Lecture 9

Nerve tissue

- Nerve tissue
- Neuron
- Synapse
- Neuroglia
- Nerve
- Saltatory signal propagation
- Development of nerve tissue
- Nerve regeneration

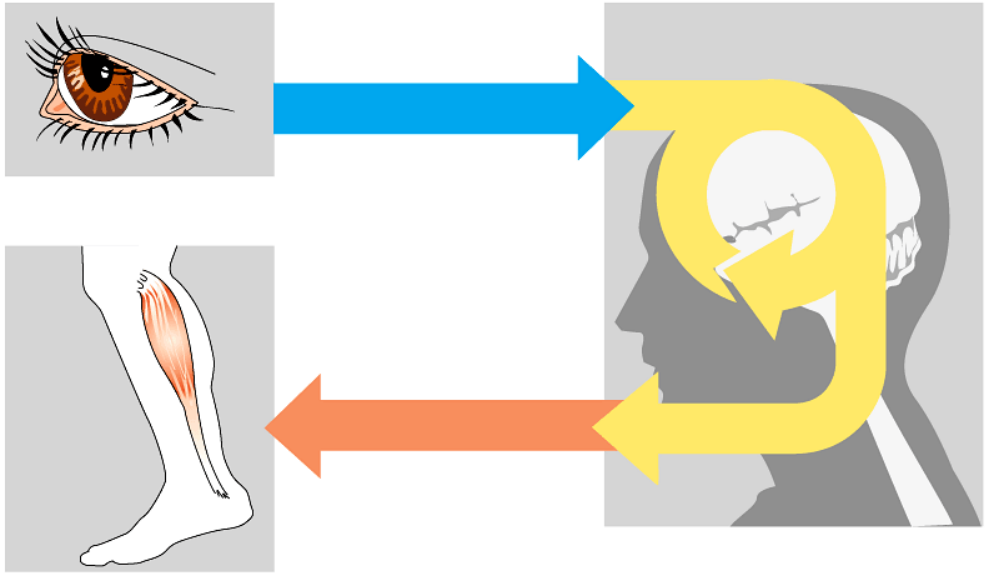
Brno, April 2021

Nerve tissue – general 1

Controls and integrates all body activities within limits that maintain life

Key functions

- **sensing changes with sensory receptors**
- **interpreting and remembering those changes**
- **reacting to those changes with effectors**



Somatic
X
Autonomous (vegetative)

Anatomical organization of nervous system 1

Central nervous system - CNS

Definition:
Unpaired, bilaterally symmetrical structures extending along the longitudinal axis of the midsagittal plane of the body.

Structures arising directly from the neural tube.

Includes:
- Brain
- Spinal cord

Peripheral nervous system - PNS

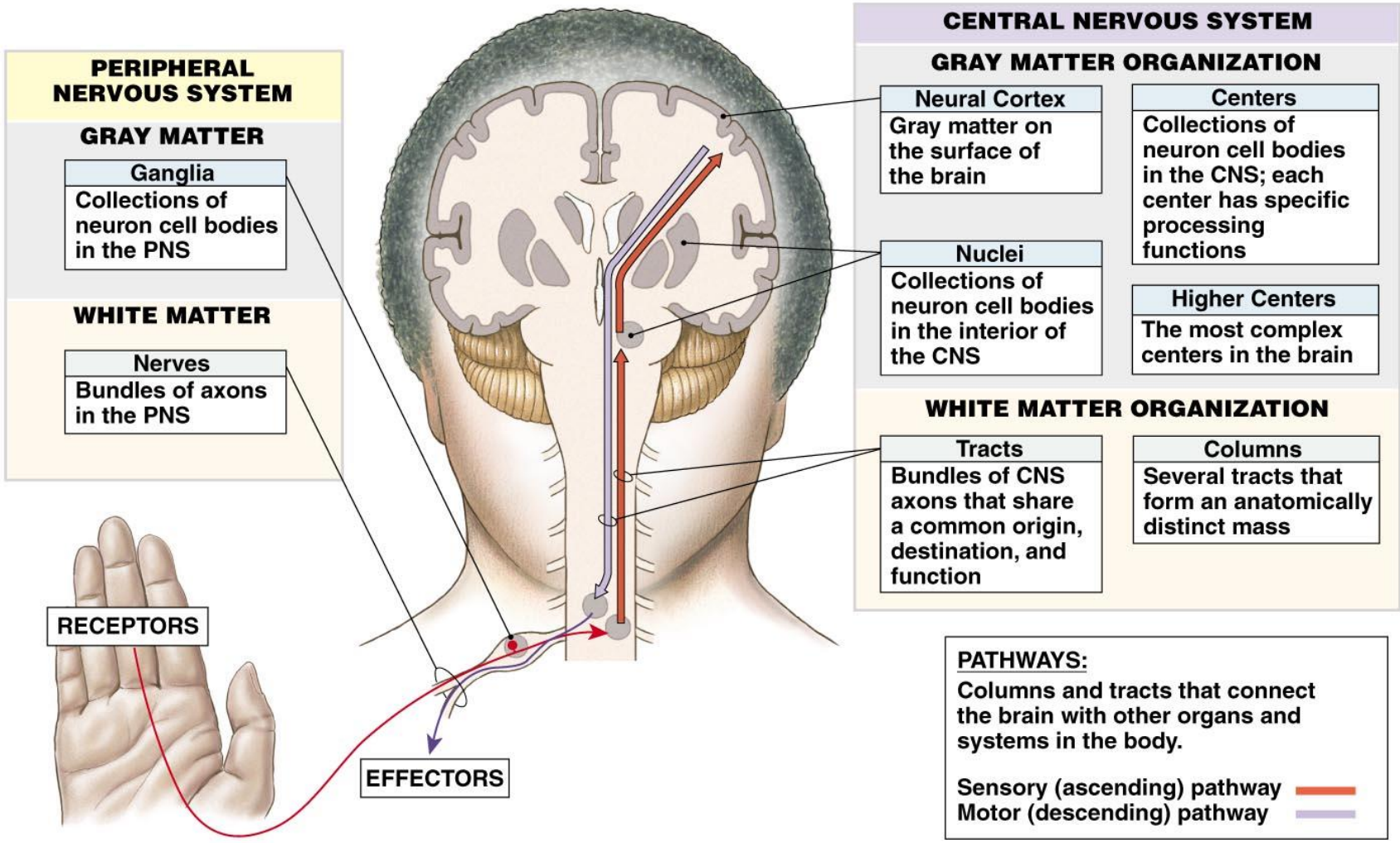
Definition:
Made up of transmission pathways carrying information between the CNS and external/internal environments.

Afferent (sensory) pathways:
Carry information to the CNS.

Efferent (motor) pathways:
Carry information from the CNS.

Includes:
- Cranial nerves (12 pairs)
- Spinal nerves (31 pairs)
- Peripheral nerves
- Ganglia

Anatomical organization of nervous system 2

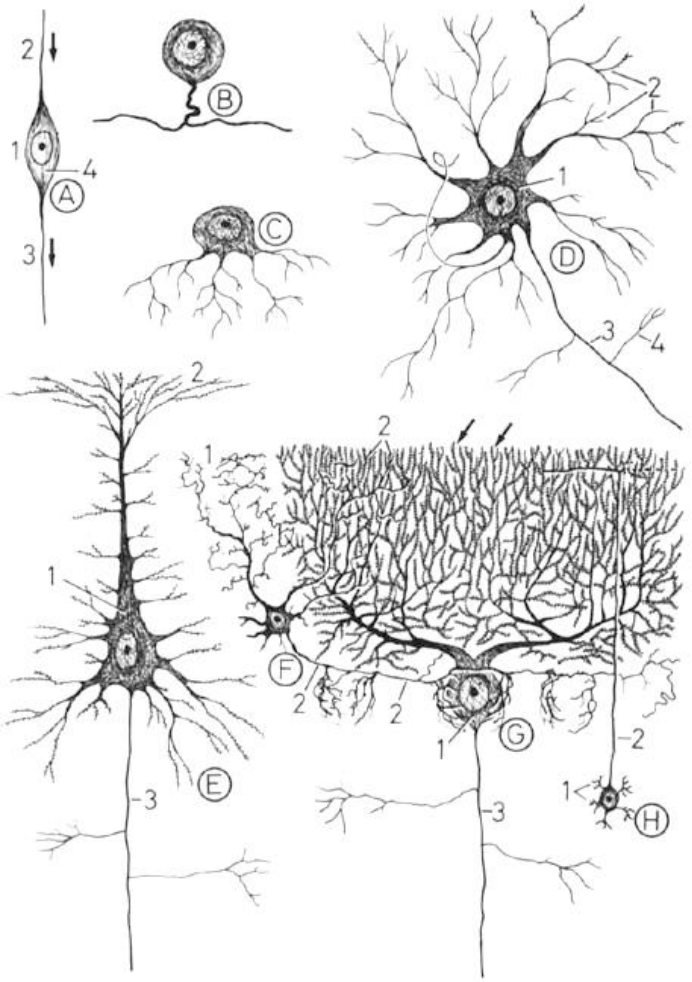


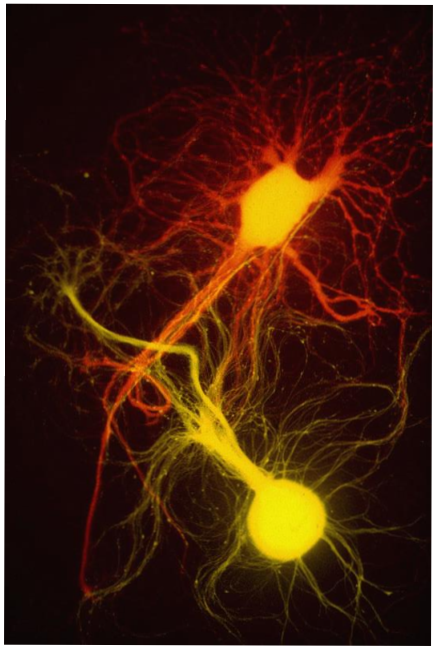
Nerve tissue – General – Neuron 1

Nervous tissue is made up of just 2 types of cells:

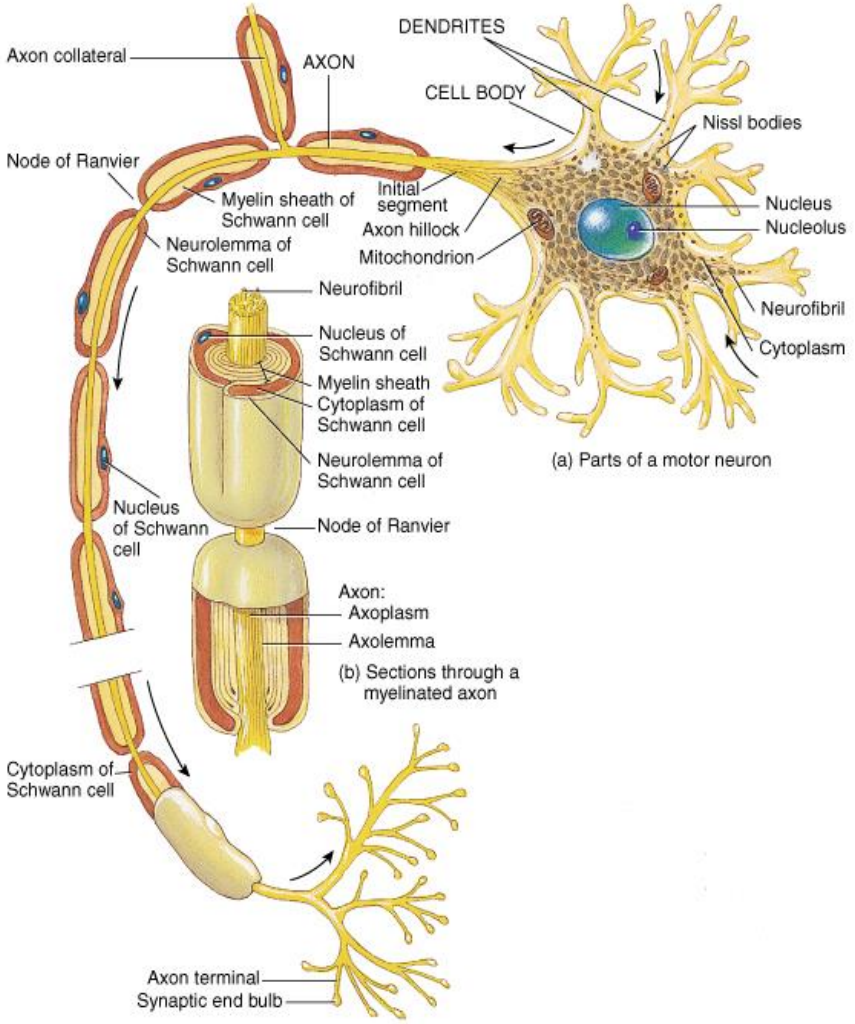
- **Neurons**
- **Neuroglia - glial cells** (supporting cells)

- Neurons are the basic functional units of nervous tissue.
- They are highly specialized to transmit nerve impulses.





Neuron 2



1. **Perikaryon (neurocyte)**

2. **Processes:**

   (one-way signal conduction)

- axon

(always only one; centrifugal conduction)

- dendrit(es)

(centripetal conduction)

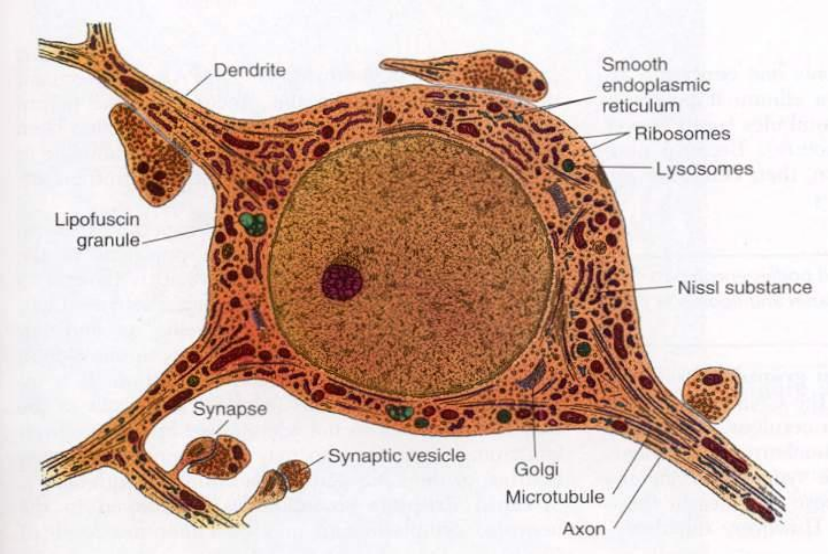
Neuron 3 - Perikaryon

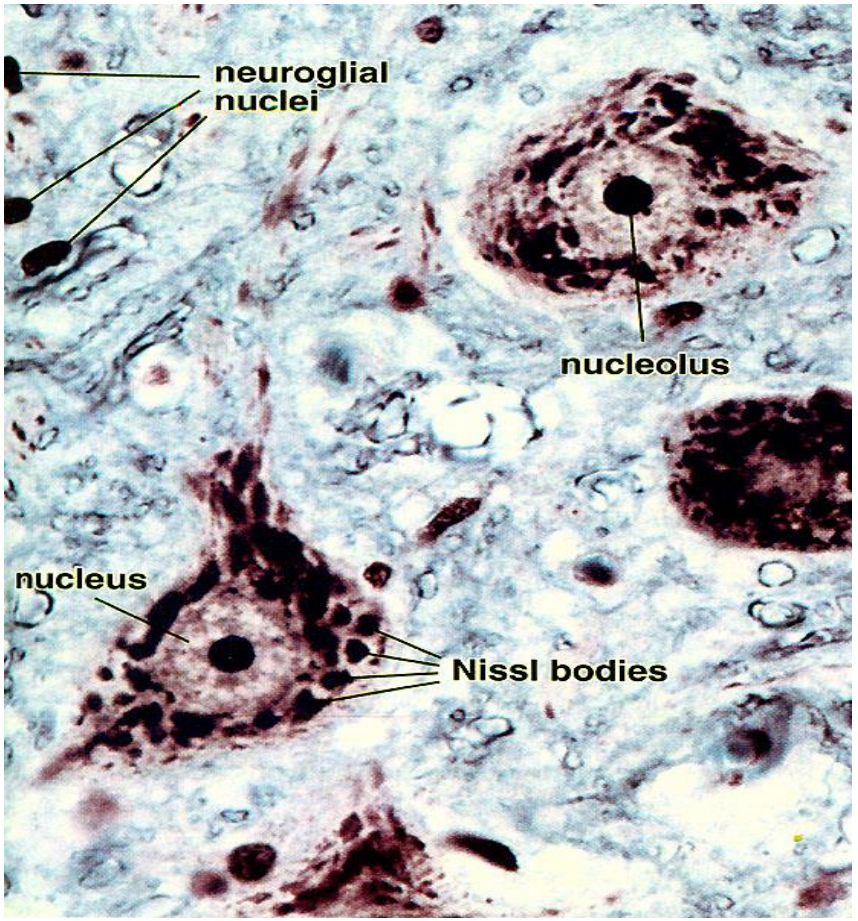
Position:
CNS – grey matter
PNS – ganglia

Shape:
pyramidal, shpherical, ovoid, peer-shaped

Size:
5 to 150 μm

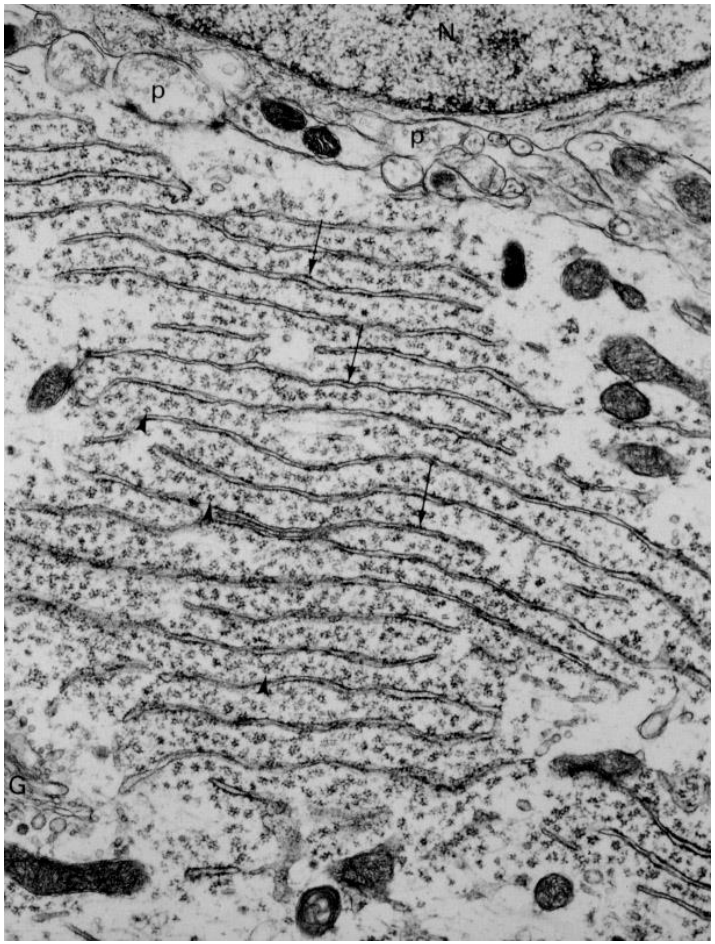
Organelles:
- Nuclues – large + pale + prominent nucleoli
- Nissl substance – rough ER
- Neurofibrils (neurofilaments + neurotubules + actin)
- Lipofuscin pigment clumps





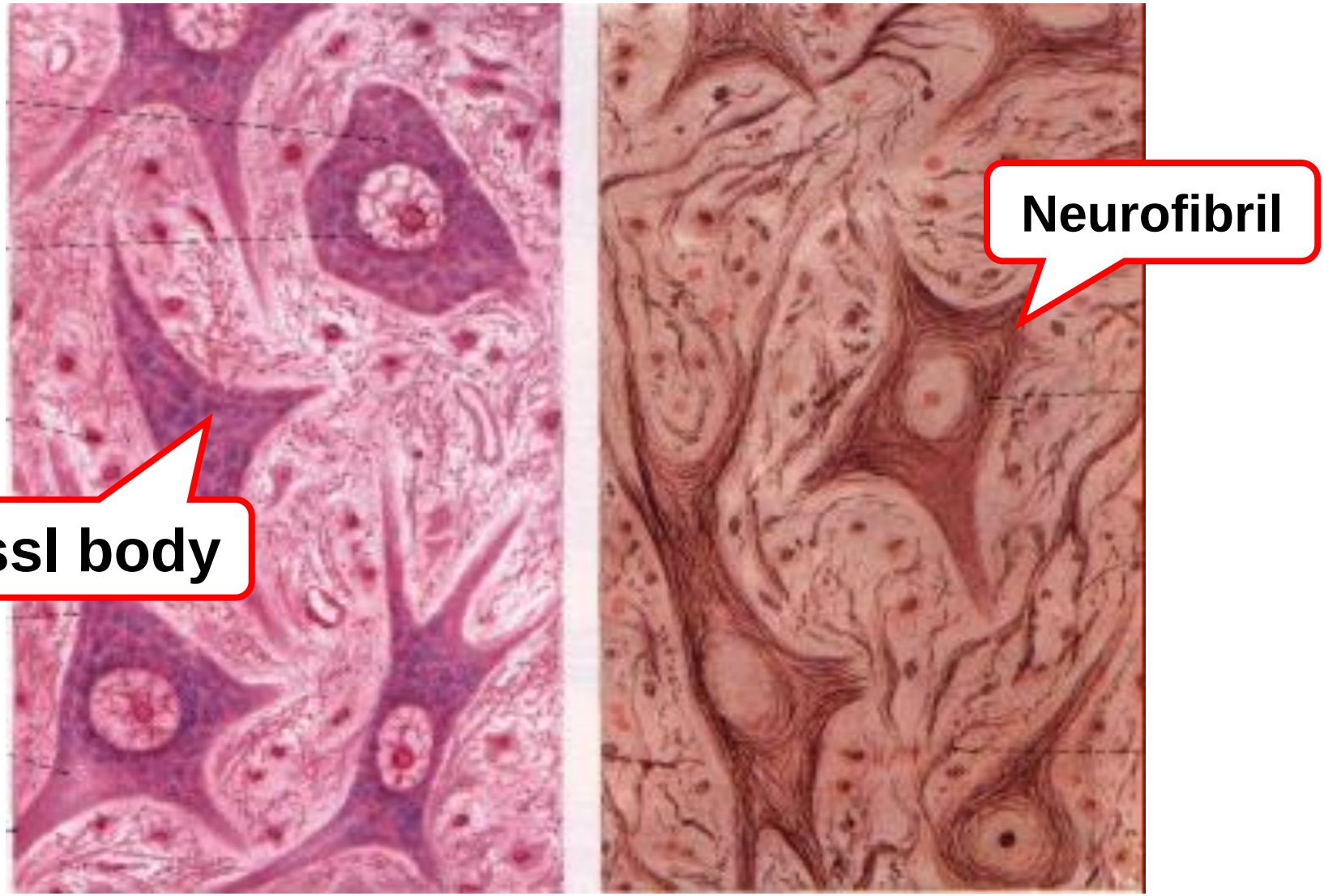
Neuron 4 - Perikaryon

Nissl substance in TEM



Cell and Tissue Ultrastructure – A Functional Perspective; 1993; Cross and Mercer, Freeman and Co.; Page 127

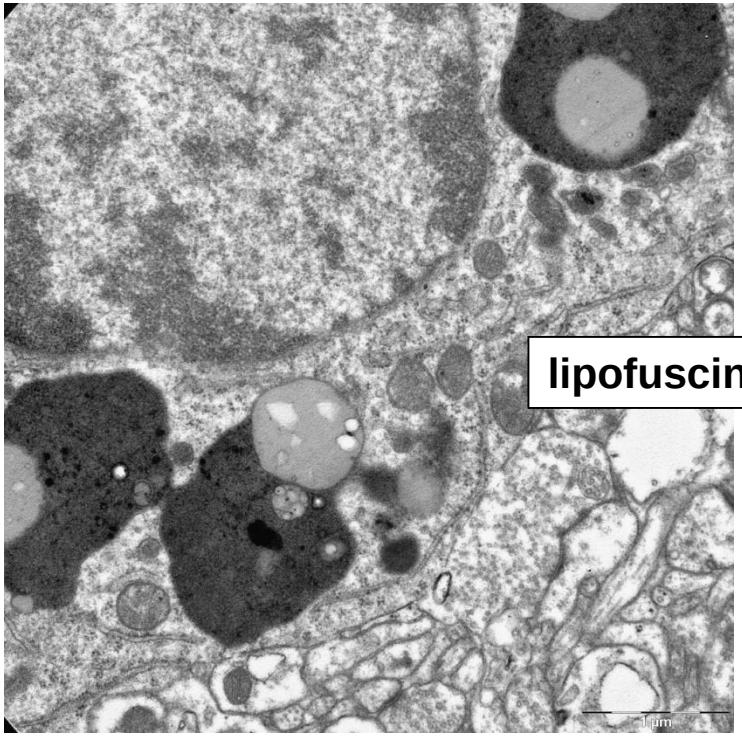
Neuron 5 - Perikaryon



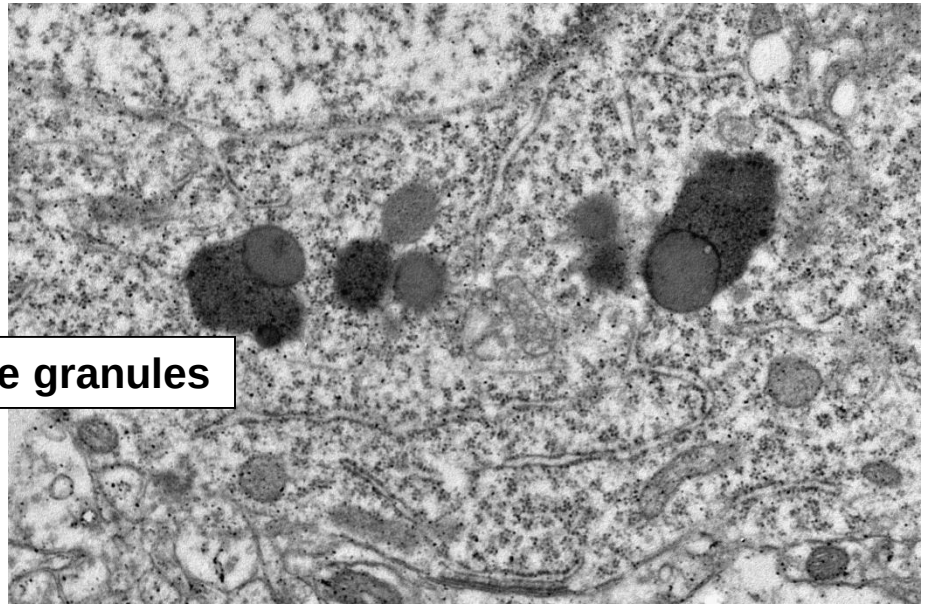
H-E stains

Silver nitrate

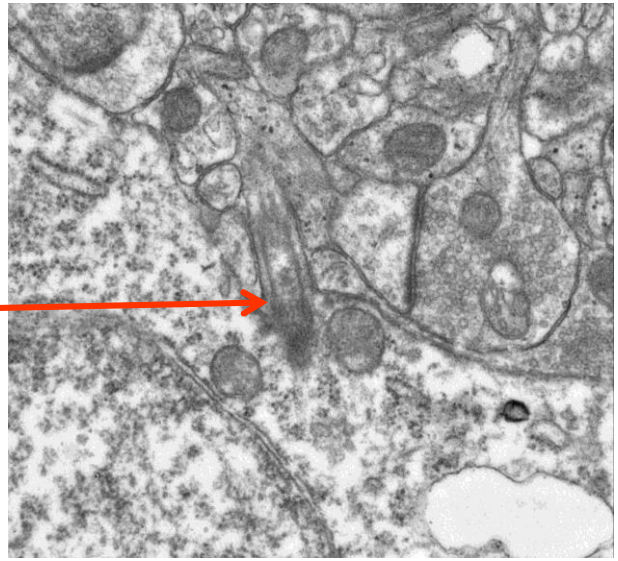
Neuron 6 - Perikaryon



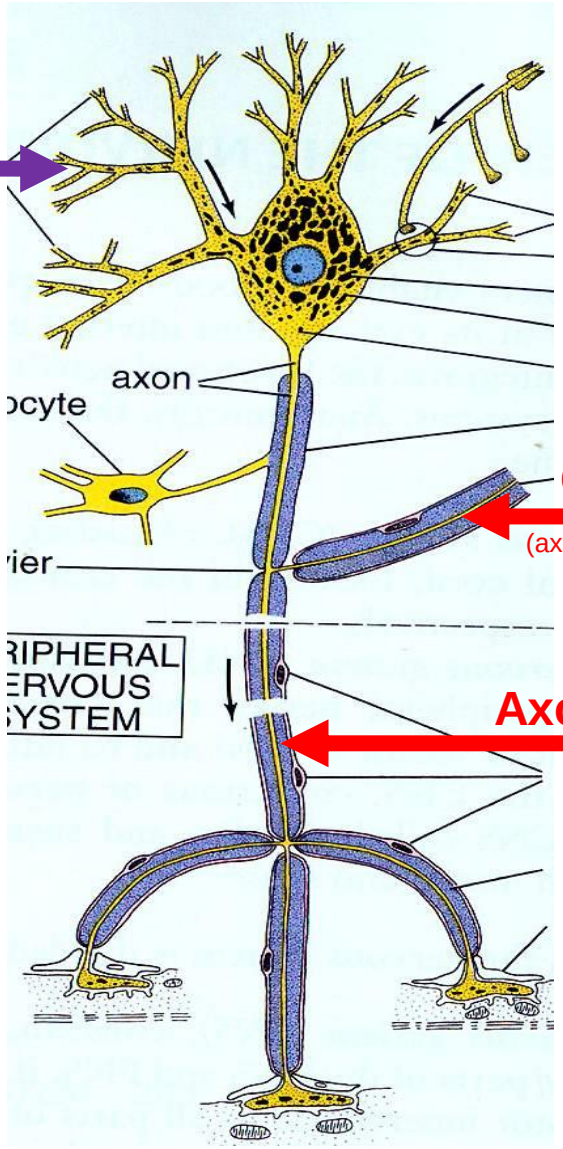
lipofuscine granules



Cilium derived from unused centriole



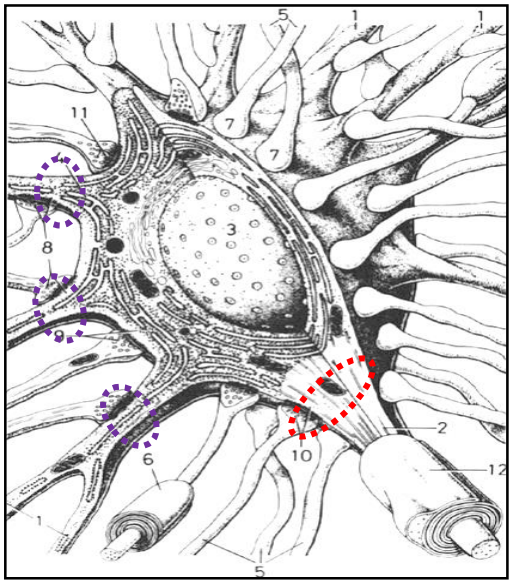
Neuron 7 – Neurites / Processes



Neuron 7 – Neurites / Processes

Dendrites

- Conducts impulses **towards the cell body**
- Typically **short, highly branched & unmyelinated**
- Surfaces specialized for contact with other neurons
- Contains **neurofibrils & Nissl bodies**
- Receptive surface for synaptic junctions
- Contain **MAP-2** (distinction from axon)
- Tens of thousands of synapses on large dendrites
- **Dendritic spines** located on surface of some dendrites
- Spines diminish with age and poor nutrition

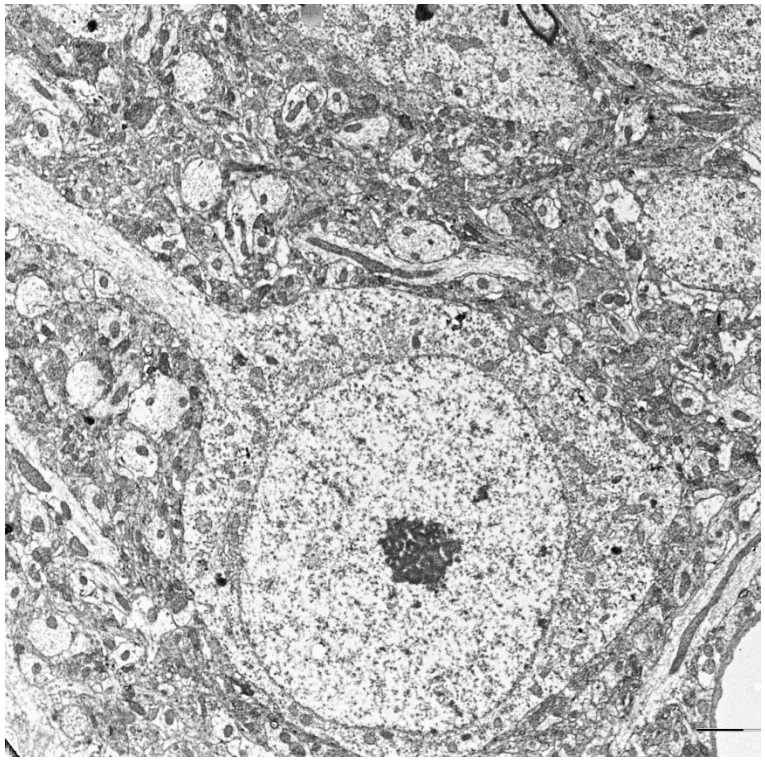


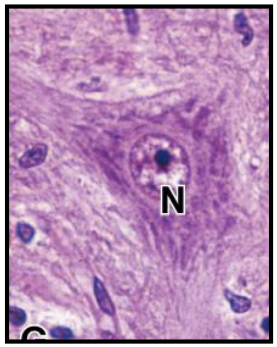
Axon (nerve fiber)

- 1 axon projects from cell body at axon hillock
- **Axon hillock** - pyramid shaped region of the soma that is **devoid of RER**
- Some axons are up to **100 cm**
- **Initial segment** = **Spike trigger zone** (a portion of axon from its origin to the beginning of myelin sheath)
- **At spike trigger zone** trigger zone summation of excitatory and inhibitory impulses occurred
- Collateral branches, Terminal arbor
- **Myelinated** or **Unmyelinated**
- Conduct impulses **away from cell body**
- Swollen tips called **synaptic knob (terminal button)** contain **synaptic vesicles** filled with neurotransmitters
- Cell membrane = **axolemma**
- Cytoplasm = **axoplasm**

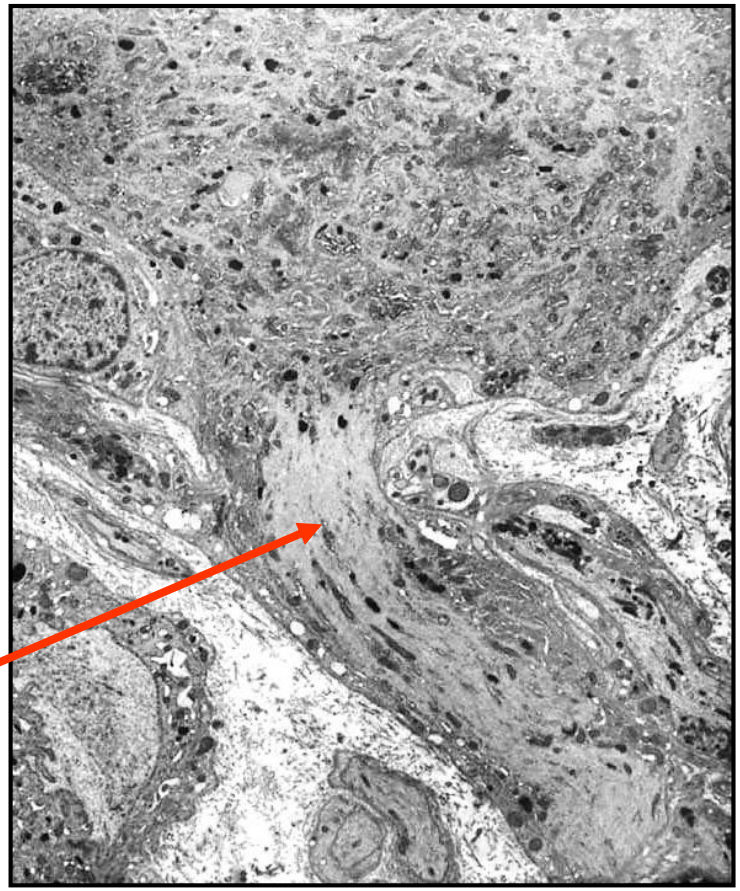
White matter: areas of myelinated axons
Gray matter: areas of unmyelinated axons, cell bodies, and dendrites

Neuron 8 – Neurites / Processes



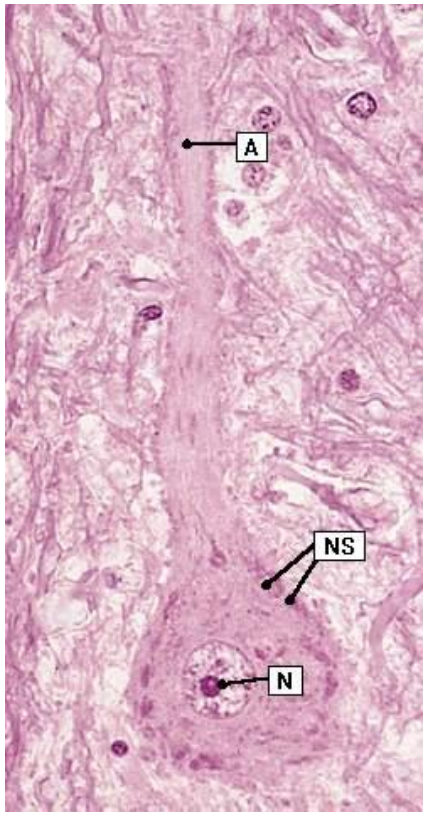


Neuron in TEM



Axon hilloc

Neuron 9 – Axonal transport



Why?

many proteins made in soma must be transported to axon and axon terminal to repair axolemma, serve as gated ion channel proteins, as enzymes or neurotransmitters

How?

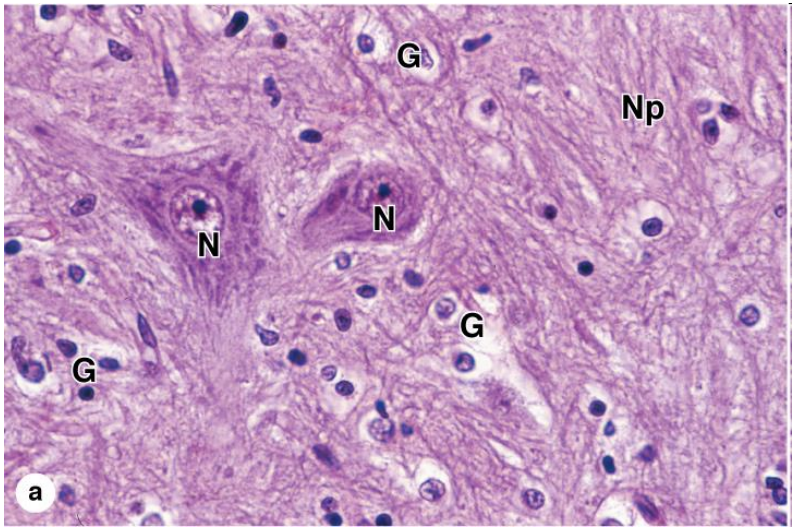
axonal transport – two-way passage of proteins, organelles, and other material along an axon

- **anterograde transport** – movement down the axon away from soma (dynein)
- **retrograde transport** – movement up the axon toward the soma
- (kinesin)

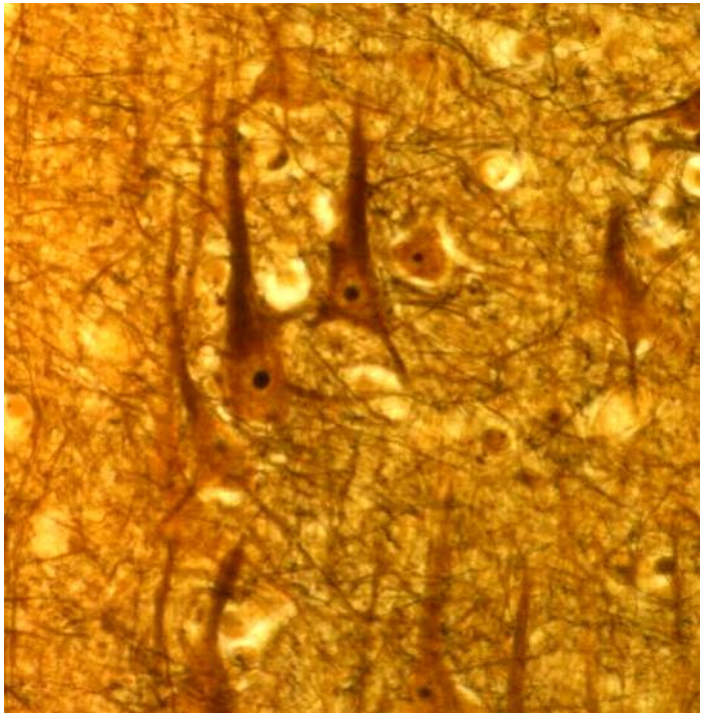
- **Slow transport:** 1-5 mm/day
- **Fast transport:** 200-400 mm/day

Nerve tissue – Neuropil 1

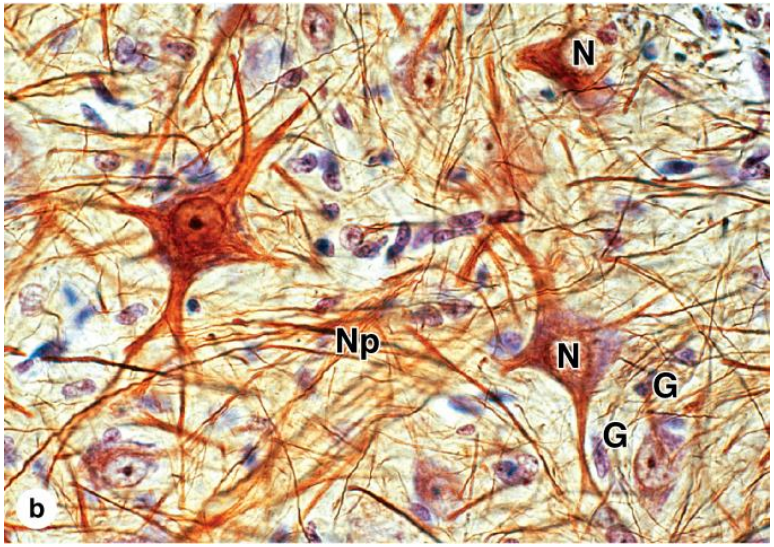
All the material filling space among the bodies of neurons and glial cells + ECM



motoneurons - HE



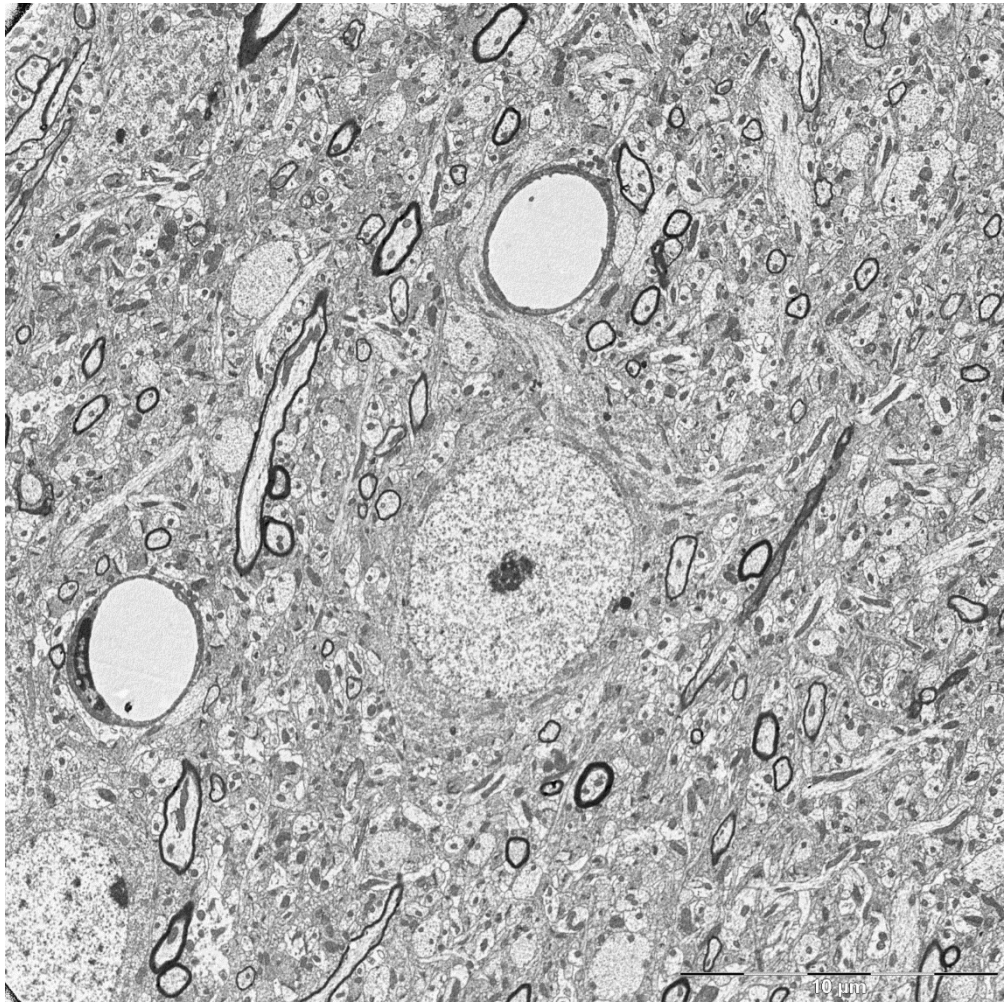
pyramidal cells - impregnation



motoneurons – combined method

Nerve tissue – Neuropil 2

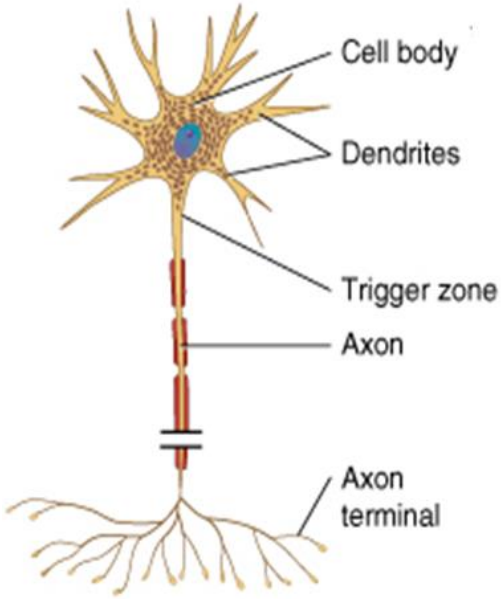
Neuropil in TEM



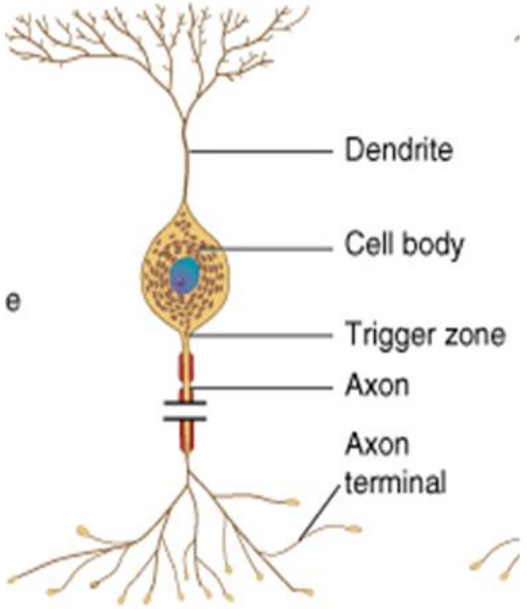
Neuron – Classification 1

According to the number of the processes

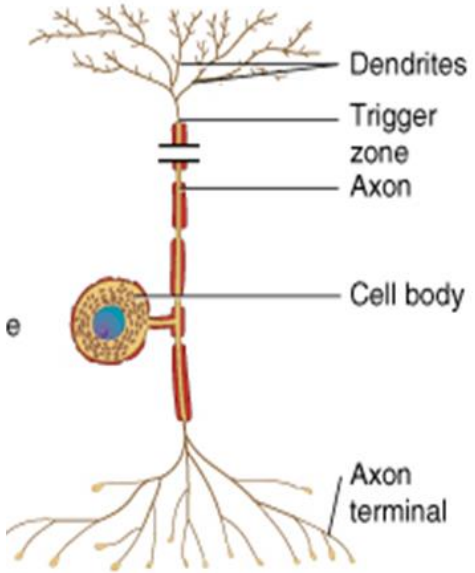
Multipolar
several dendrites & one axon
(most common cell type)



Bipolar
one main dendrite & one axon
(in retina, vestibular and cochlear ganglion)

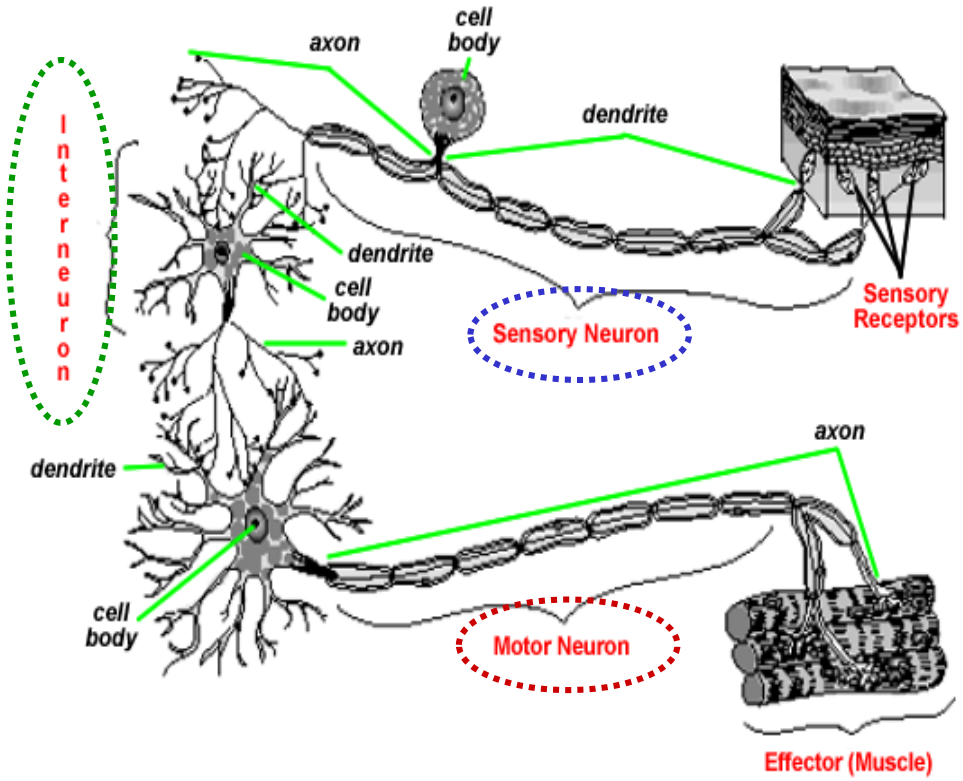


Unipolar (pseudounipolar)
one process only
(develop from a bipolar)
(always sensory, in spinal ganglia)



Neuron – Classification 2

According to the function



Motor (efferent) neurons:
- conduct impulses to muscles, neurons, glands

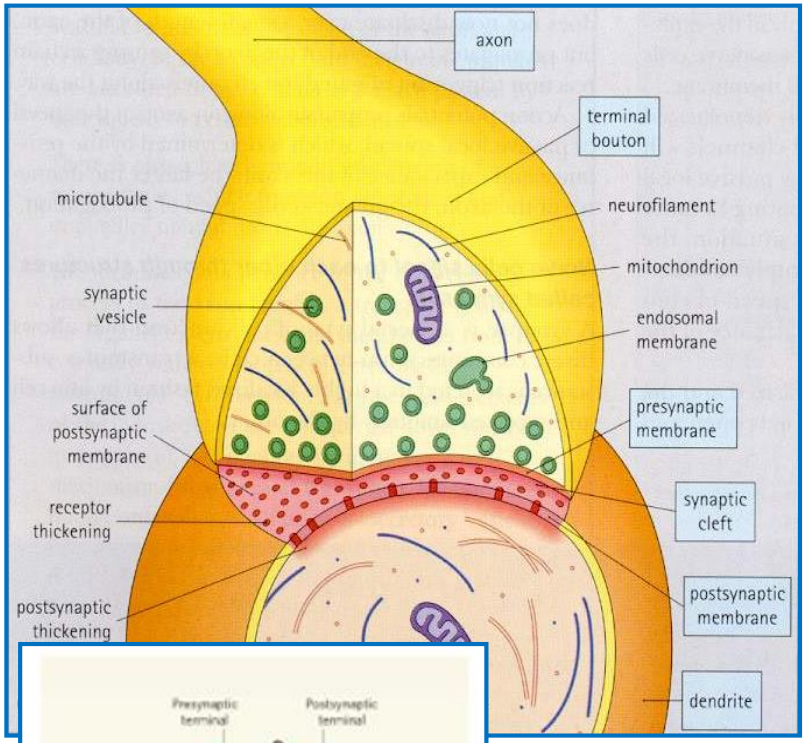
Sensory (afferent) neurons:
- receive sensation

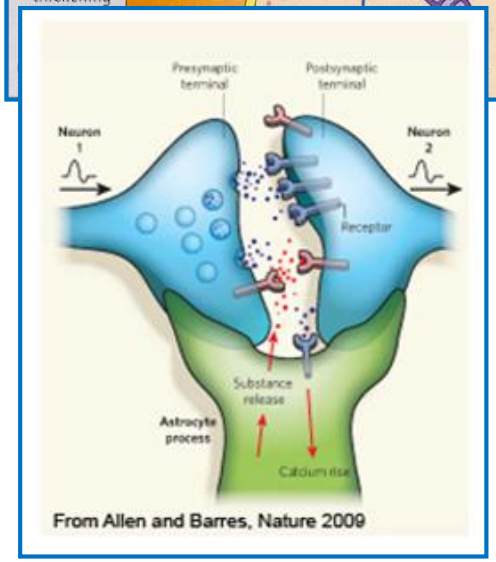
Interneurons:
- local circuit neurons

Synapse 1

Definition

Synapses are highly specialized intercellular junctions, which link the neurons of each nervous pathway





- **Axon terminal** forms **bouton terminal**
- **Presynaptic membrane -** contains mitochondria, and an abundance of **synaptic vesicles with neurotransmitter**
- **Presynaptic dense projections -** are associated with synaptic vesicles form active sites of synapse
- **Synaptic vesicles** (smaller + larger – storage)
- **Postsynaptic membrane -** contains receptors and some dense materials
- **Synaptic cleft -** 20-30 nm width, occupied by fine filaments
- **Glial cells** increase synaptic efficacy
- **Asymmetric synapses are excitatory** (a thick postsynaptic membrane and a 30 nm synaptic cleft)
- **Symmetric synapses are inhibitory** (thin postsynaptic membrane and a 20 nm synaptic cleft)
- Need **special staining** to see by light microscopy

Synapse 2

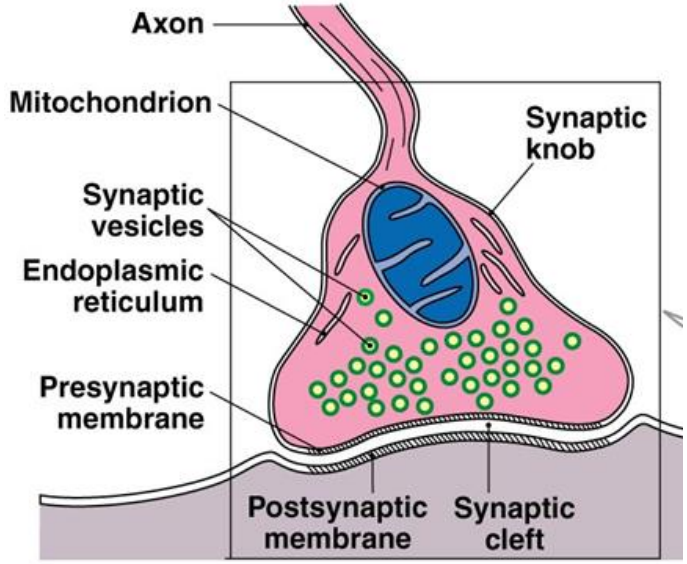
Excitatory synapses

- postsynaptic Na+ channels open
- influx of Na+
- **depolarizition** of membrane of postsynaptic neuron

X

Inhibitory synapses

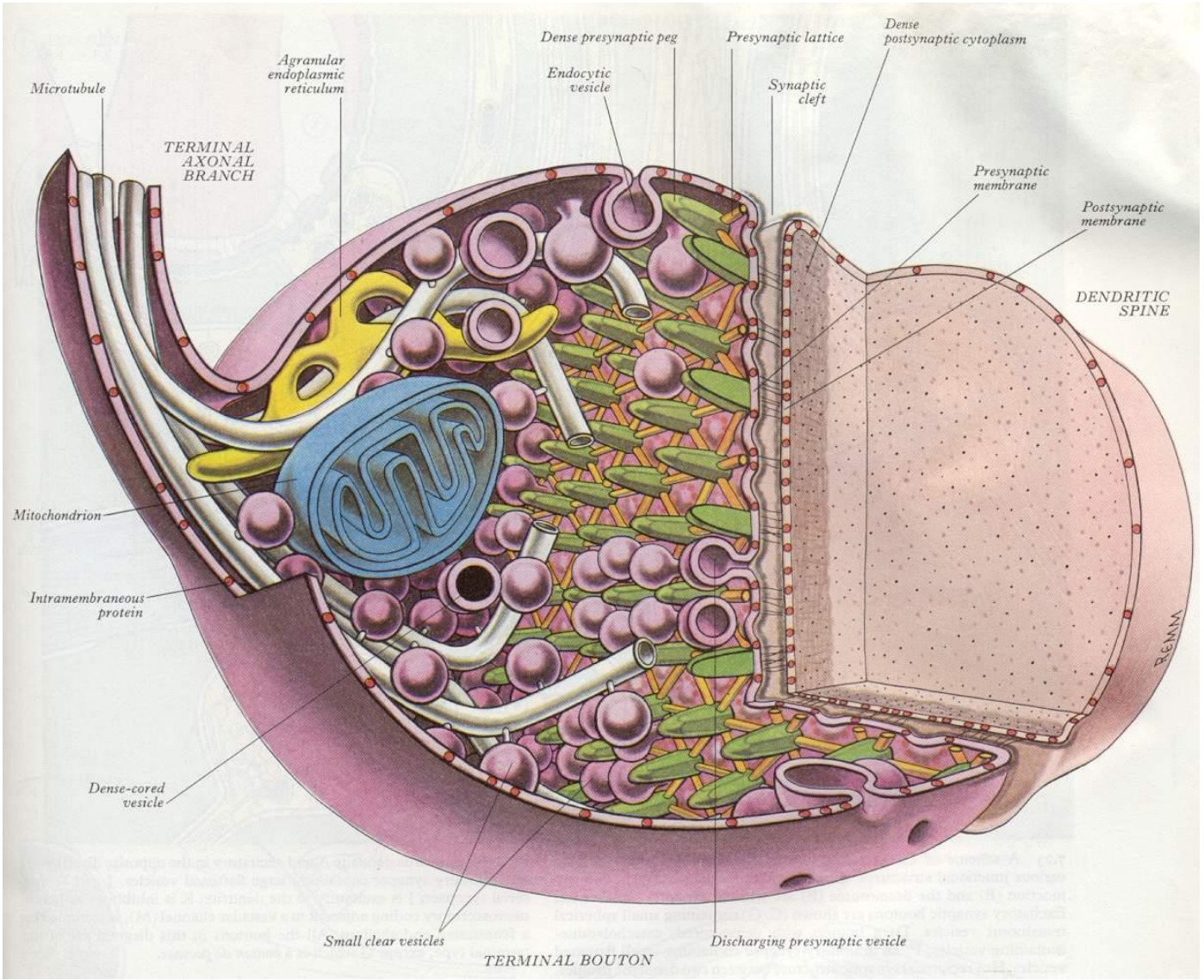
- postsynaptic Cl- (or other anion) channels open
- influx of anions
- **hyperpolarizition** of membrane of postsynaptic neuron



Neurotransmitters

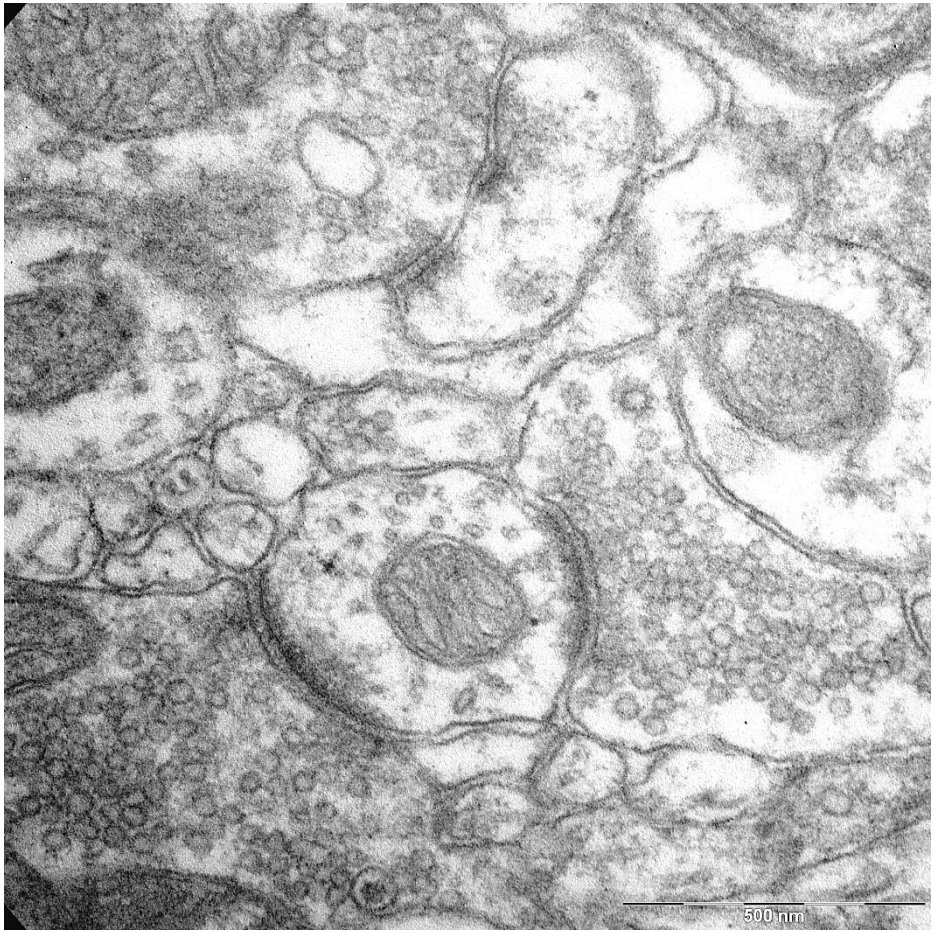
- **Acetylcholine**
- **Amioacids** – gluatamate, glycin, GABA (gamma-amminobutyric acid)
- **Monoamines** – serotonin, catecholamines, dopamine, adrenaline, …
- **Neuropeptides** – enkefalin, somatostatin, neurotensin, ….
- **Others** – adenosine, nitric oxide

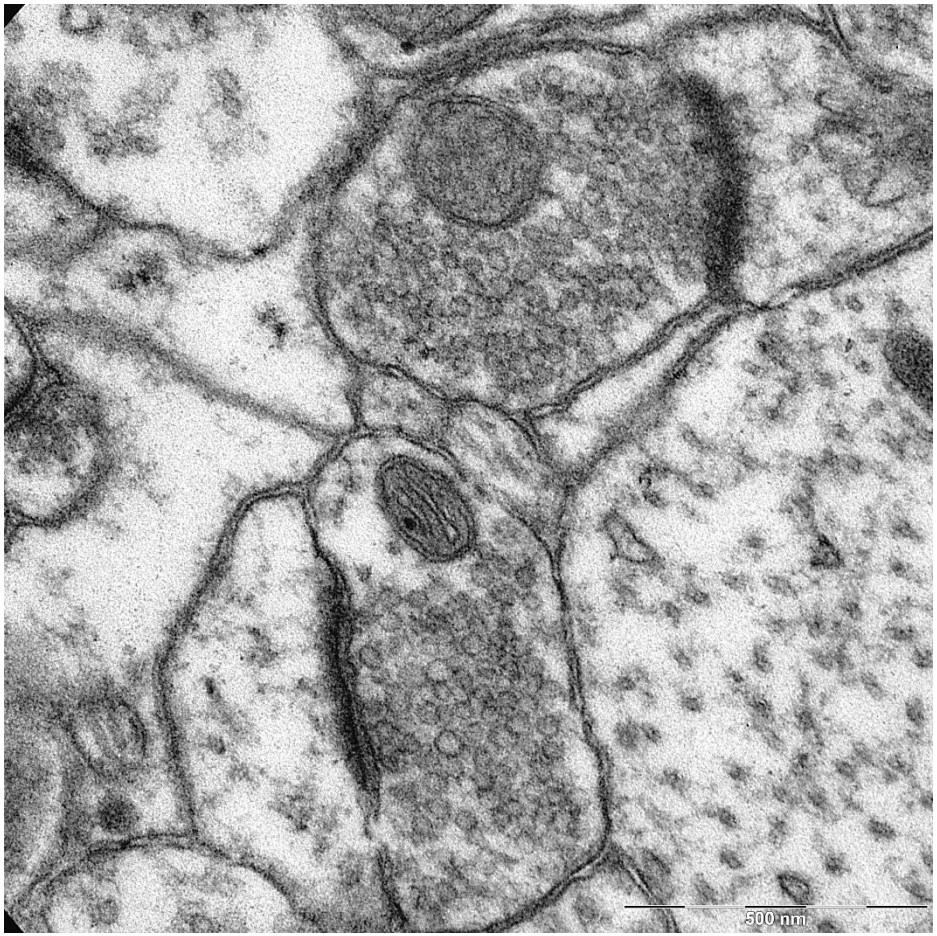
Synapse 3


Microtubule
Agranular endoplasmic reticulum
Dense presynaptic peg
Presynaptic lattice
Dense postsynaptic cytoplasm
Endocytic vesicle
Synaptic cleft
TERMINAL AXONAL BRANCH
Presynaptic membrane
Postsynaptic membrane
DENDRITIC SPINE
Mitochondrion
Intramembraneous protein
Dense-cored vesicle
Small clear vesicles
Discharging presynaptic vesicle
TERMINAL BOUTON
REINNA

Synapse 4

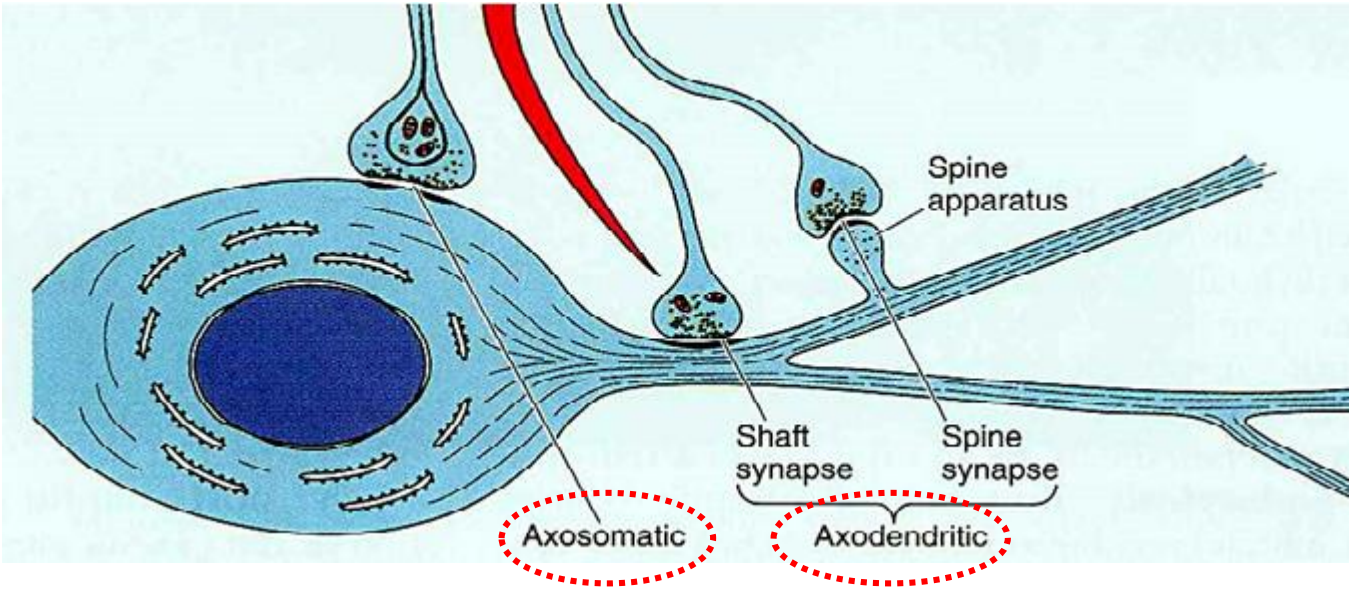
Synapse in TEM





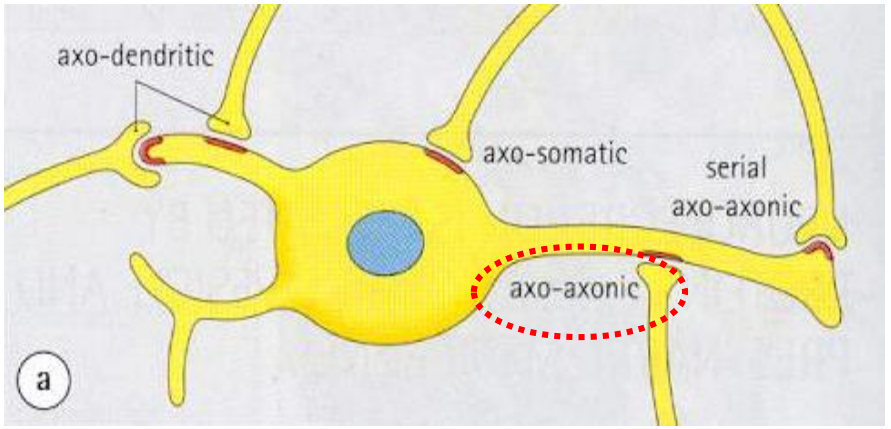
Synapse 5

Classification according to the constitution

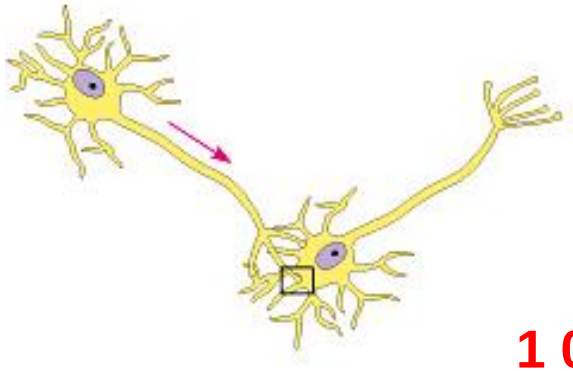


Axodendritic
Axosomatic
Axoaxonic

Note:
Neuromuscular junction – synapse between neuron and effector muscle fibre

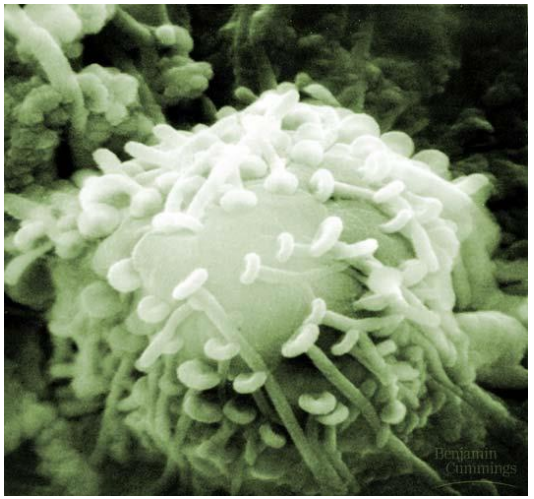


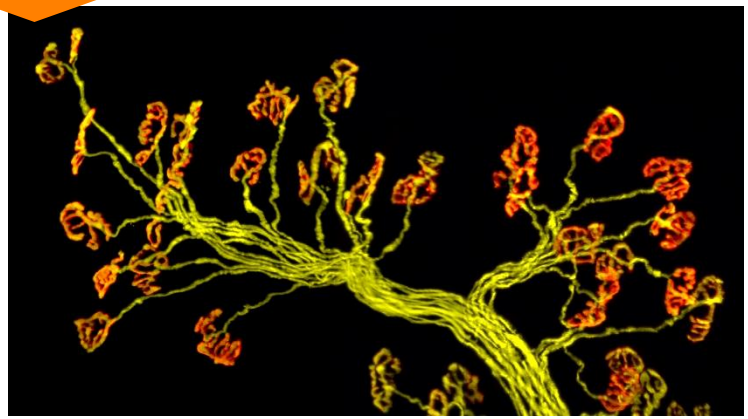
Synapse 7



One neuron may have

1 000 to 10 000 synapses !!!





Neuroglia

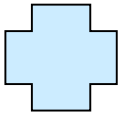
General features

- **non-neuronal** cells of several types
- support and protect the neurons
- bind neurons together and **form framework for nervous tissue**
- in fetus, **guide migrating neurons** to their destination
- if mature neuron is not in synaptic contact with another neuron it is covered by glial cells
- prevents neurons from touching each other
- gives **precision to conduction pathways**
- only nuclei visible by light microscopy without special staining
- there are several glial cells for each neuron

Number of **neurons**: about **100 billions to 1 trillion**
Number of **glial cells**: **50x more** then neurons

Central neuroglia

- Astrocytes
- Oligodendrocytes
- Microglia
- Ependymal cells



Peripheral neuroglia

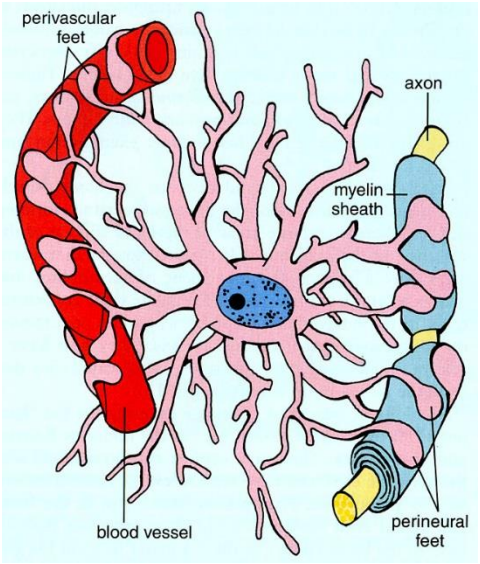
- Schwann cels
- Satelite cells

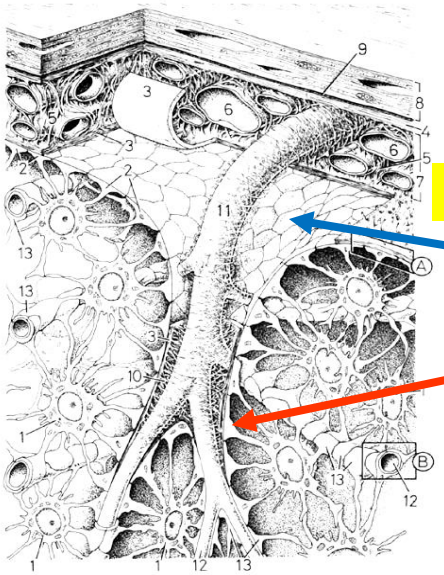
Neuroglia - Astrocytes

- **most abundant glial cell in CNS**
- **covers entire brain surface and most non-synaptic regions of the neurons in the gray matter of the CNS**

- **diverse functions:**

✓ form a **supportive framework** of nervous tissue
✓ have extensions (**perivascular feet**) that contact blood capillaries that stimulate them to form a tight seal called the **blood-brain barrier**
✓ convert blood glucose to **lactate** and supply this to the neurons for nourishment
✓ **nerve growth factors** secreted by astrocytes promote neuron growth and synapse formation
✓ communicate electrically with neurons and may **influence synaptic signaling**
✓ regulate chemical composition of tissue fluid by absorbing excess neurotransmitters and ions
✓ **astrocytosis** or **sclerosis** – when neuron is damaged, astrocytes form hardened scar tissue and fill space formerly occupied by the neuron
✓ contains **GFAP**



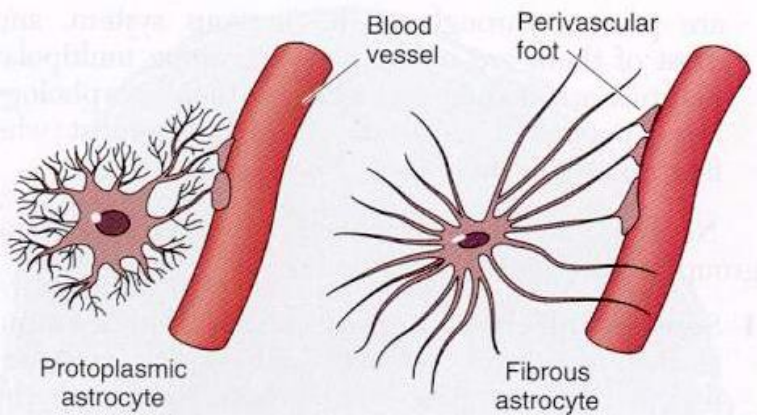


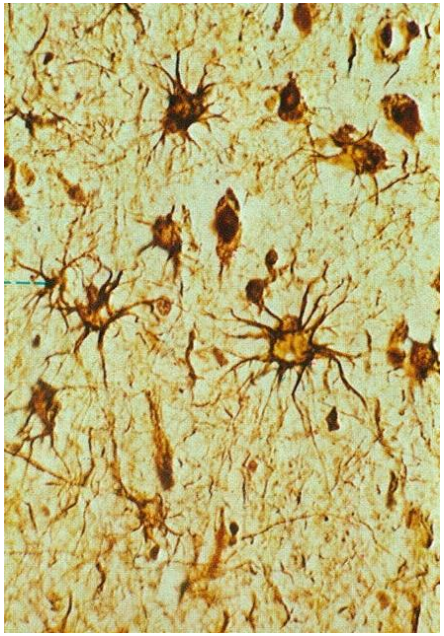
Membrana limitans gliae…

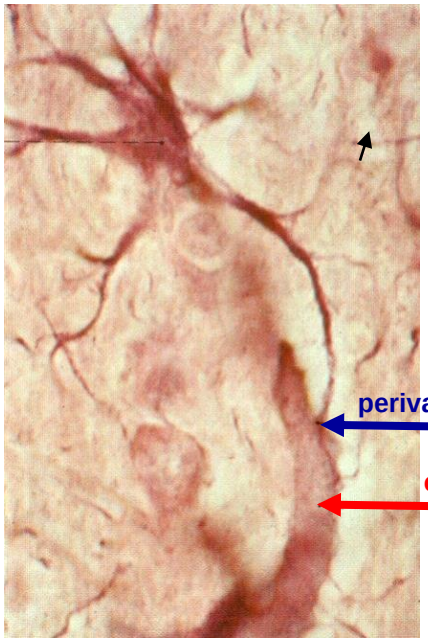
…superficialis

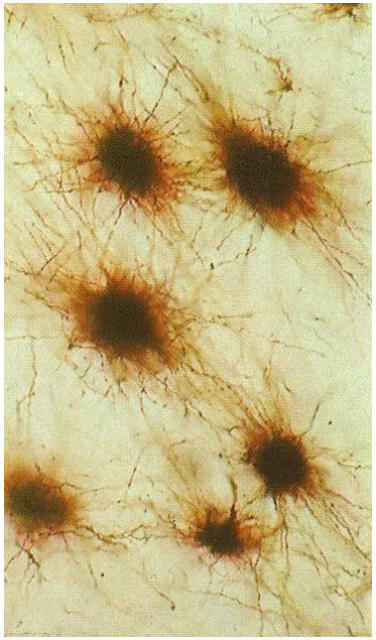
…perivascularis

Neuroglia - Astrocytes









protoplasmic astrocyte

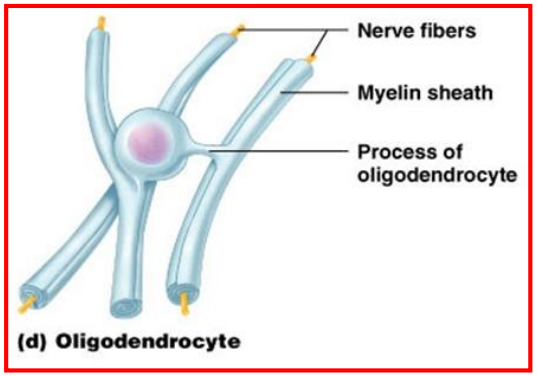
(predominant in grey matter)

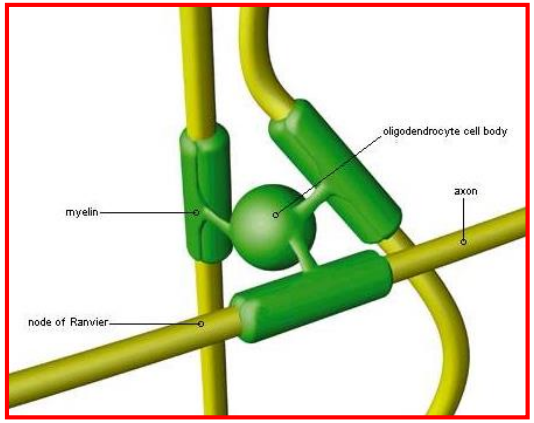
fibrous astrocyte

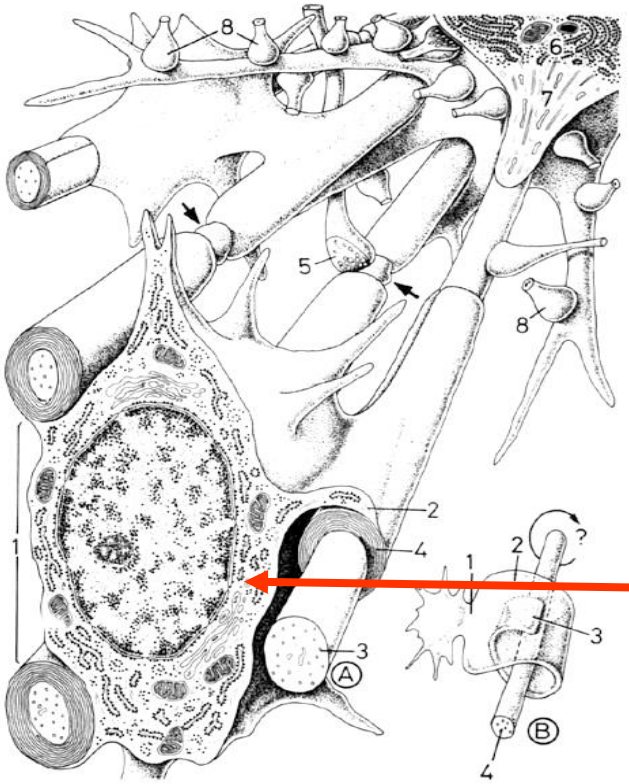
(predominant in white matter)

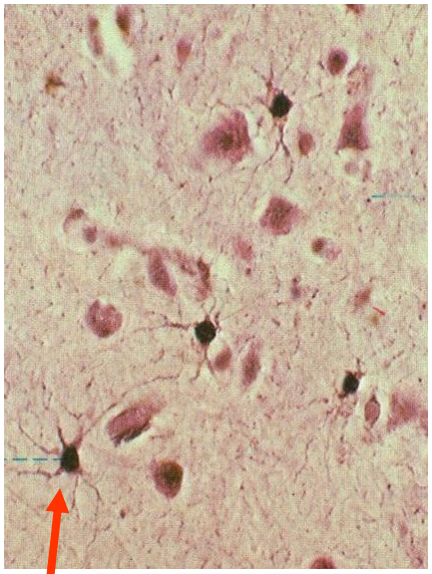
Neuroglia - Oligodendrocytes

- ✓ smaller than astrocytes; darker, round nucleus, abundant RER, well developed golgi apparatus
- ✓ form **myelin sheaths in CNS**
- ✓ one cell **serves more then one axon**
- ✓ **cannot migrate around axons** (unlike Schwann cells) must push newer layers of myelin under the older ones so myelination spirals inward toward nerve fiber
- ✓ nerve fibers in CNS have **no Schwann sheath (neurilemma) or endoneurium**
- ✓ each arm-like process wraps around a nerve fiber forming an **insulating** layer that speeds up signal conduction
- ✓ damaged in **multiple sclerosis**





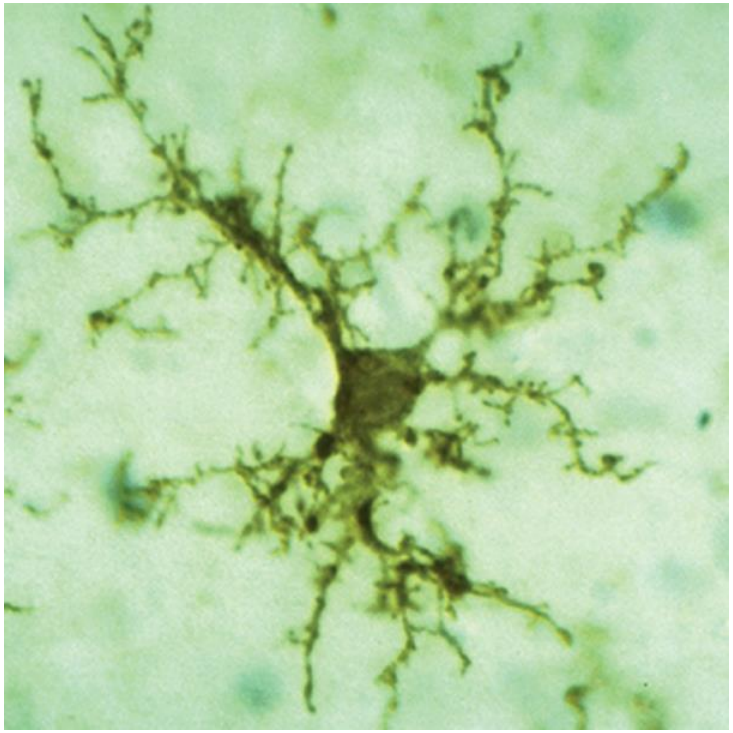


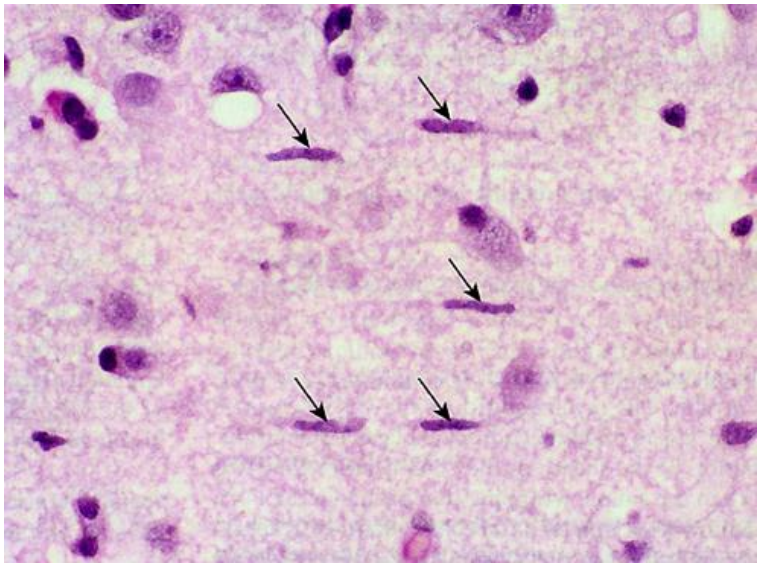


oligodendrocyte

Neuroglia - Microglia

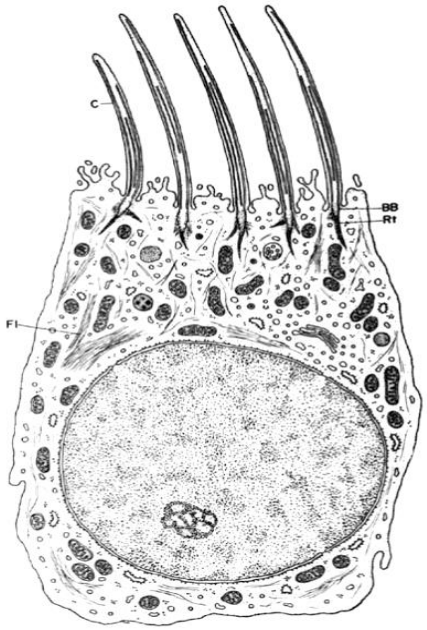
- ✓ **smallest** neuroglial cell
- ✓ small, dark, **elongated nuclei**
- ✓ possess **phagocytotic** properties
- ✓ when activated – **antigen presenting** cell
- ✓ originate in bone marrow (**mesodermal** origin)

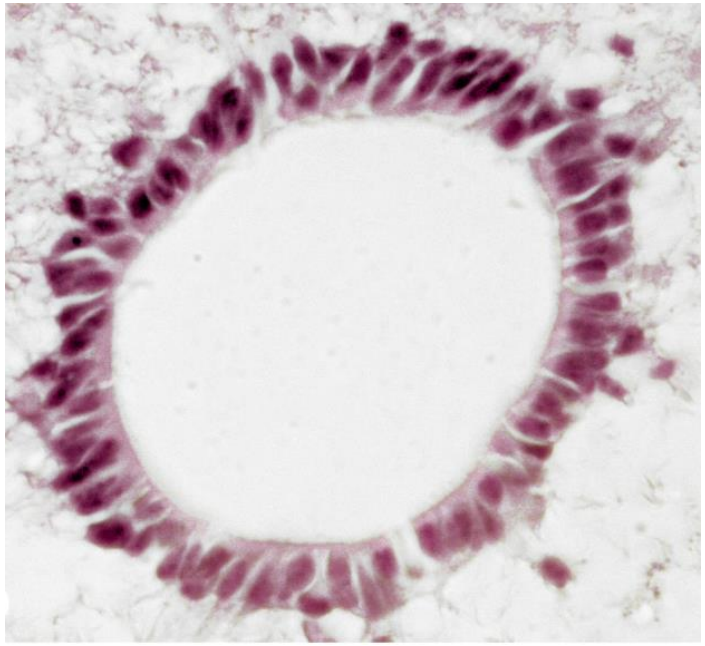




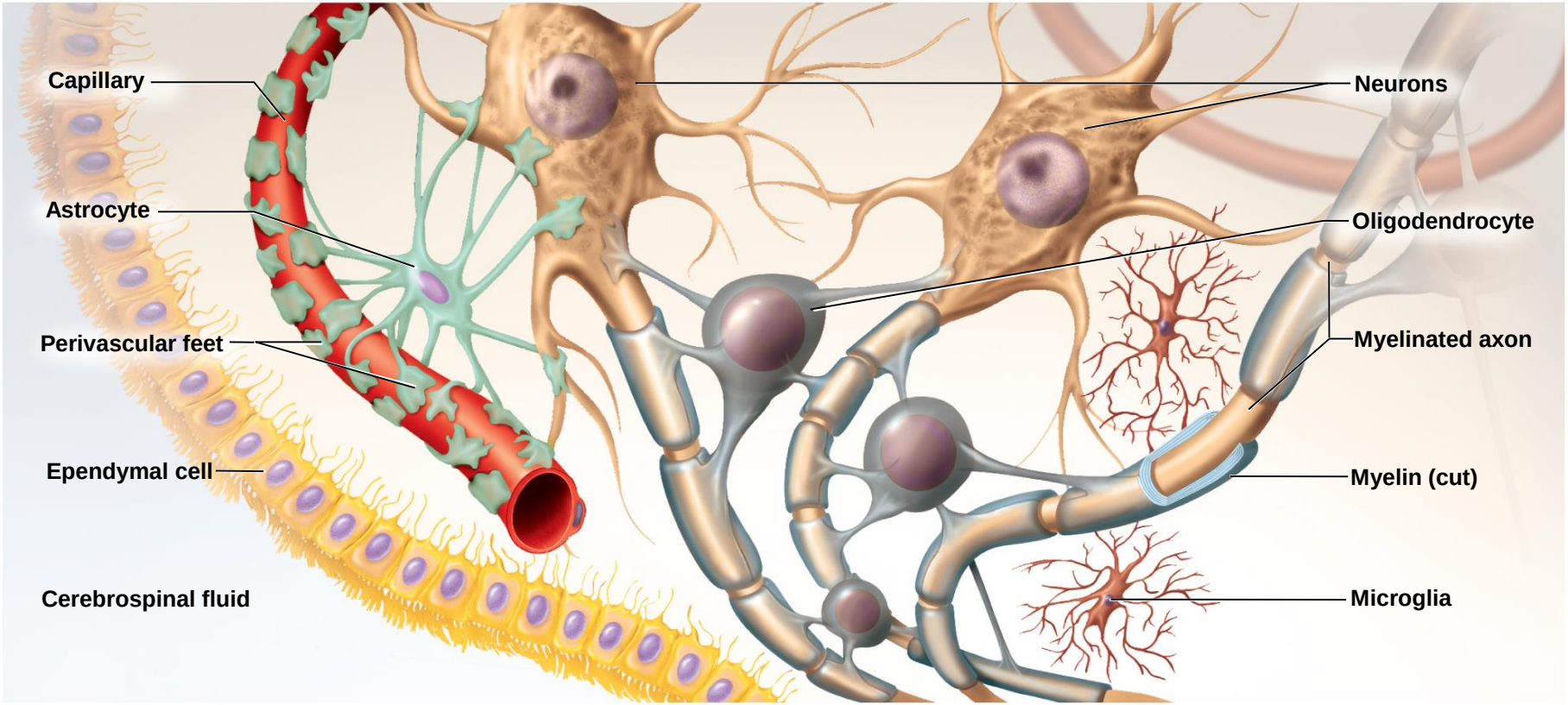
Neuroglia – Ependymal cells

- ✓ **line ventricles of CNS and central canal of spinal cord**
- ✓ **cuboidal** or low **columnar** shape
- ✓ no basal lamina
- ✓ **secrete** cerebrospinal fluid (CSF)
- ✓ some are **ciliated**, facilitate movement of CSF
- ✓ participate in formation of **Choroid plexus**





Neuroglia – Central - Summary

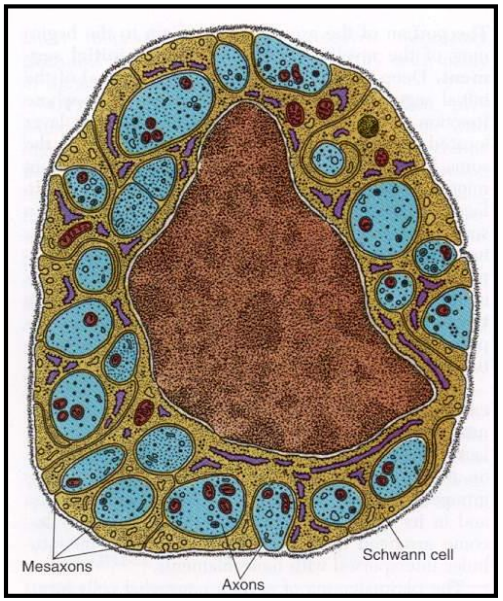


Neuroglia in PNS – Schwann cells 1

- cells that encircle all axons in PNS
- provide structural and metabolic support to axons
- provide guidance for axonal growth

Small diameter axons

Enveloping by only cytoplasm

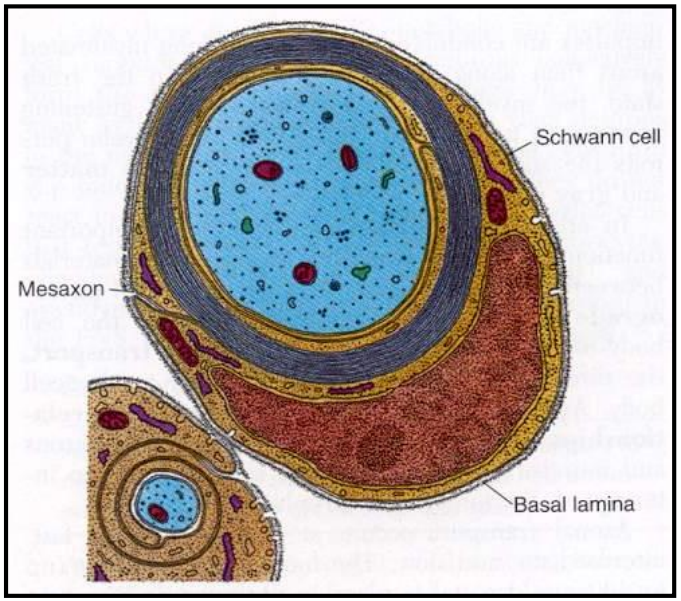


only Schwann sheath – gray nerve fiber

X

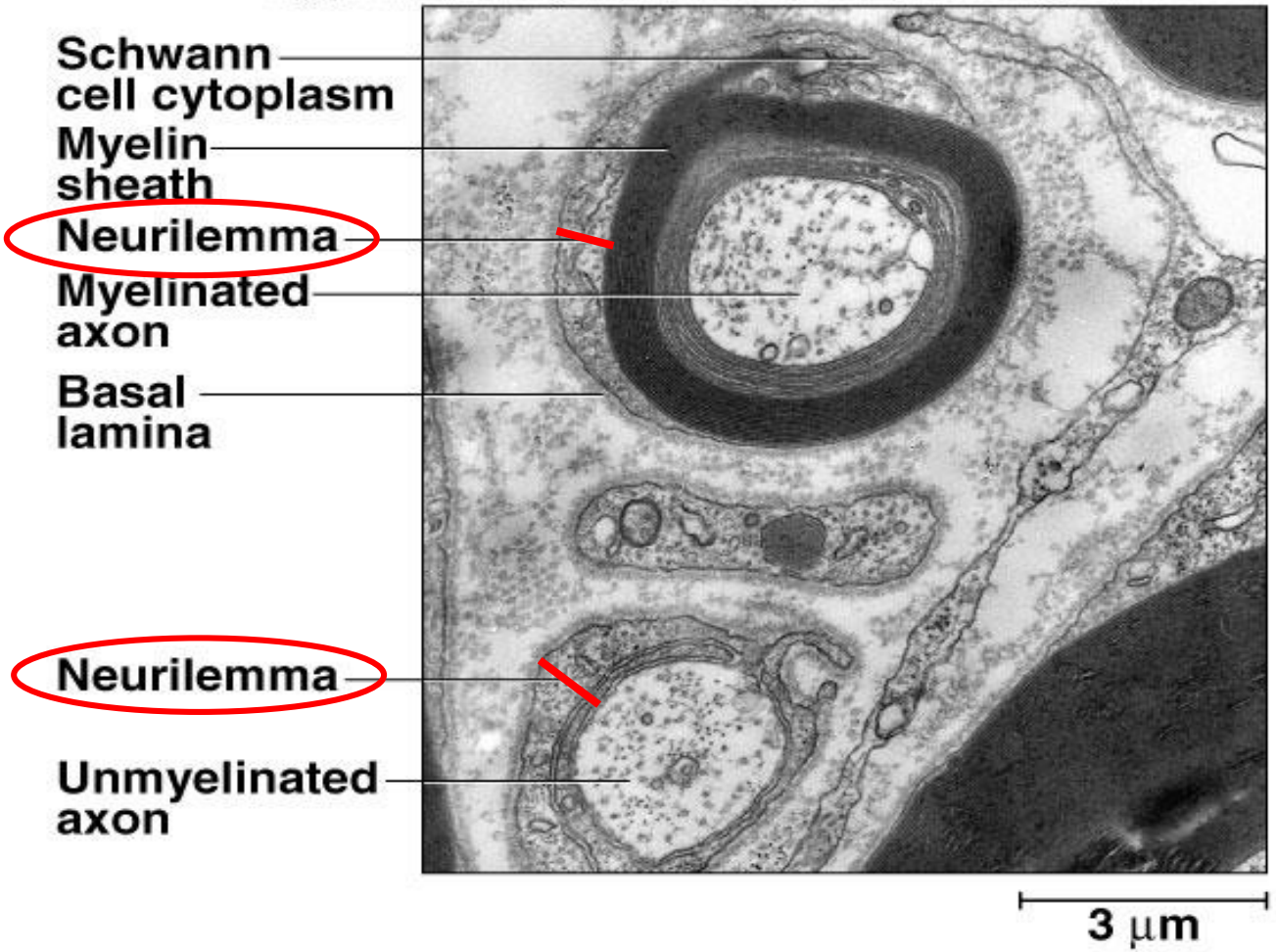
Large diameter axons

Wrapping by myelin sheaths



Schwann + myelin sheath– double contoured nerve fiber

Neuroglia in PNS – Schwann cells 2

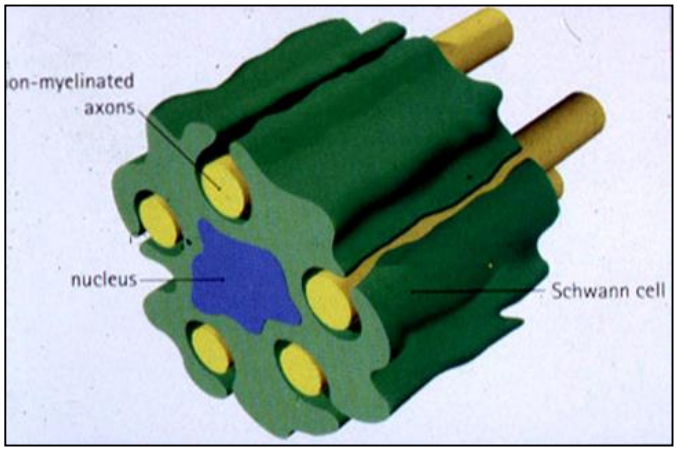


Neuroglia in PNS – Schwann cells 3

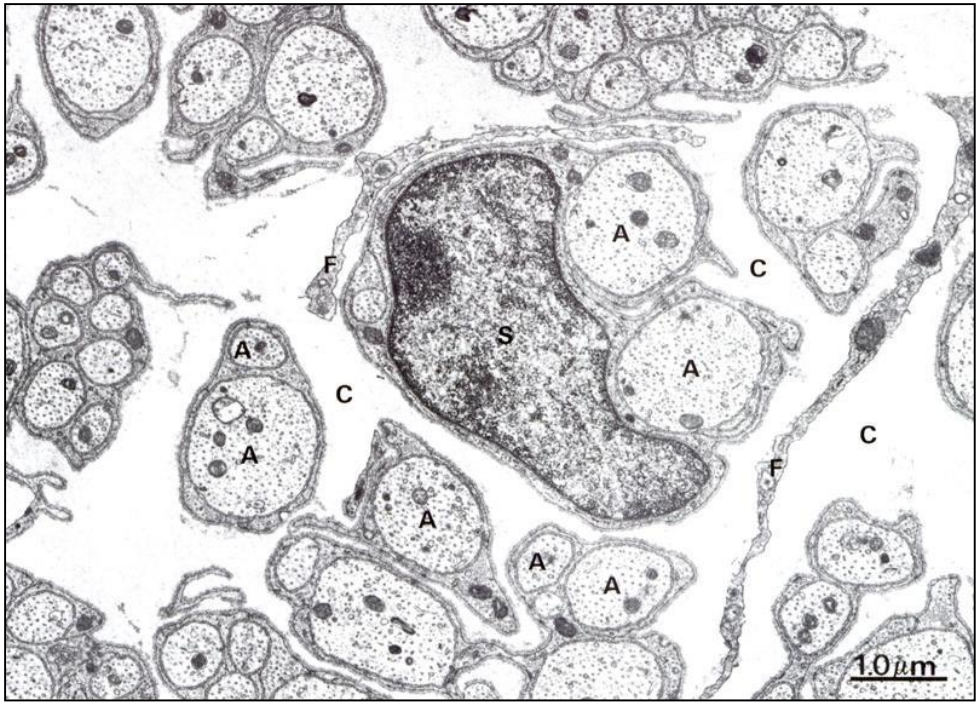
Small diameter axons ⇨ **Non-myelinated fibers**

(typical for autonomous nerve system)

only Schwann sheath – gray nerve fiber



One Schwann cell can ensheath multiple axons

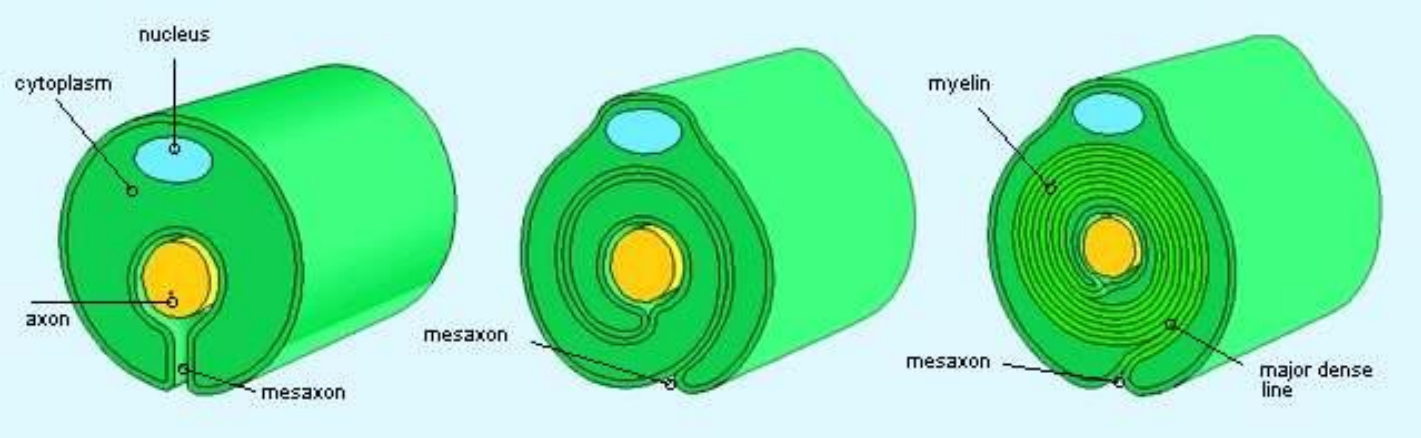


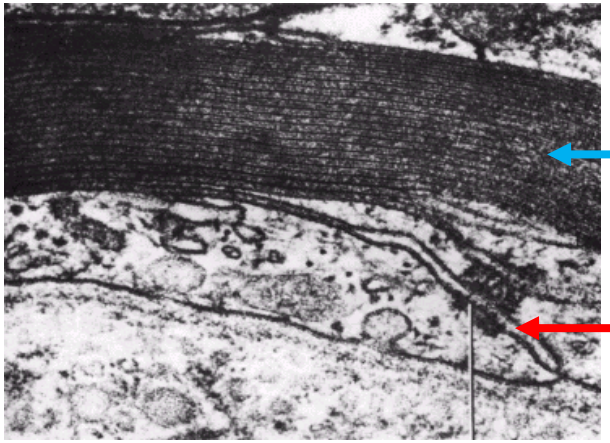
Neuroglia in PNS – Schwann cells 4

Large diameter axons ⇨ **Myelinated fibers**

Myelination

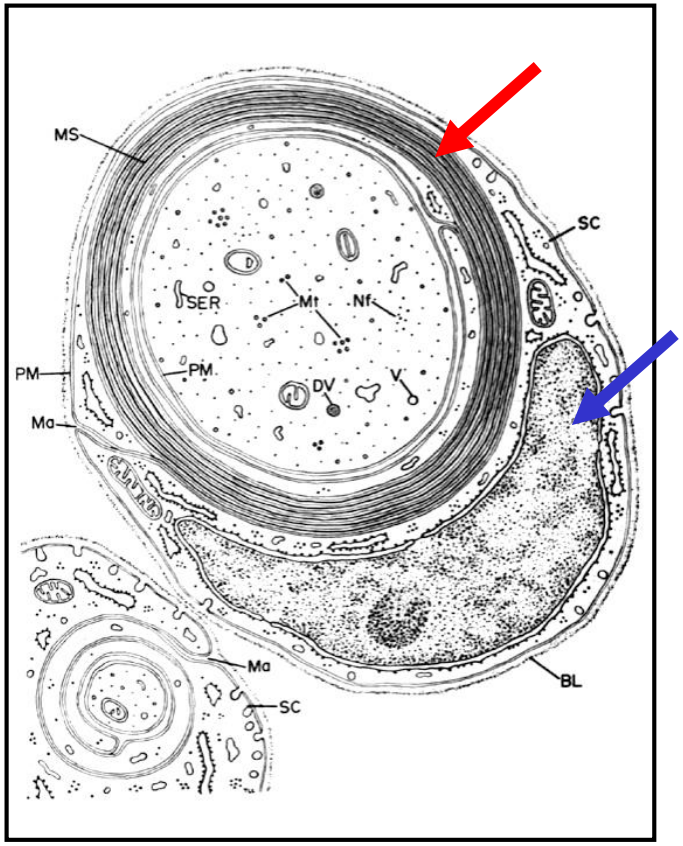
- begins 14th week of development
- proceeds rapidly during infancy
- completed in adolescence

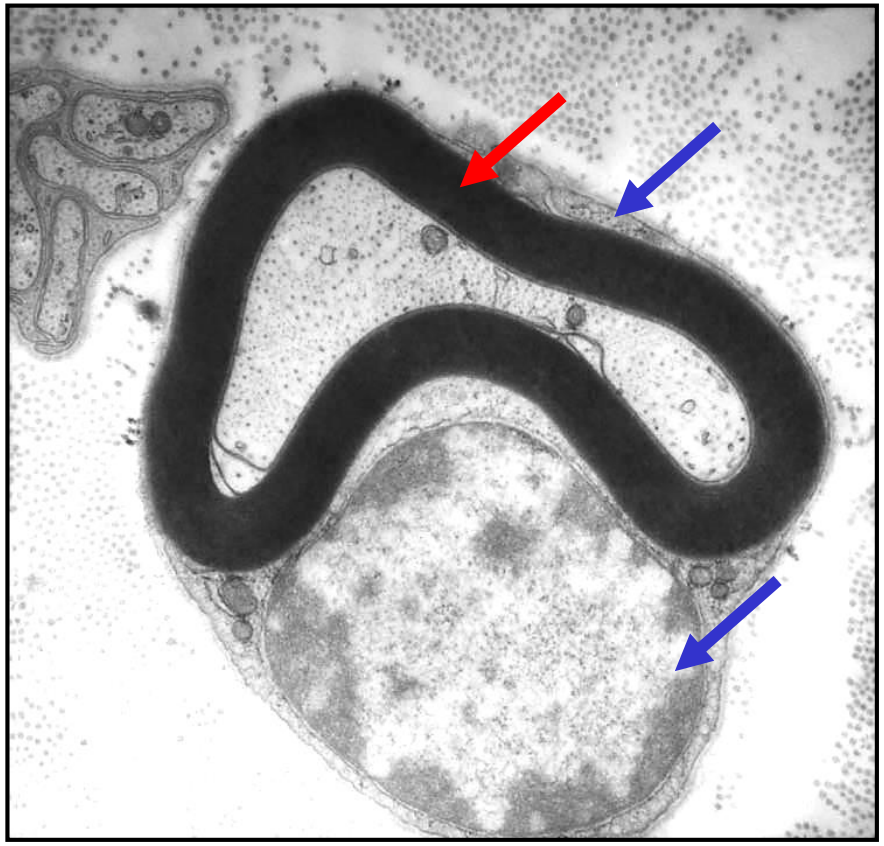




Neuroglia in PNS – Schwann cells 5

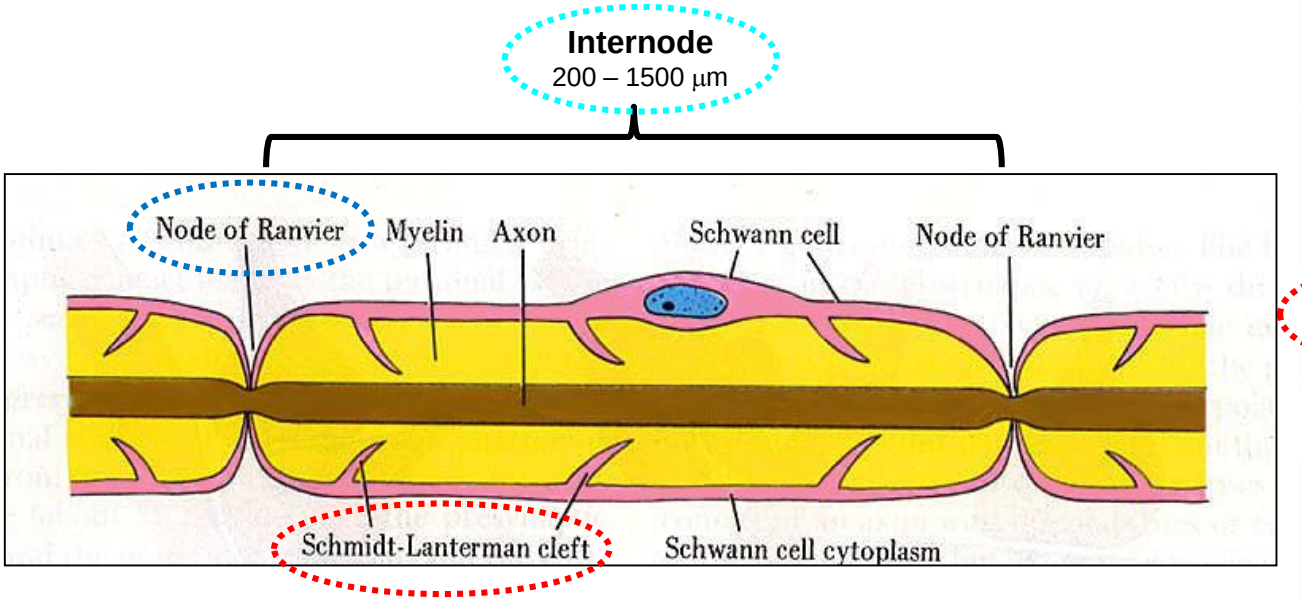
Double contoured nerve fiber ⇨ **Schwann sheath** **= Neurilemma**
+
Myelin sheath

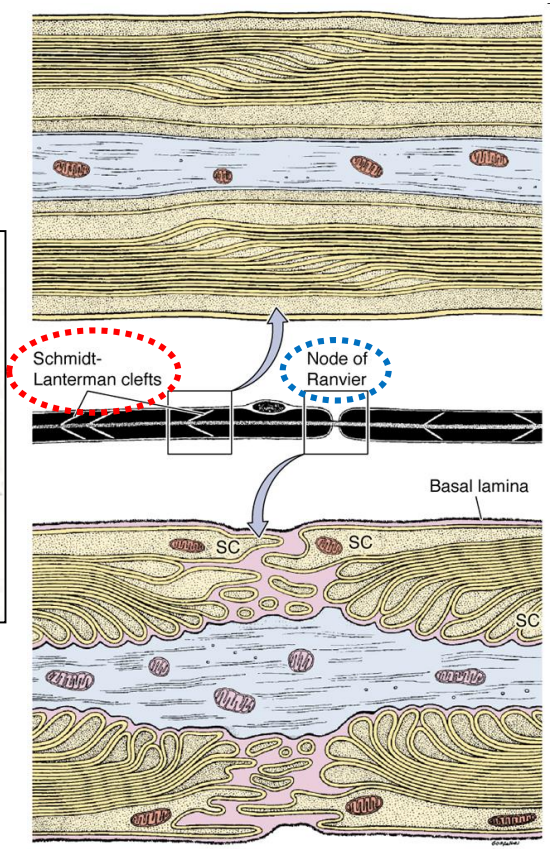




Neuroglia in PNS – Schwann cells 6

Myelin sheath is segmented = Many Schwann cells are needed to cover one nerve fibre

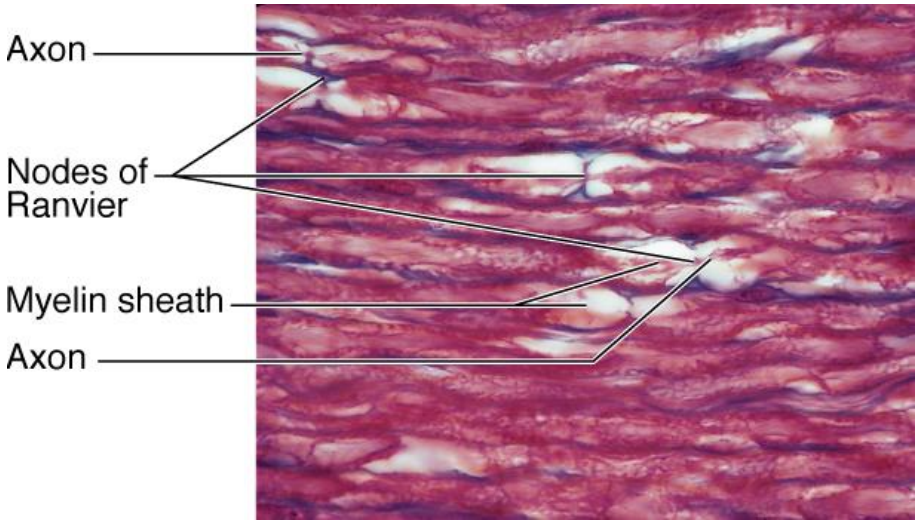


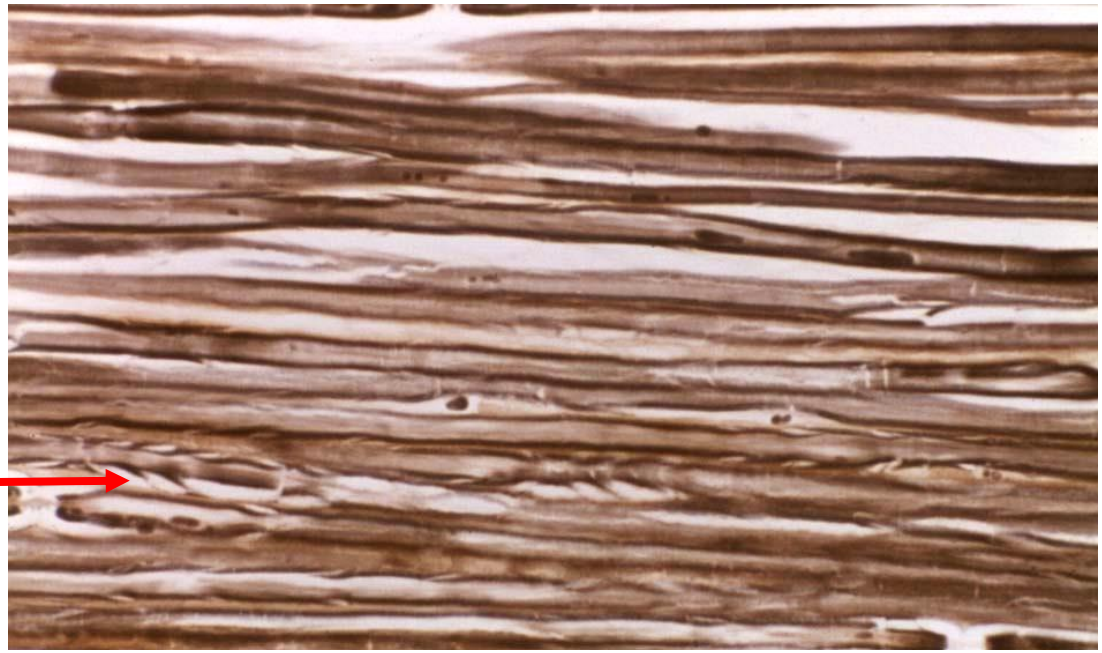


Schmidt-Lanterman clefts

- Schwann cell cytoplasm trapped within the lamellae of myelin

Neuroglia in PNS – Schwann cells 7



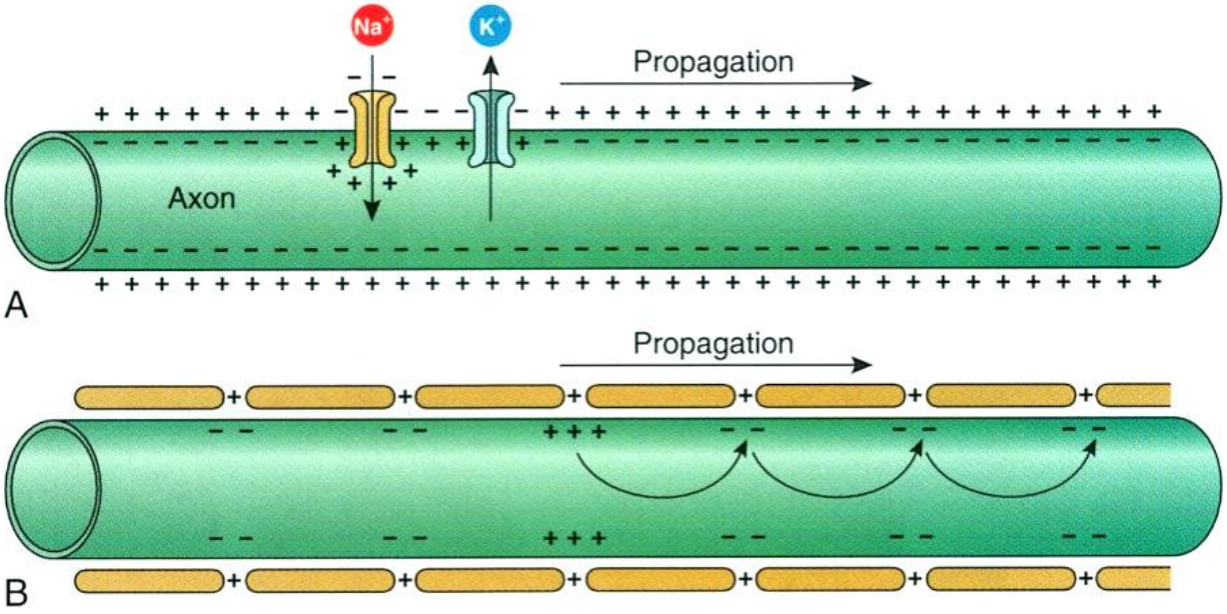


Neuroglia – Functional effect of myelination

Signal propagation

Non-myelinated axons – slow (0.5 – 2 m/s)

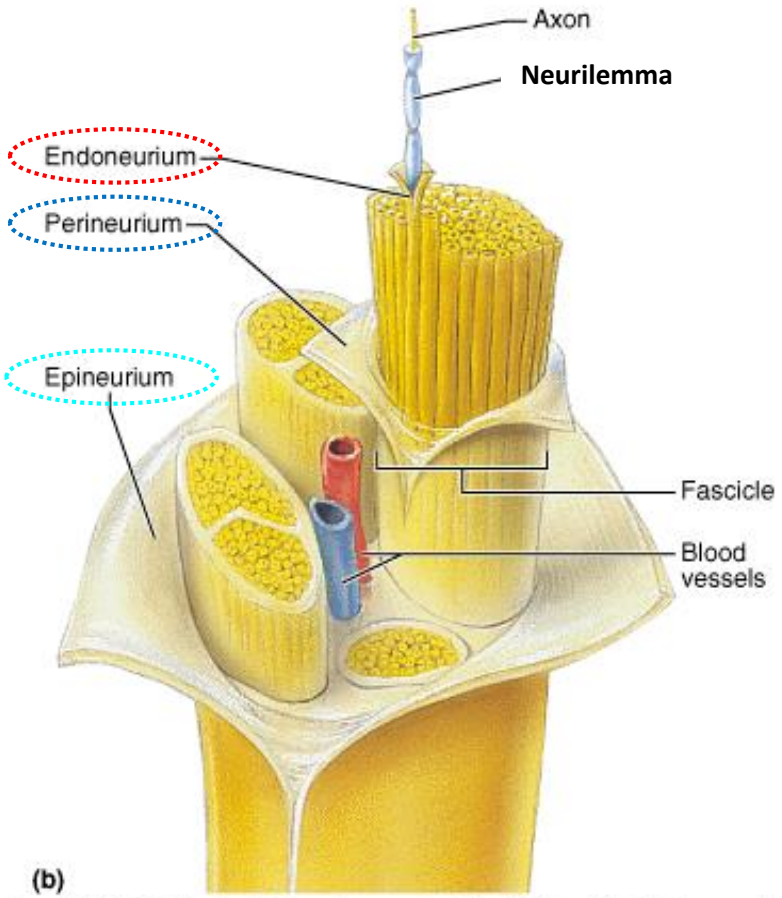
Myelinated axons – fast (15 – 20 m/s)



Saltatory (salta=jump)

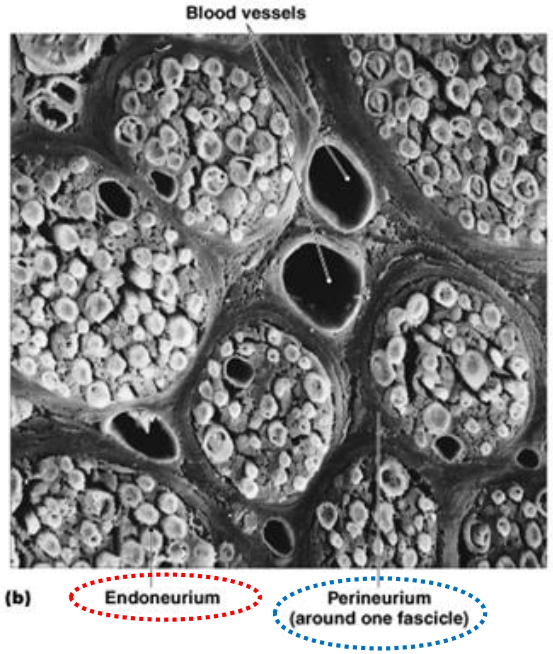
Peripheral nerve – Organization 1

Consists of 100's to 100,000's of myelinated and unmyelinated axons (nerve fibers).

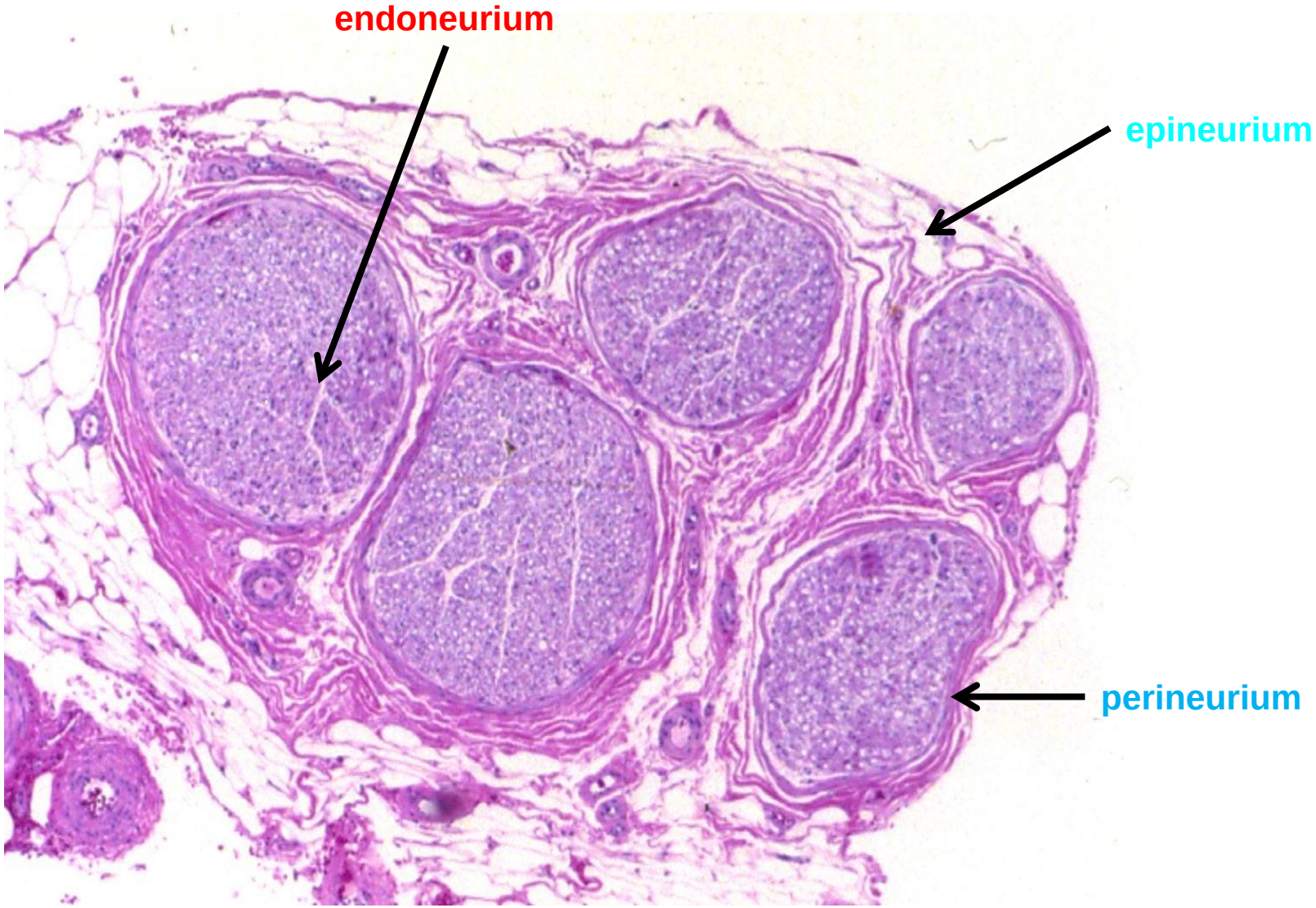


Connective tissue layers composing nerves:

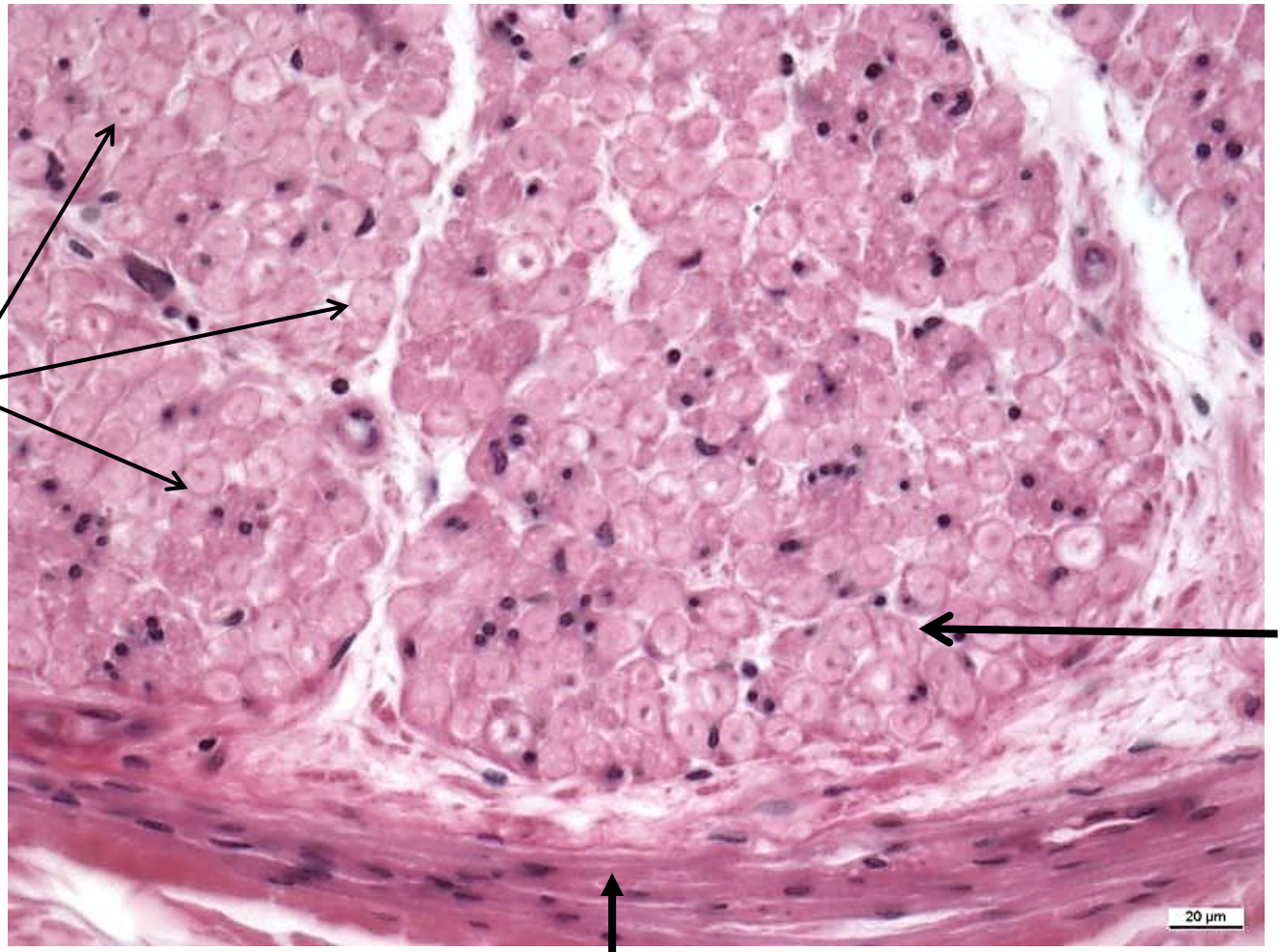
- **Endoneurium** - surrounds axons
- **Perineurium** - surrounds fascicles
- **Epineurium** - surrounds the entire nerve



Peripheral nerve – Organization 2



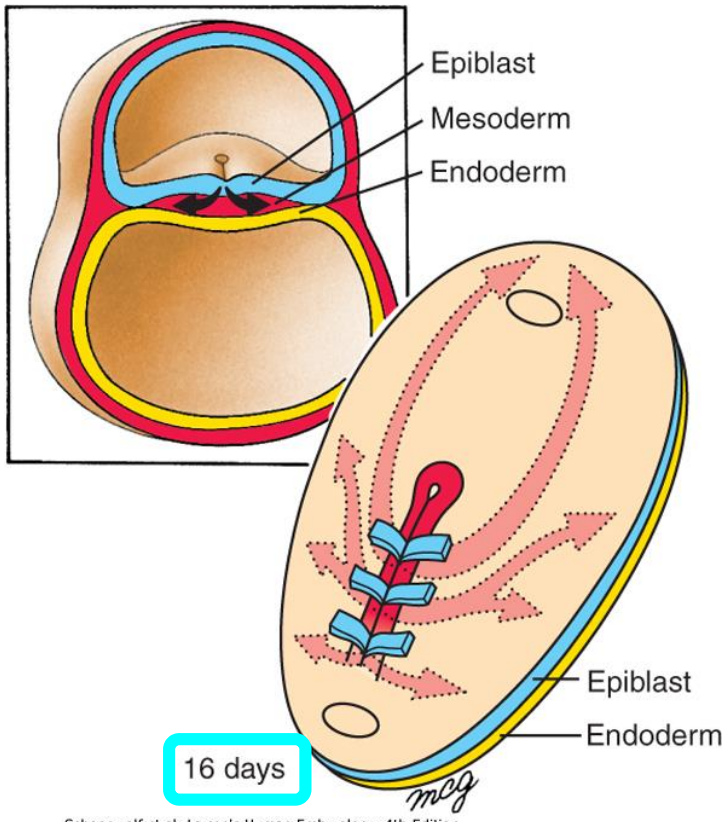
Peripheral nerve – Organization 3



Nerve tissue – Development 1

Gastrulation

Formation of the three germ layers



Ectoderm: outside, surrounds other layers later in development, generates **skin** and **nervous tissue.**

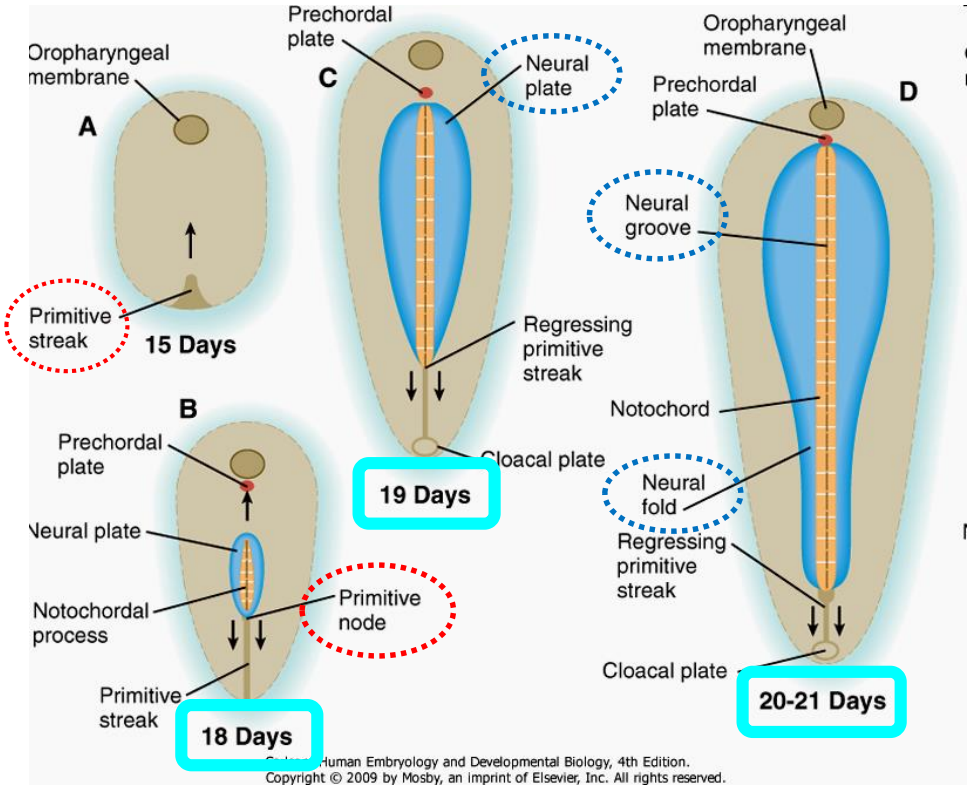
Mesoderm: middle layer, generates most of the **muscle, blood** and **connective tissues** of the body and placenta.

Endoderm: eventually most interior of embryo, generates the **epithelial lining** and associated **glands** of the **gut**, **lung**, and **urogenital tracts.**

Nerve tissue – Development 2

Neural Induction

In addition to patterning the forming mesoderm, the **primitive node** **also sets up the** **neural plate**



Endoderm + Mesoderm

BMP-4

Ectoderm to Skin

X

Primitive node

noggin
chordin
follistatin

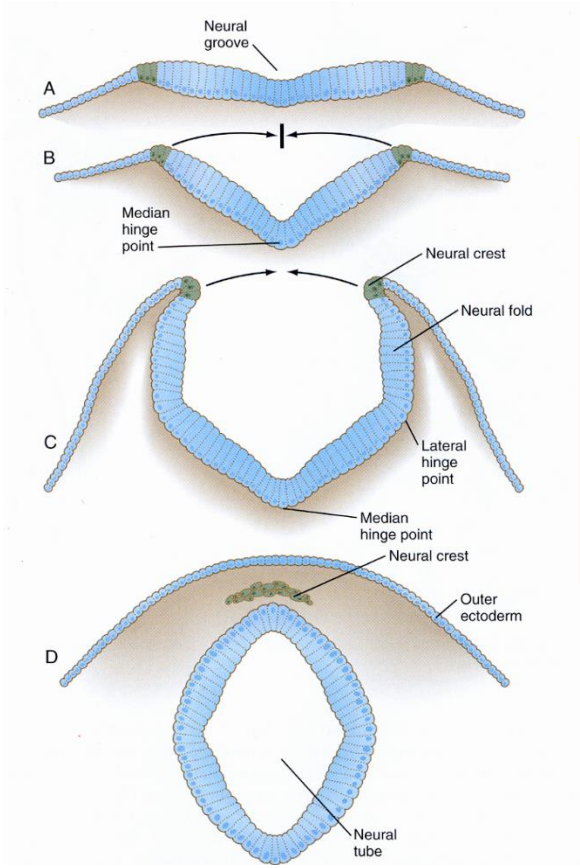
BMP-4 antagonists

Ectoderm to Nerve tissue

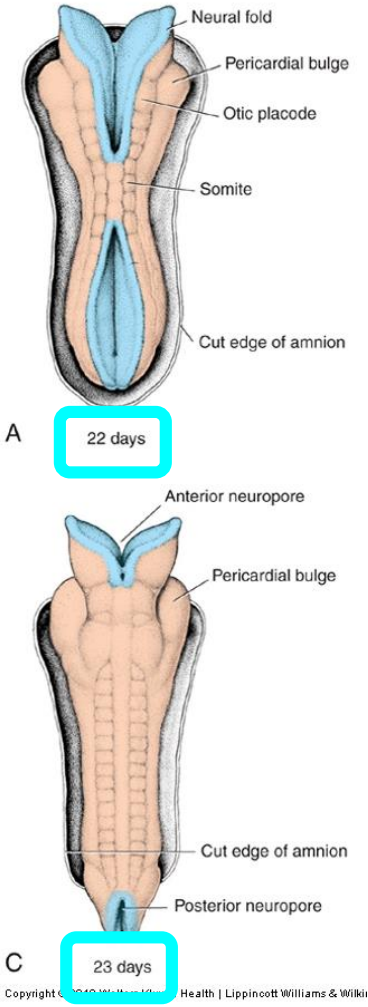
Nerve tissue – Development 3

Neurulation

Folding and closure of the neural plate



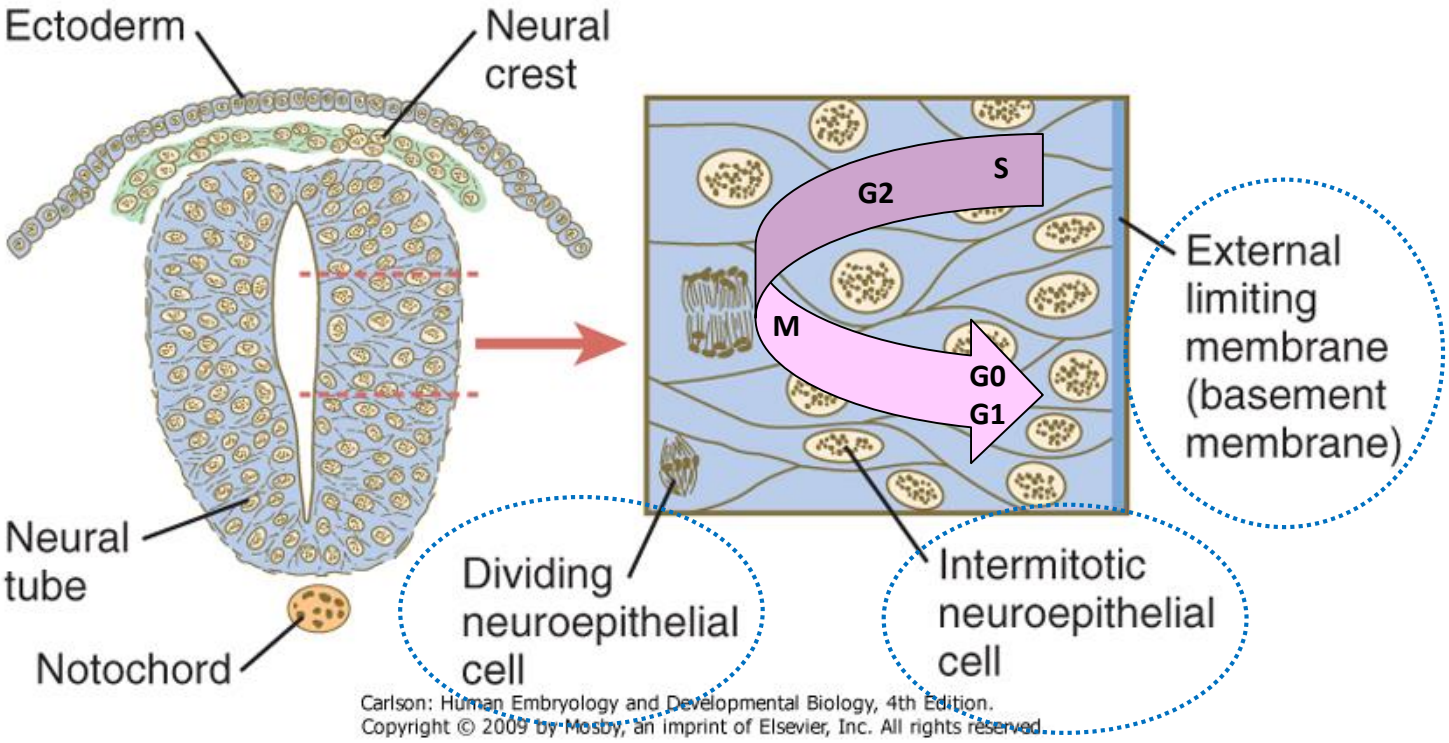
- **neural folds close**
- **neural crest delaminates** and migrates away
- **closure** happens **first in middle** of the tube and then **zips rostrally and caudally**
- **anterior neuropore closes** around **day 25**
- **posterior neuropore closes around day 28**



Nerve tissue – Development 4

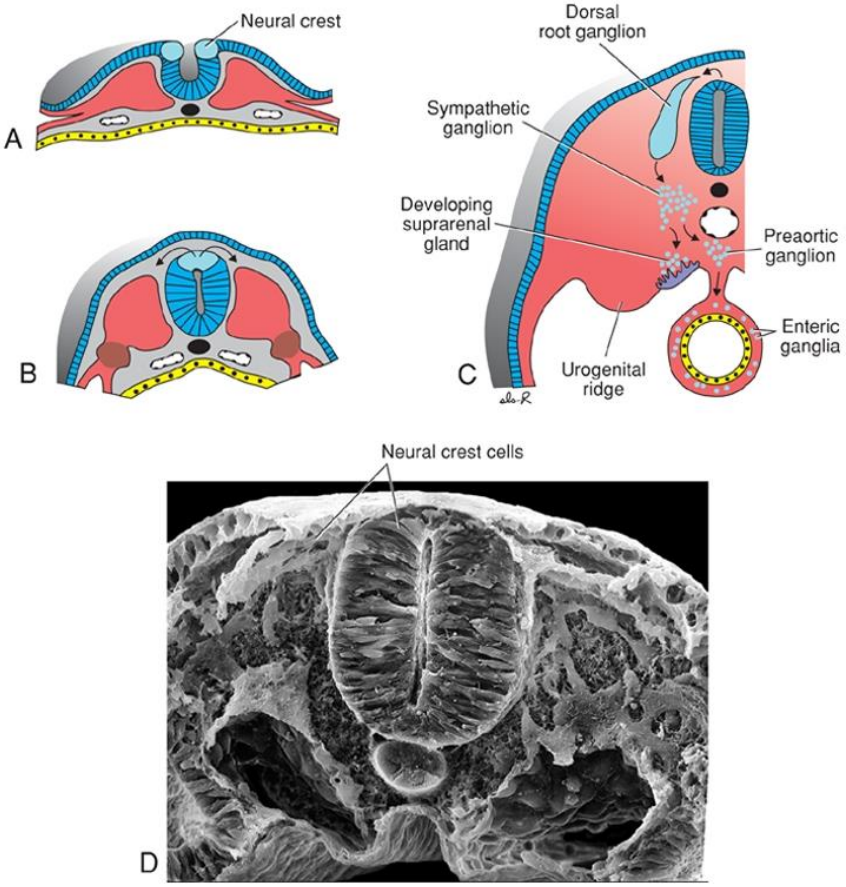
The **early neural tube** is a pseudostratified epithelium

- The **"apical" portion** abuts the **central canal**
- The **"basal" portion** abuts the **surrounding tissue** (e.g. somites, notochord, etc.).
- Cell division occurs in the apical portion.



Nerve tissue – Development 5

Neural crest
the "4th germ layer"



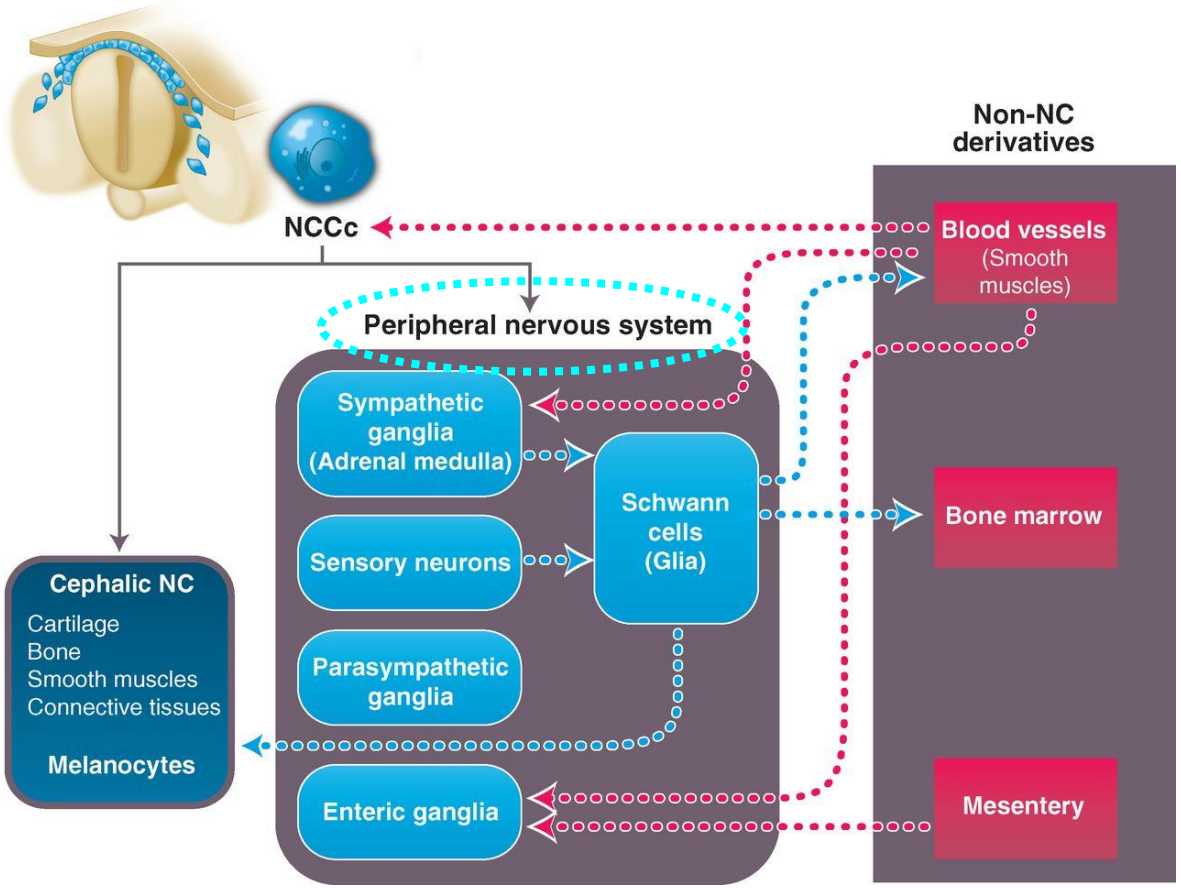
Signals from:
- Mesoderm
- Adjacent skin
- Neural plate

Neural crest cells

- Down-regulate cadherin
- Delaminate from neuroepithelium
- Transform into migratory mesenchymal cells
- Give rise to many cell types

Nerve tissue – Development 5

Neural crest derivatives

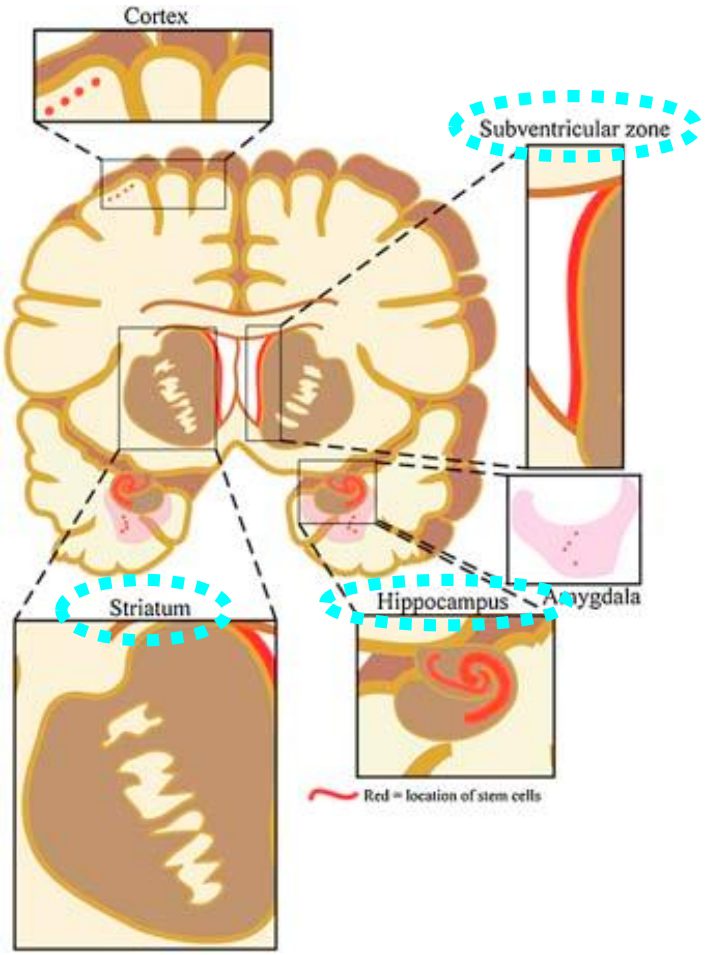


Nerve tissue regeneration - CNS

Stem / progenitor cells resiging in some areas of adult brain

Life-long plasticity of CNS

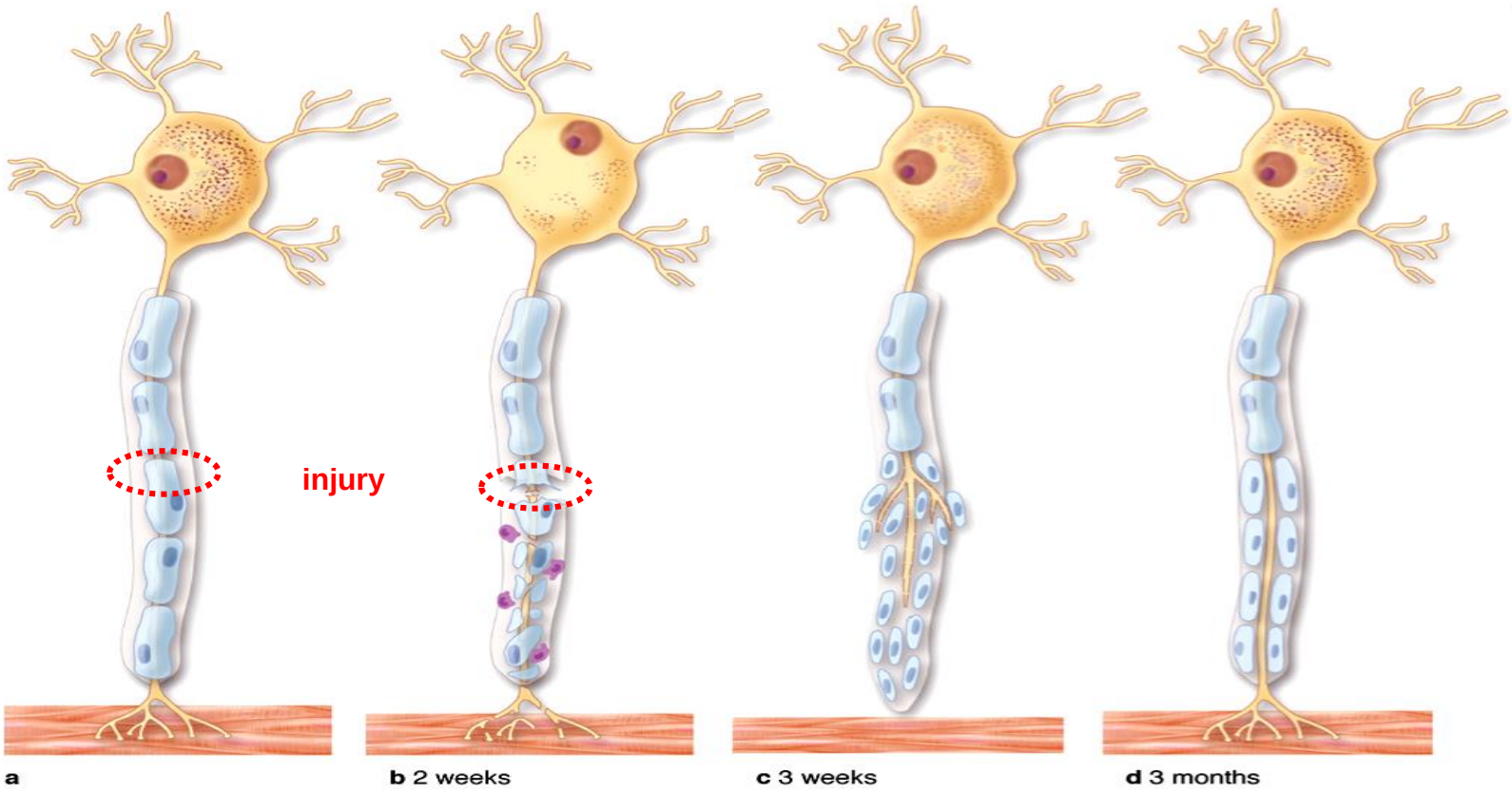
- Sprouting new dendrites
- Synthesis of new proteins
- Changes of synaptic contacts



Nerve tissue regeneration - PNS

Axons and dendrites may be repaired if:

- Neuron cell body remains intact
- Schwann cels remains active and form tube
- Scar tissue does not form too rapidly



Breakdown of axon
Breakdown of myelin sheath

Schwann cells divide
Axon begins to grow
(1.5 mm/day)
Navigaion by Schwann cells
Collaterals will die

Thank you for your attention !

Questions and comments at:
ahampl@med.muni.cz