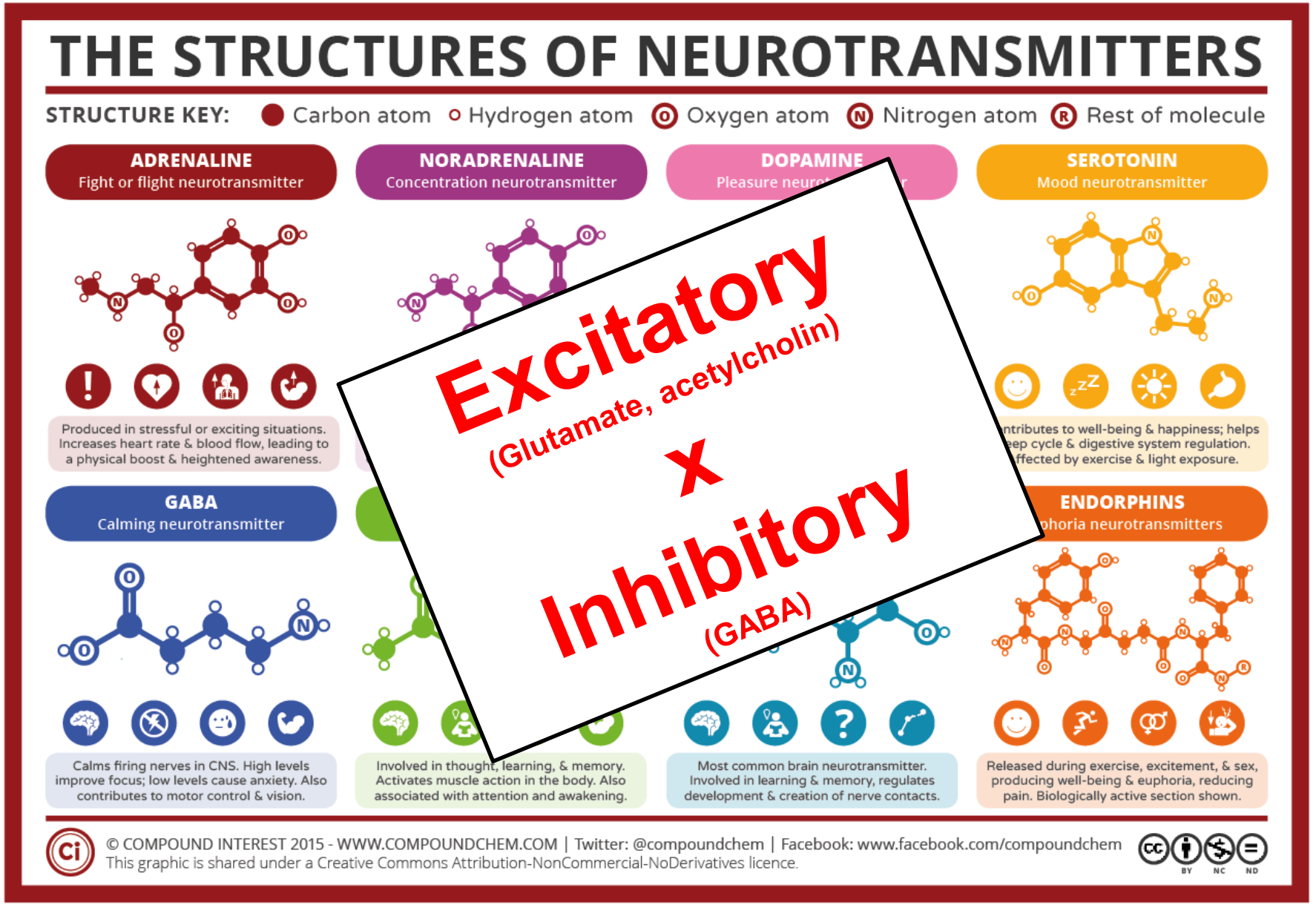

http://www.compoundchem.com/2015/07/30/neurotransmitters/

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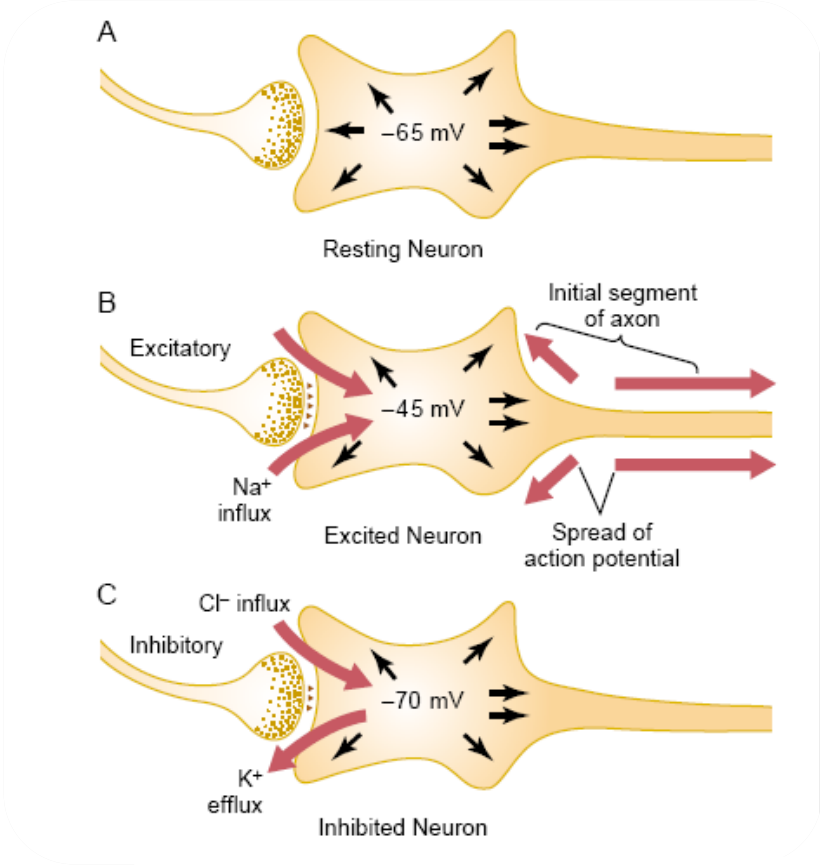
Excitatory/inhibtory postsynaptic potencial



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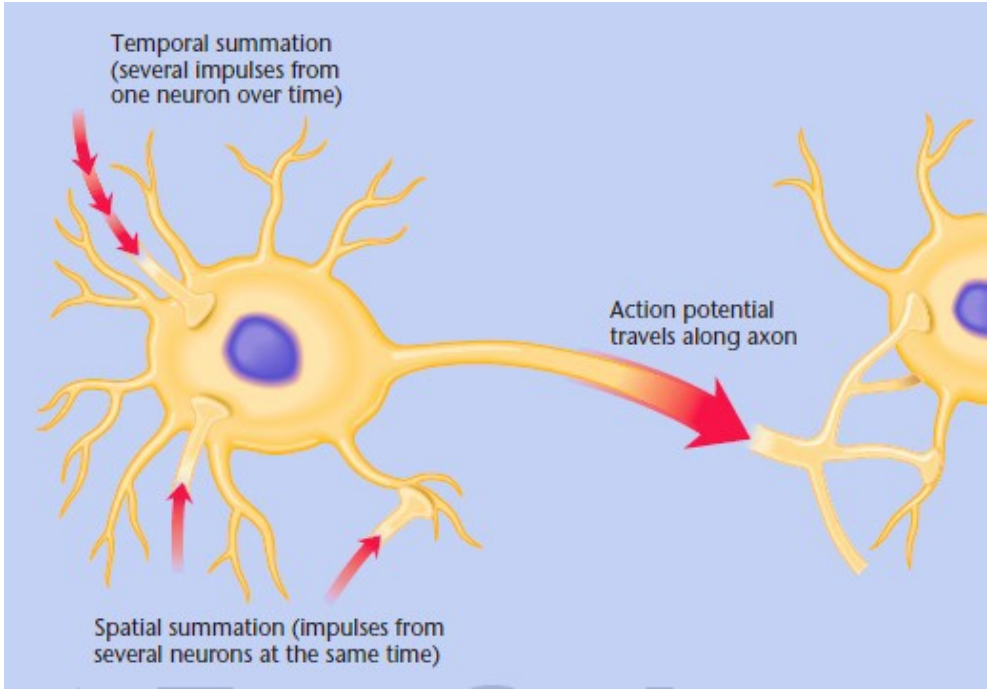
Signal summation

- Temporal
- Spatial



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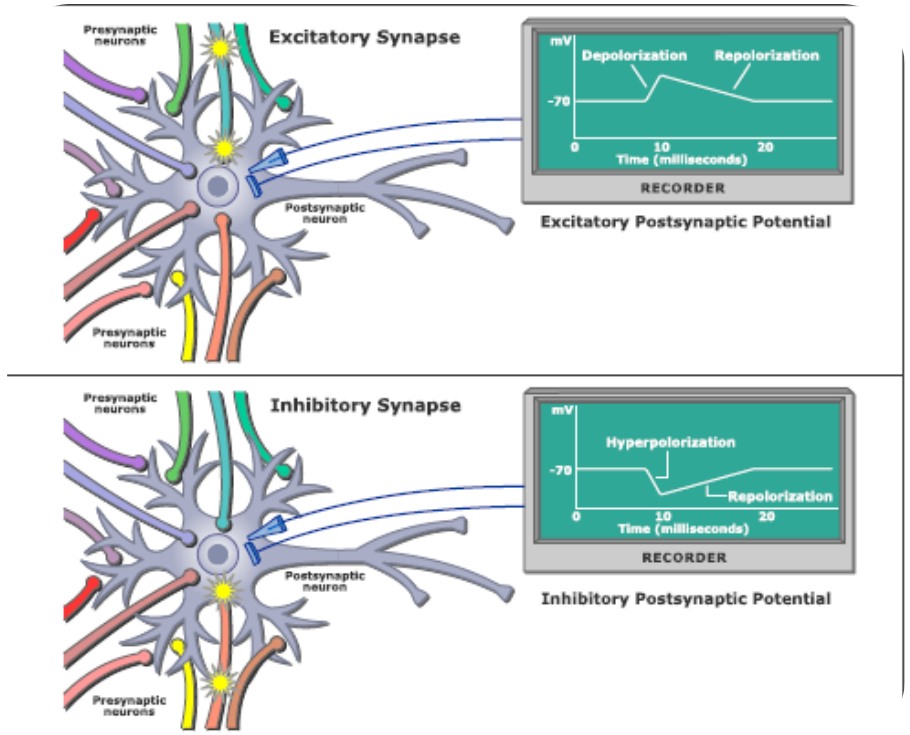

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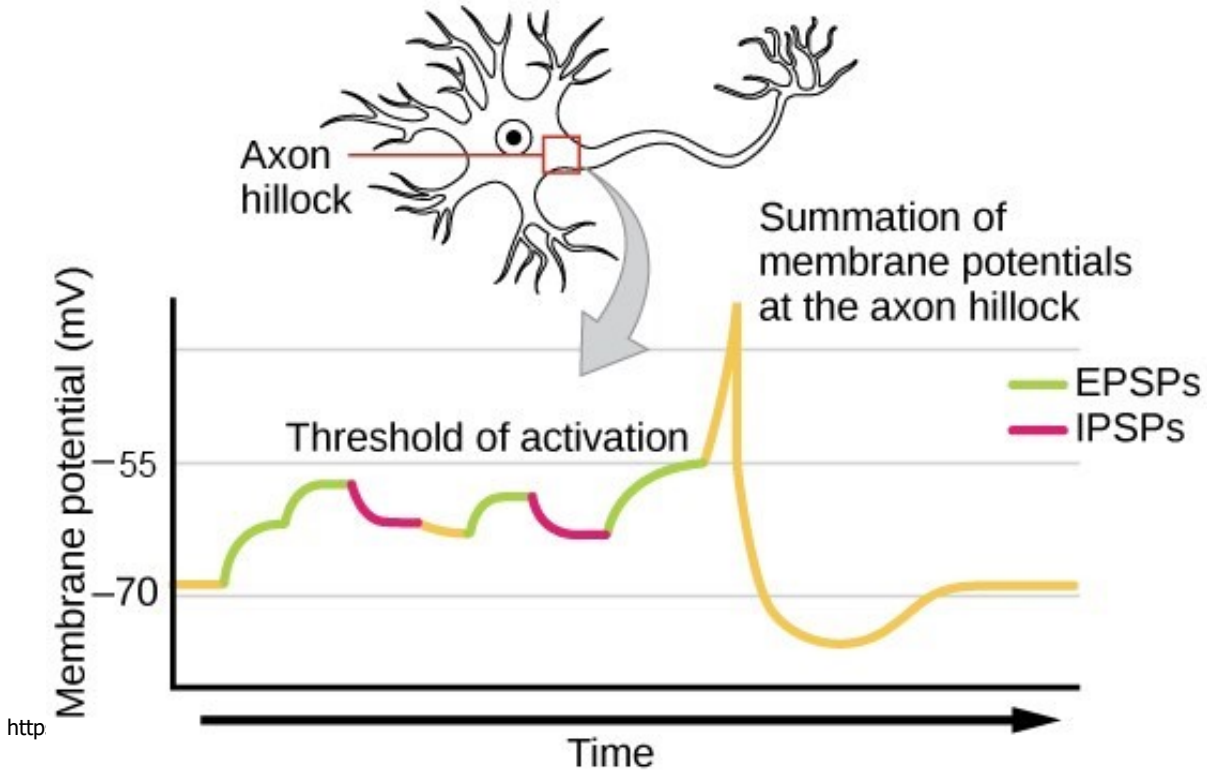
Signal summation



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

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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

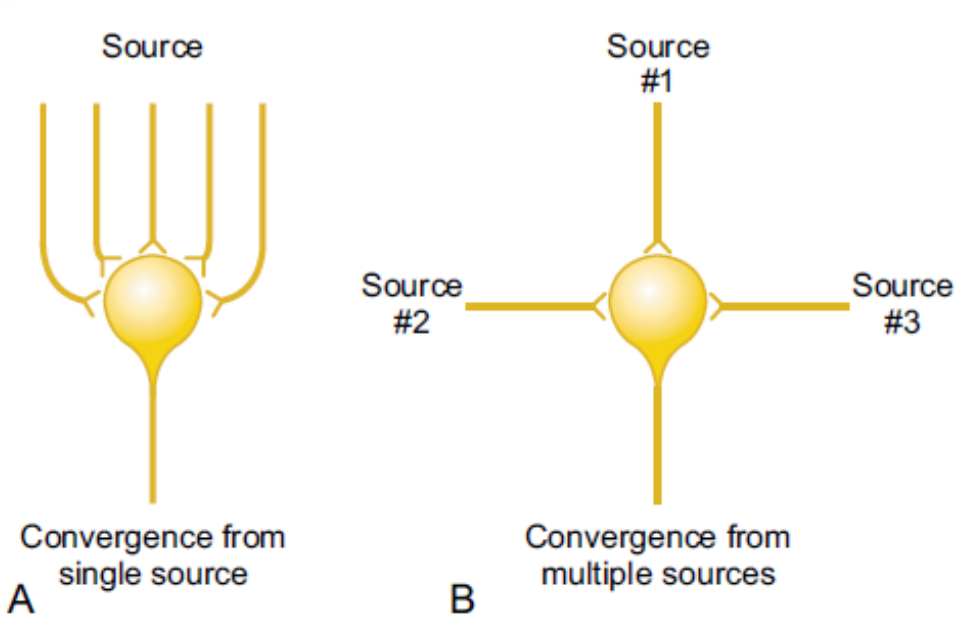

Figure 46–12

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

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Synaptic divergence

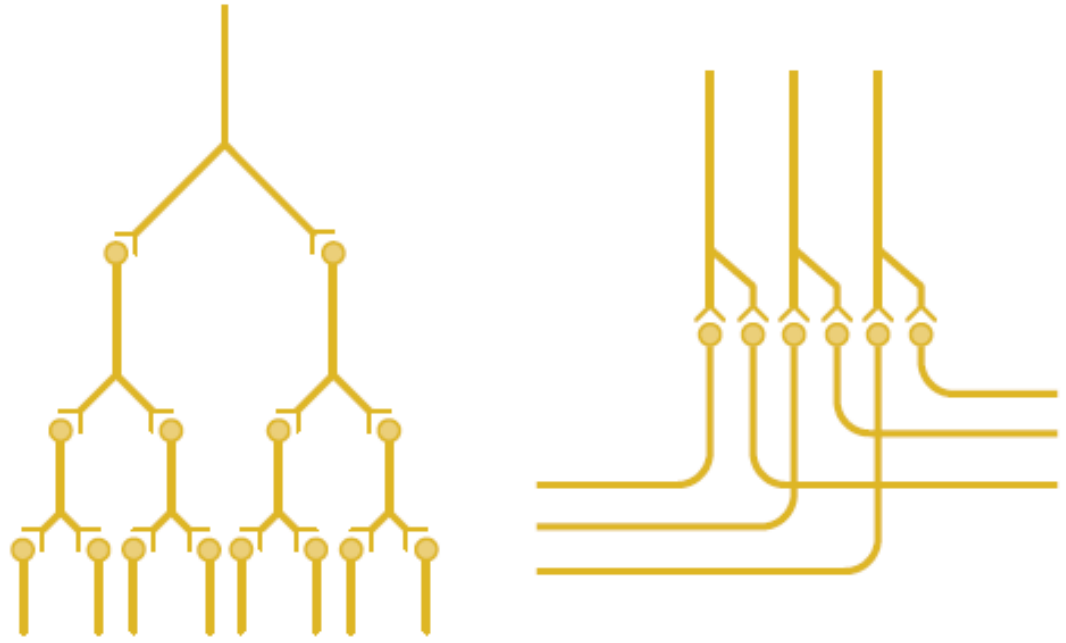

Figure 46–11

"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.

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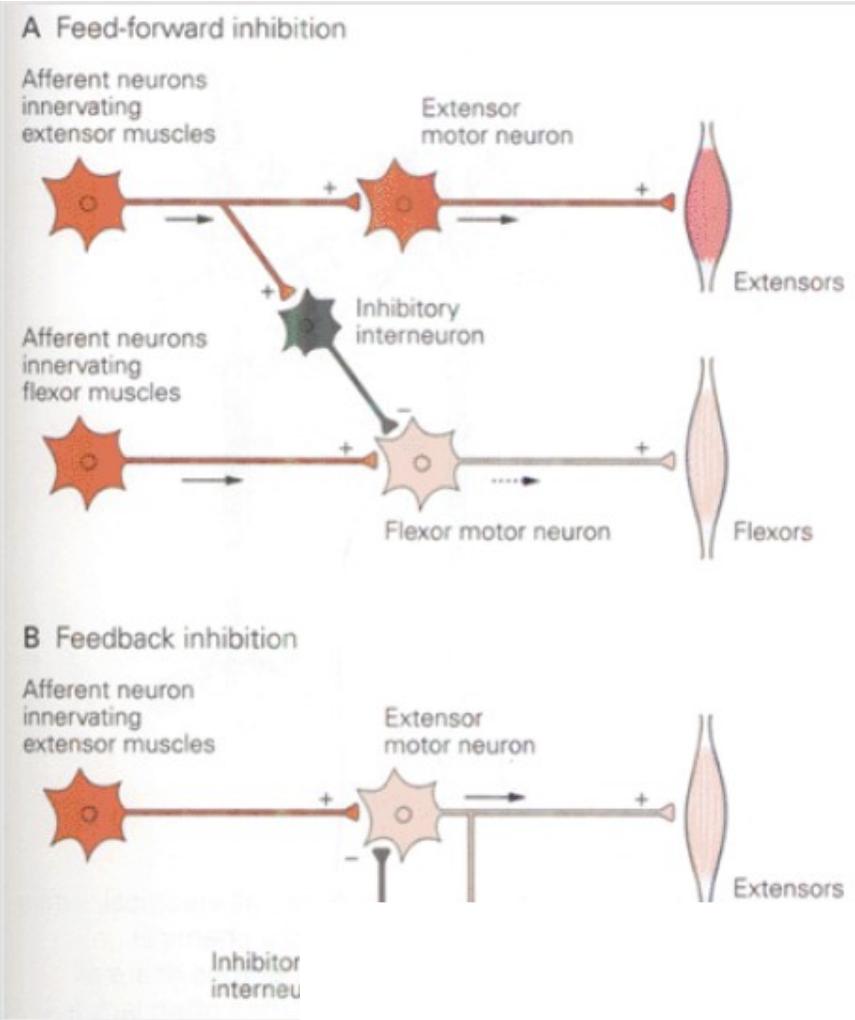
Networking



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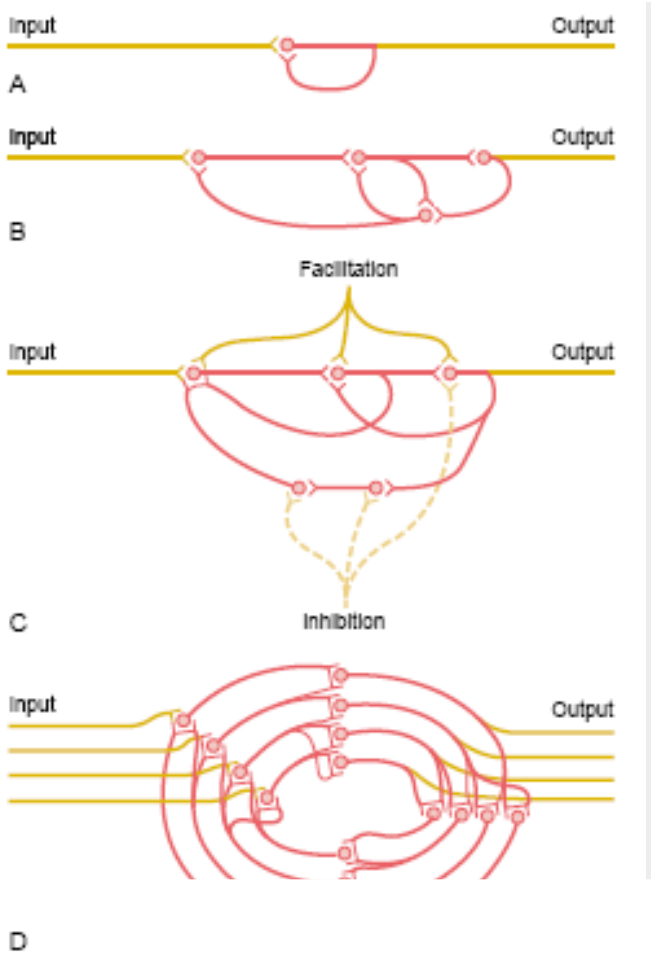
Networking



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Neurotransmission vs. Neuromodulation

- Information transmission

- Regulation of NS activity

Neurotransmission vs. Neuromodulation

- Information transmission
- Specific

- Regulation of NS activity
- Diffuse (volume transmission)

Neurotransmission vs. Neuromodulation

- Information transmission
- Specific
- Receptors – ion channels

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

Neurotransmission vs. Neuromodulation

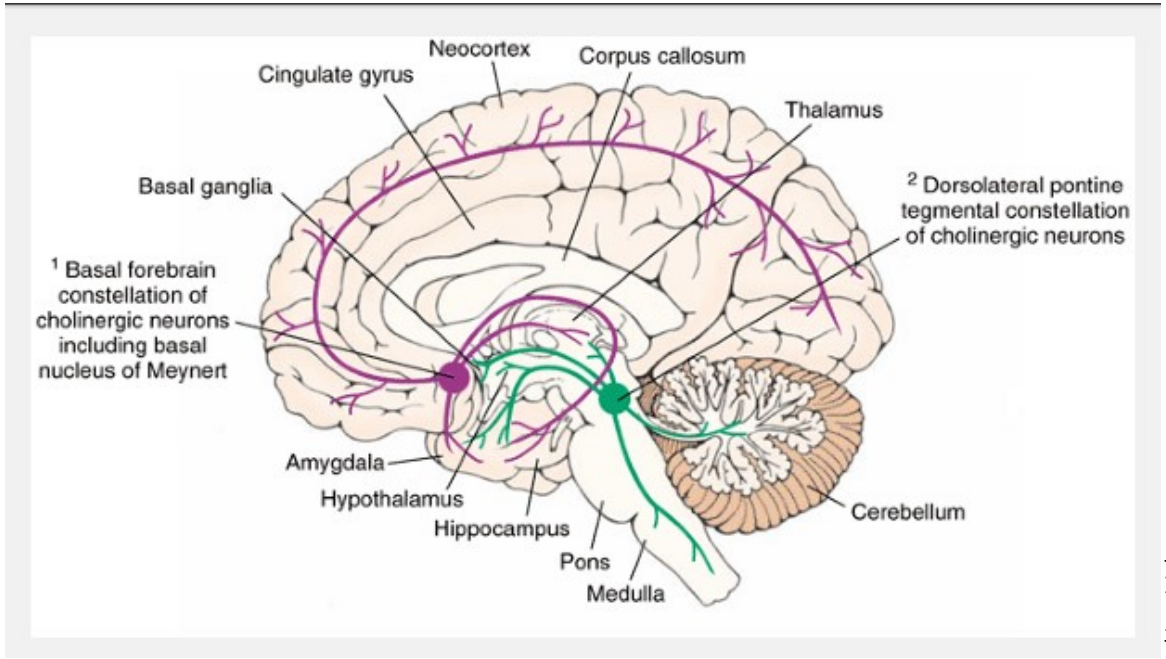
- Information transmission
- Specific
- Receptors – ion channels
- Short duration
  - membrane potential changes

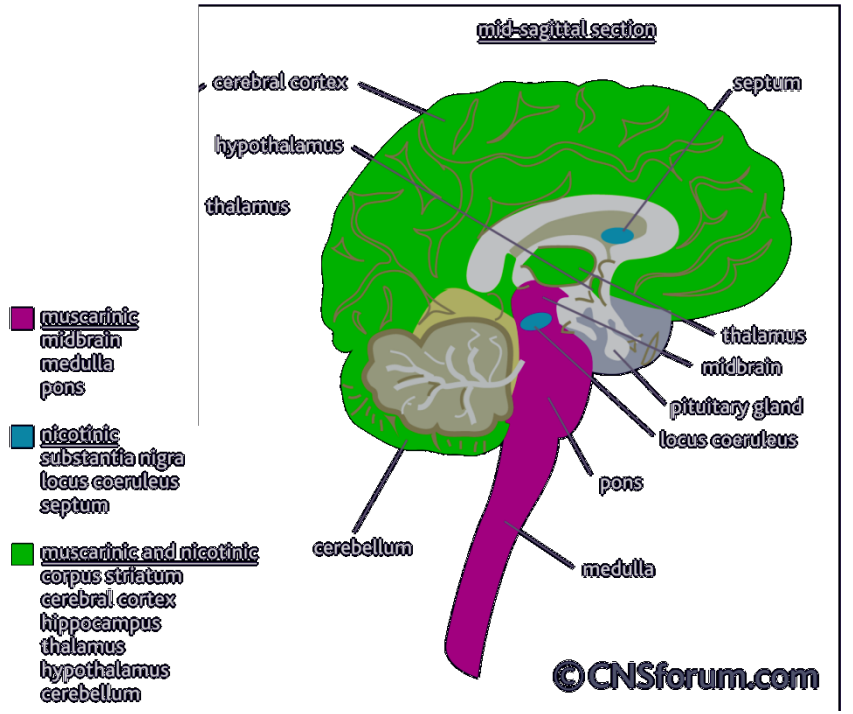
- Regulation of NS activity
- Diffuse (volume transmission)
- Receptors – G-proteins
- Longer duration
  - changes in synaptic properties

Acetylcholine

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

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





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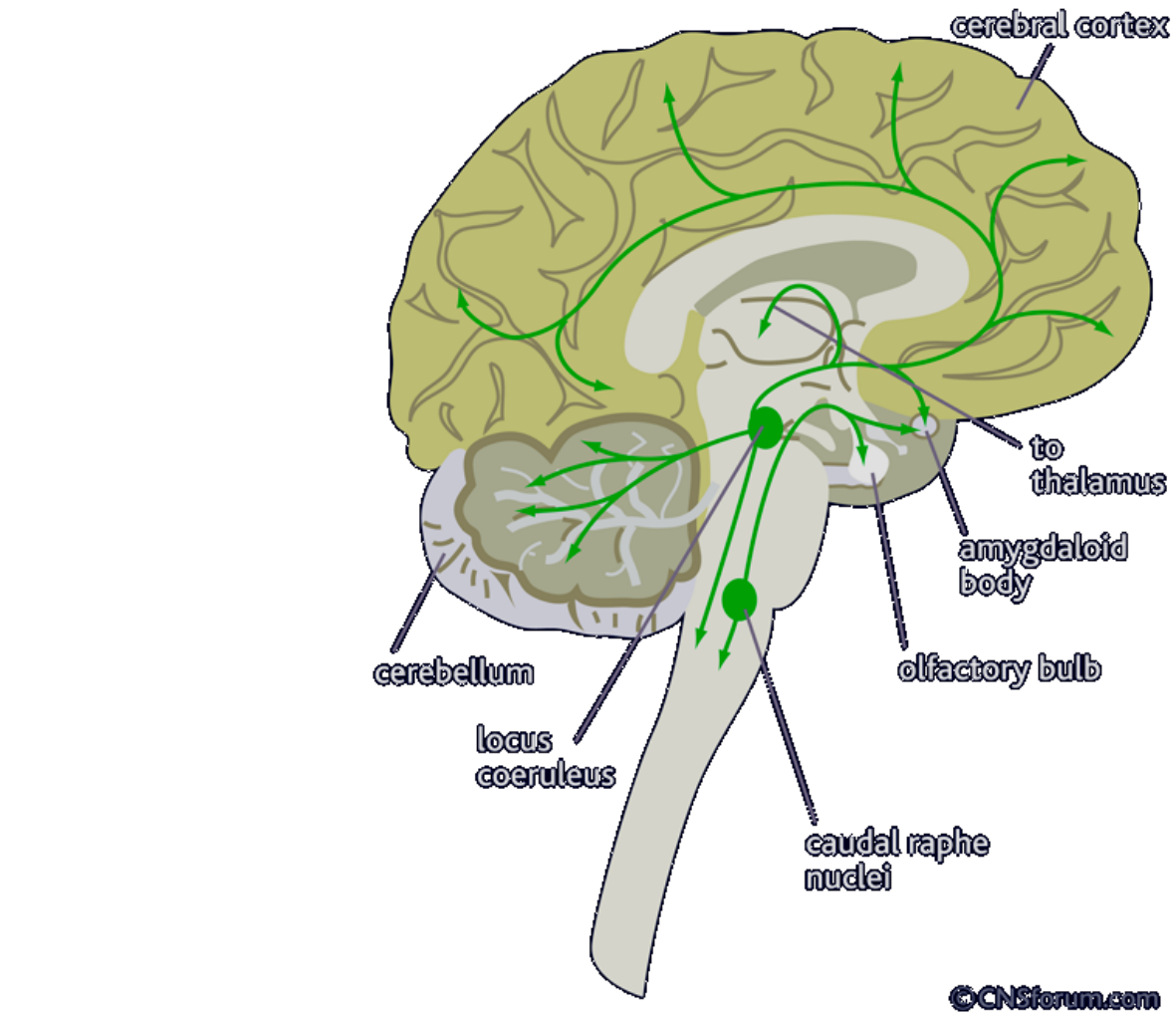
Noradrenalin

- Locus coeruleus
- Nuclei raphe caudalis

- Vigilance
- Responsiveness to unexpected stimuli
- Memory
- Learning



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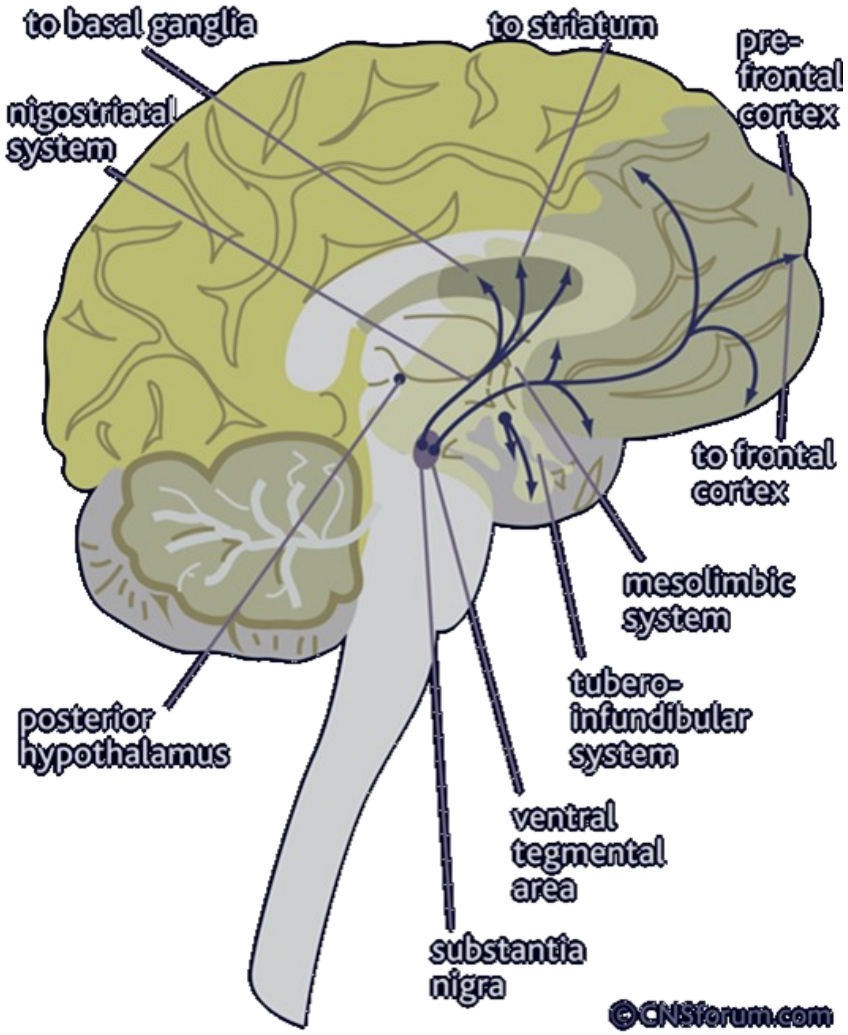
Dopamin

- Nigrostriatal system
  - Movement
  - Sensory stimuli
- Ventrotegmentno-mesolimbic-frontal system
  - Reward
  - Cognitive function
  - Emotional behavior
- Tubero-infundibular system
  - Hypotalamic-pituatory regulation
- D1 receptors – excitatory
- D2 receptors - inhibitory



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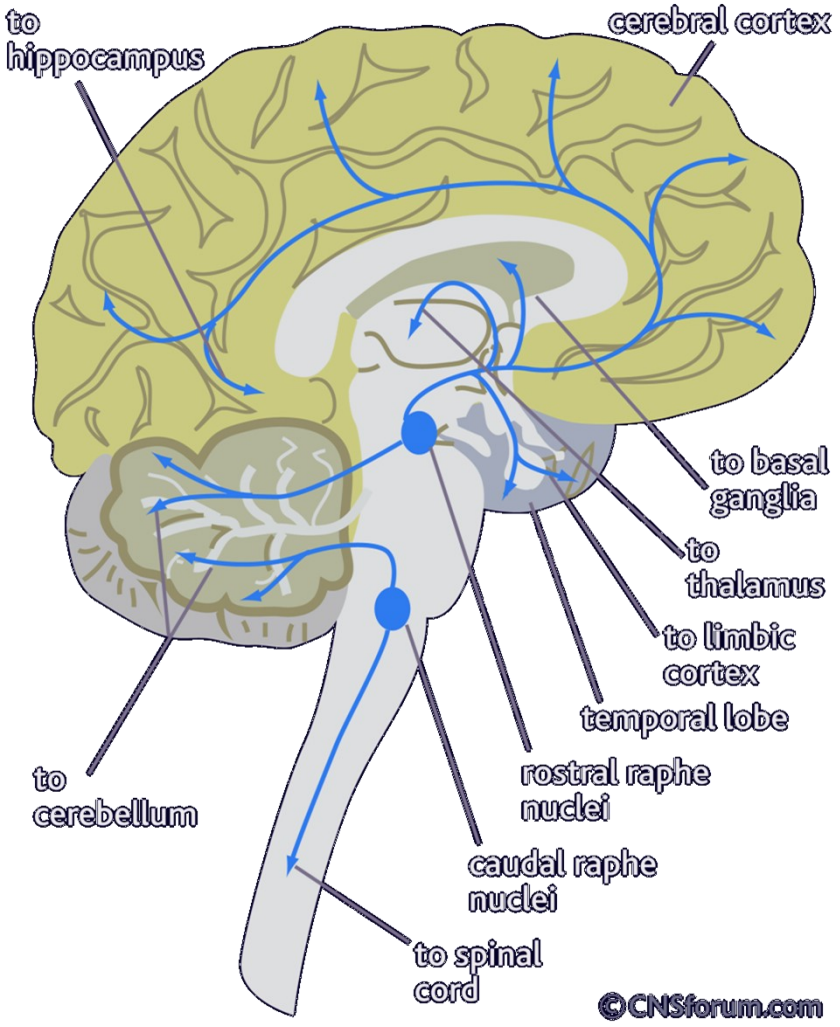
Serotonin

- Nuclei raphe rostralis
- Nuclei raphe caudalis

- Anxiety/relaxation
- Impulsive behavior
- Sleep



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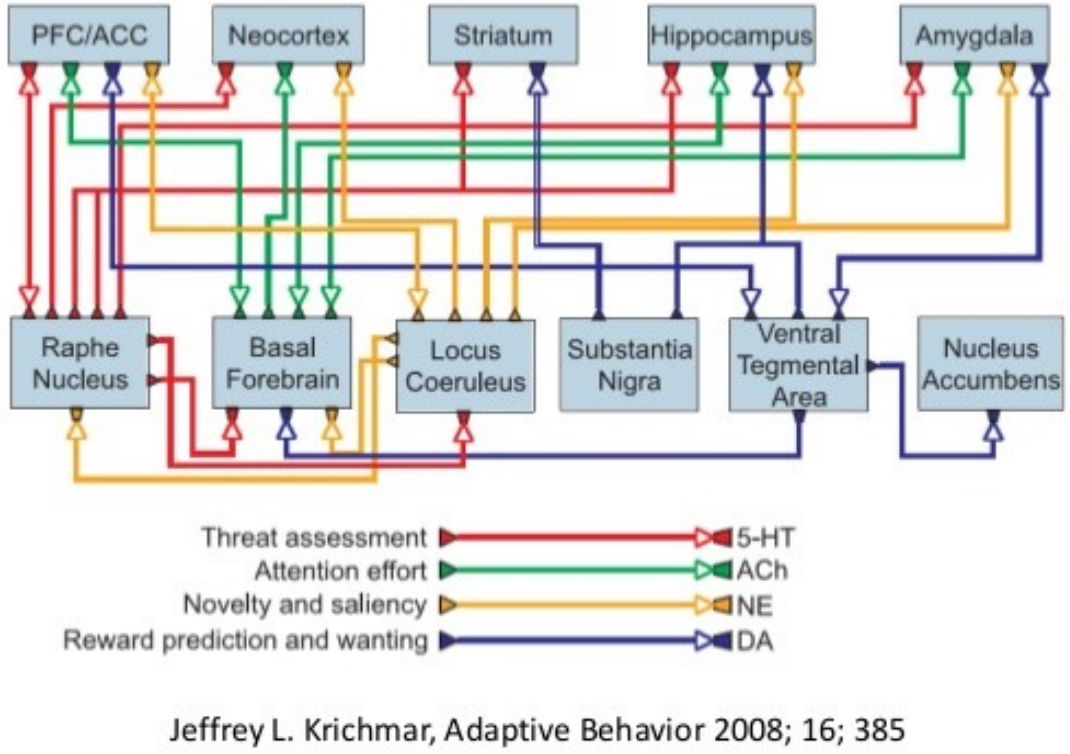
Neuromodulatory systems



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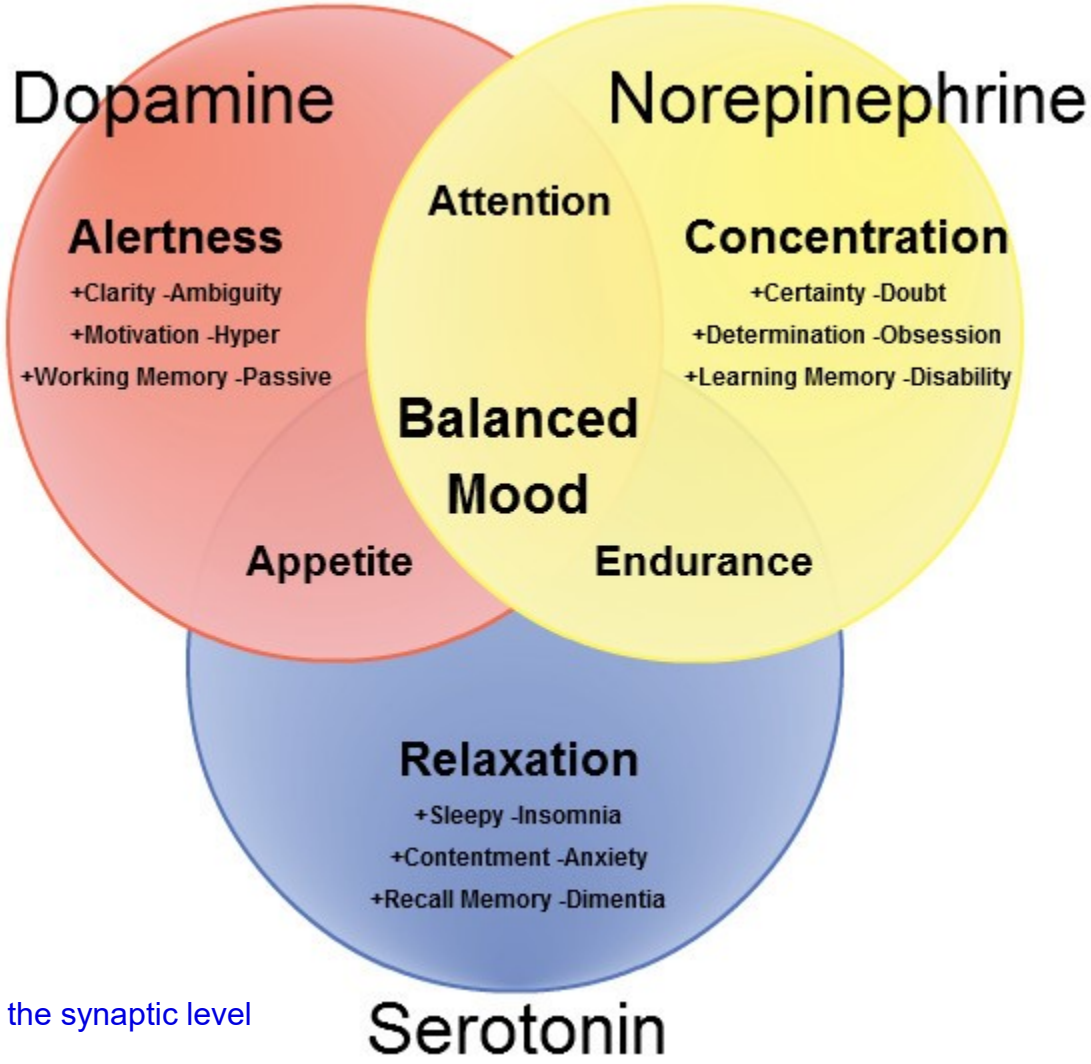
Neuromodulatory systems



http://ausm.org.uk/wp-content/uploads/2015/02/Dopamine_Norepinephrine_Serotonin.jpg

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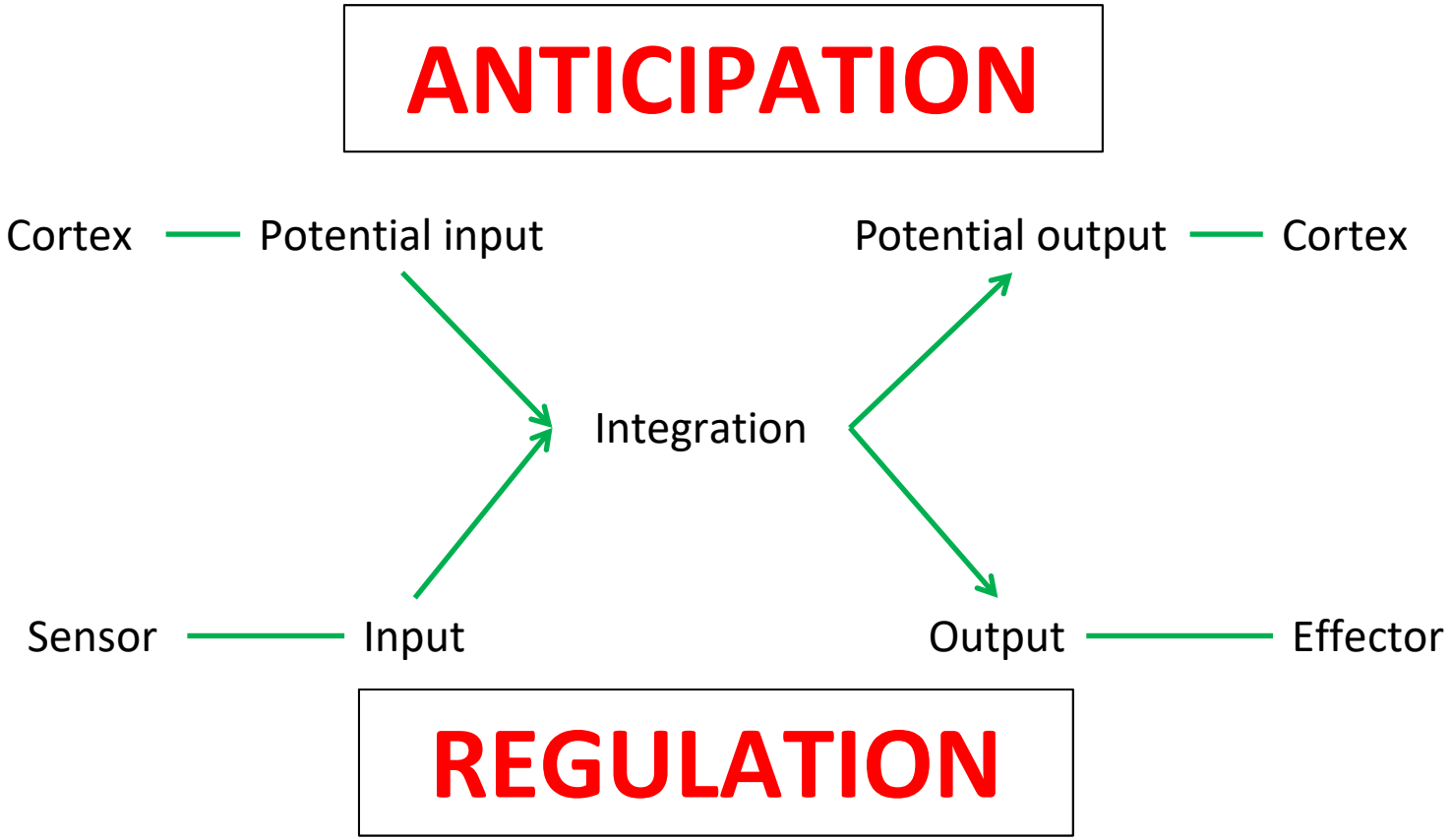
Somatosensitivity, pain

The role of nervous system



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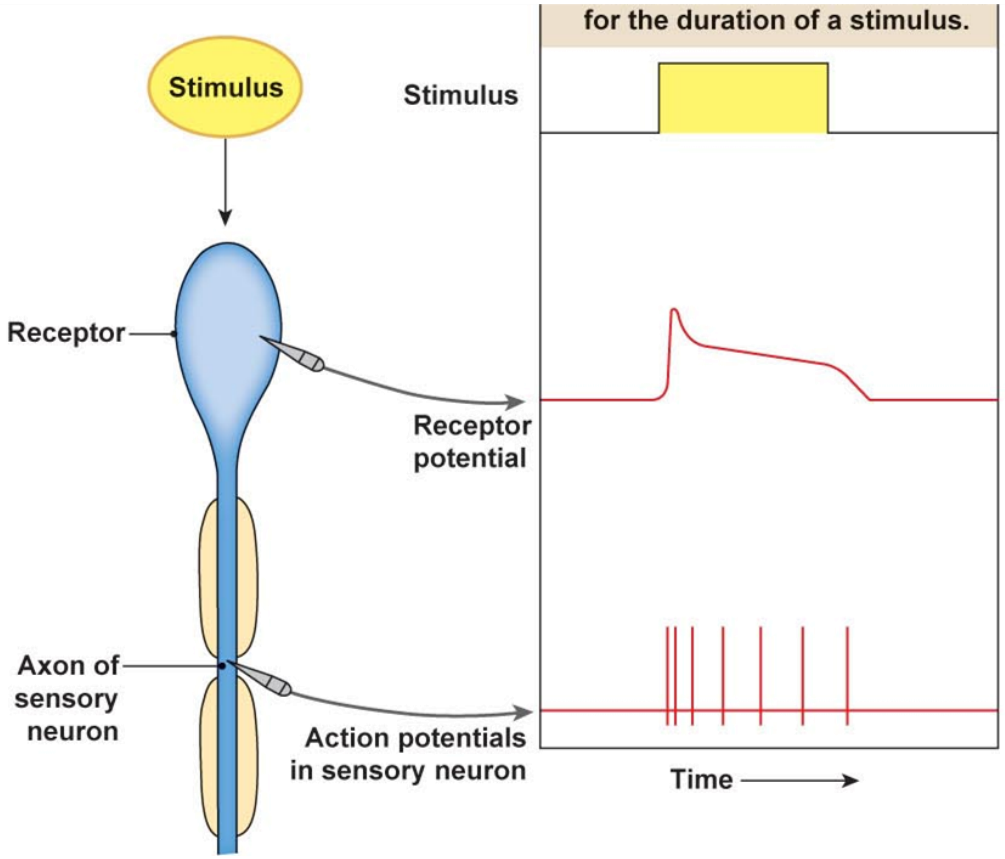
Receptors/sensors

- Energy convertor
  - Signal reception
  - Signal transformation
- Receptor potential
  - Generator potential
- Action potential



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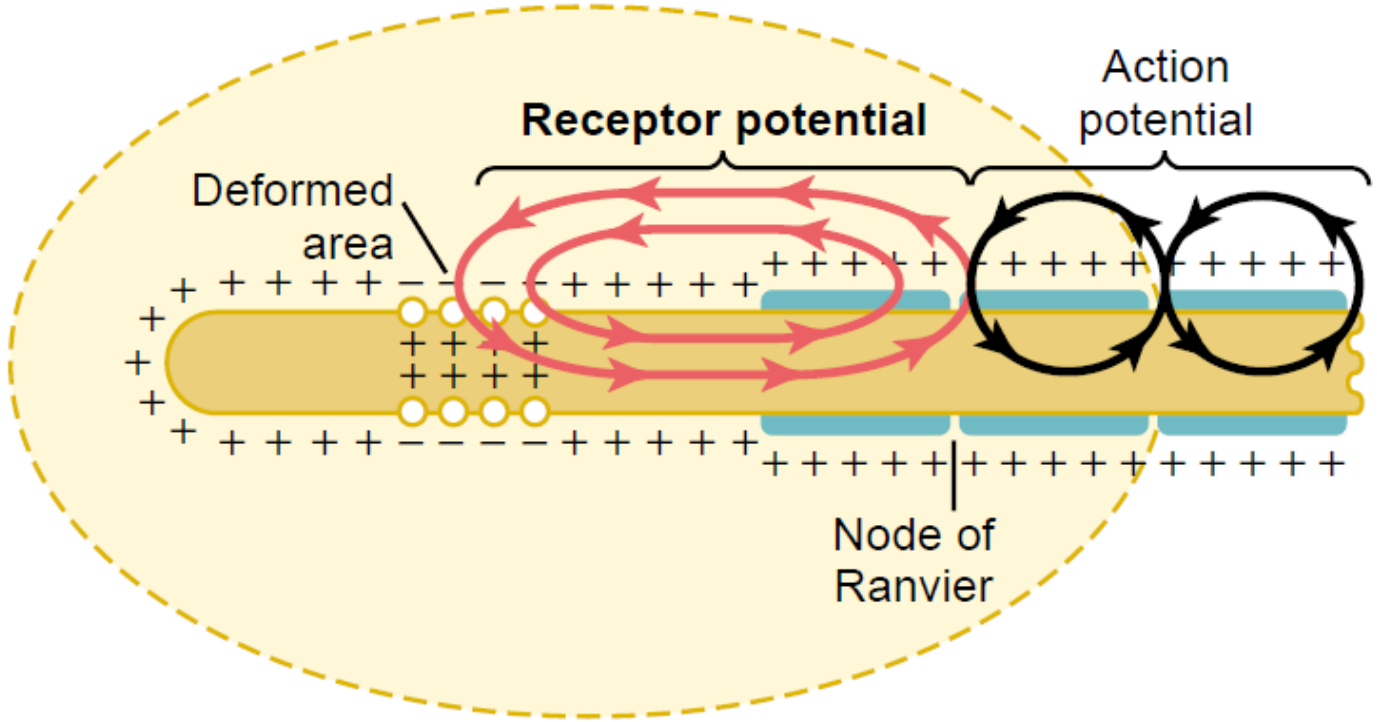
Receptor/generator and action potential



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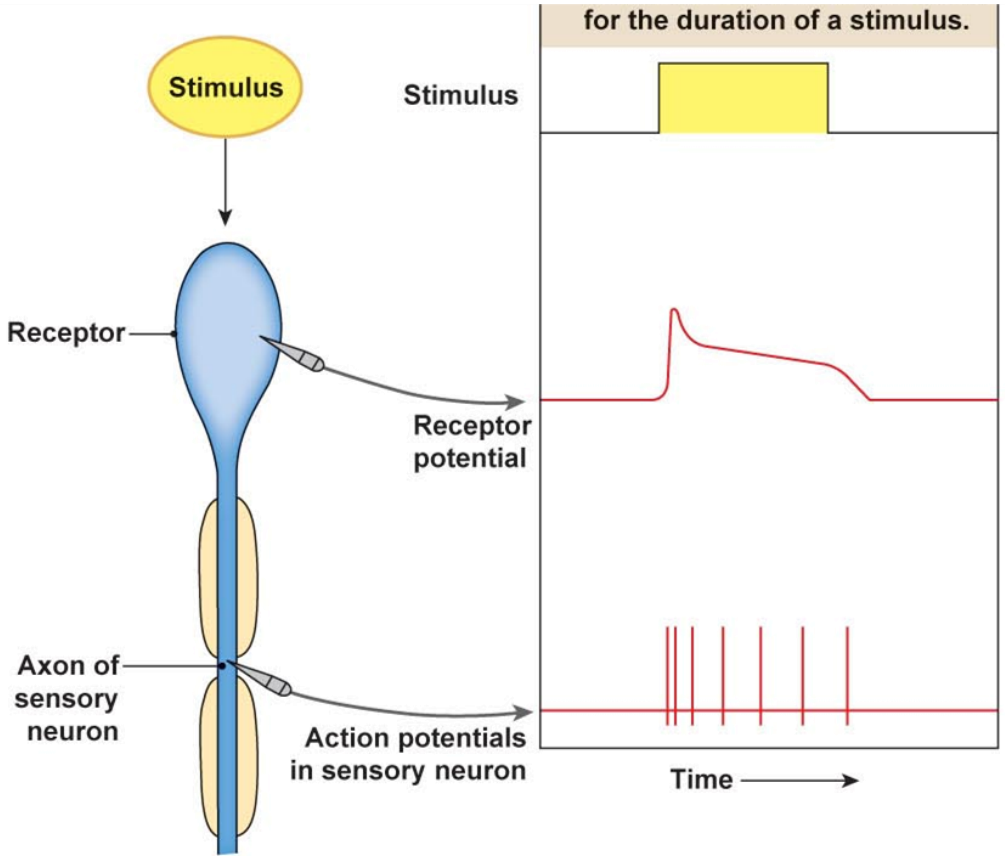
Receptors/sensors

- Energy convertor
  - Signal reception
  - Signal transformation
- Receptor potential
  - Generator potential
- Action potential
- Adequate stimulus
- Non adequate stimulus



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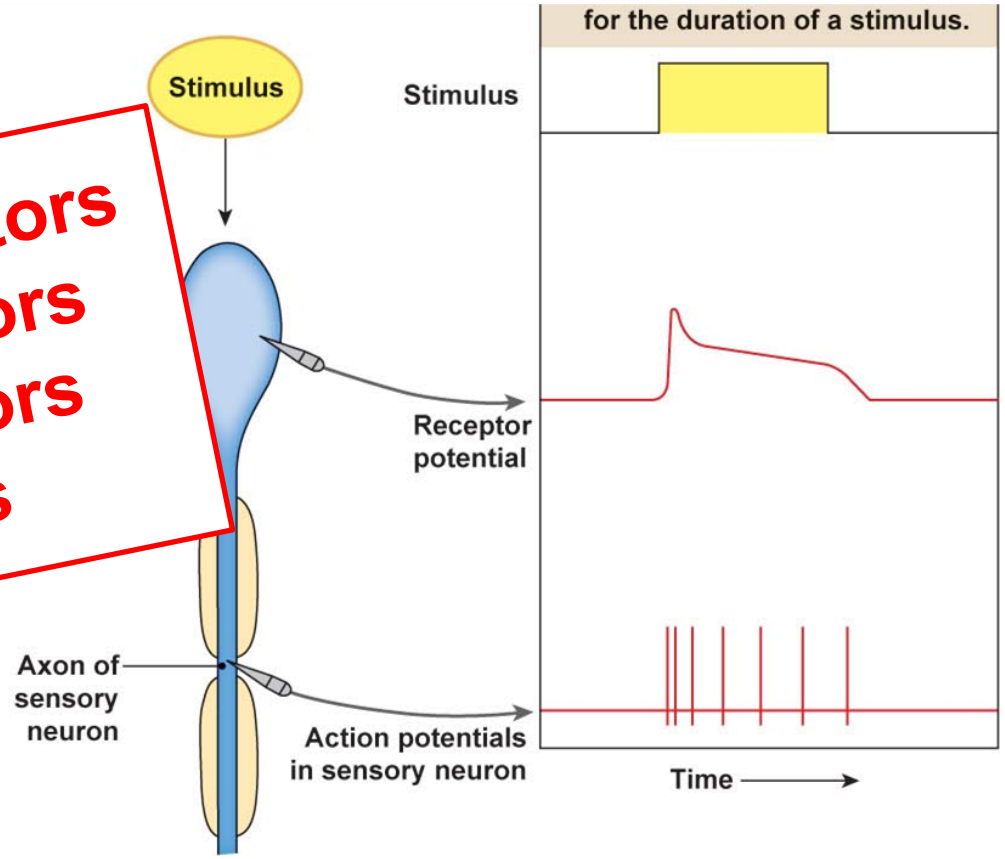
Receptors/sensors

- Energy convertor
  - Signal reception
  - Signal transformation
- Receptor potentia
  - Generator potentia
- Action potential
- Adequate stimulus
- Non adequate stimulus

✓ Mechanoreceptors
✓ Thermoreceptors
✓ Chemoreceptors
✓ Fotoreceptors



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Receptors/sensors

- Energy convertor
  - Signal reception
  - Signal transformatio
- Receptor pot
  - Generator p
- Action potentia
- Adequate stimul
- Non adequate stim

Basic attributes of stimulus

Qualitative

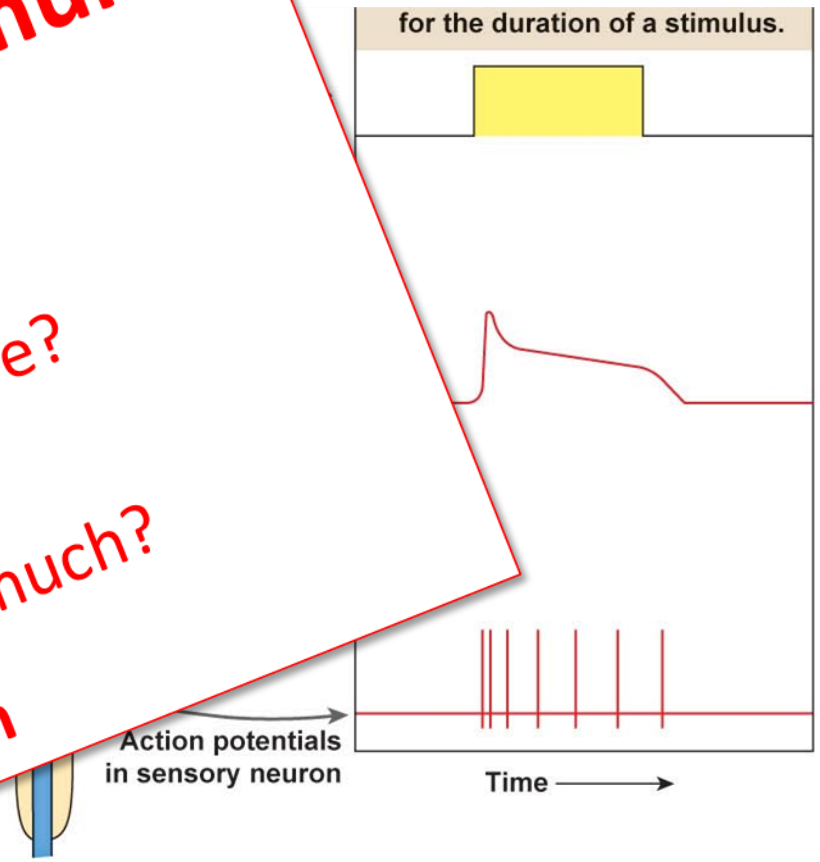
Modality - What?

Localization - Where?

Quantitative

Intensity - How much?

Duration



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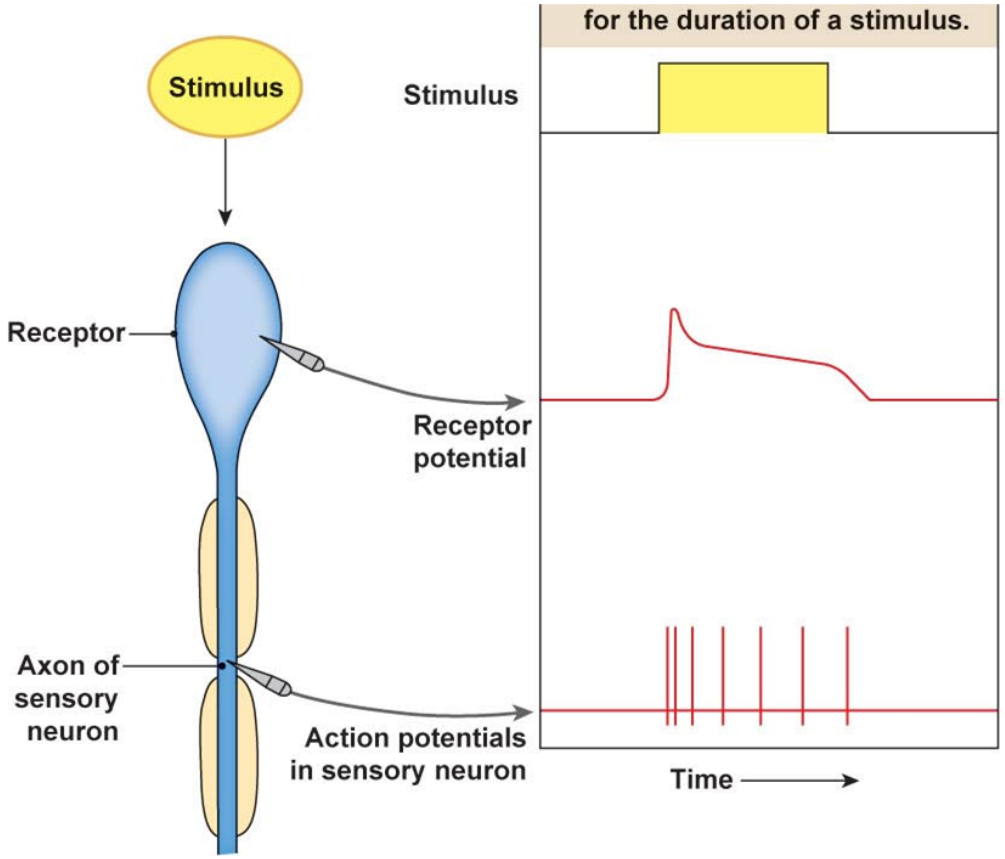
Intensity coding

How much?

- Amplitude of receptor potential is transtucted into the frequency of AP



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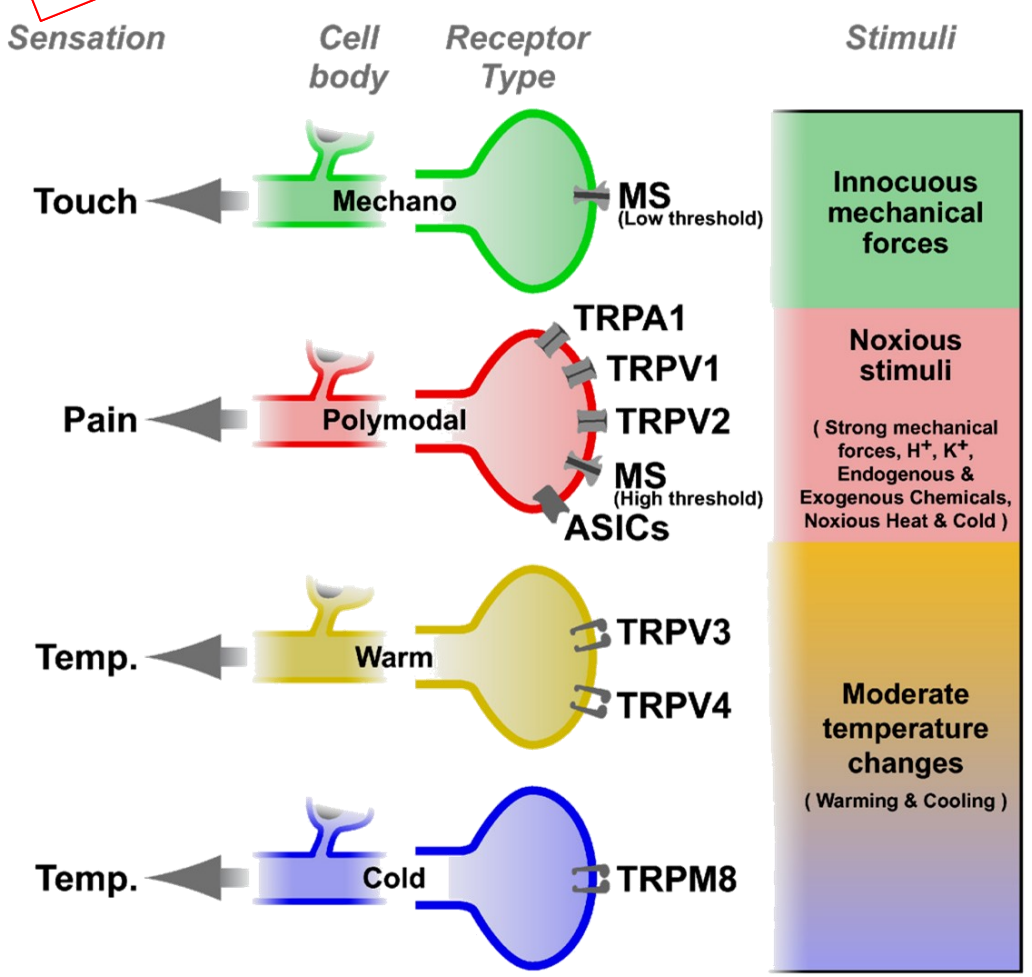
Qualitative information

What?
Where?

- **The law of specific nerve energies:**

  The nature of perception is defined by the pathway over which the sensory information is carried

- Labeled line coding define the information about quality



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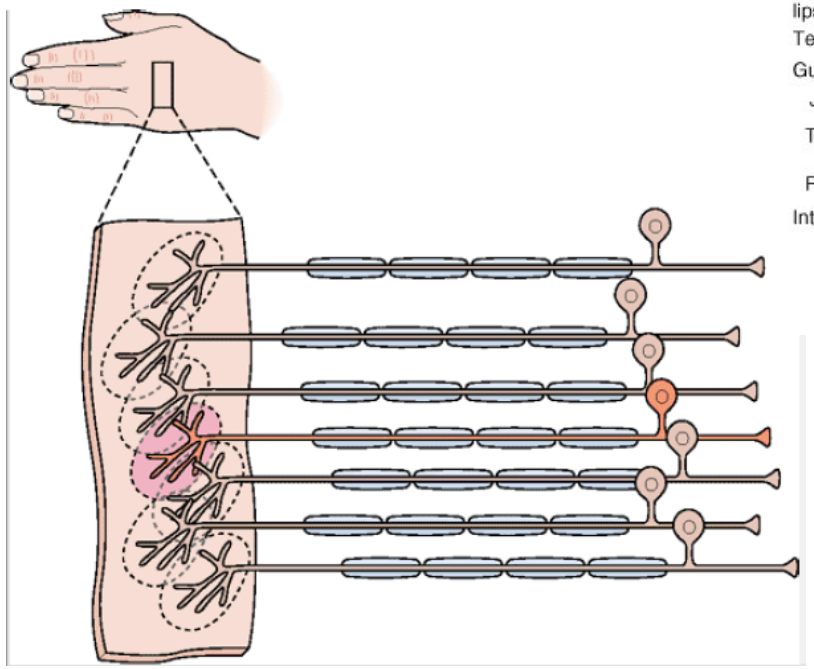
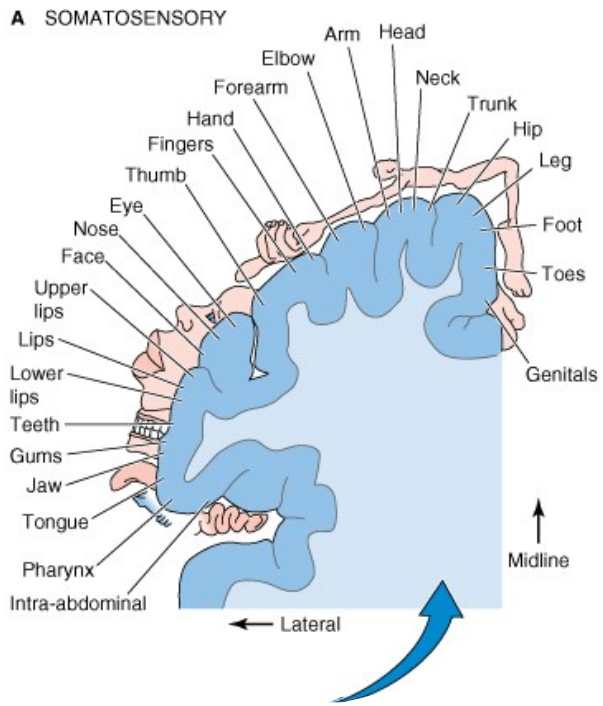
Qualitative information

What?
Where?

- Labeled line coding
- Receptive field
- Nerve stimulation mimics receptor stimulation





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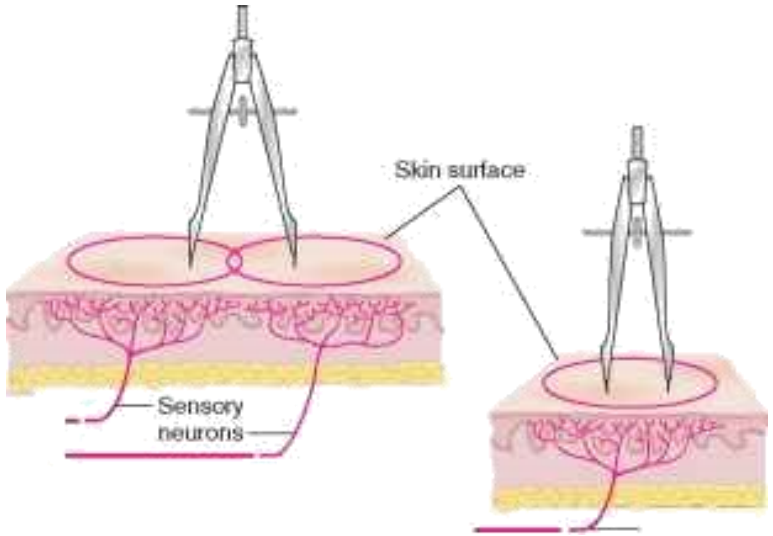
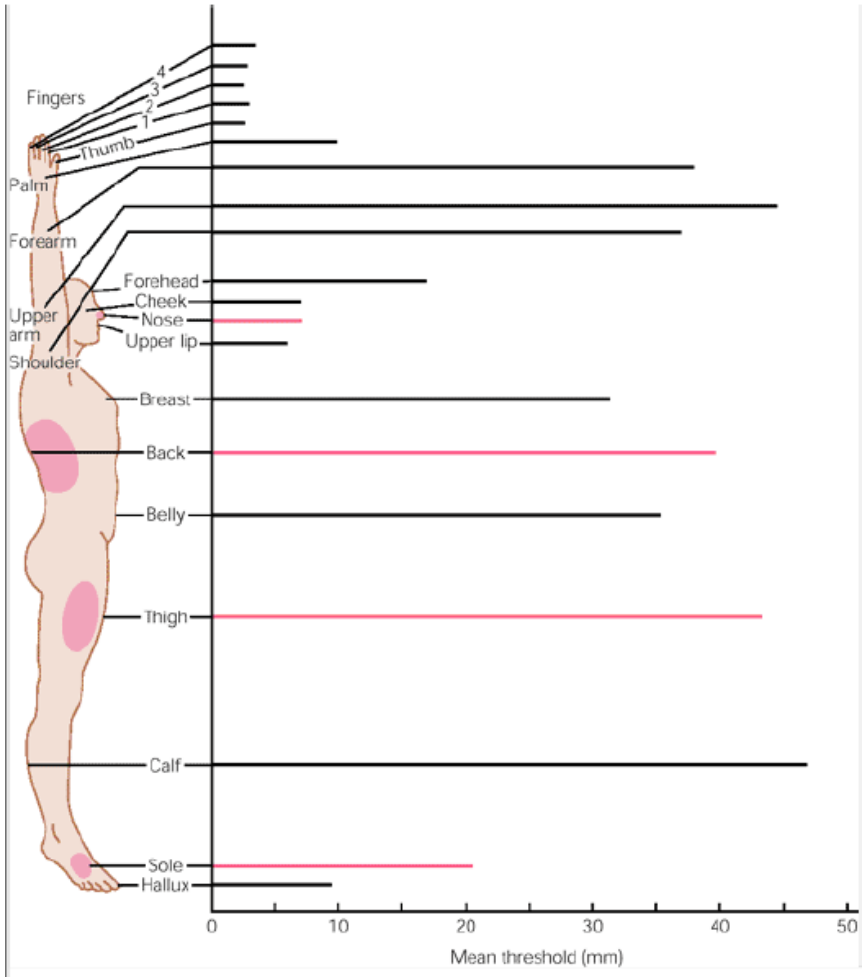
Receptive fields

- Various size and overaly
- Small receptive field – high resolution
- Spatial resolving power increased by lateral inhibition





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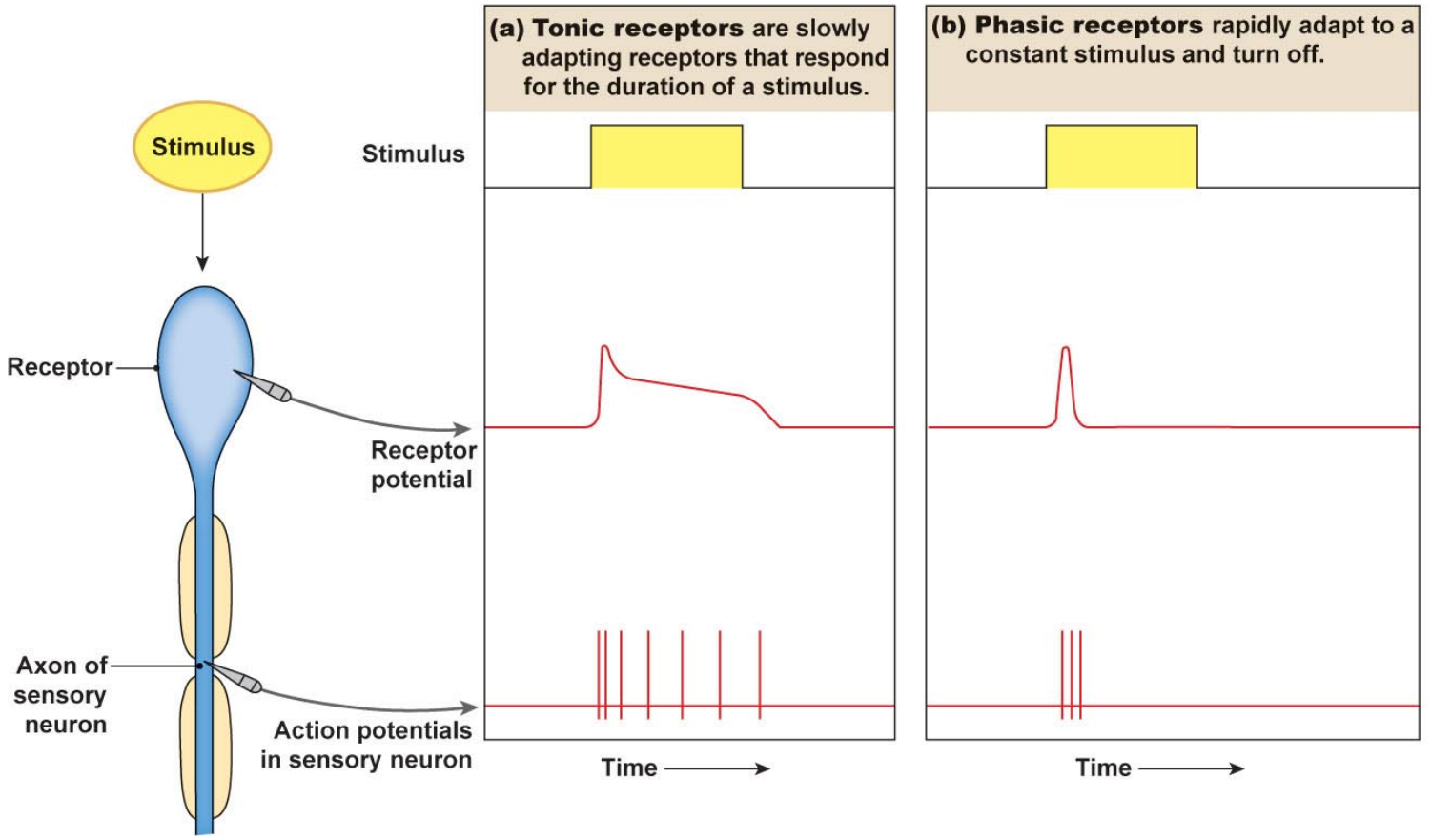
Receptor adaptation

- The decline of receptor responses in spite of stimulus presence
- Tonic receptors – slow adaptation – presence of stimulus, position
- Phasic receptors – rapid adaptation – change of stimulus



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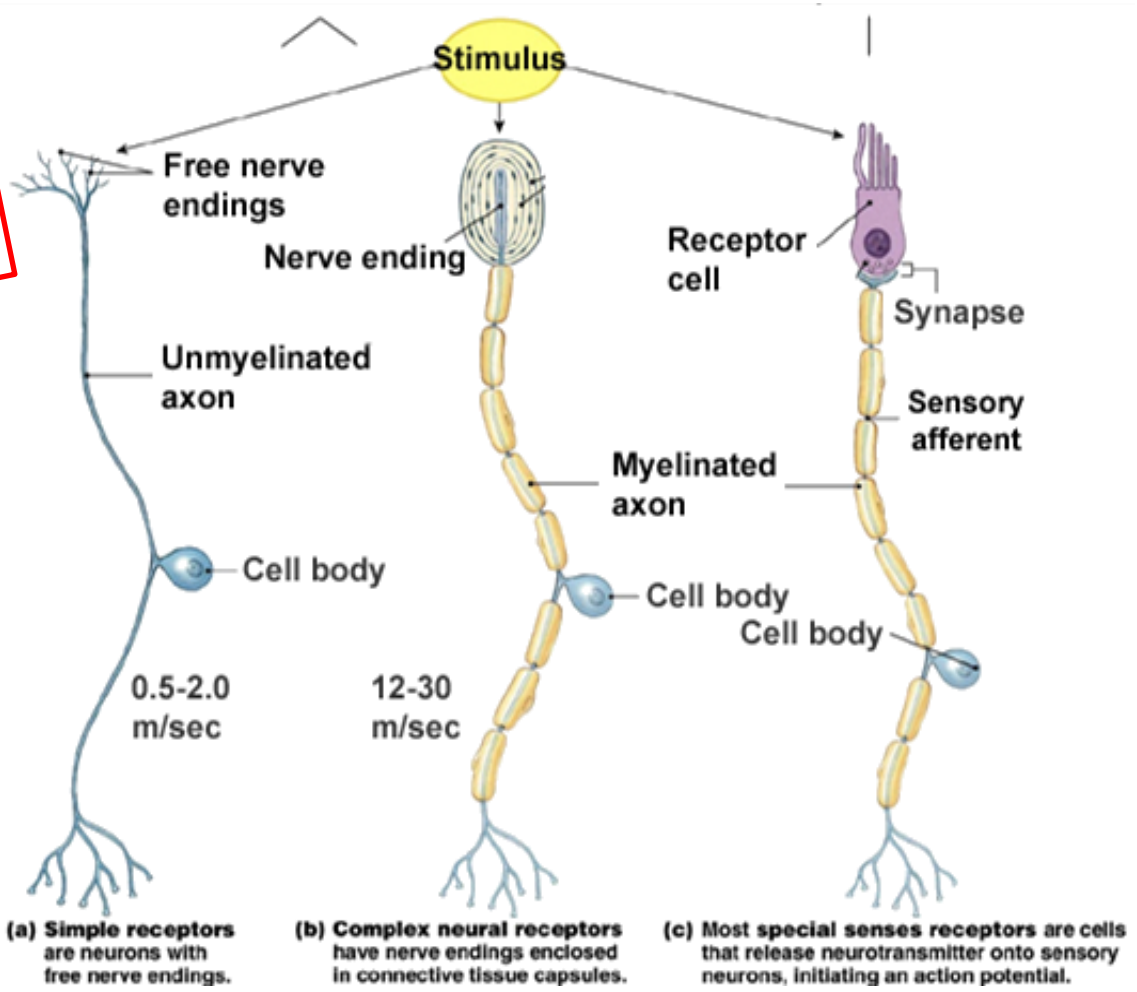
Receptors

- Simple
- Complex

- General
  - Superficial – somatosensors
  - Deep – viscerosensors
  - Muscles, tendons, joints – proprioceptors

- Special
  - Part of sensory organs

✓ Mechanoreceptors
✓ Thermoreceptors
✓ Chemoreceptors
✓ Fotoreceptors



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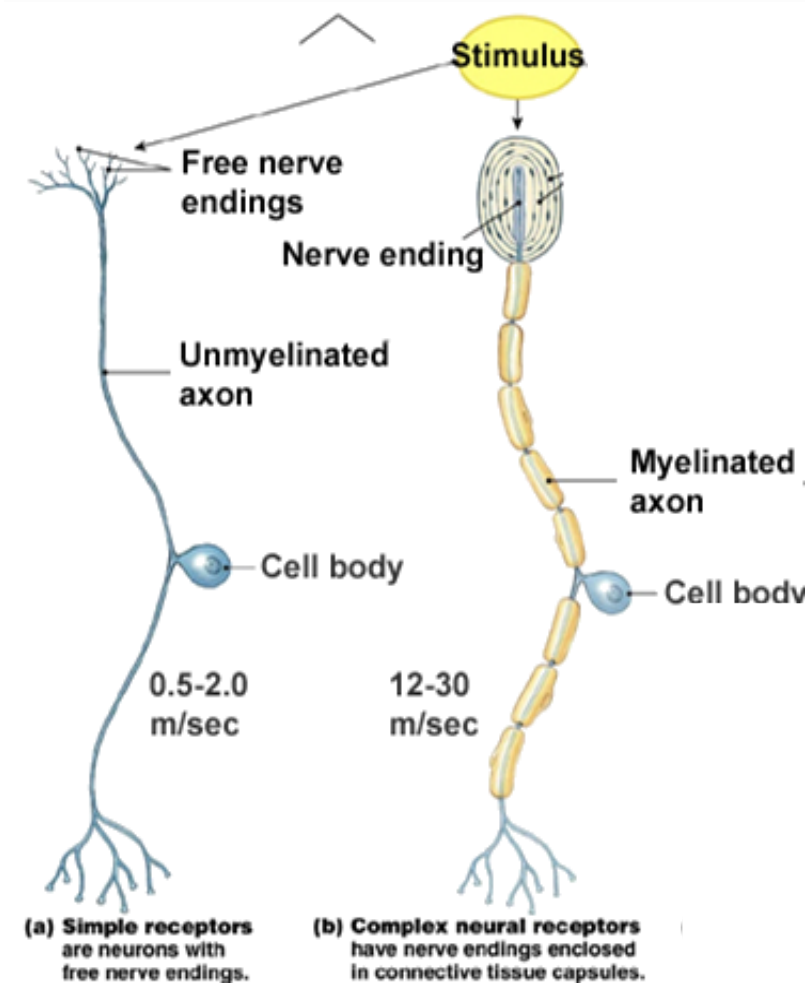
Evolutionary point of view

- The signals indicating potential damage are the most important and the corresponding systems evolved early
  - Pain
  - Temperature

- The touch signals have adaptive value and evolved later



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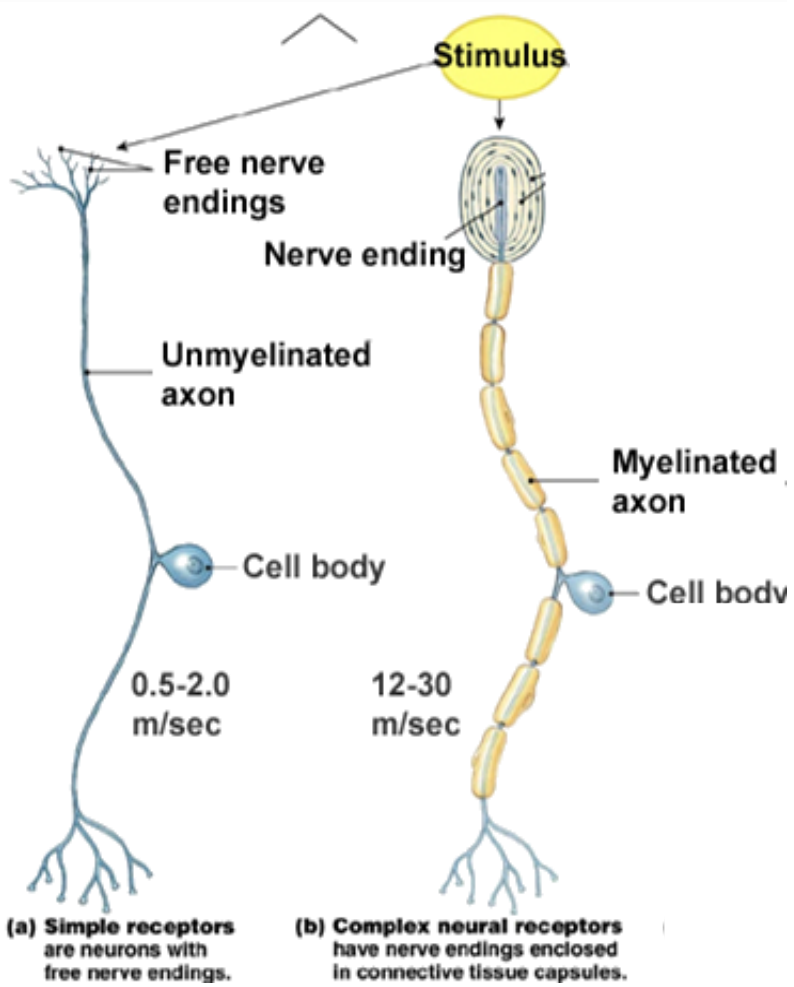
Evolutionary point of view

- The signals indicating potential damage are the most i… the correspo… volved earl…
  - …
  - Temperature
- The to… daptive value and …ter

Immediate survival

Long-term survival



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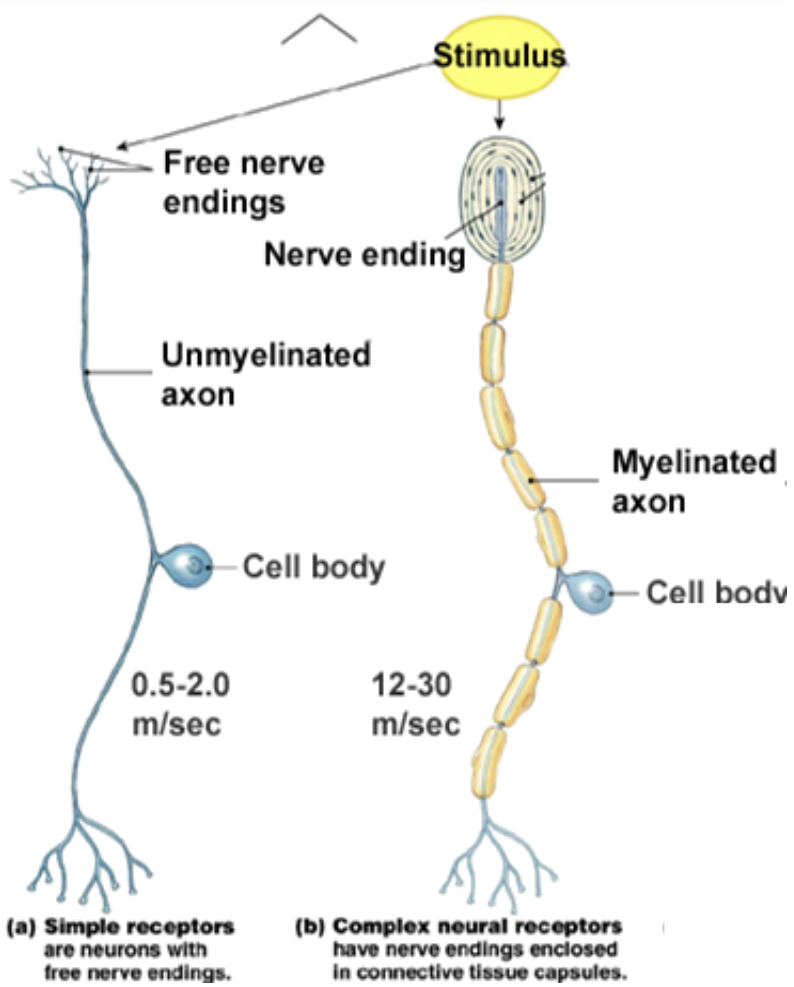
Evolutionary point of view

- The signals indicating potential damage are the most i… the correspo… volved earl…
  - …
  - Temperature
- The to… adaptive value and …ter
- The structure of the receptor, nerve fibers and pathways reflects the evolution

Immediate survival

Long-term survival



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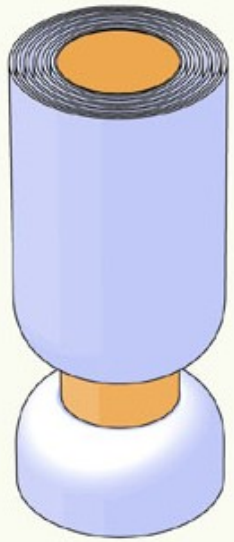
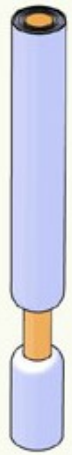
Nerve fibres

Axons from skin	Aα	Aβ	Aδ	C
Axons from muscles	Group I	II	III	IV
				
Diameter (μm)	13–20	6–12	1–5	0.2–1.5
Speed (m/sec)	80–120	35–75	5–30	0.5–2
Sensory receptors	Proprioceptors of skeletal muscle	Mechanoreceptors of skin	Pain, temperature	Temperature, pain, itch

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

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Viscerosensitivity

- An information from visceral and cardiovascular system
- Linked to the autonomic nervous system

- The most of information does not reach higher structures than hypothalamus

- The most of informatic

✓ Parasympathetic nervous system (VII., IX., **X., sacral PNS**)
– „Operational information“ (blood pressure, pO2, pCO2)

✓ Sympathetic nervous system
– „Potential danger“ (pressure, pain, cold)

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Proprioception

- Information from
  - Muscles
  - Tendons
  - Joints

- Important for
  - Precise coordination of movements
  - Overload protection

Somatosensory pathways

- Three systems

- (Archispinothalamic)
  - Interconnection of adjacent segments (tr. Spinospinalis)
- Paleospinothalamic
  - tr. Spinoreticularis, tr. Spinotectalis…
- Neospinothalamic
  - tr. Spinothalamicus
- Dorsal column system
  - tr. Spinobulbaris

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Somatosensory pathways

- Three systems
- (Archispinothalamic)
  - Interconnection of adjacent
- Paleospinot
- Ne
  -
- Dors
  - tr.

EVOLUTION….

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

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Somatosensory pathways

- Paleospinothalamic
  - Low resolution – dull, diffuse pain („slow pain“)
- Neospinothalamic
  - High resolution – sharp, localized pain („fast pain“), temperature
  - Low resolution – touch
- Dorsal column system
  - High resolution – fine touch

Somatosensory pathways

- Paleospinothalamic
  - Low resolution – dull, diffuse pain („slow pain“)
- Neospinothalamic
  - High resolution – sharp, localized pain („fast pain“), temperature
  - Low resolution – touch
- Dorsal column system
  - High resolution – fine touch

Immediate survival

Long-term survival

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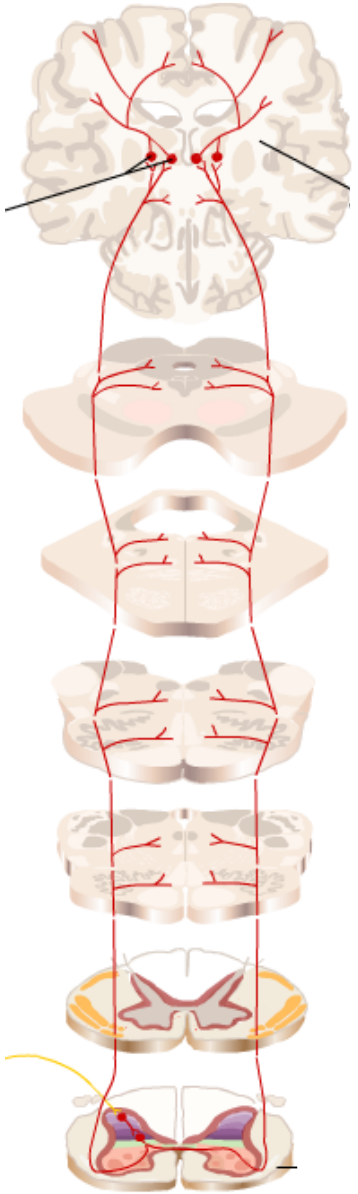
Paleospinothalamic system

- Tr. Spinoreticularis, spinotectalis…
- Evolved before neocortex
- The primary connection to the subcortical structures
- Basic defensive reactions and reflexes - vegetative response, reflex locomotion - opto-acoustic reflexes etc.
- Secondarily connected to cortex (after its evolution; tr. Spino-reticulo-thalamicus), but this system has a small resolutions – dull diffuse pain
- This tract is not designed for „such a powerful processor as neocortex“
- Approximately half of the fibers cross the midline



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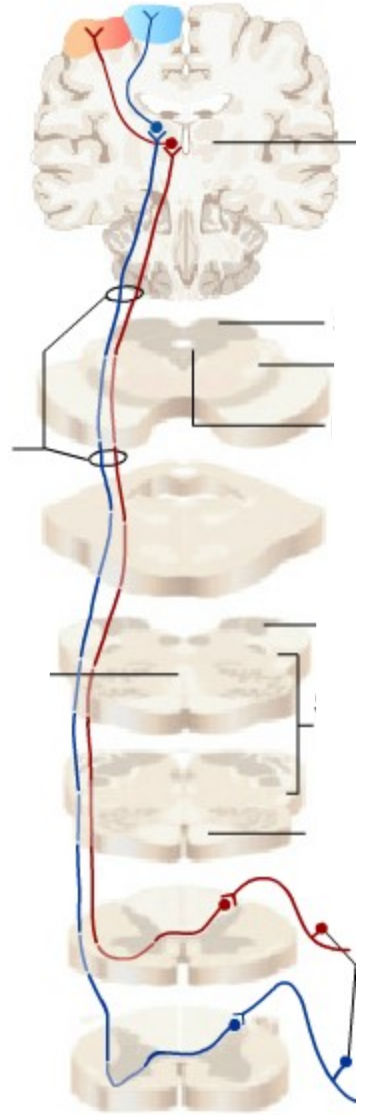
Neospinothalamic system

- Tr. Spinothalamicus
- Younger structure primarily connected to neocortex
- „High capacity/resolution“
- Detail information about pain stimuli (sharp, localized pain)
- Information about temperature
- Crude touch sensation
- The fibers cross midline at the level of entry segment



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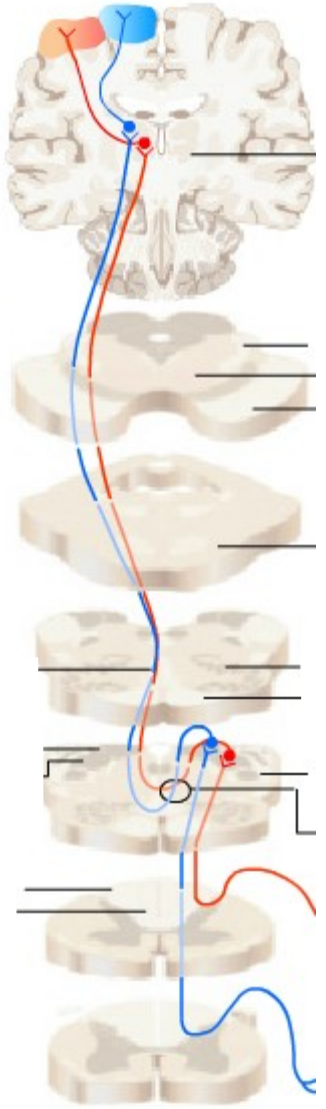
Dorsal column system

- Tr. Spinobulbaris
- The youngest system
- High capacity
- Tactile sensation
- Vibration
- Fine motor control
- Better object recognition
- Adaptive value
- The fibers cross midline at the level of medulla oblongata



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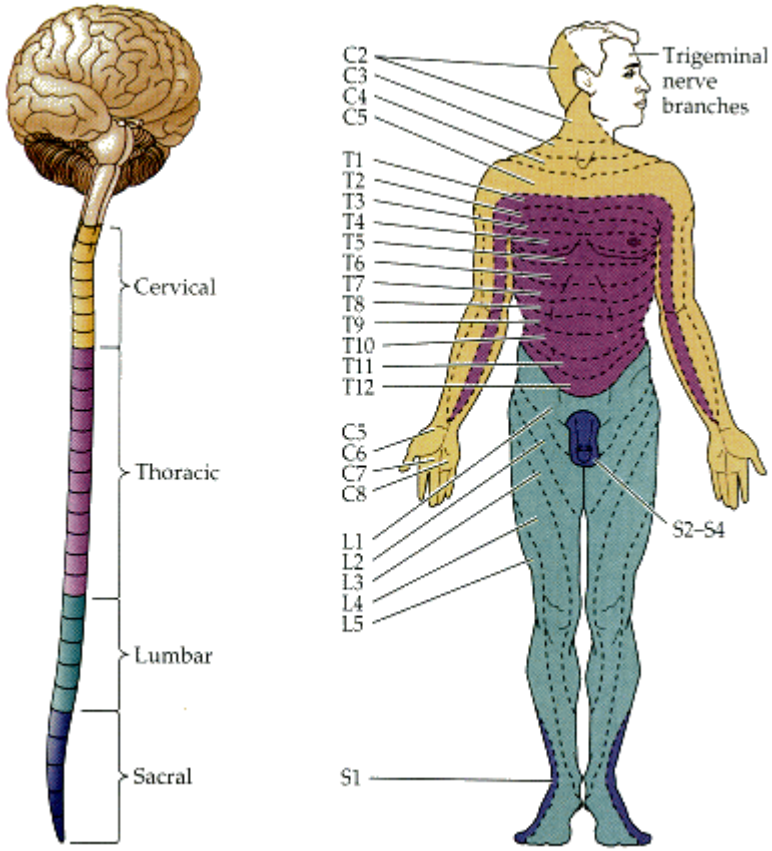
Dermatoms

- Somatotopic organization somatosensitve nerves



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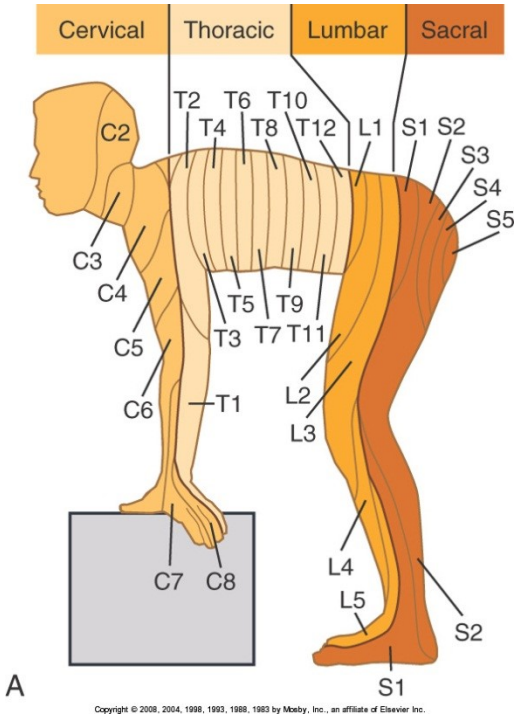

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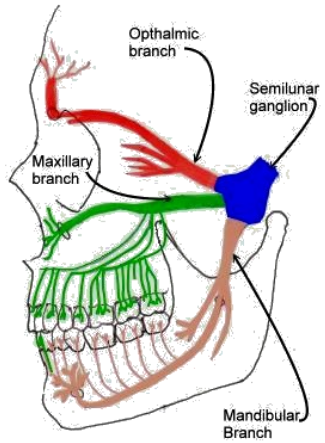
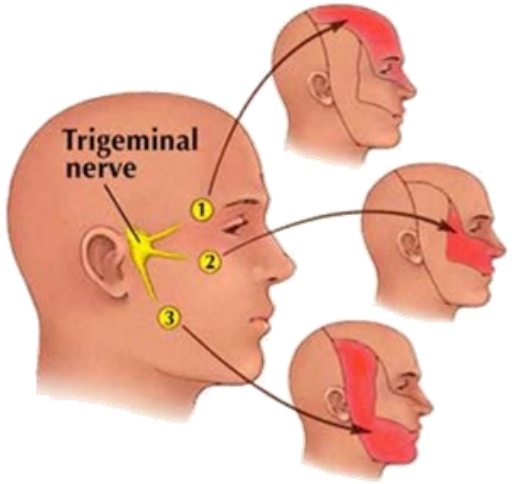
Trigeminal system

- Spinal TS
  - Pain, temperature
- Main sensory TS
  - Touch, proprioception





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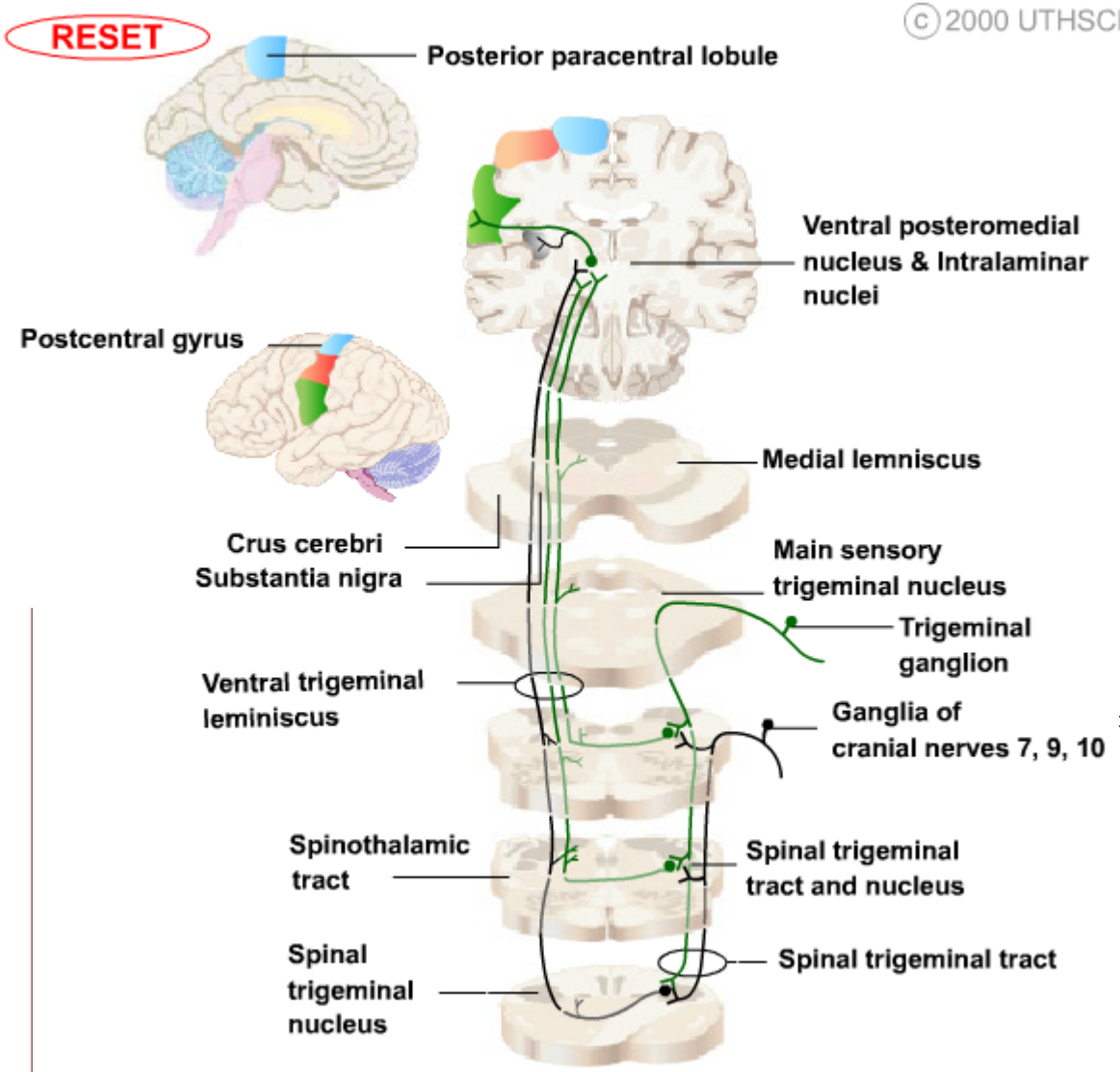

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Somatosensory pathways

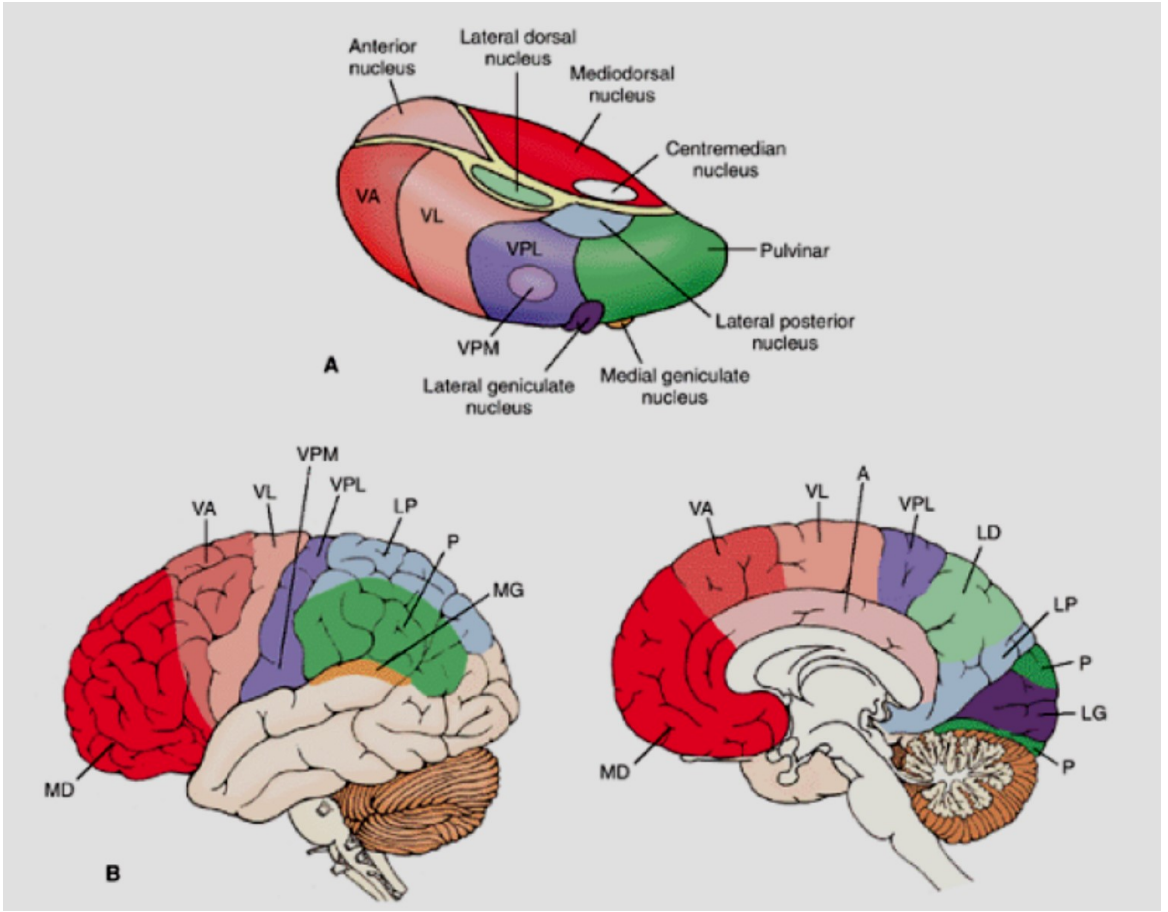
Table I
The Sensory Modalities Represented by the Somatosensory Systems

Modality	Sub Modality	Sub-Sub Modality	Somatosensory Pathway (Body)	Somatosensory Pathway (Face)
Pain	sharp cutting pain		Neospinothalamic	Spinal Trigeminal
	dull burning pain		Paleospinothalamic	
	deep aching pain		Archispinothalamic	
Temperature	warm/hot		Paleospinothalamic	
	cool/cold		Neospinothalamic	
Touch	itch/tickle & crude touch		Paleospinothalamic	
	discriminative touch	touch	Tr. spinobulbaris	Main Sensory Trigeminal
		pressure		
		flutter		
		vibration		
Proprioception	Position: Static Forces	muscle length		
		muscle tension		
		joint pressure		
	Movement: Dynamic Forces	muscle length		
		muscle tension		
		joint pressure		
		joint angle		

http://neuroscience.uth.tmc.edu/s2/chapter02.html

Thalamus and neocortex

- Almost all the afferent information gated in the thalamus
- Olfaction is an exception
- Bilateral connections between neocortex and thalamus



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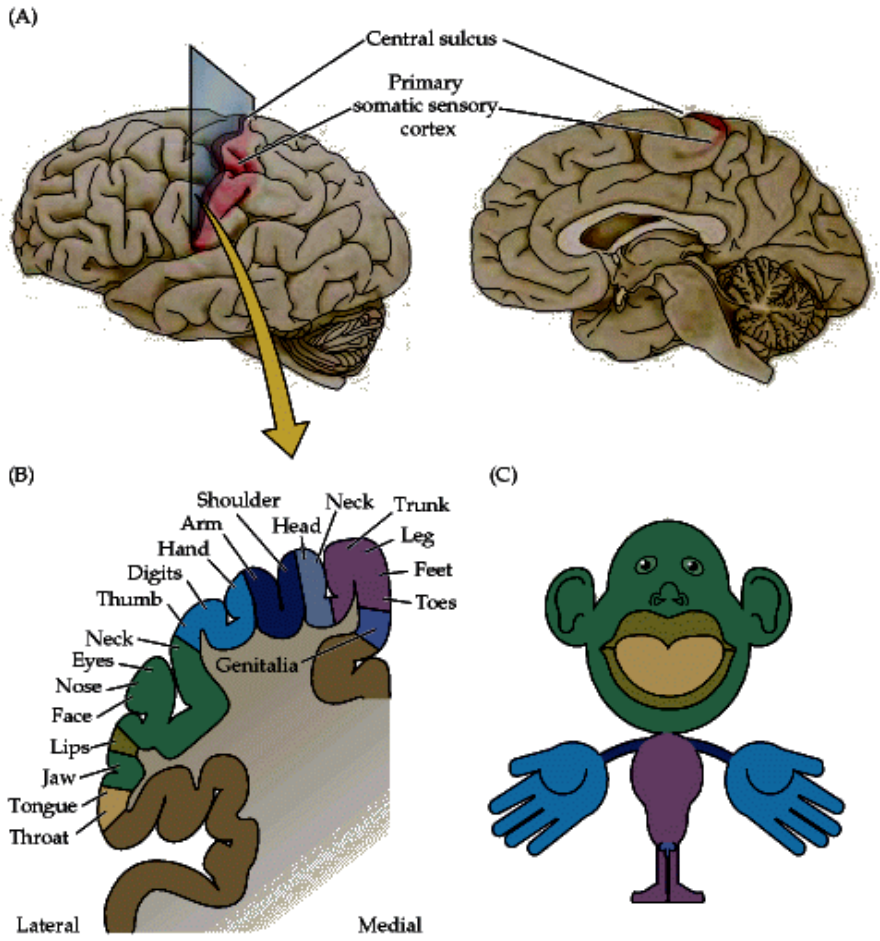
Neocortex

- Somatotopic organization
- Cortical magnification



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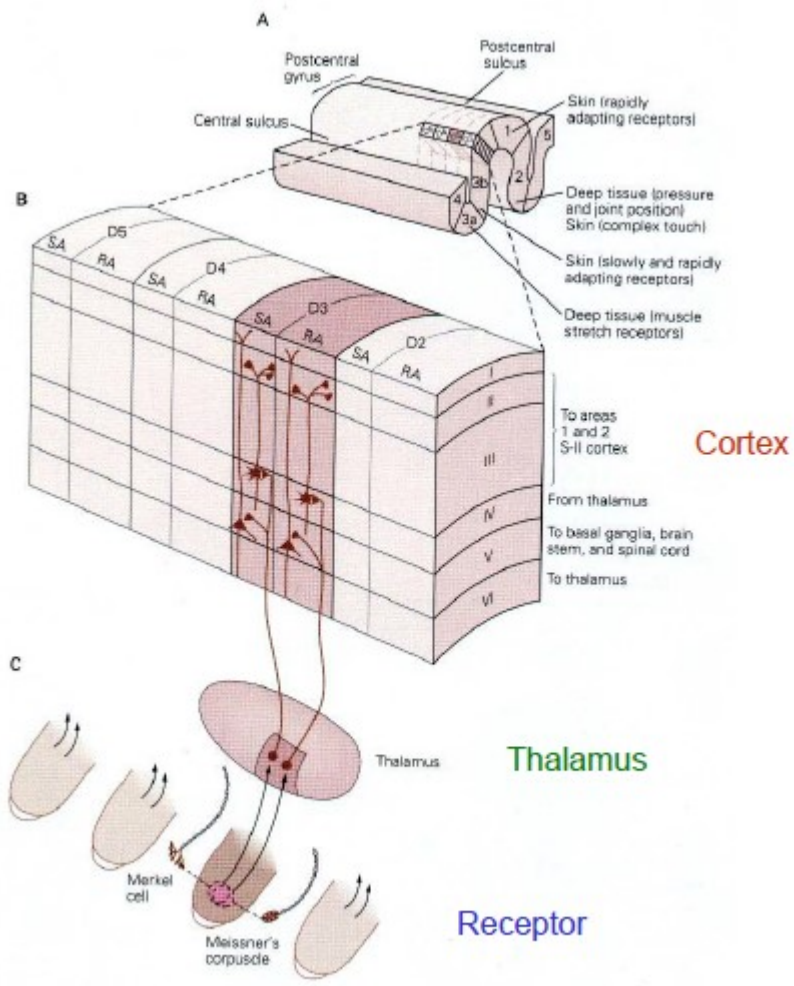

http://www.shadmehrlab.org/Courses/physfound_files/wang_5.pdf

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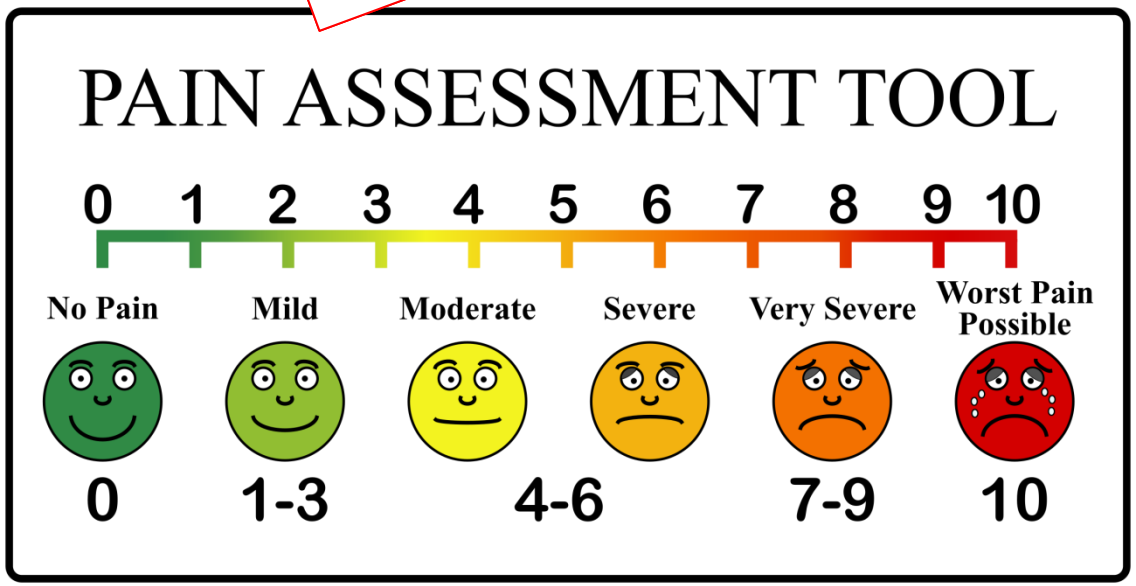
Pain

- Distressing feeling associated with real or potential tissue damage
- Sensor x psychological component
- Physiological pain (nociceptor activation)
- Pathological pain (not mediated by nociceptors)
- Acute (up to 6months) – „activiting“
- Chronic (more than 6 months) – „devating“

Subjective character



https://www.cheatography.com/uploads/davidpol_1460561912_Pain_Scale__Arvin61r58.png

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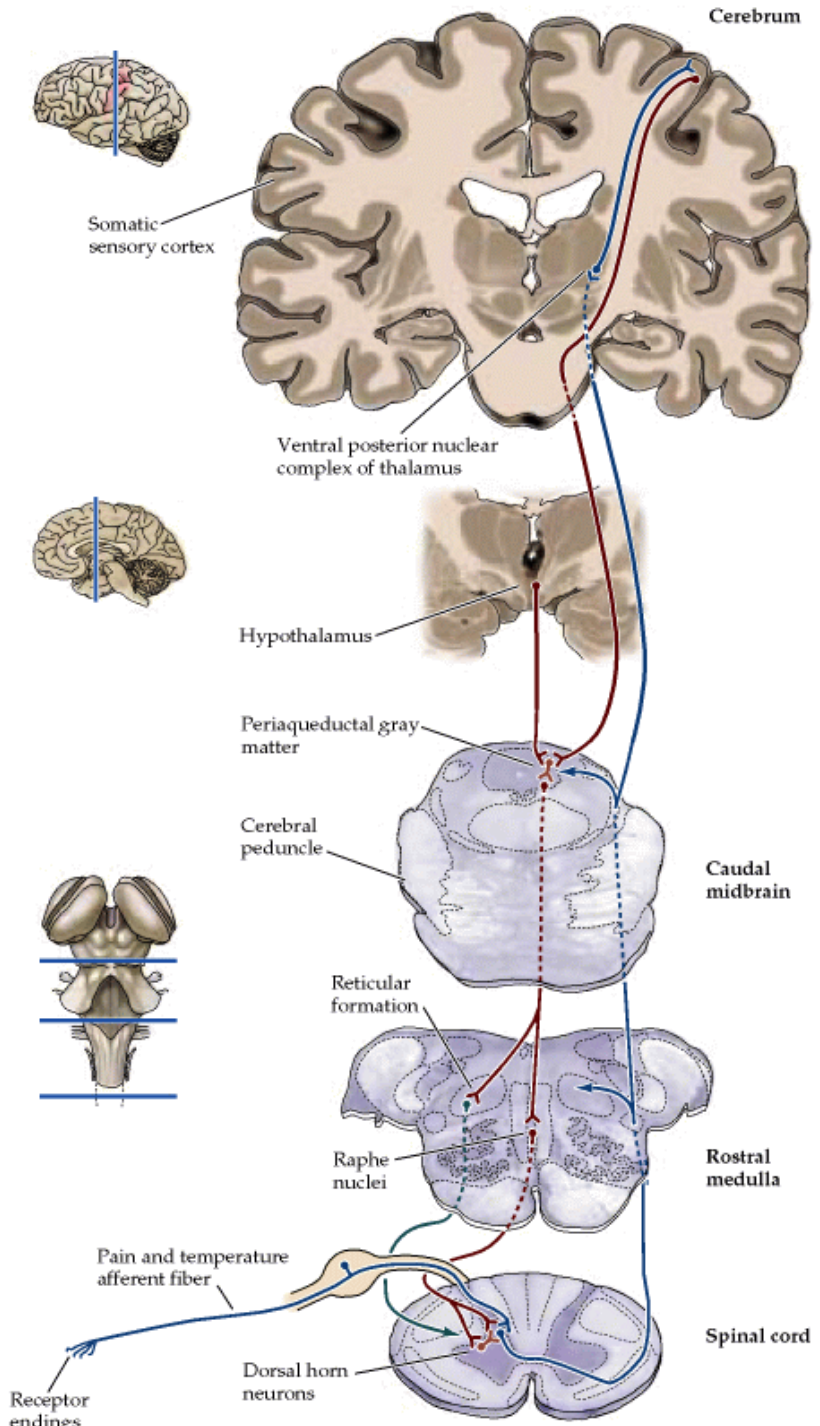
Descendent pathways modulating pain

- Somatosemcoric cortex
- Hypotalamus
- Periaquaeductal gray
- Nuclei raphe



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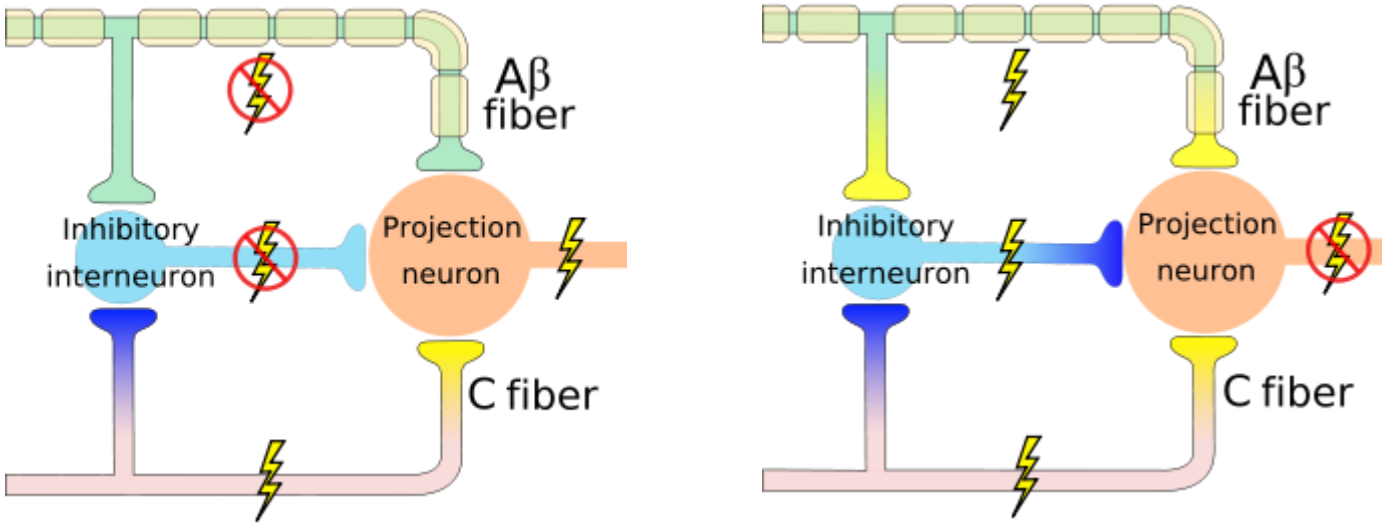
Pain modulation on the spinal level

Gate control theory of pain



https://en.wikipedia.org/wiki/Gate_control_theory

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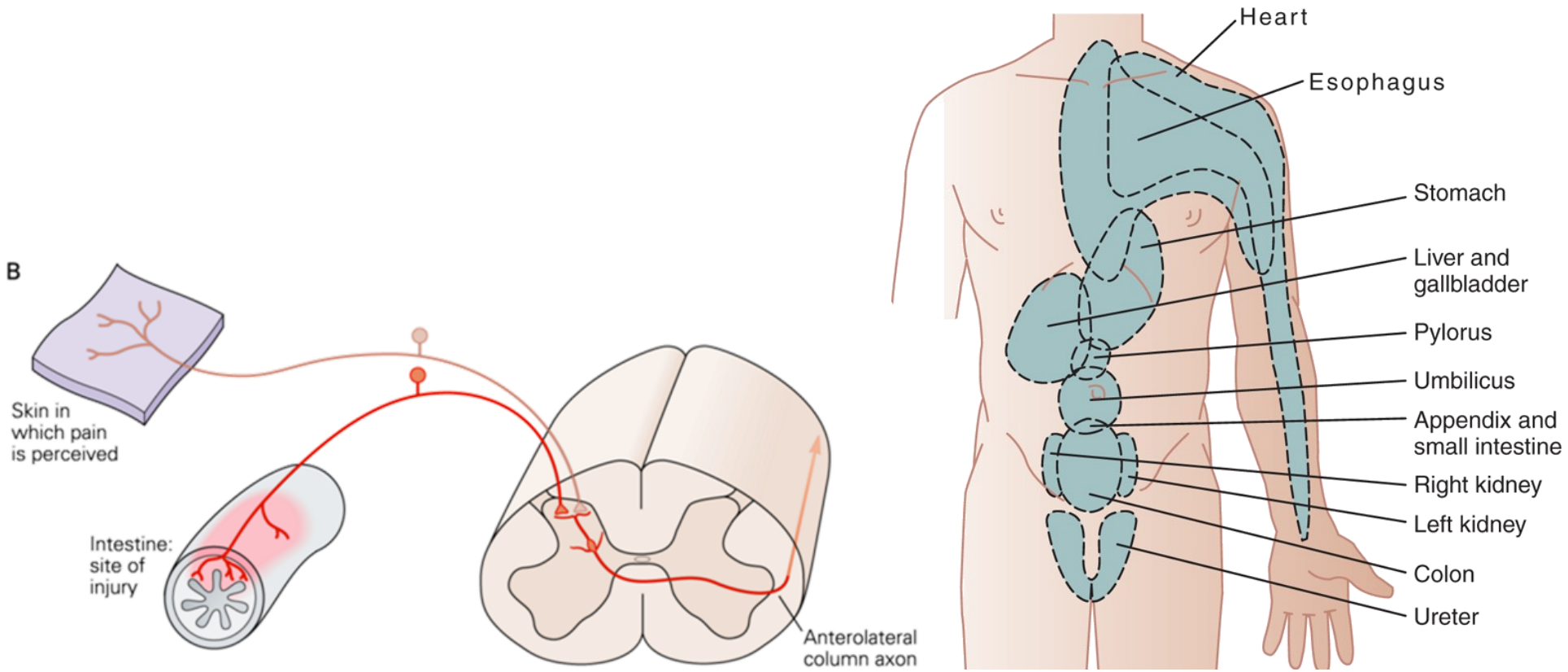
Referred pain



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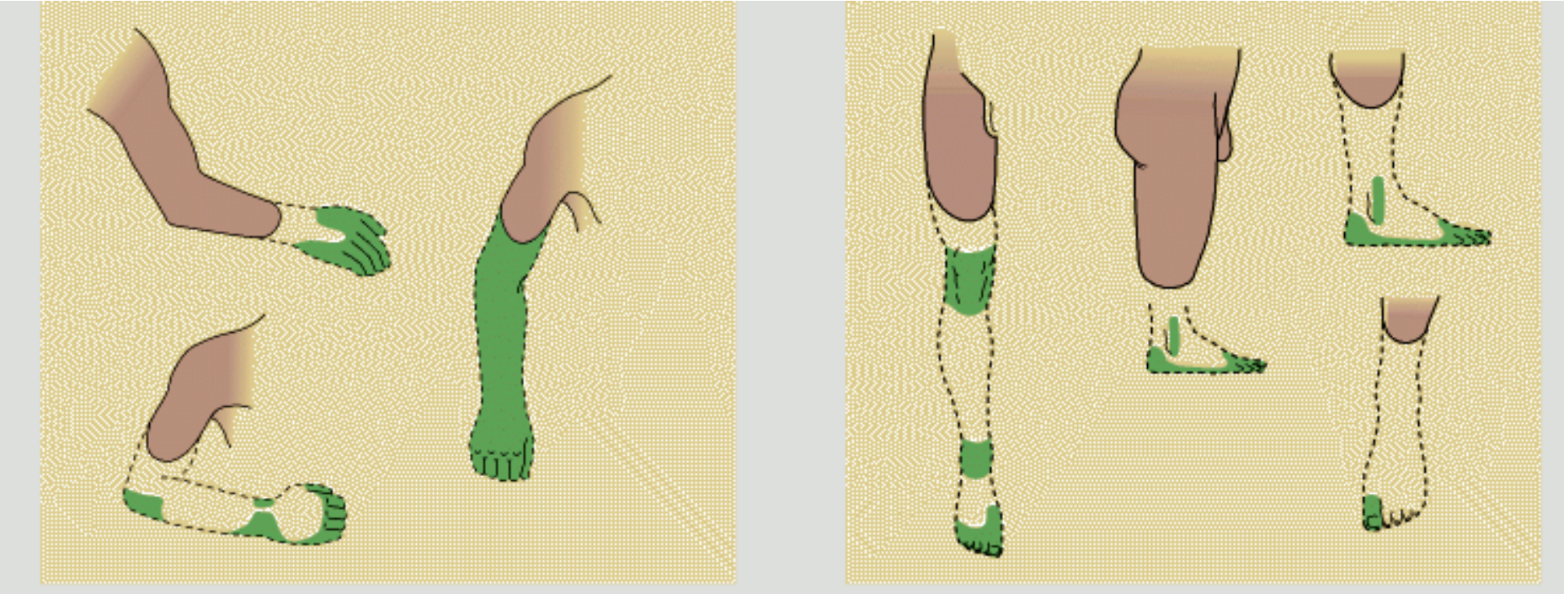
Phantom limb pain



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