

M U N I

M E D

M U N I
M E D

3

Intracranial compartment, Cellular base of nervous system

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
 - Organ els
- There are
- Properties/c among different compartments

The brain homeostasis is maintained within a narrow range thanks to hematoencephalic barrier and astrocyte activity

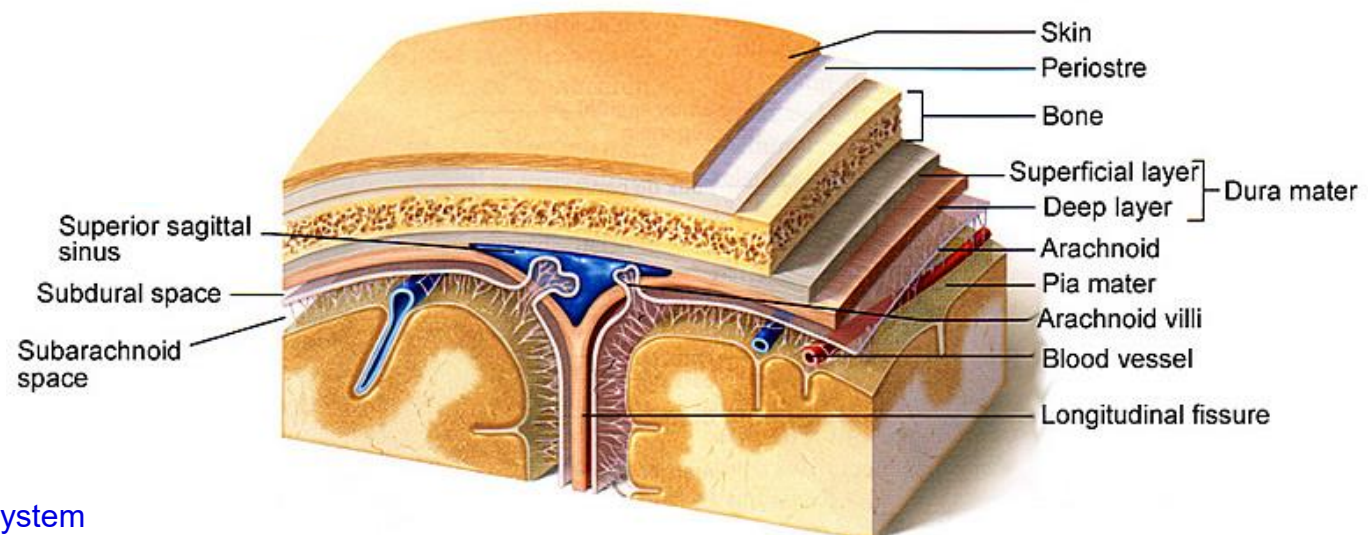
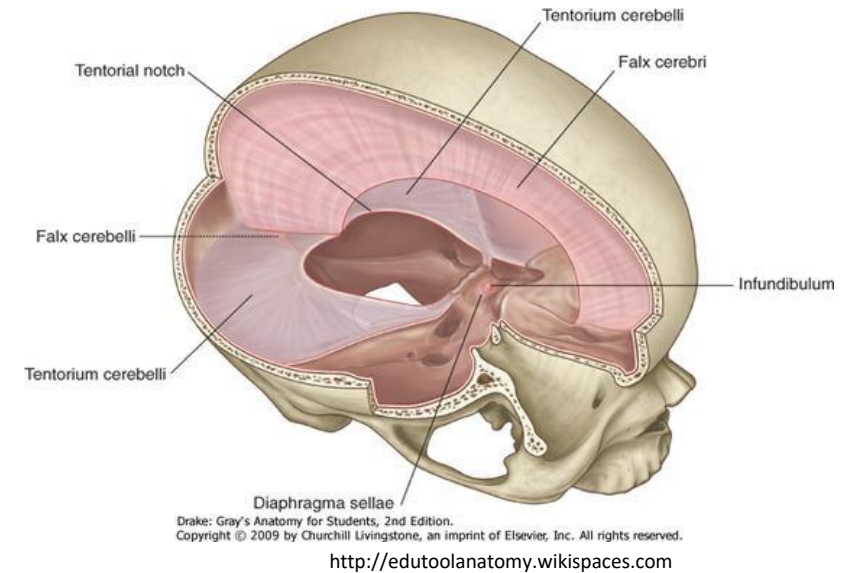
Compartmentalization

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

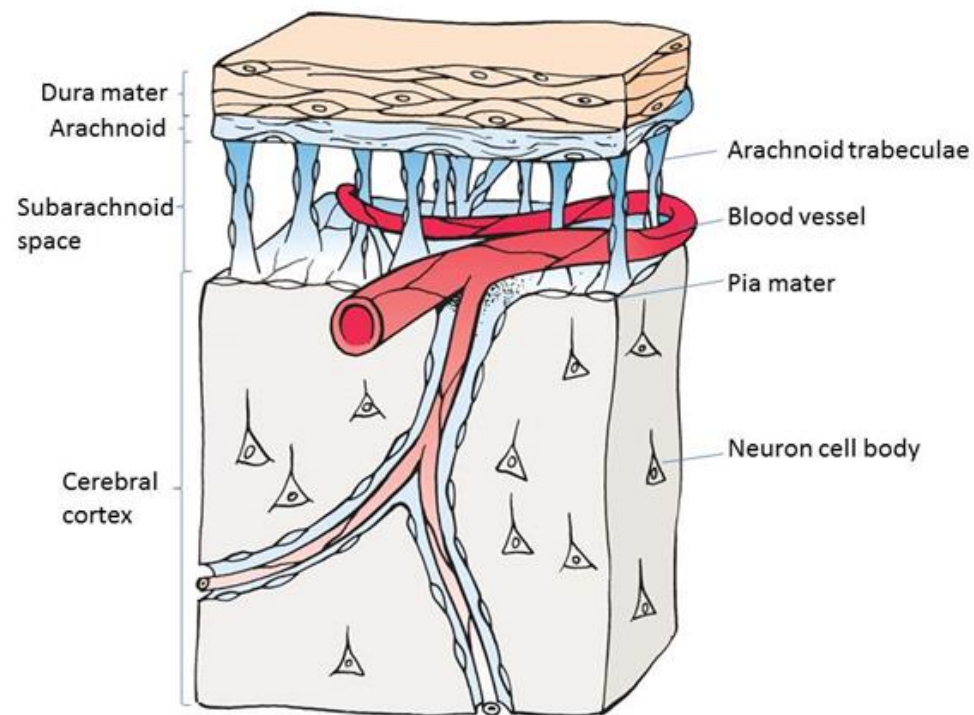
The brain homeostasis is maintained within a narrow range thanks to hematoencephalic barrier and astrocyte activity
This allows neuronal cells to live for the entire life of the individual

Intracranial compartment

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

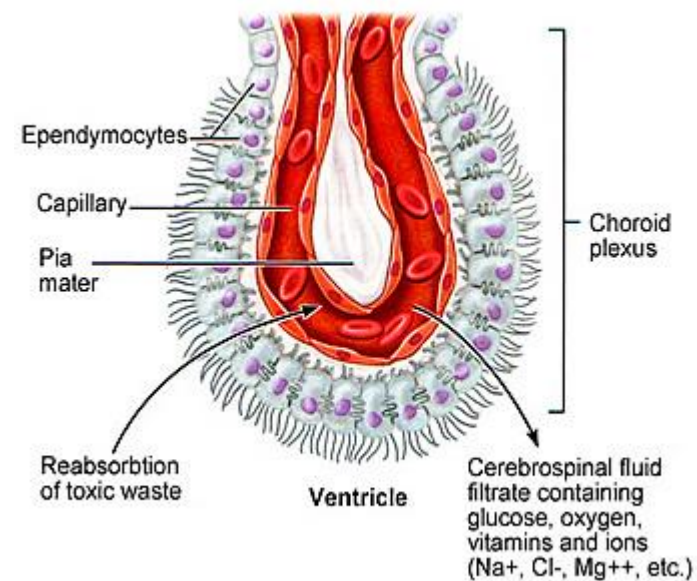


Meningeal and hematoliquor barrier



Adopted from: M.H.Ross and W. Pawlina. Histology: a text and atlas, Lippincott Williams & Wilkins, 2011

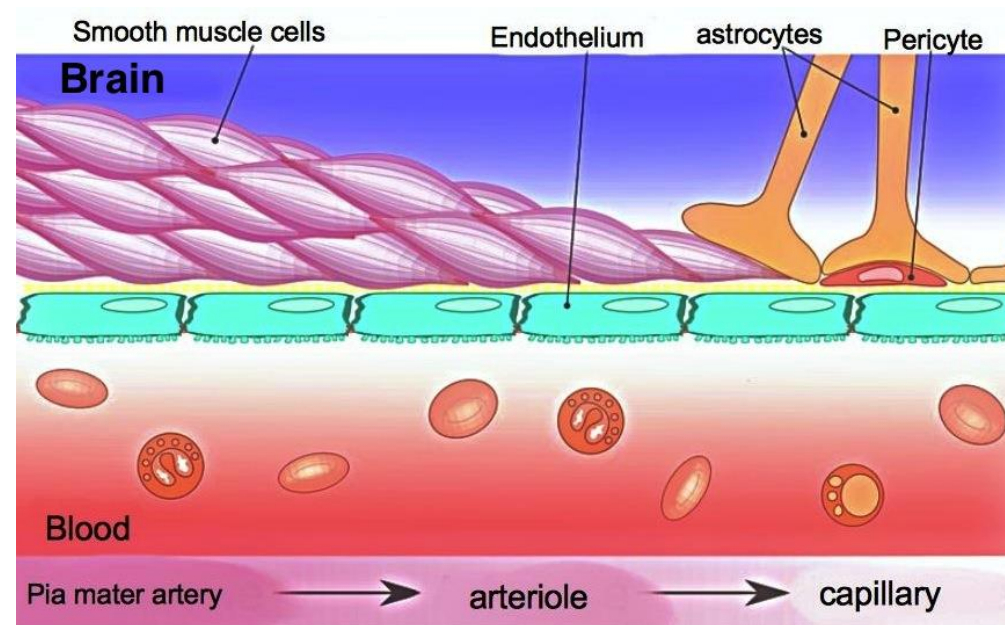
<https://sisu.ut.ee/histology/meninges>



<https://sisu.ut.ee/histology/meninges>

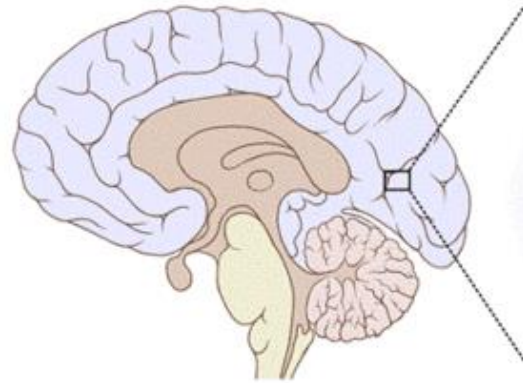
Hematoencephalic barrier

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

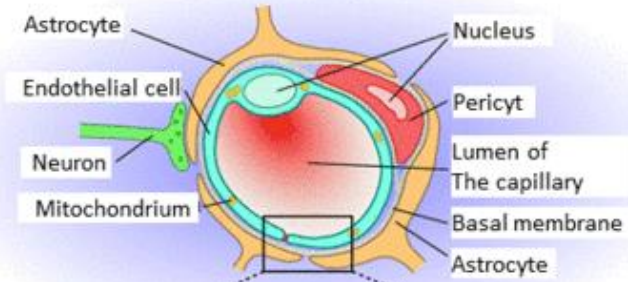


https://upload.wikimedia.org/wikipedia/commons/1/12/Blood_vessels_brain_english.jpg

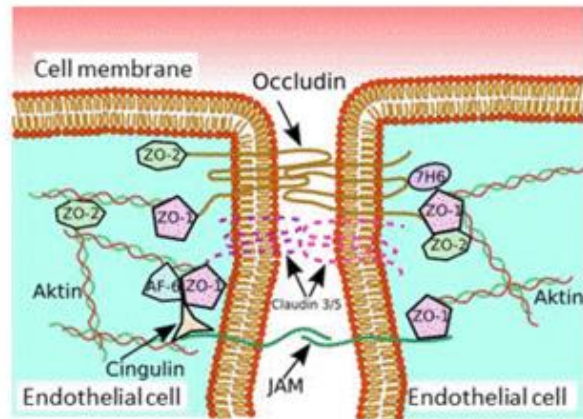
Hematoencephalic barrier



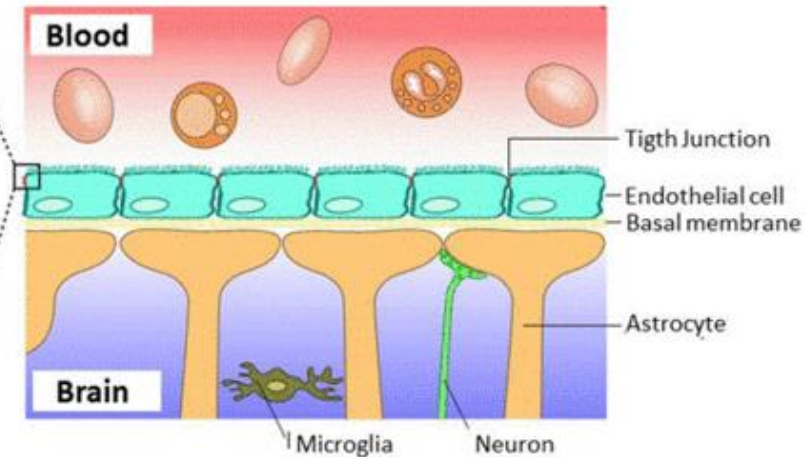
Cross section of blood vessel



Junction between Endothelial cells

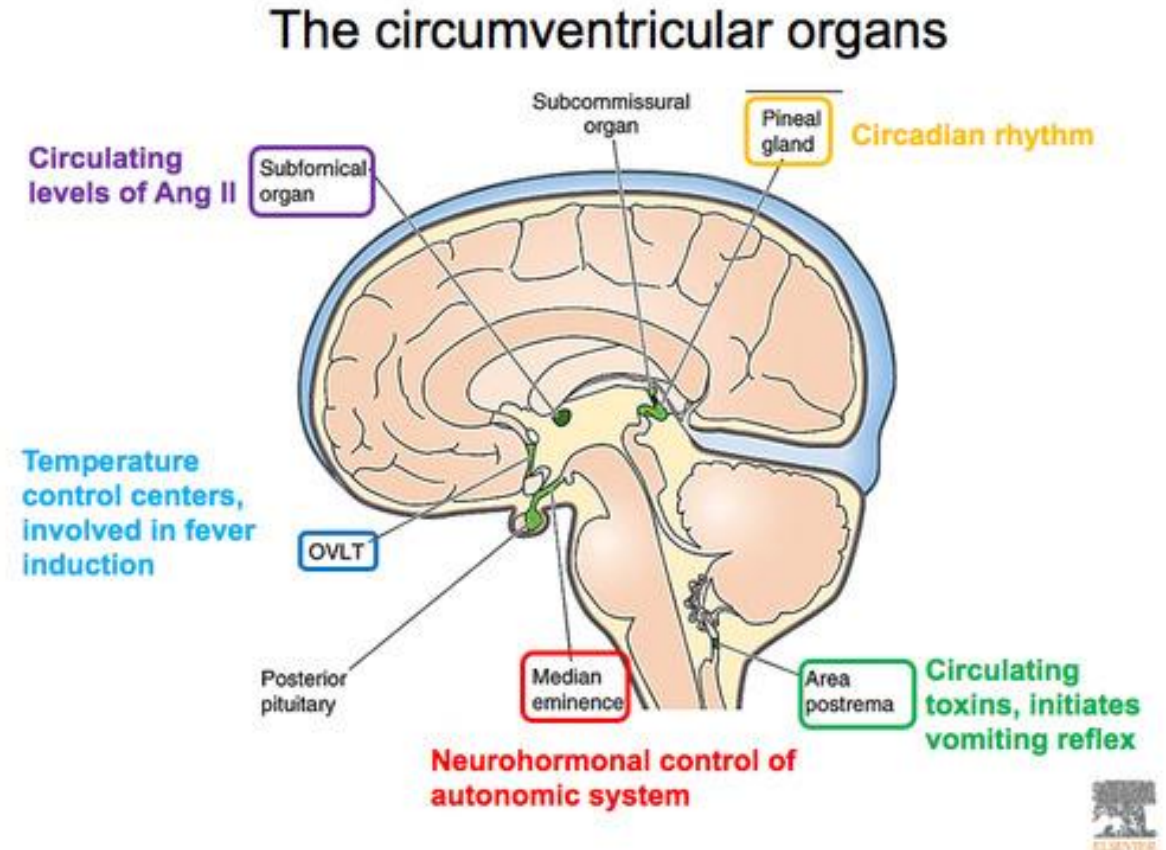


Longitudinal section of blood vessel



Circumventricular organs

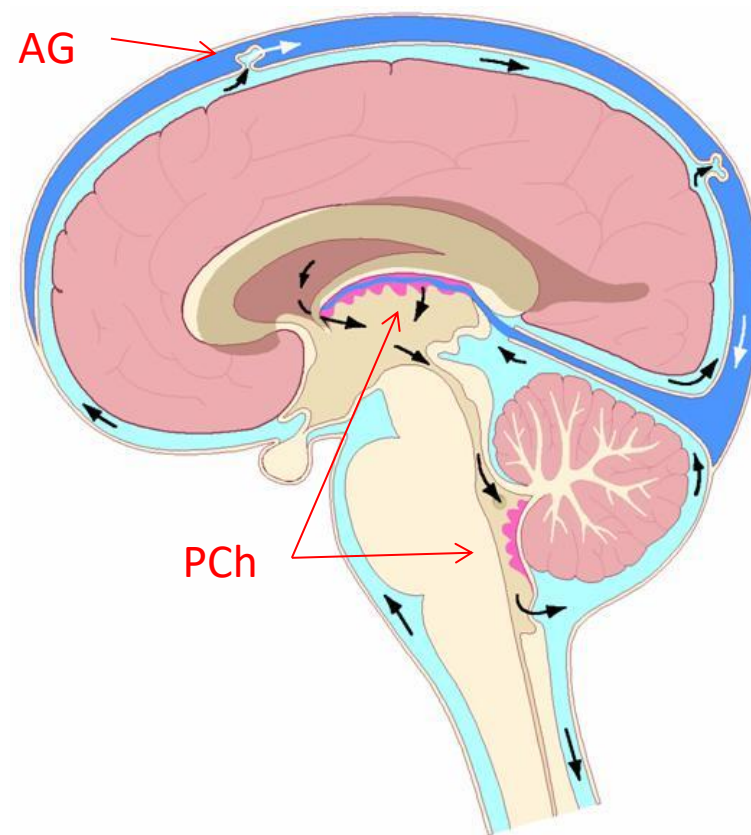
- Rich vascularisation
- Modified hematoencephalic barrier
- Sensors
- Secretion



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

Cerebrospinal fluid

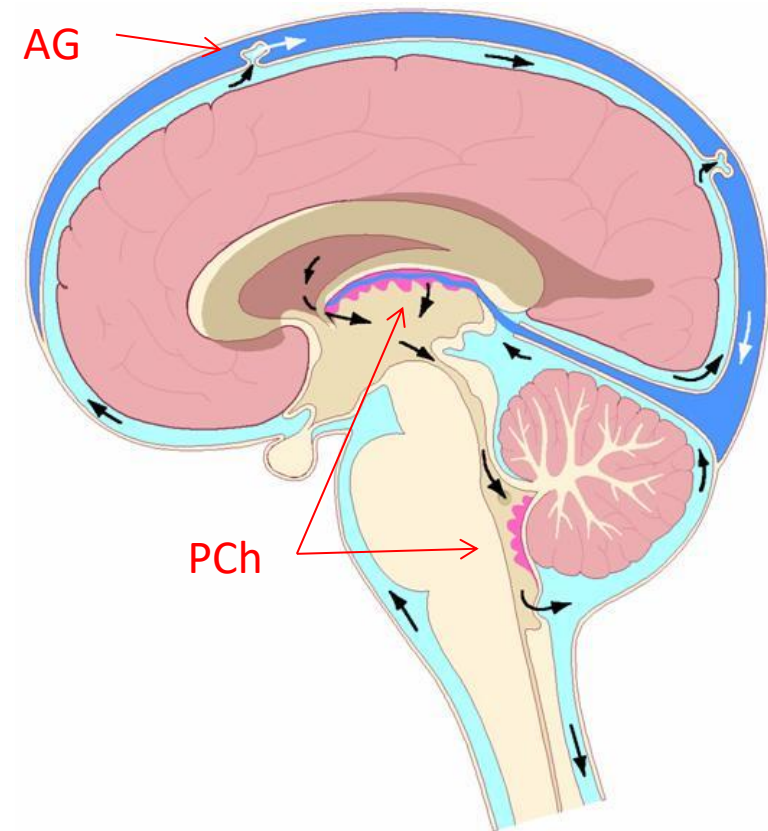
- Content
 - ✓ High levels of Mg^{+} and Na^{+}
 - ✓ Low levels of K^{+} and Ca^{2+}
 - ✓ Almost no cells (max 5/ml)
- Function
 - ✓ Protection
 - ✓ Microenvironment of neurons and glia
 - Metabolic functions
 - Immunologic functions
 - Transport functions and so on



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

Cerebrospinal fluid

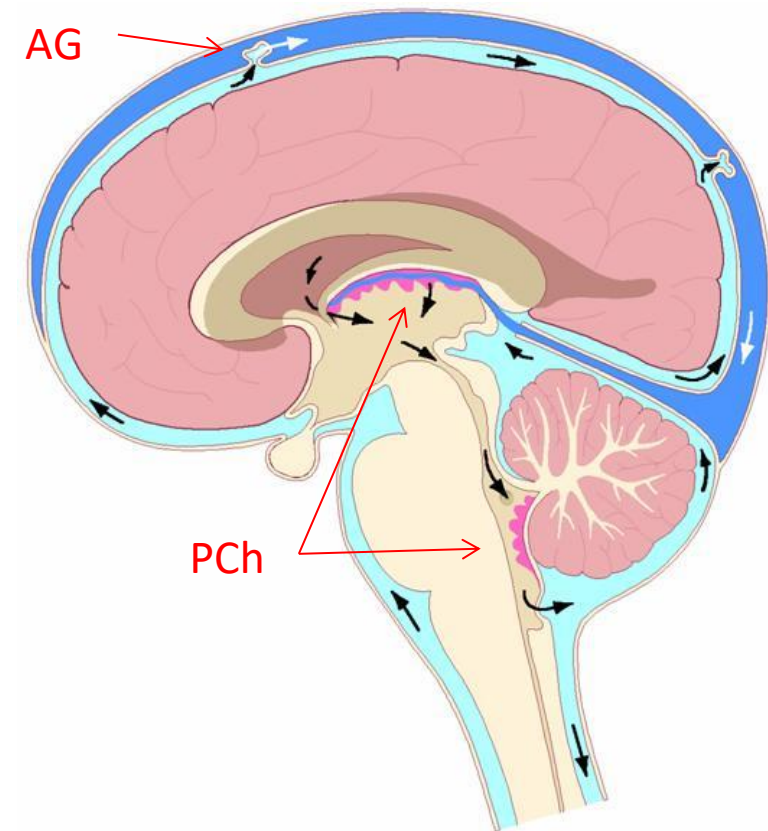
- Clear fluid produced by active secretion
- Liquor space
 - lined by ependymal cells
 - 150-250 ml



<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)

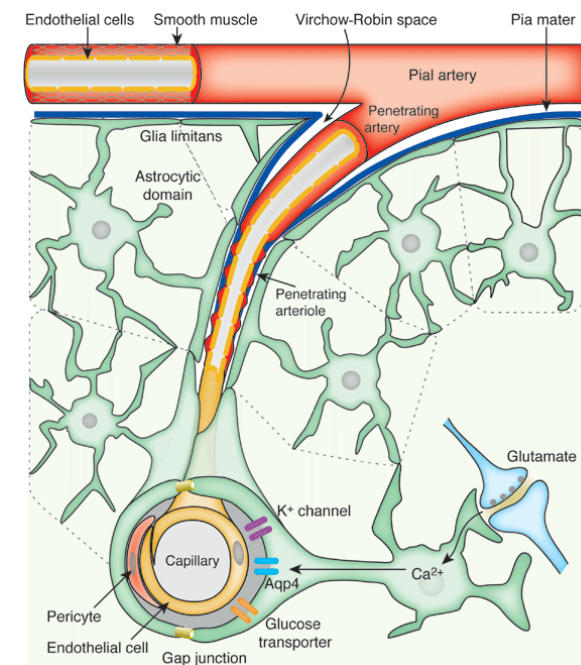
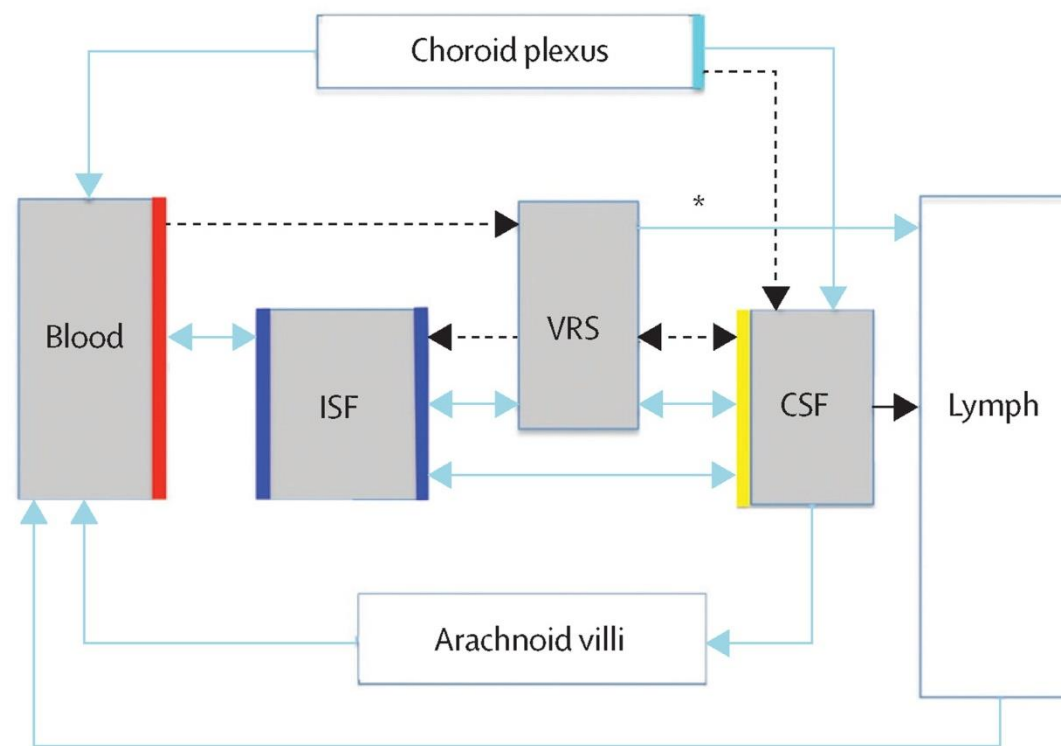


<http://www.control.tfe.umu.se>

New insight into the production and resorption of CSF

Ducros A, Biousse V. Headache arising from idiopathic changes in CSF pressure. *The Lancet Neurology*. 2015;14:655–668.

- CSF – cerebrospinal fluid
- ISF – interstitial fluid
- VRS – Virchow Robin space (space between the pia mater and an artery or a vein, but not capillaries)



<http://visnu528.blogspot.cz/2014/09/glymphatics-and-virchow-robin-space.html>

CNS lymphatic drainage

- Cervical lymph nodes
 - Nasal lymphatics
 - Dural lymphatics
 - Alongside nerves
 - Alongside vessels (not APCs)
- Lumbar lymph nodes
 - Alongside nerve roots

Engelhardt, B., Carare, D., & Weller, R. O. (2016). Gateways of the central nervous system. *Neuropathologica*, 132, 3. <https://doi.org/10.1007/s00006-016-0500-0>

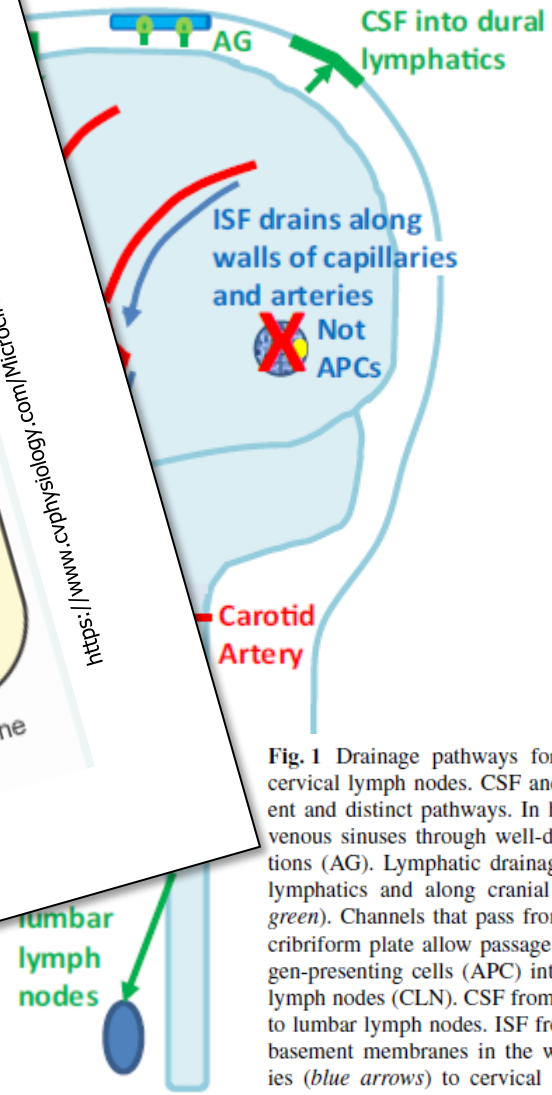
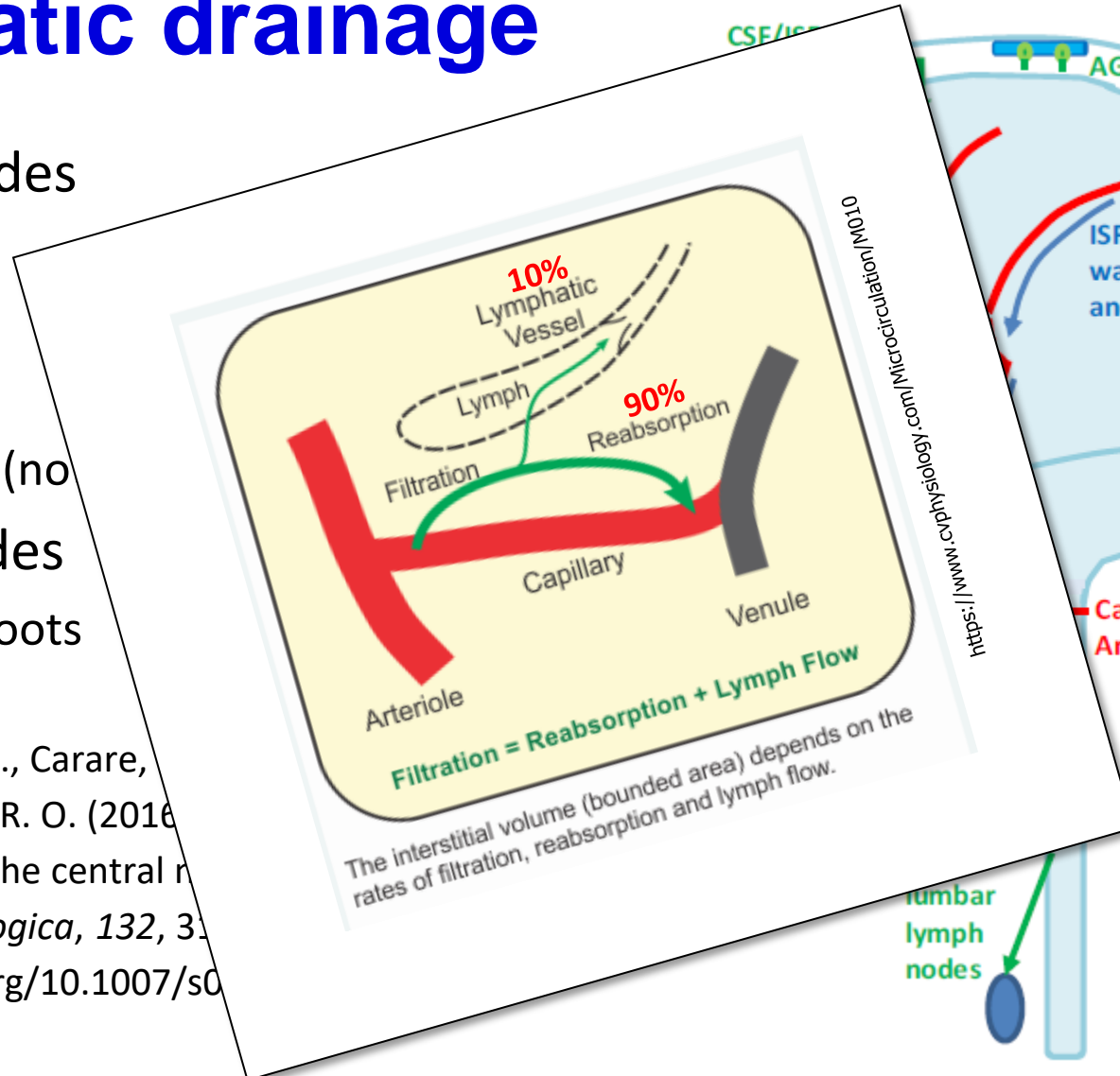


Fig. 1 Drainage pathways for CSF and interstitial fluid (ISF) to cervical lymph nodes. CSF and ISF drain to lymph nodes by different and distinct pathways. In humans, CSF drains into the blood of venous sinuses through well-developed arachnoid villi and granulations (AG). Lymphatic drainage of CSF occurs via nasal and dural lymphatics and along cranial and spinal nerve roots (outlined in green). Channels that pass from the subarachnoid space through the cribriform plate allow passage of CSF (green line) T cells and antigen-presenting cells (APC) into nasal lymphatics (NL) and cervical lymph nodes (CLN). CSF from the lumbar subarachnoid space drains to lumbar lymph nodes. ISF from the brain parenchyma drains along basement membranes in the walls of cerebral capillaries and arteries (blue arrows) to cervical lymph nodes adjacent to the internal carotid artery just below the base of the skull. This narrow intramural perivascular drainage pathway does not allow the traffic of APC. There is interchange between CSF and ISF (convective influx/lymphatic system), as CSF enters the surface of the brain alongside penetrating arteries

CNS lymphatic drainage

- Cervical lymph nodes
 - Nasal lymphatics
 - Dural lymphatics
 - Alongside nerves
 - Alongside vessels (not APC)
- Lumbar lymph nodes
 - Alongside nerve roots

Engelhardt, B., Carare, R. O., Bechmann, I., Flügel, A., Laman, J. D., & Weller, R. O. (2016). Vascular, glial, and lymphatic immune gateways of the central nervous system. *Acta Neuropathologica*, 132, 317–338.
<https://doi.org/10.1007/s00401-016-1606-5>

Routes for drainage of CSF and ISF to cervical and lumbar lymph nodes

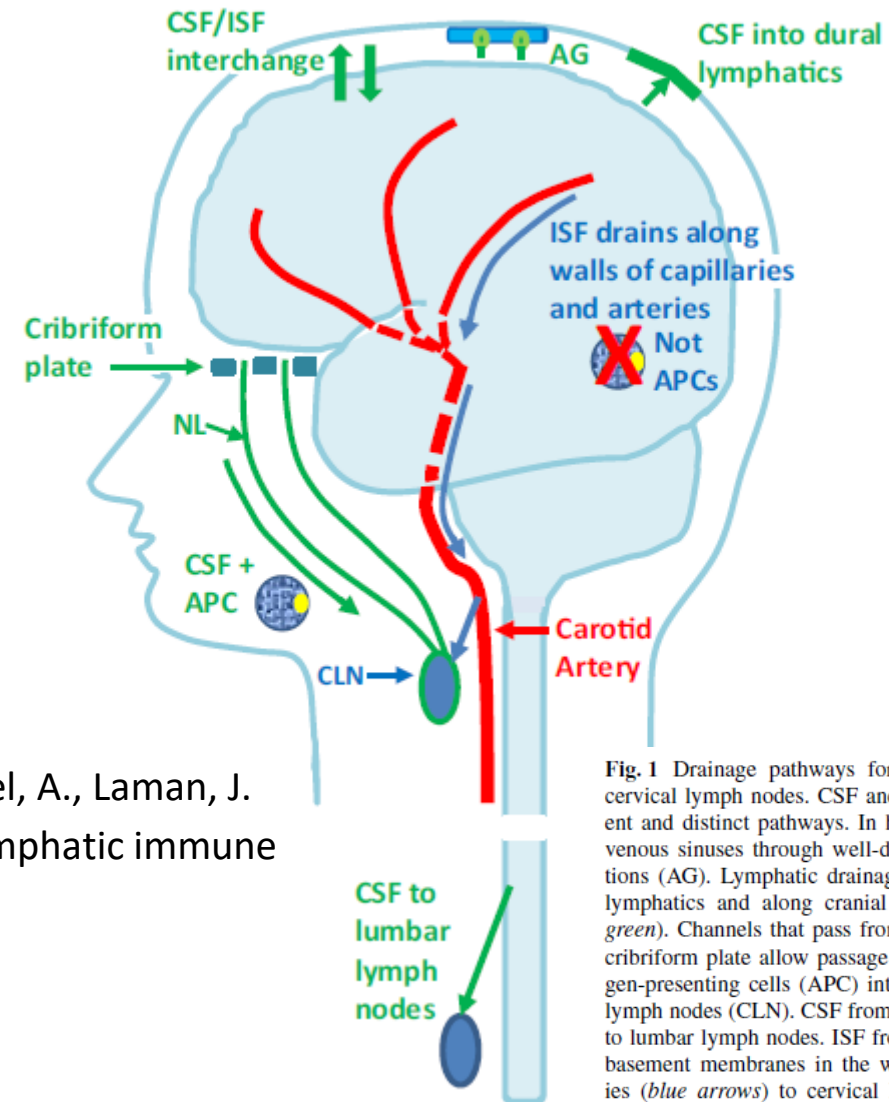
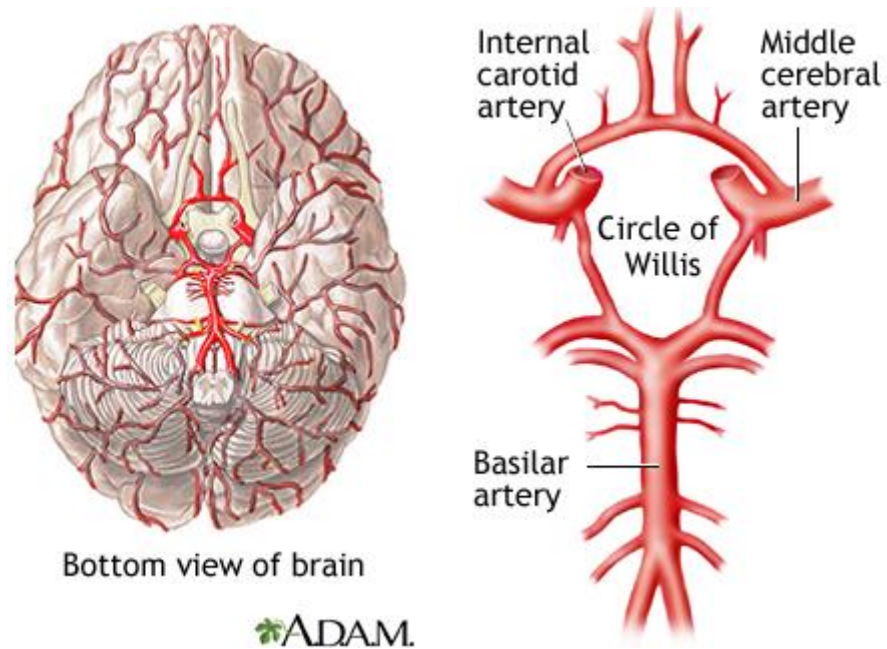
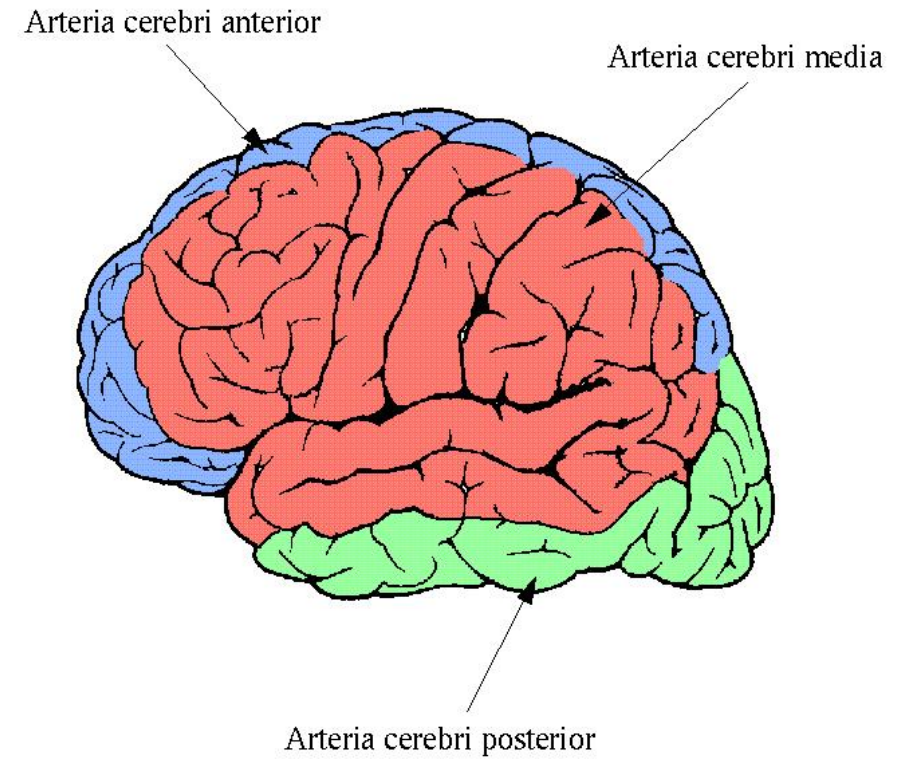


Fig. 1 Drainage pathways for CSF and interstitial fluid (ISF) to cervical lymph nodes. CSF and ISF drain to lymph nodes by different and distinct pathways. In humans, CSF drains into the blood of venous sinuses through well-developed arachnoid villi and granulations (AG). Lymphatic drainage of CSF occurs via nasal and dural lymphatics and along cranial and spinal nerve roots (outlined in green). Channels that pass from the subarachnoid space through the cribriform plate allow passage of CSF (green line) T cells and antigen-presenting cells (APC) into nasal lymphatics (NL) and cervical lymph nodes (CLN). CSF from the lumbar subarachnoid space drains to lumbar lymph nodes. ISF from the brain parenchyma drains along basement membranes in the walls of cerebral capillaries and arteries (blue arrows) to cervical lymph nodes adjacent to the internal carotid artery just below the base of the skull. This narrow intramural perivascular drainage pathway does not allow the traffic of APC. There is interchange between CSF and ISF (convective influx/lymphatic system), as CSF enters the surface of the brain alongside penetrating arteries

Blood compartment



<https://medlineplus.gov/ency/imagepages/18009.htm>



<http://www.ims.uni-stuttgart.de>

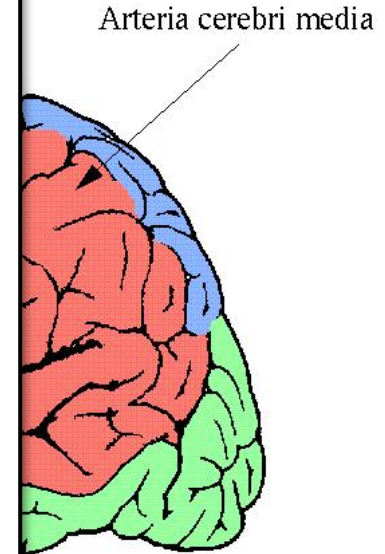
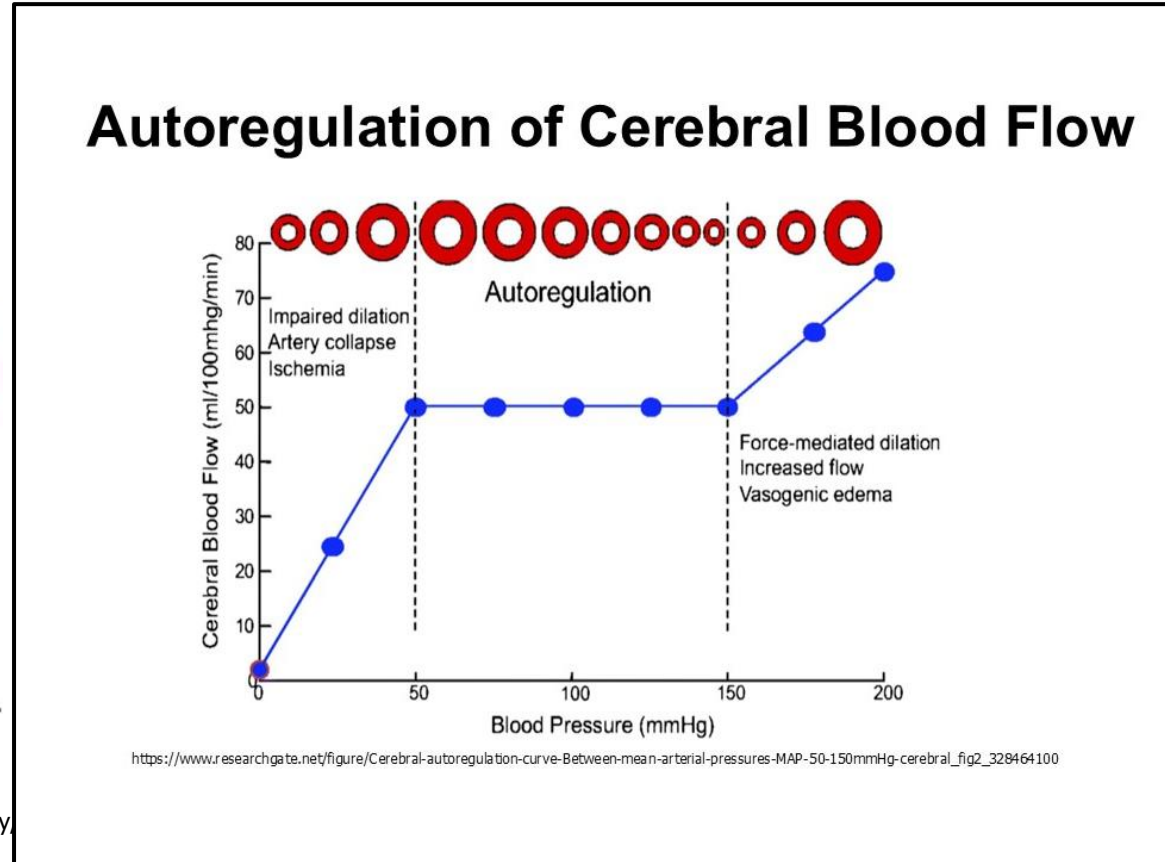
Blood compartment



Bottom view of brain

ADAM.

<https://medlineplus.gov/ency>

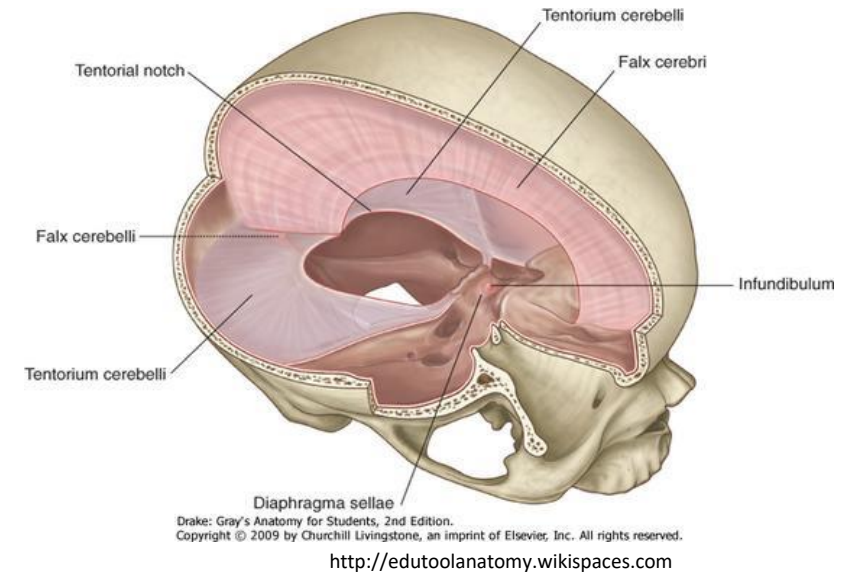


terior

tgart.de

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

- Neuronal cells
 - Reception, integration and propagation of information
 - Unique, irreplaceable
- Neuroglial cells
 - Support for neuronal cells
 - Easily replaceable

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., 2000)
 - 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

Neuroglial cells

Central nervous system

- Astrocytes
 - Hematoencephalic b.
 - Homeostasis maintaining
 - Metabolism of neurotransmitters
 - Important during brain development
- Oligodendrocytes
 - Myelin sheat

Neuroglial cells

Central nervous system

- Astrocytes
 - Hematoencephalic b.
 - Homeostasis maintaining
 - Metabolism of neurotransmitters
 - Important during brain development
- Oligodendrocytes
 - Myelin sheat
- Microglia
 - Immune funtion

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)

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

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

Neuroglial cells

Central nervous system

- Astrocytes
 - Hematoencephalic b.
 - Homeostasis maintaining
 - Metabolism of neurotransmitters
 - Important during brain development

- Oligodendrocytes

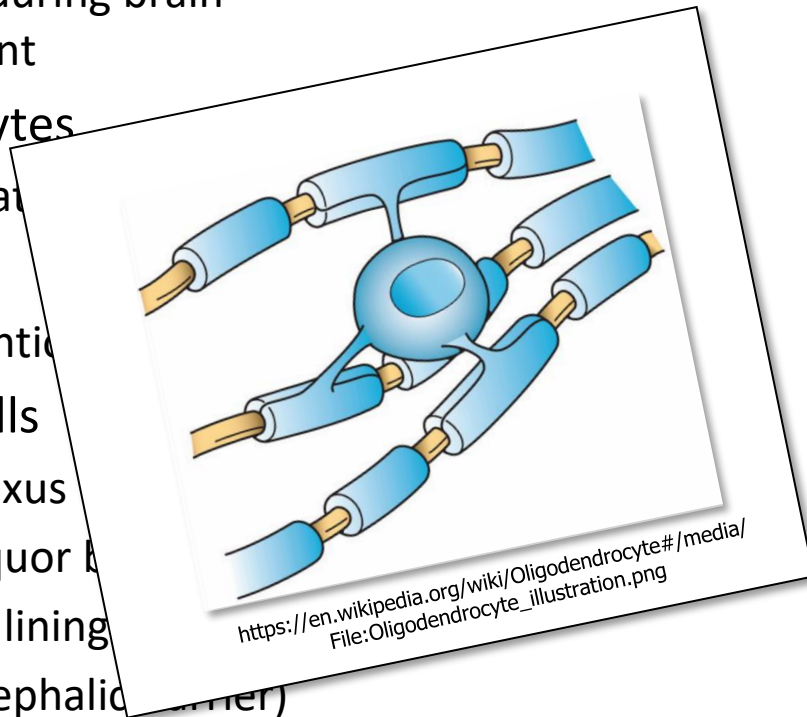
- Myelin sheath

- Microglia

- Immune function

- Ependymal cells

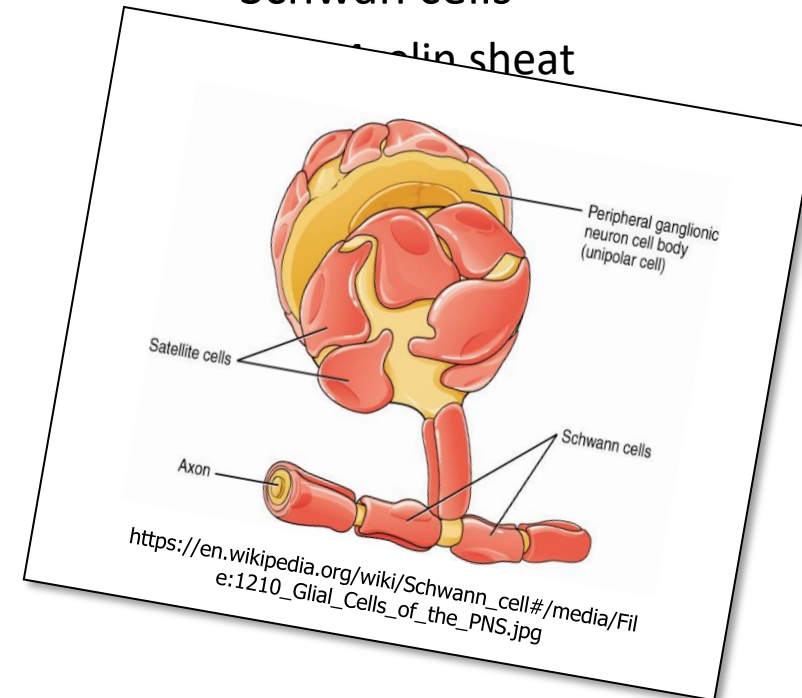
- Choroid plexus
- (hemato-liquor barrier)
- Ventricular lining
- (liquoro-encephalic barrier)



Peripheral nervous system

- Satellite cells
 - Support functions in PNS

- Schwann cells



Neuron

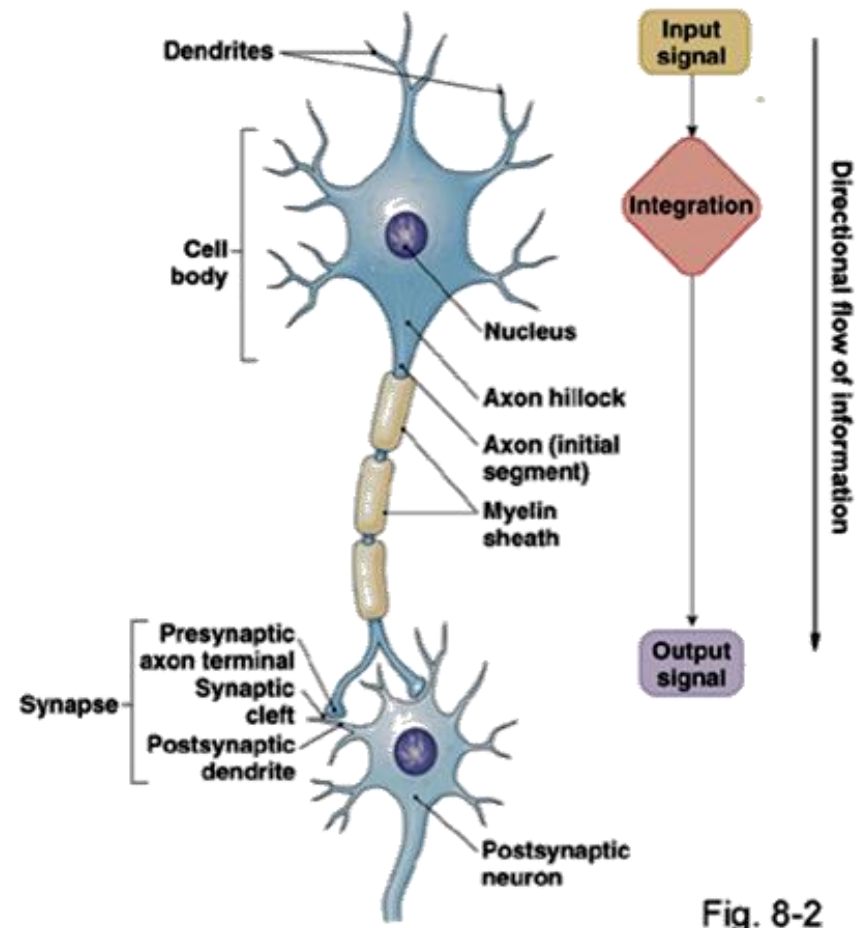


Fig. 8-2

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

Background Activity

The cytoplasm

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

Neuron

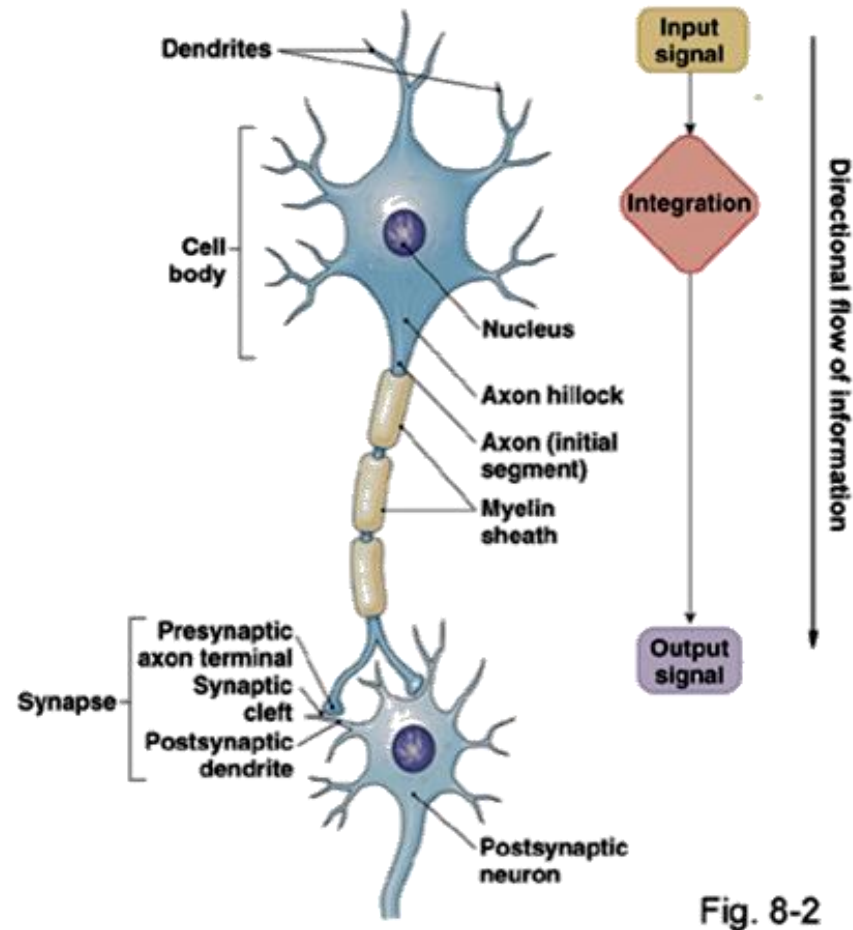


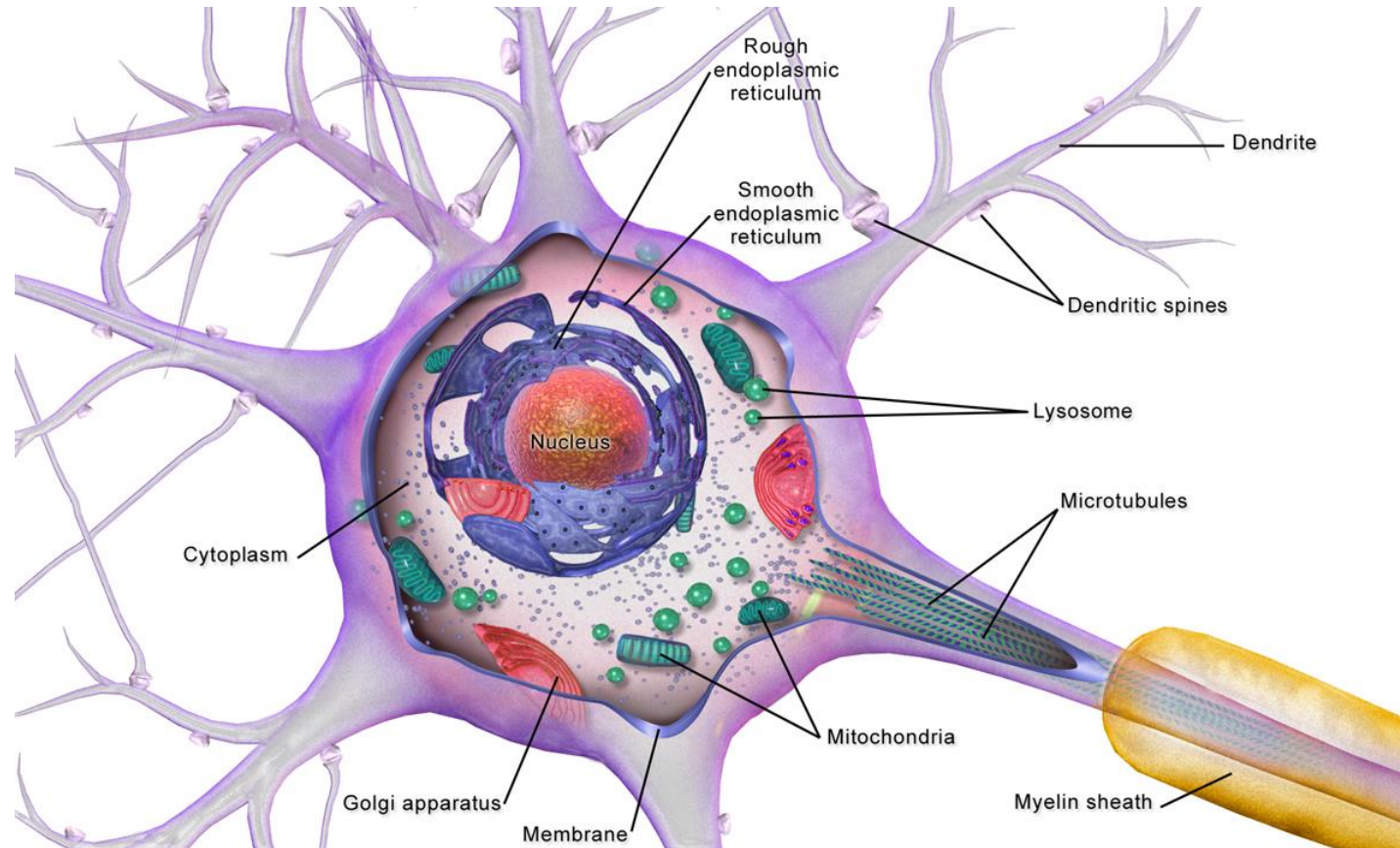
Fig. 8-2

Information processing and transmission

The membrane

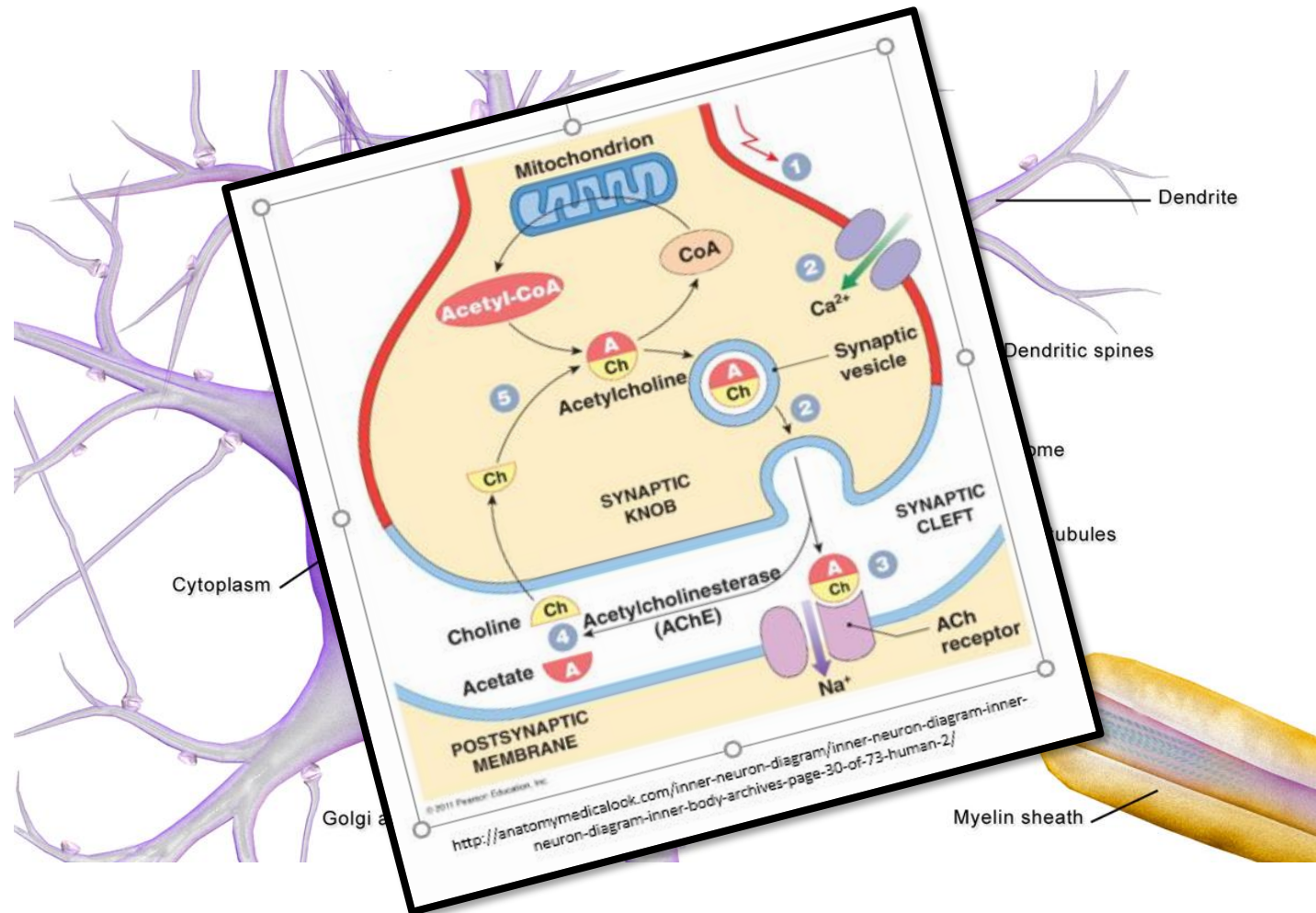
- ✓ Signal reception
- ✓ Signal integration
- ✓ AP generation
- ✓ AP propagation
- ✓ Signal transmission

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

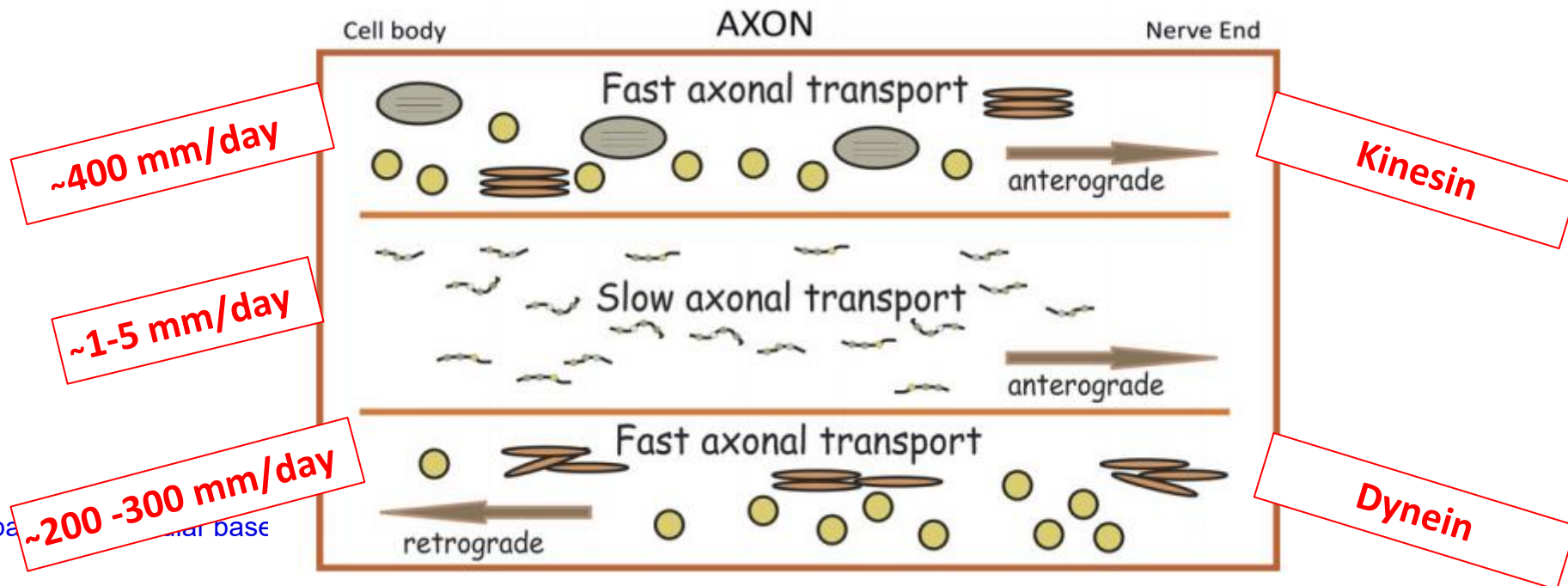
Golgi derived vesicles
lysosomes, mitochondria
structural elements of
endoplasmic reticulum

Slow axonal transport

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

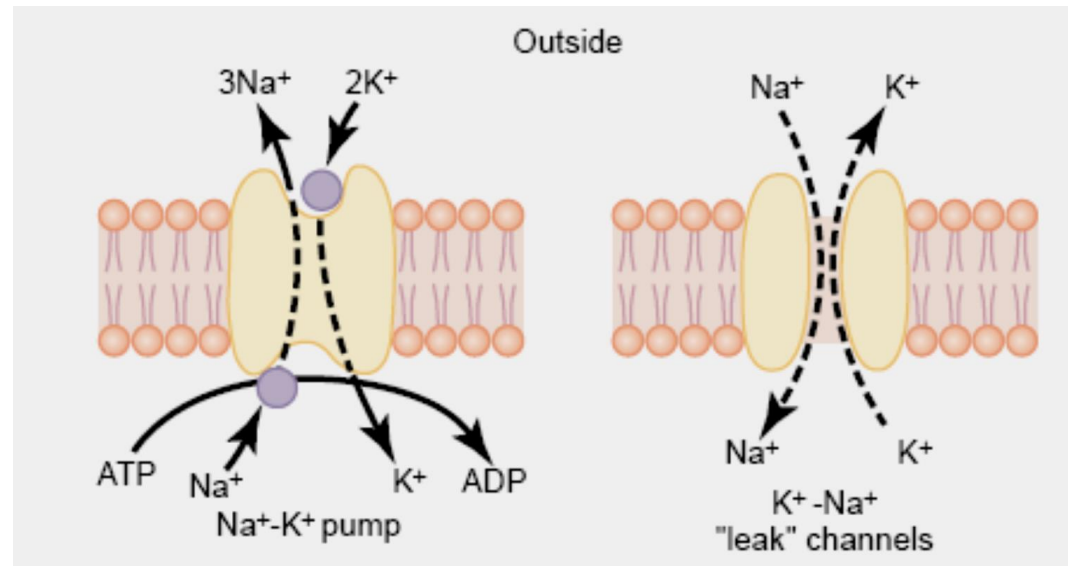
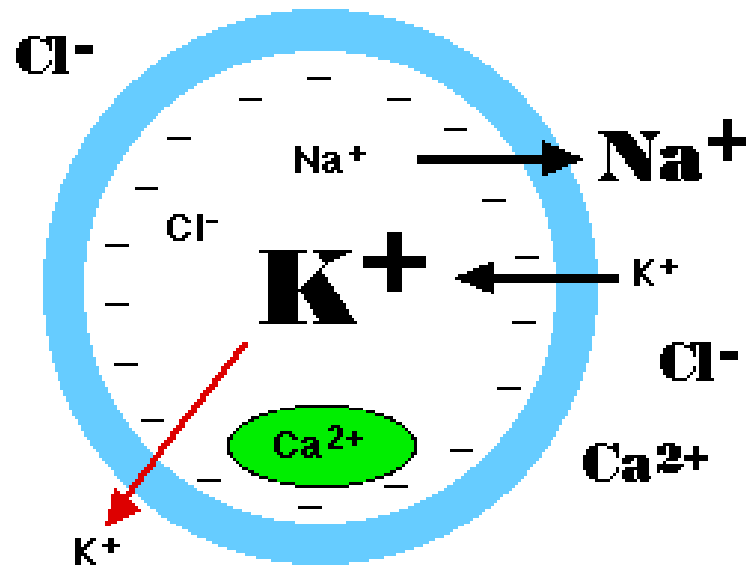
Slow axonal transport

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.uhi.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

Threshold potential around -55 mV

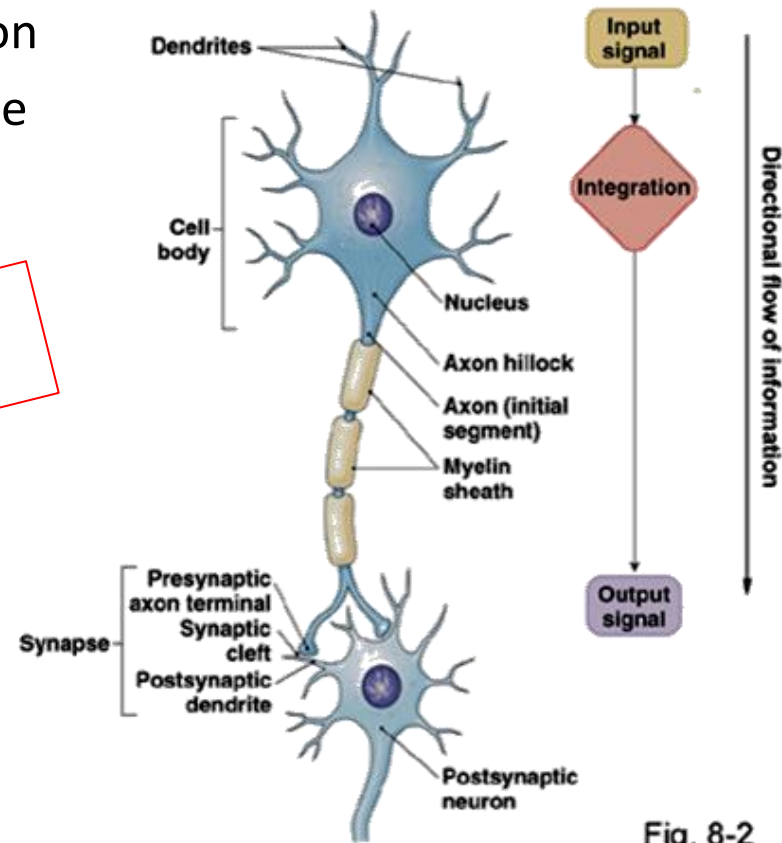
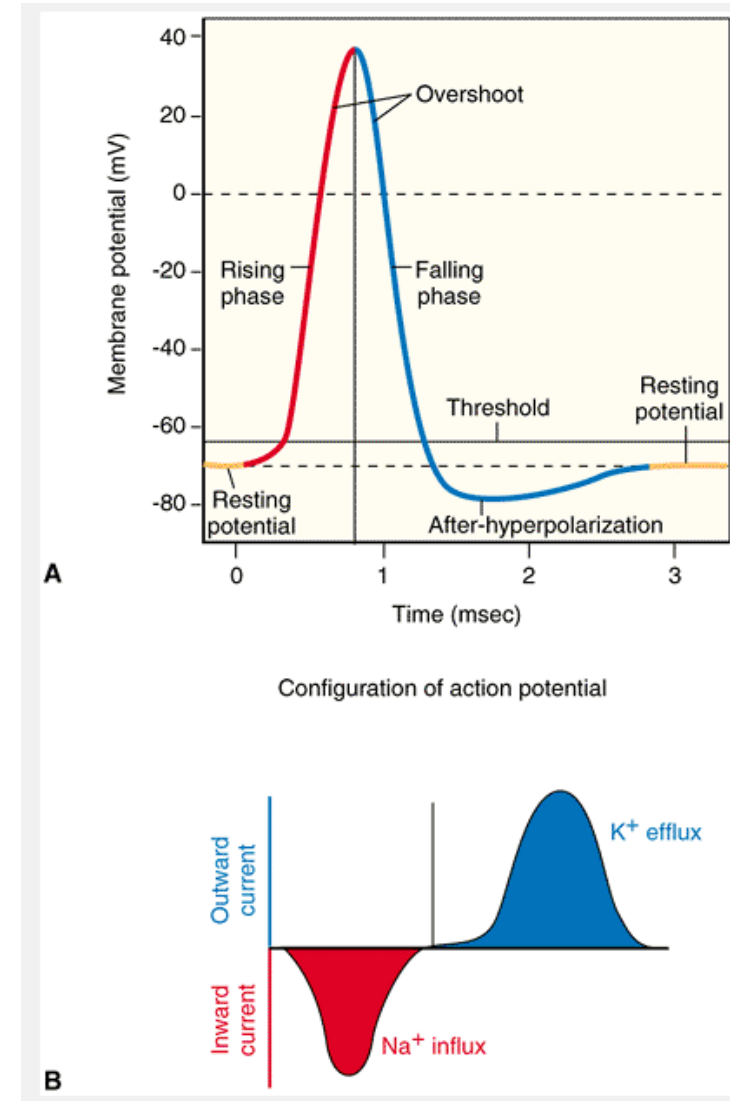
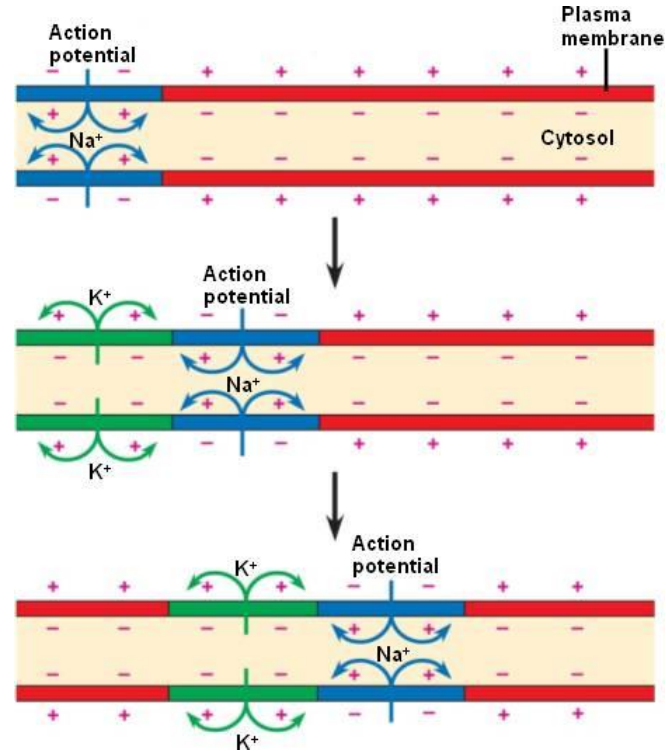
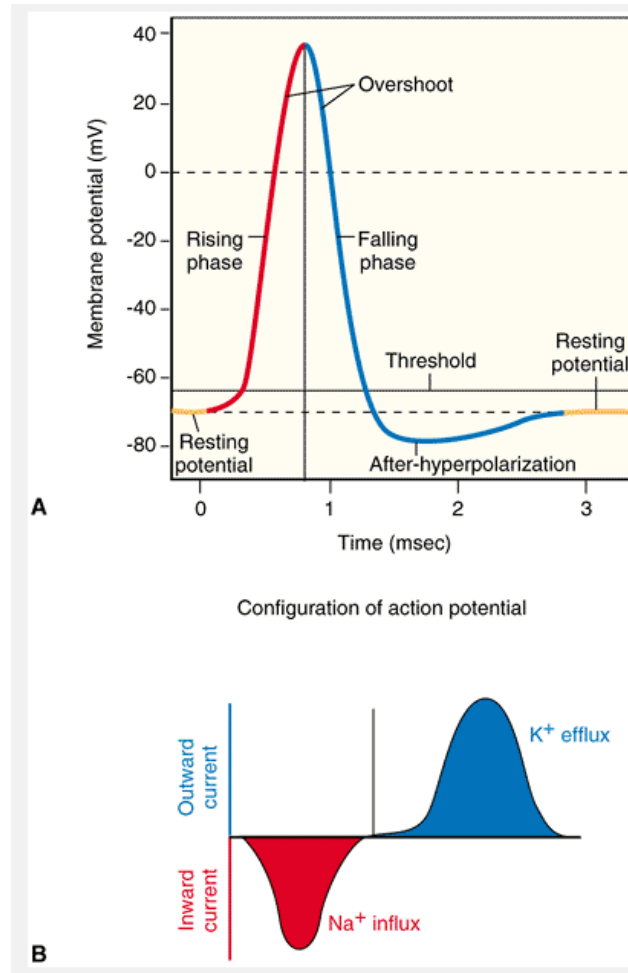


Fig. 8-2



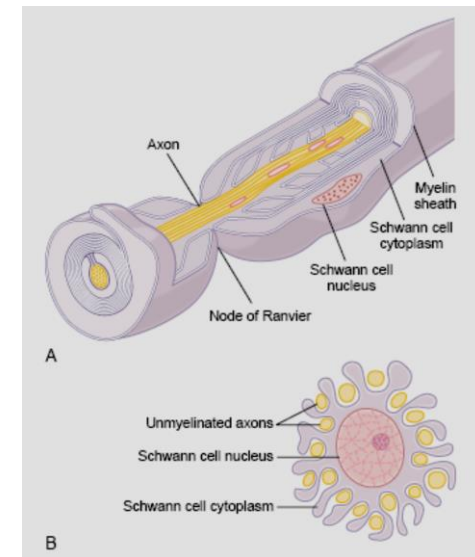
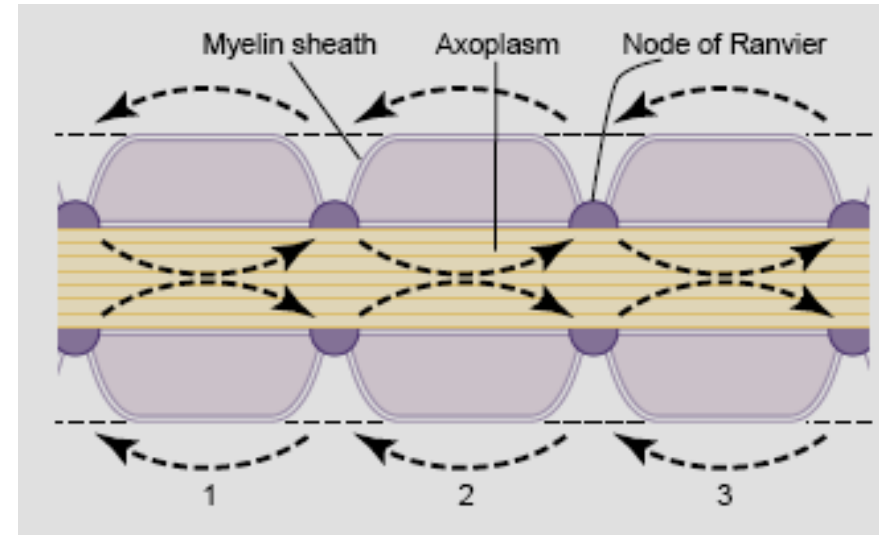
Action potential spreading



- Local currents
- Anterograde

Saltatory conduction

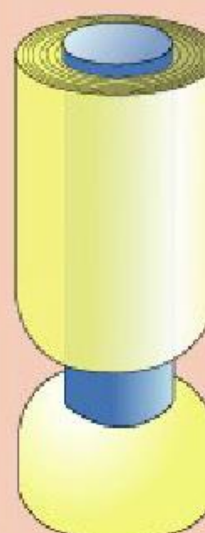
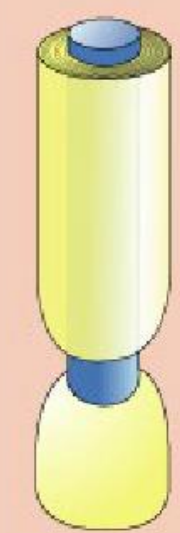


- Myelin sheath
- Nodes of Ranvier
- Economy
- Speed of conduction
- Speed of conduction also dependent of nerve fibre diameter
 - the electrical resistance is inversely proportional to area of cross-section



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

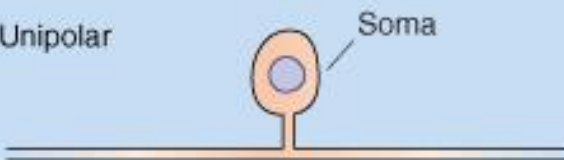

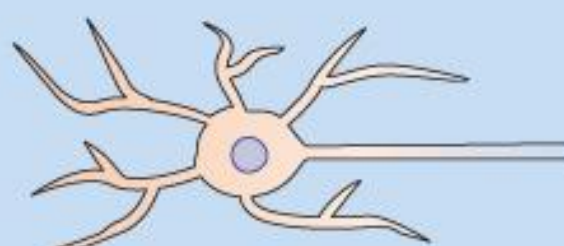
Classification of nerve fibers

- 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

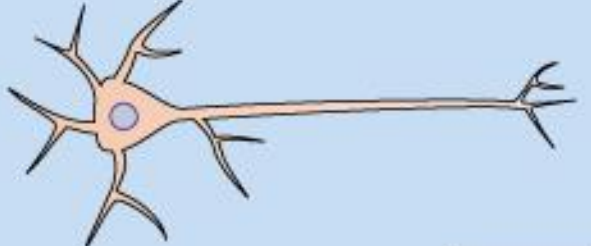
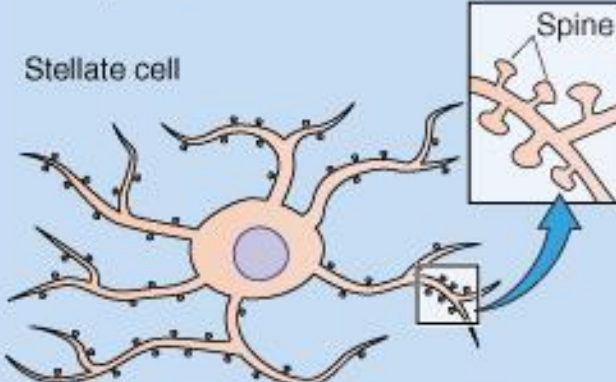
<http://neuroscience.uth.tmc.edu/s2/chapter04.html>

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> 

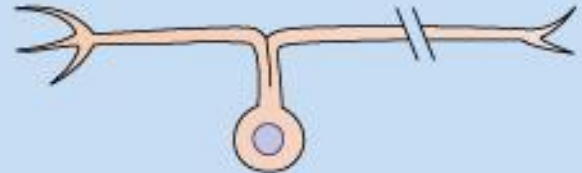

<http://www.slideshare.net/CsillaEgri/presentations>

Neuronal classification

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

<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>	Projection neuron or Principal neuron or Golgi type I cell (cortical motor neuron)	Affects different brain areas	<p>Dorsal root ganglion cell</p> 
<p>Stays in a local brain area</p>	Intrinsic neuron or Interneuron or Golgi type II cell (cortical inhibitory neuron)	Affects only nearby neurons	<p>Retinal bipolar cell</p> 

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

68. Cellular base of nervous system

- ✓ Neuroglial cells
 - Classification and functional overview
- ✓ Neuronal cells
 - Characterization, classification, anatomy
 - Functions of neurons
 - Background activity (cytoplasm)
 - Synthesis (soma)
 - Transport (categorization, characterization)
 - Information processing and transmission (membrane)
 - Main points of question No. 70

69. Intracranial compartment, intracranial pressure

- ✓ Content of intracranial compartment (brain, blood, CSF)
- ✓ Barriers among compartments (meningeal, hematoencephalic, hematoliquor)
 - HEB description
 - Circumventricular organs
- ✓ CSF
 - Function
 - Production, circulation, absorption
- ✓ Intracranial pressure
 - Definition, equation, implications

70. Membrane voltage, action potential – generation and propagation through nerve fibers

- ✓ Membrane potentials
 - General characteristics and ionic mechanisms description
- ✓ Resting potential in neuron (characteristics)
- ✓ Action potential
 - Characteristics
 - Ionic mechanisms
 - Signal conduction
 - Role of myelin, saltatory conduction
- ✓ Classification of nerve fibres

M U N I

M E D