# Nerve tissue

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

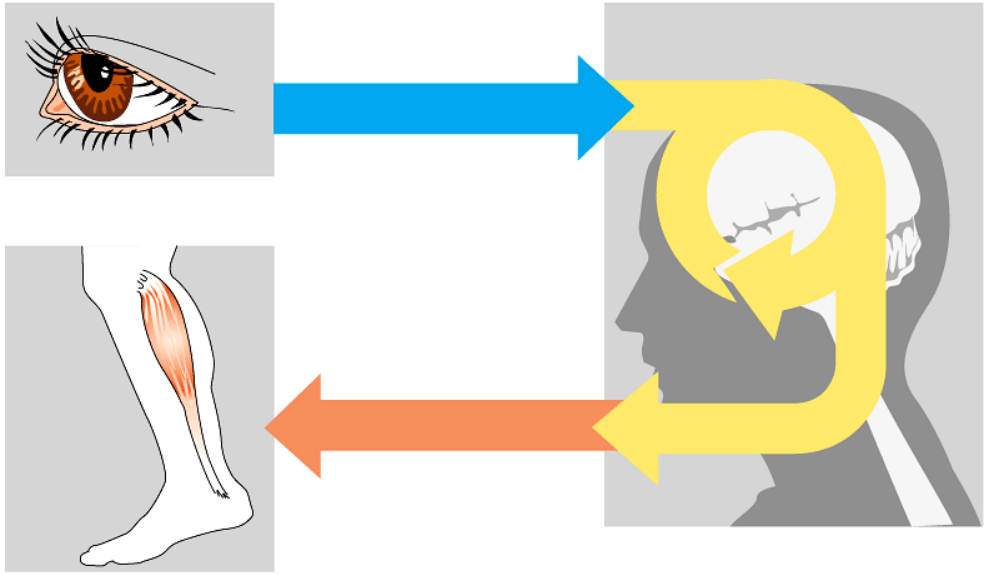
Brno, April 2024

# 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

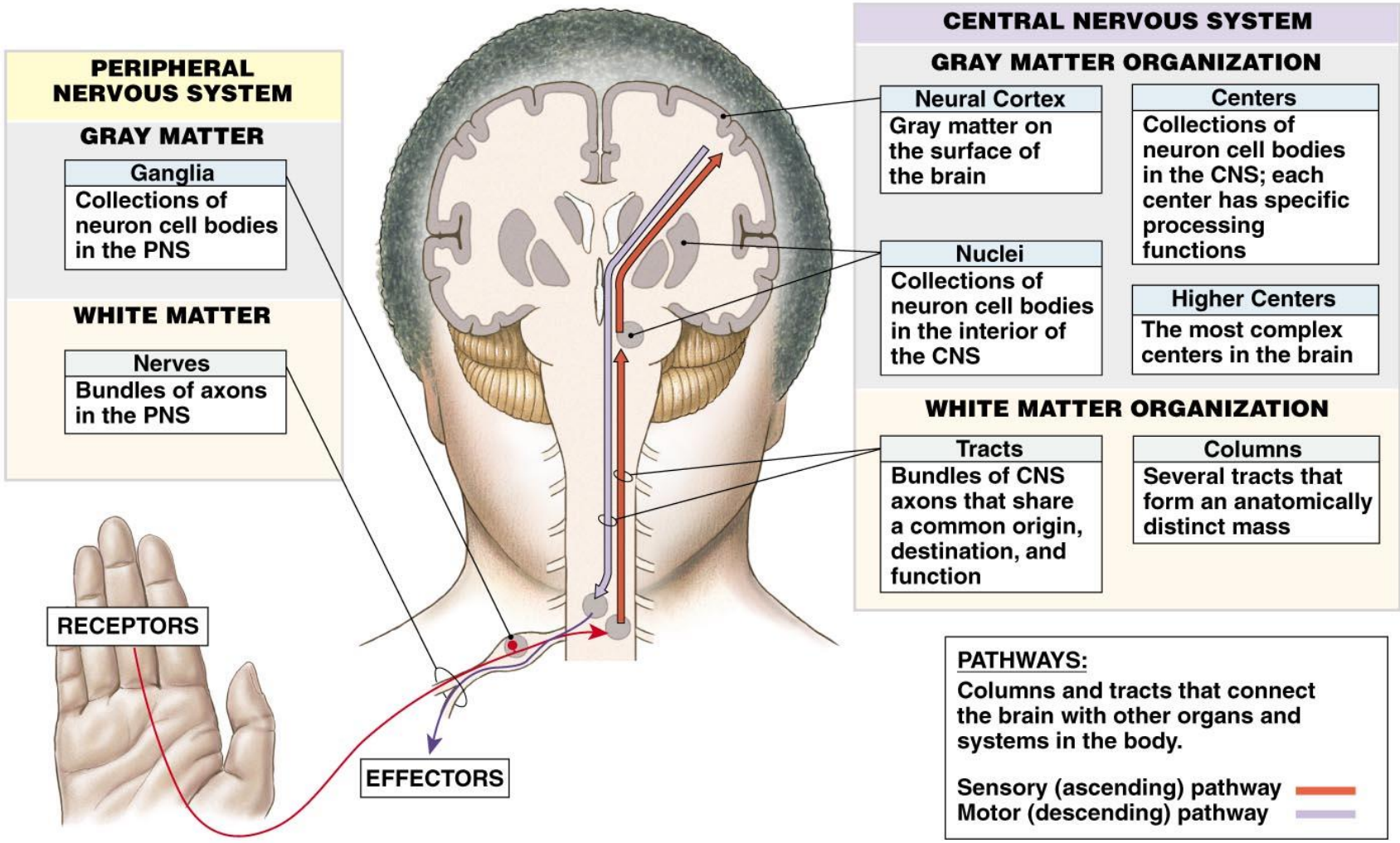
Definition:
Made up of transmission pathways carrying information between the CNS and external/internal environments.

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

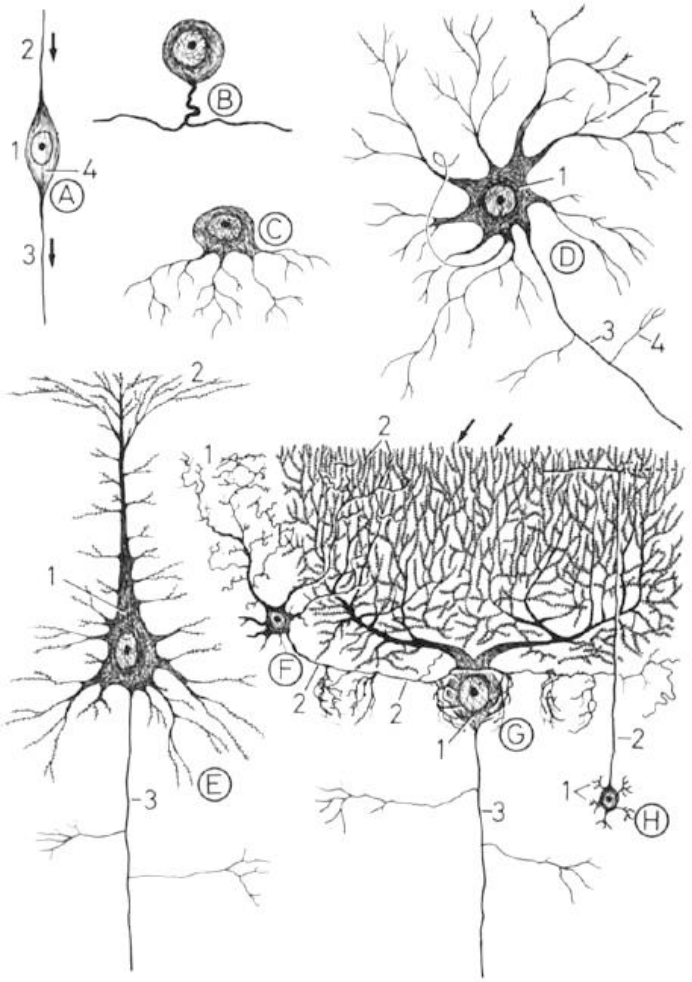


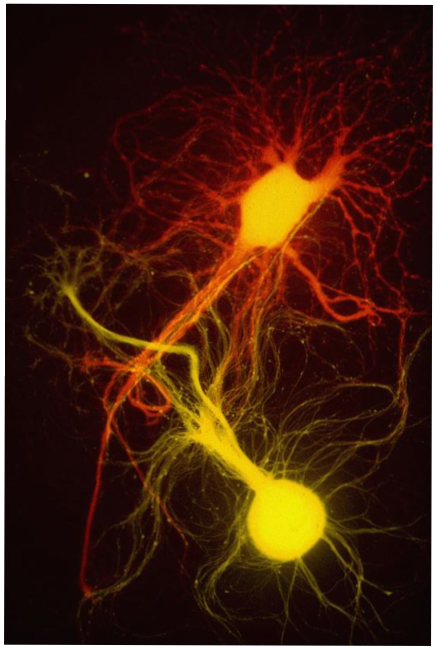
# Nerve tissue – General – Neuron 1

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

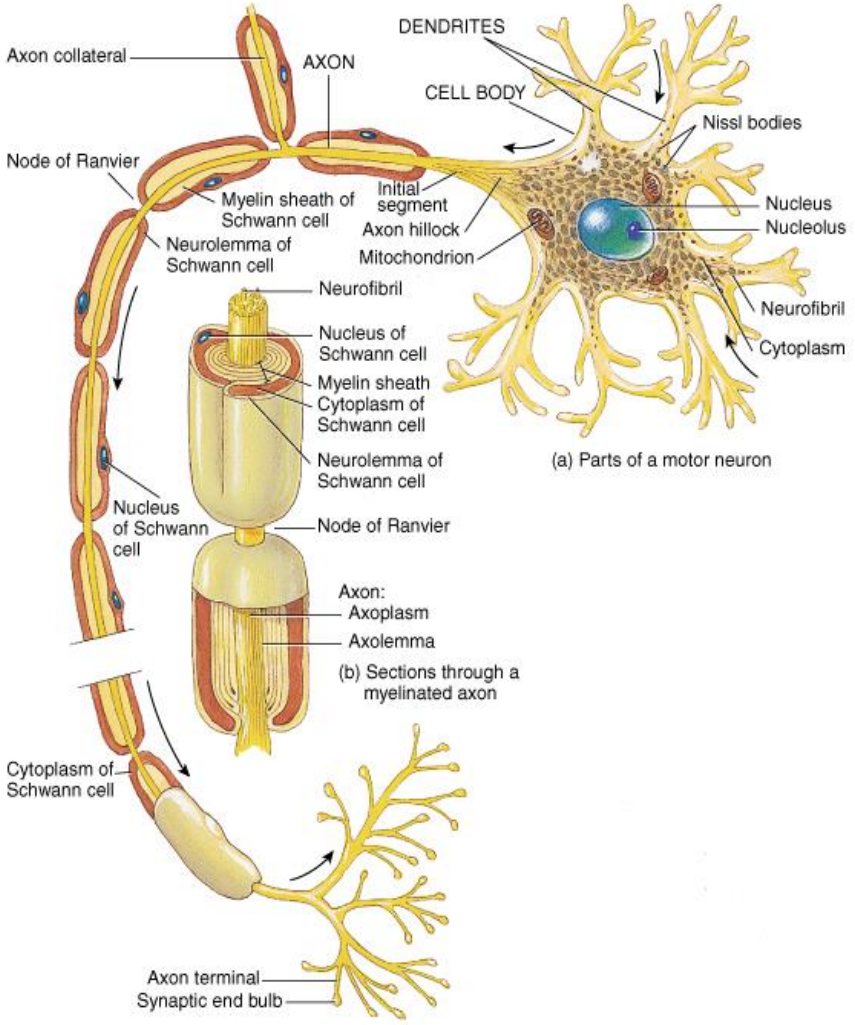
- **Neurons**
- **Neuroglia - glial cells** (supporting cells)

- 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)

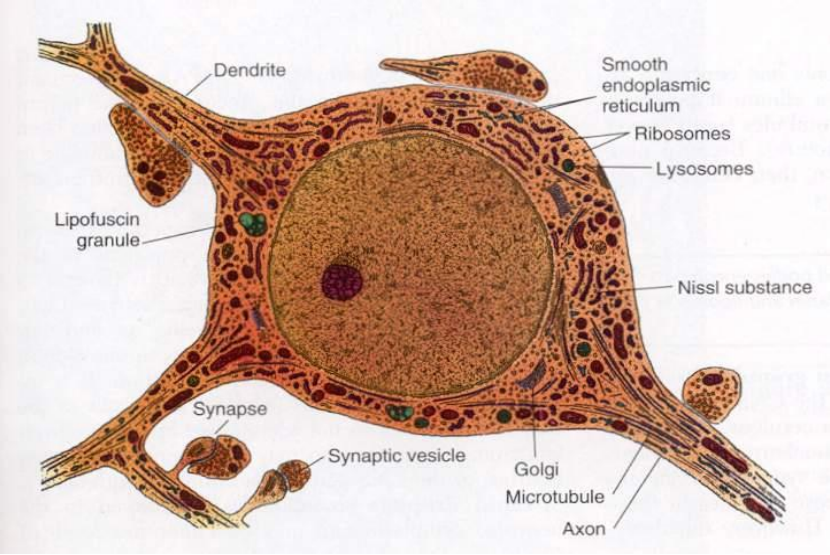
# Neuron 3 - Perikaryon

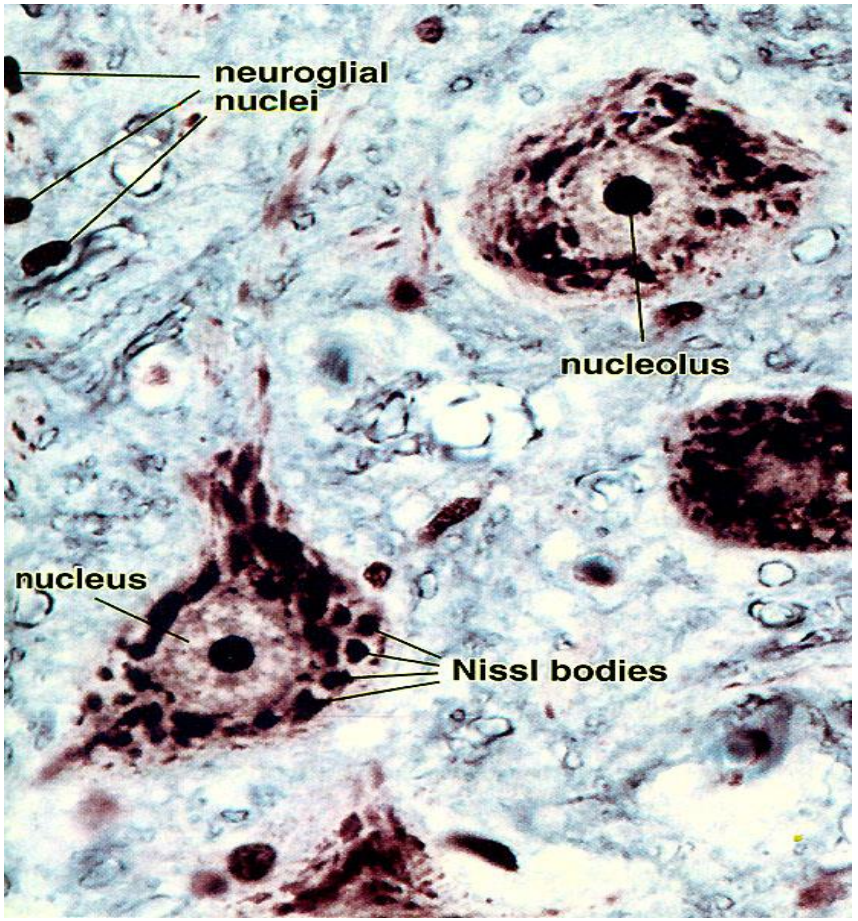
**Position:**
CNS – grey matter
PNS – ganglia

**Shape:**
pyramidal, shpherical, ovoid, peer-shaped

**Size:**
5 to 150 μm

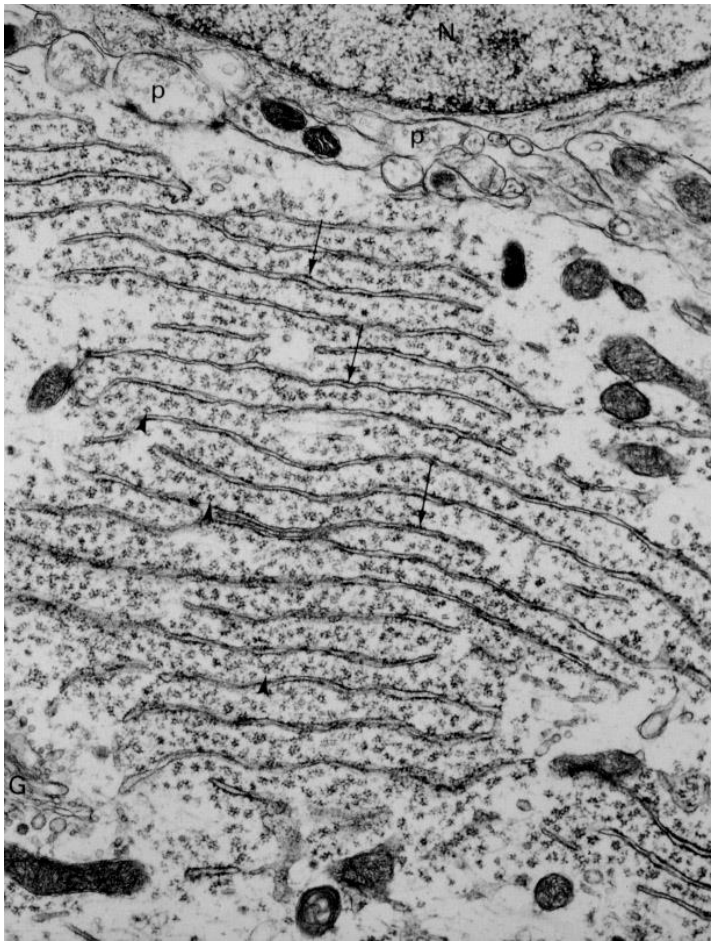
**Organelles:**
- Nuclues – large + pale + prominent nucleoli
- Nissl substance – rough ER
- Neurofibrils (neurofilaments + neurotubules + actin)
- Lipofuscin pigment clumps



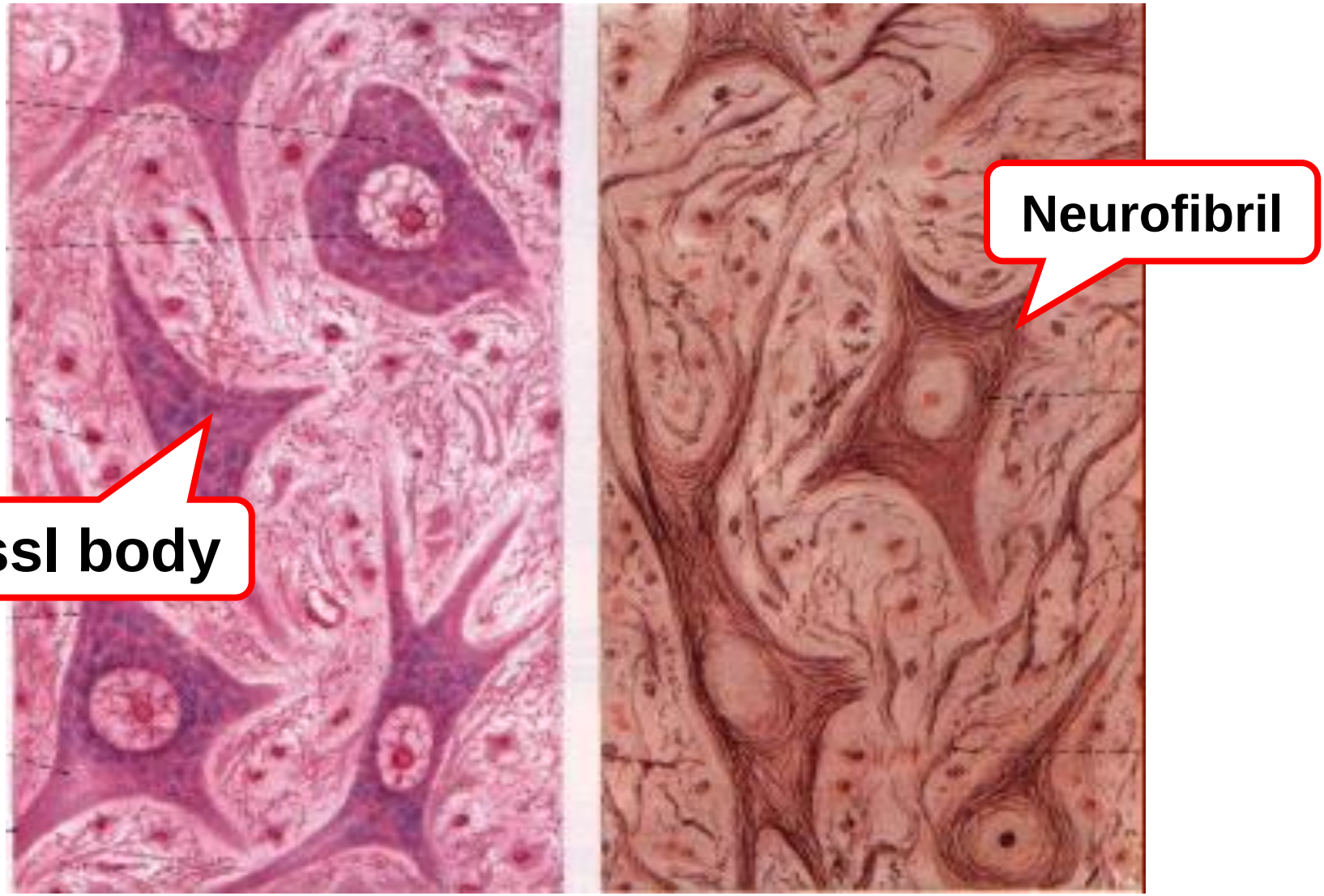
# Neuron 4 - Perikaryon

## Nissl substance in TEM




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

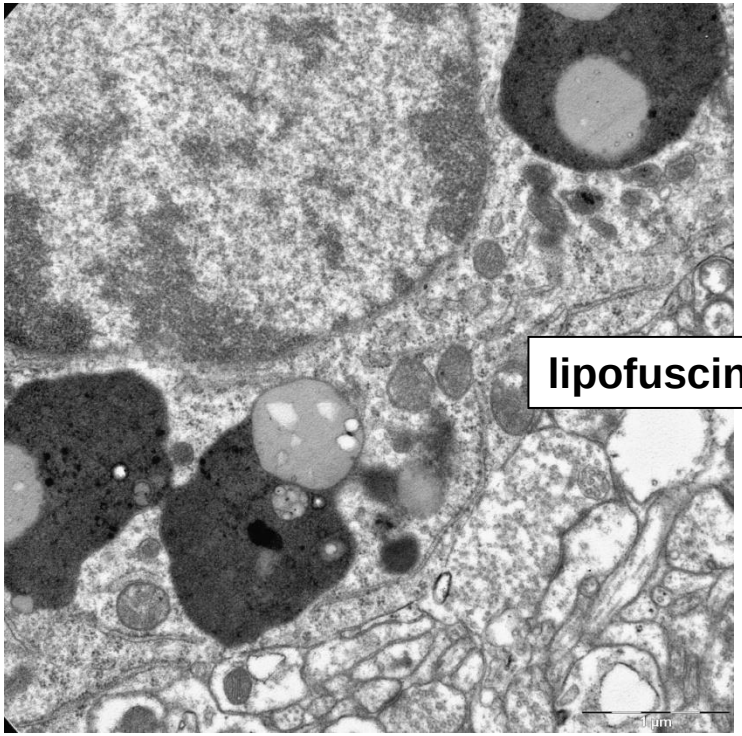
# Neuron 5 - Perikaryon

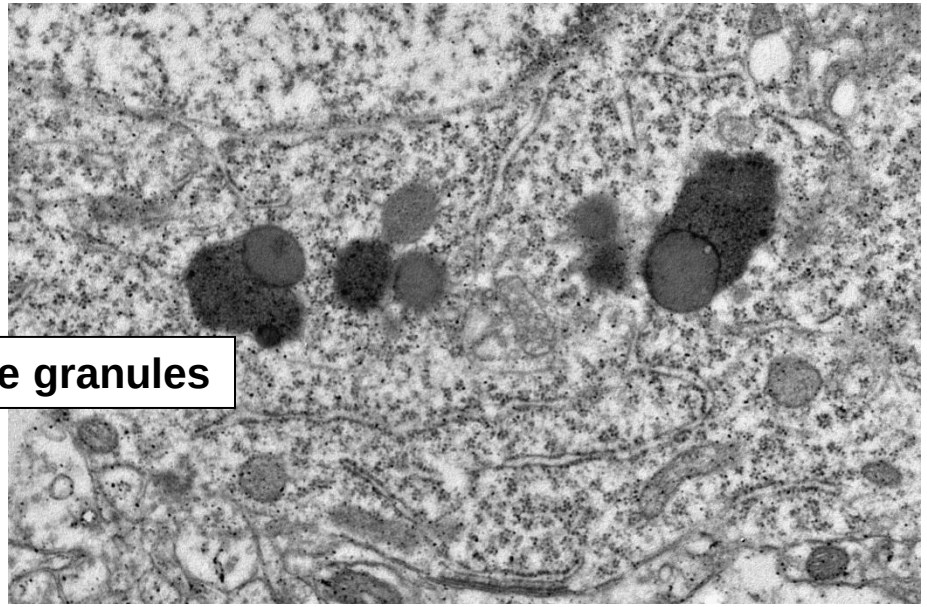



H-E stains

Silver nitrate

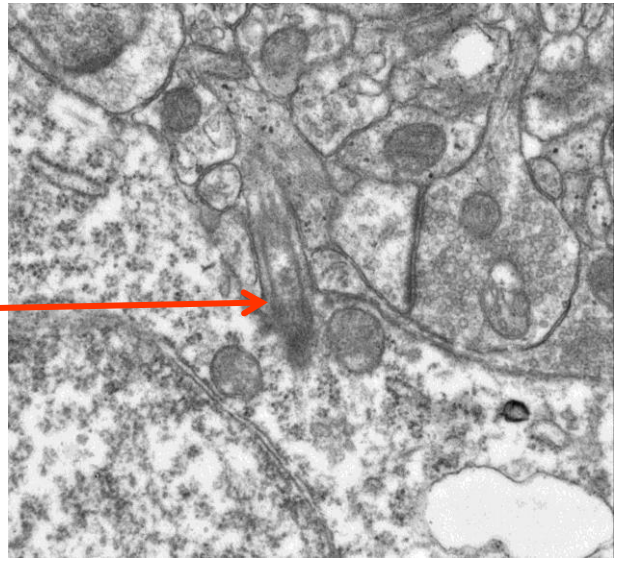
# Neuron 6 - Perikaryon



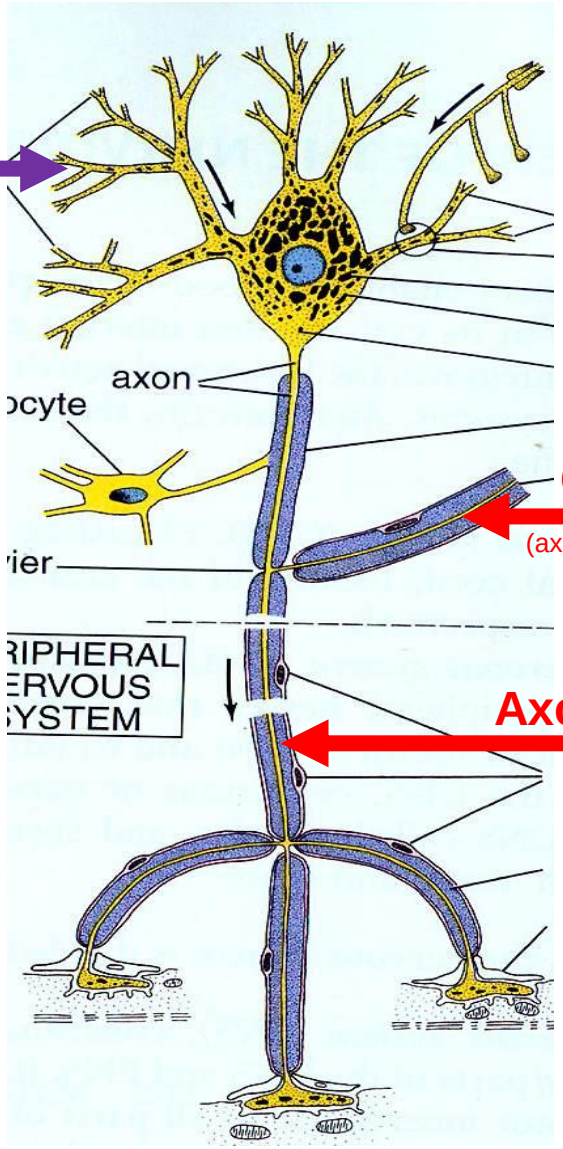


lipofuscine granules

Cilium derived from unused centriole



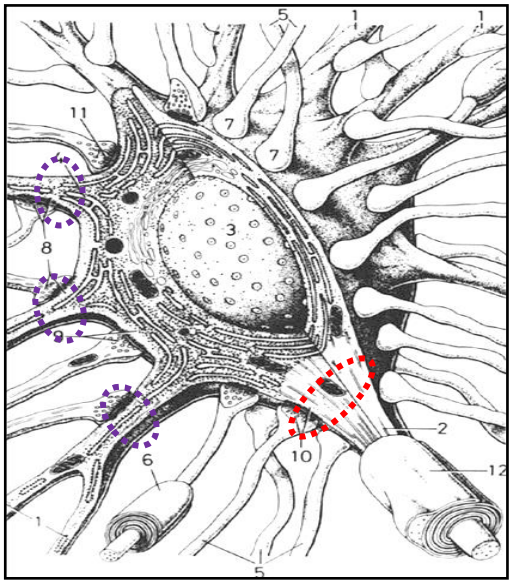
# Neuron 7 – Neurites / Processes



# 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

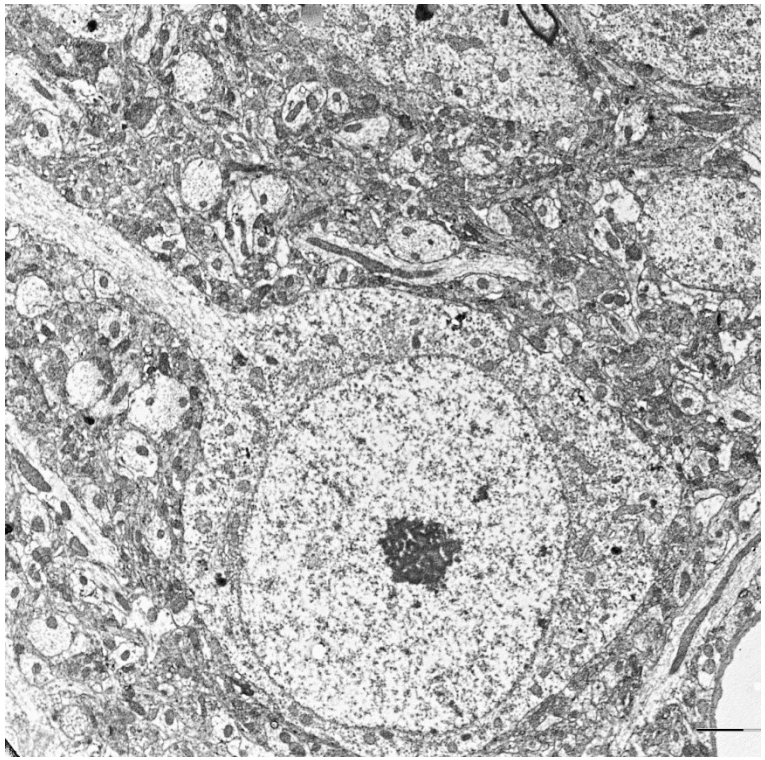


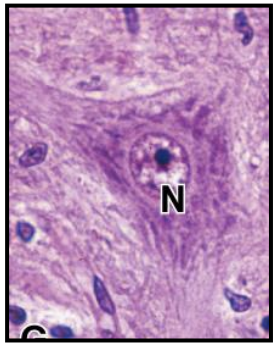

## **Axon** (nerve fiber)

- 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**

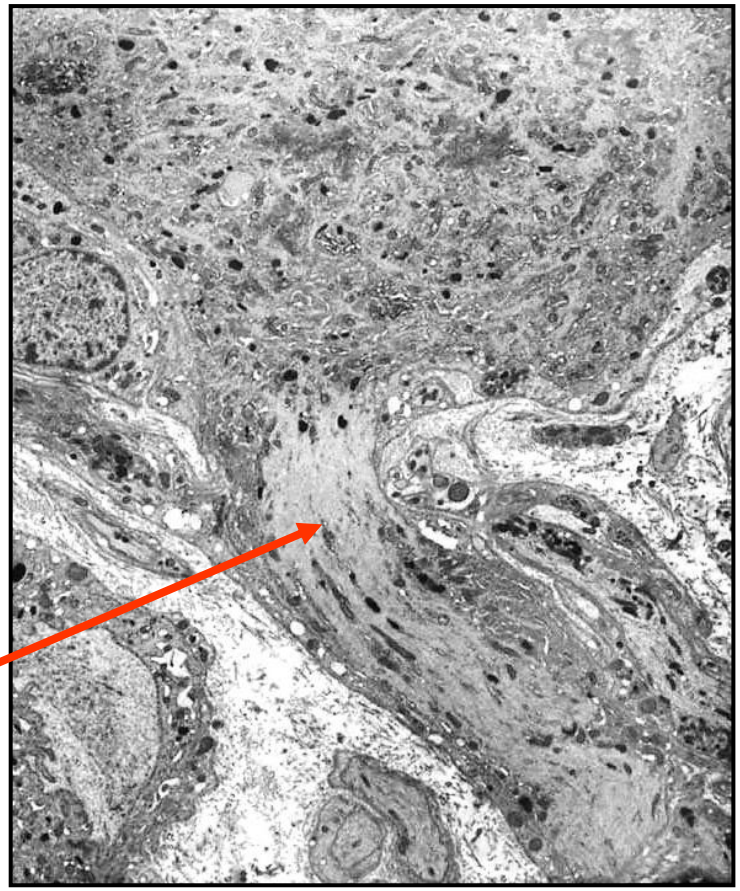
**White matter:** areas of myelinated axons
**Gray matter:** areas of unmyelinated axons, cell bodies, and dendrites

# Neuron 8 – Neurites / Processes



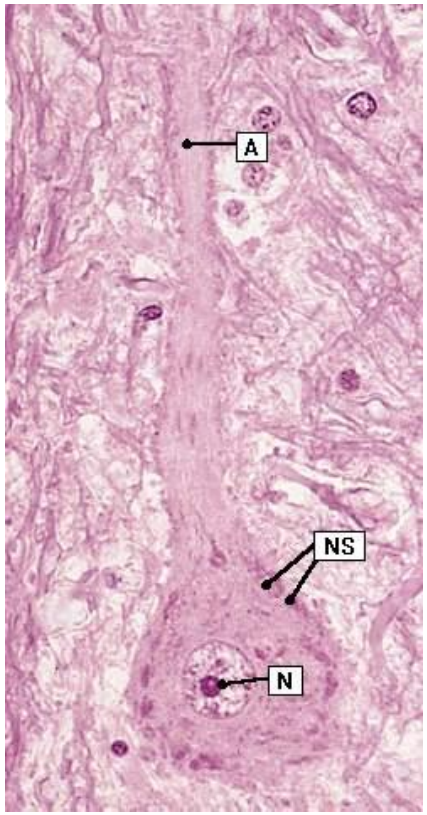



**Neuron in TEM**



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?

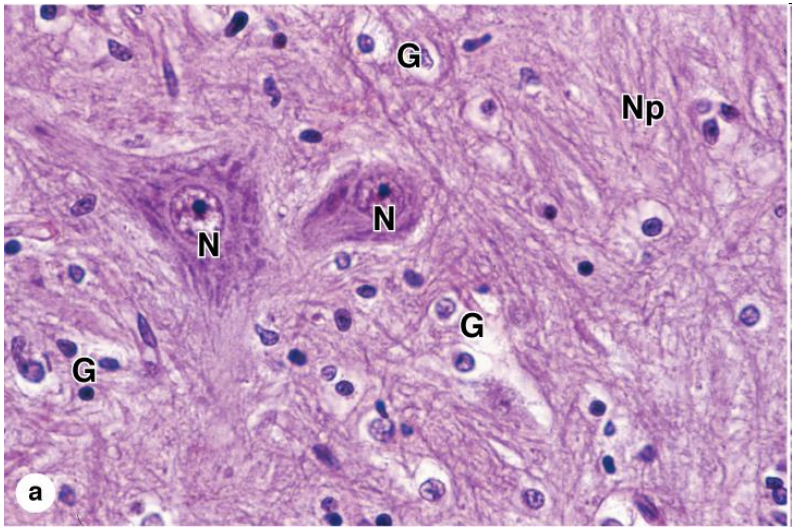
**axonal transport** – two-way passage of proteins, organelles, and other material along an axon

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

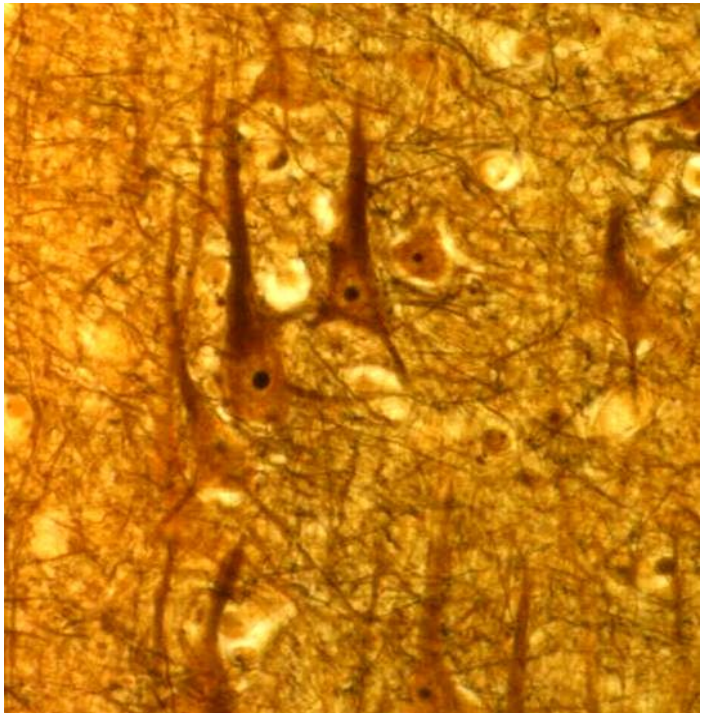
- **Slow transport:** 1-5 mm/day
- **Fast transport:** 200-400 mm/day

# Nerve tissue – Neuropil 1

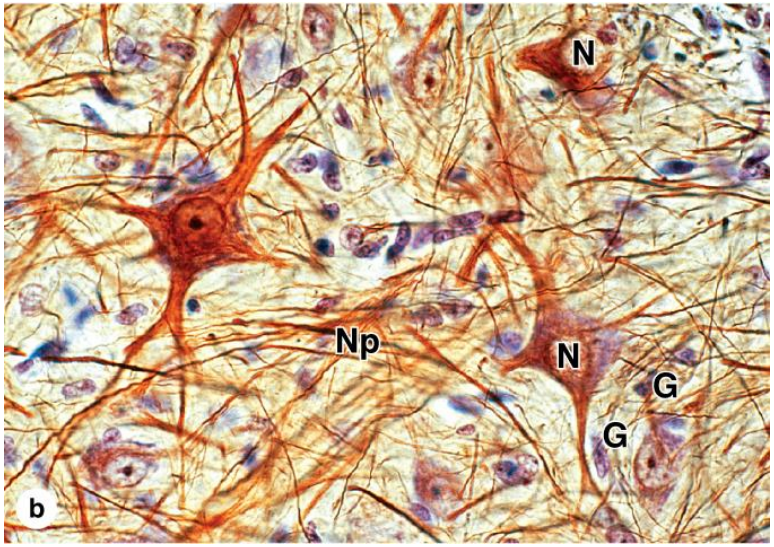
All the material filling space among the bodies of neurons and glial cells + ECM




motoneurons - HE



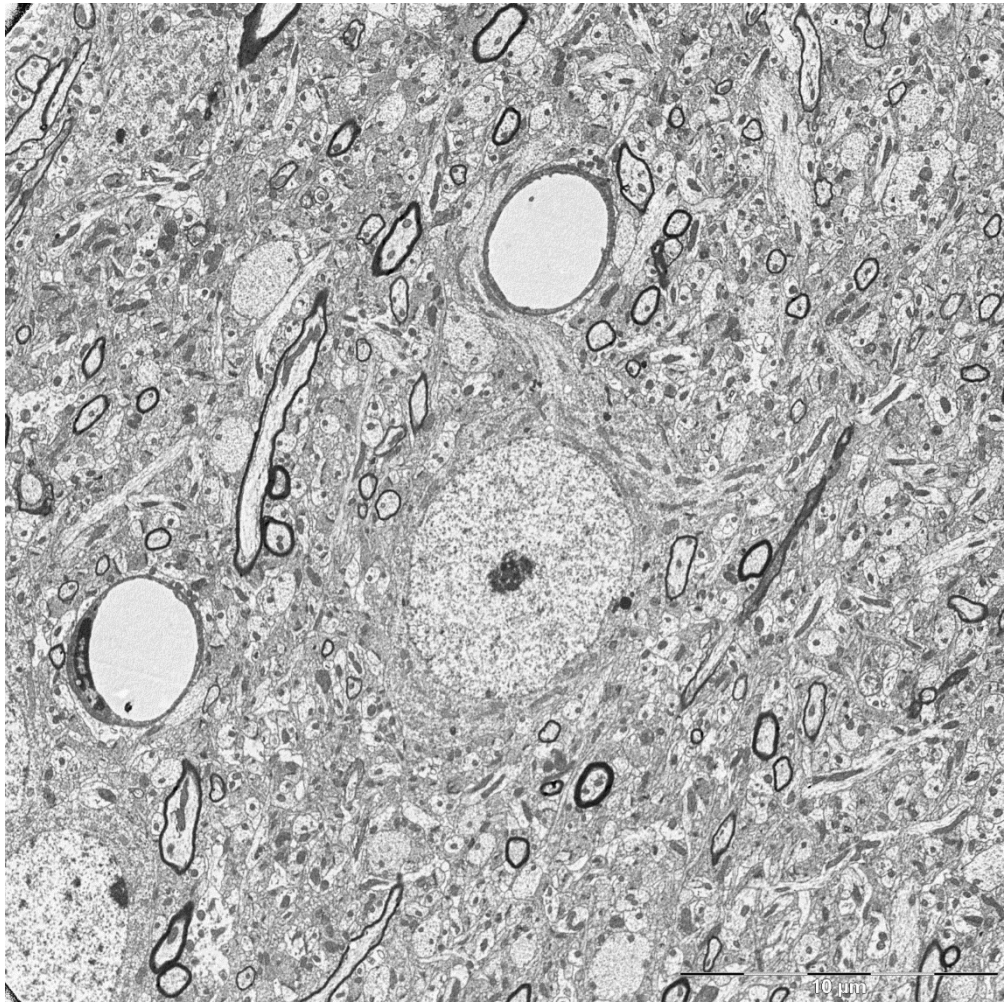
pyramidal cells - impregnation




motoneurons – combined method

# Nerve tissue – Neuropil 2

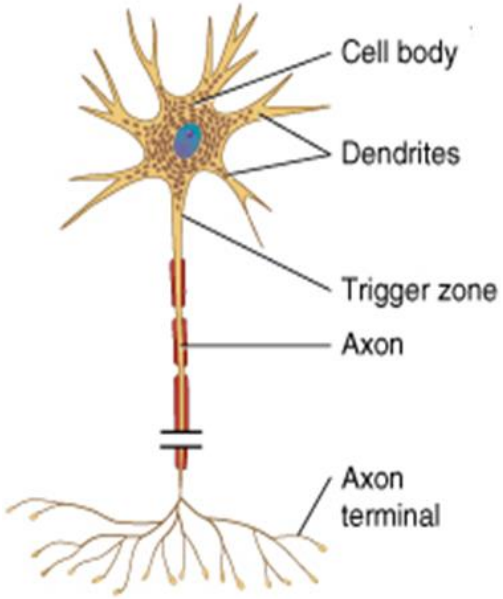
## Neuropil in TEM



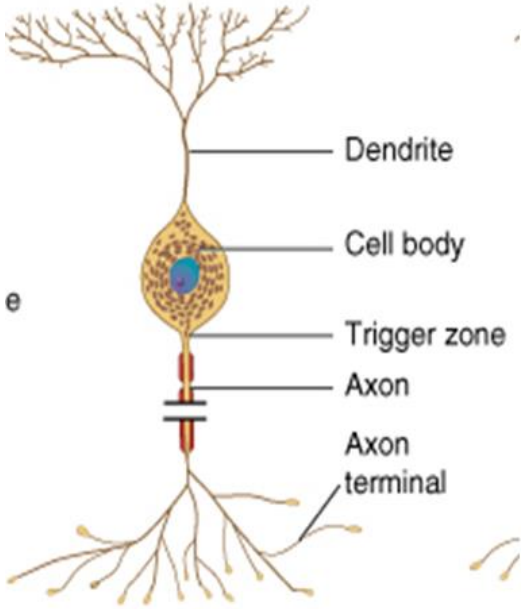
# Neuron – Classification 1

## According to the number of the processes

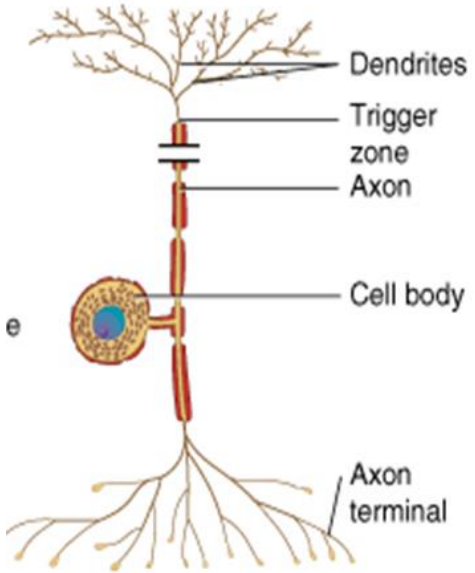
**Multipolar**
several dendrites & one axon
*(most common cell type)*




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

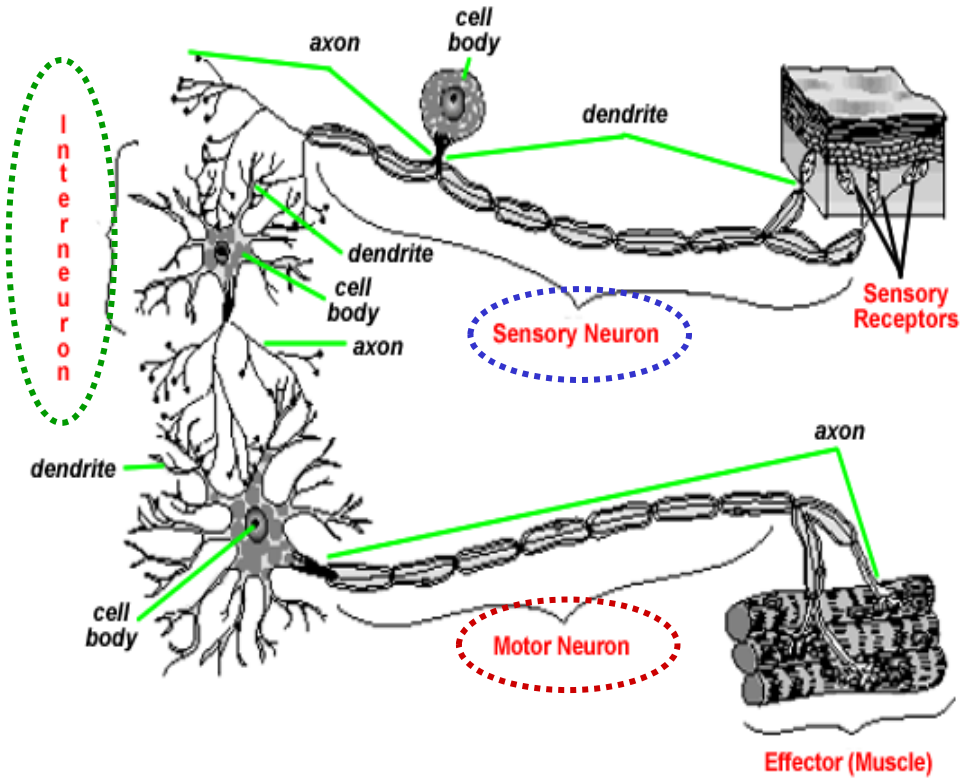



**Unipolar** (pseudounipolar)
one process only
(develop from a bipolar)
*(always sensory, in spinal ganglia)*



# Neuron – Classification 2

## According to the function




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

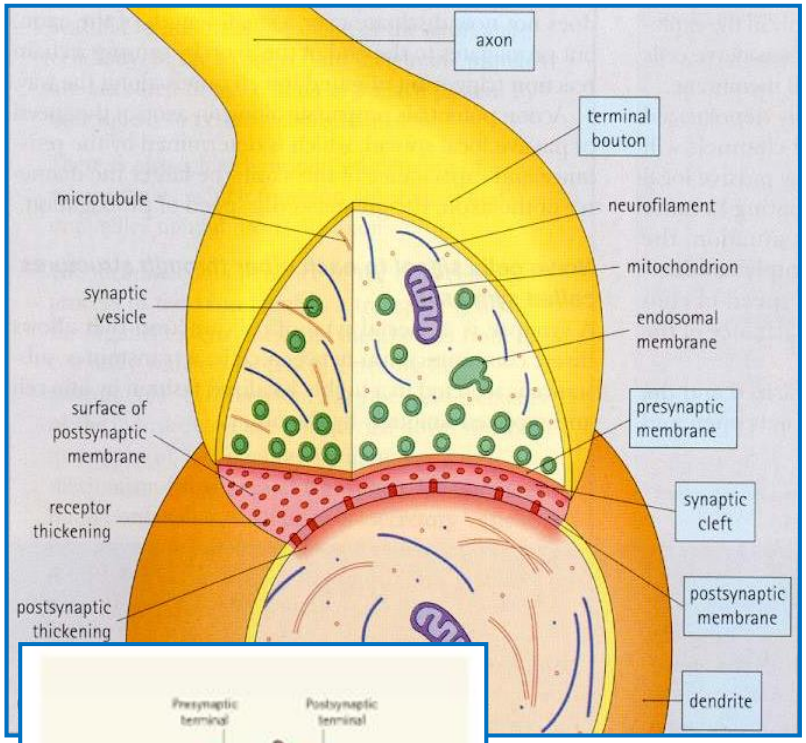
**Sensory (afferent) neurons:**
- receive sensation

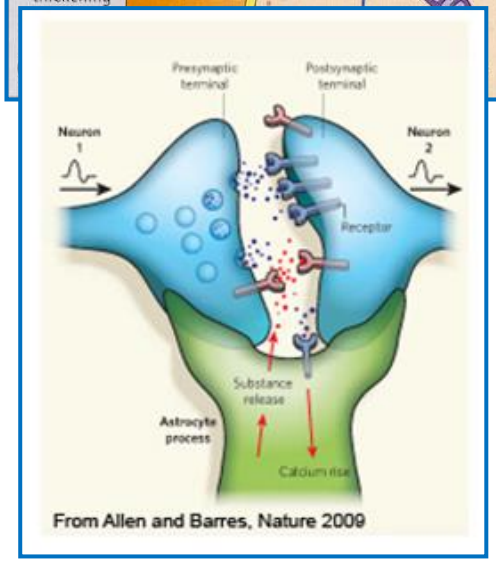
**Interneurons:**
- local circuit neurons

# 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

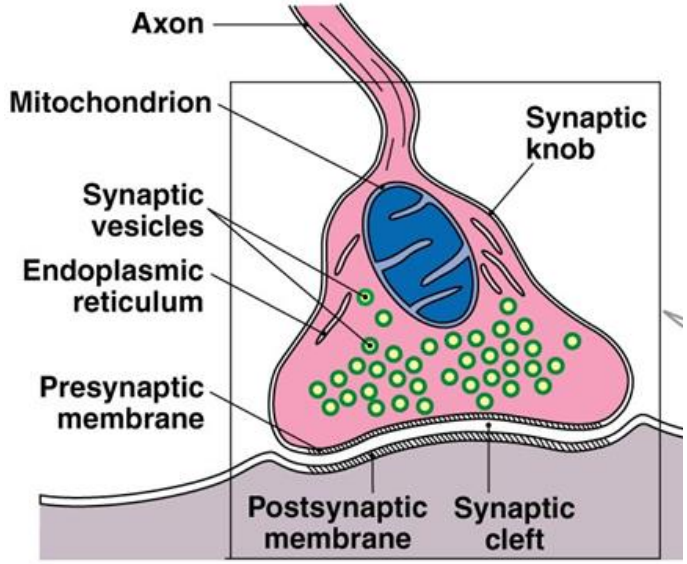
**Excitatory synapses**

- 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

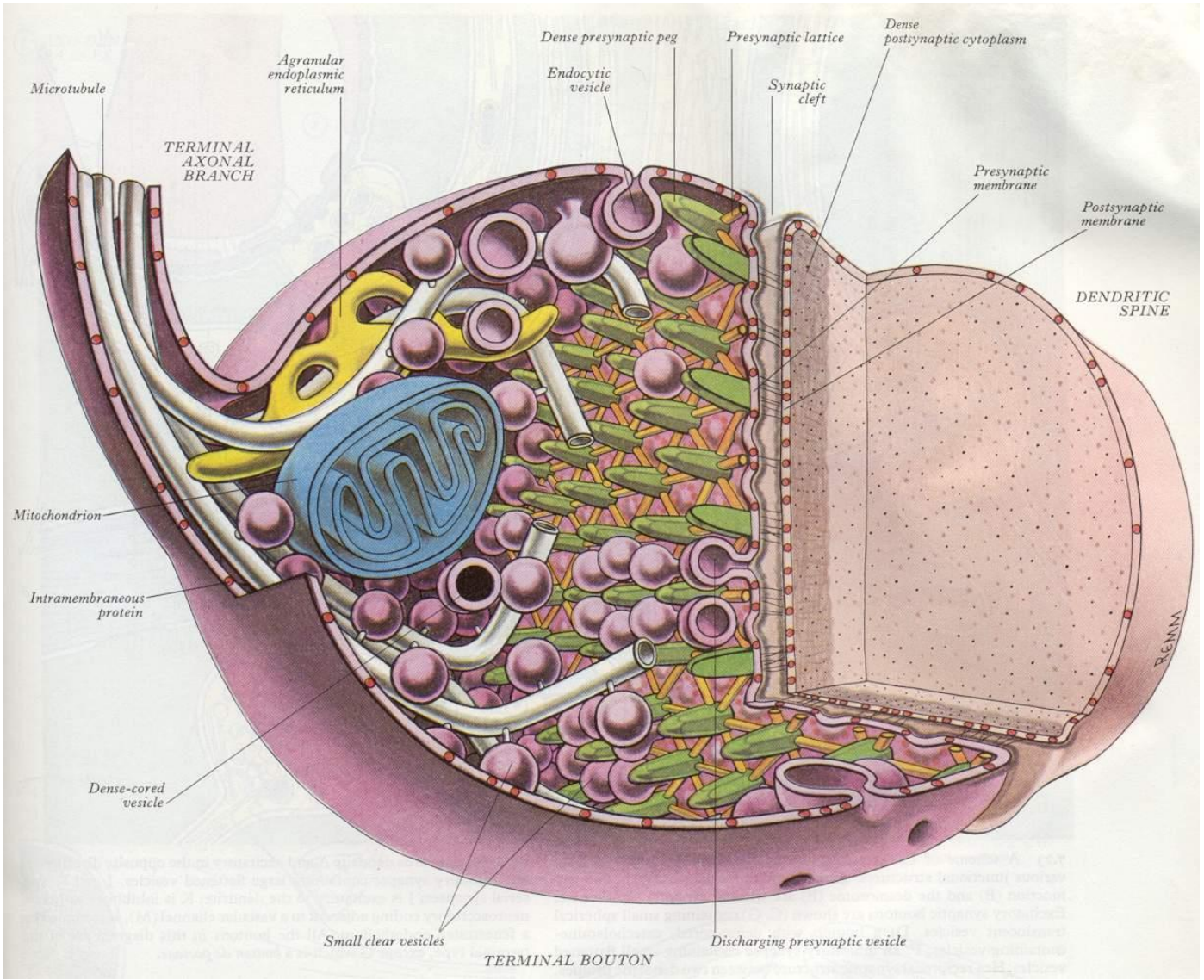




## Neurotransmitters

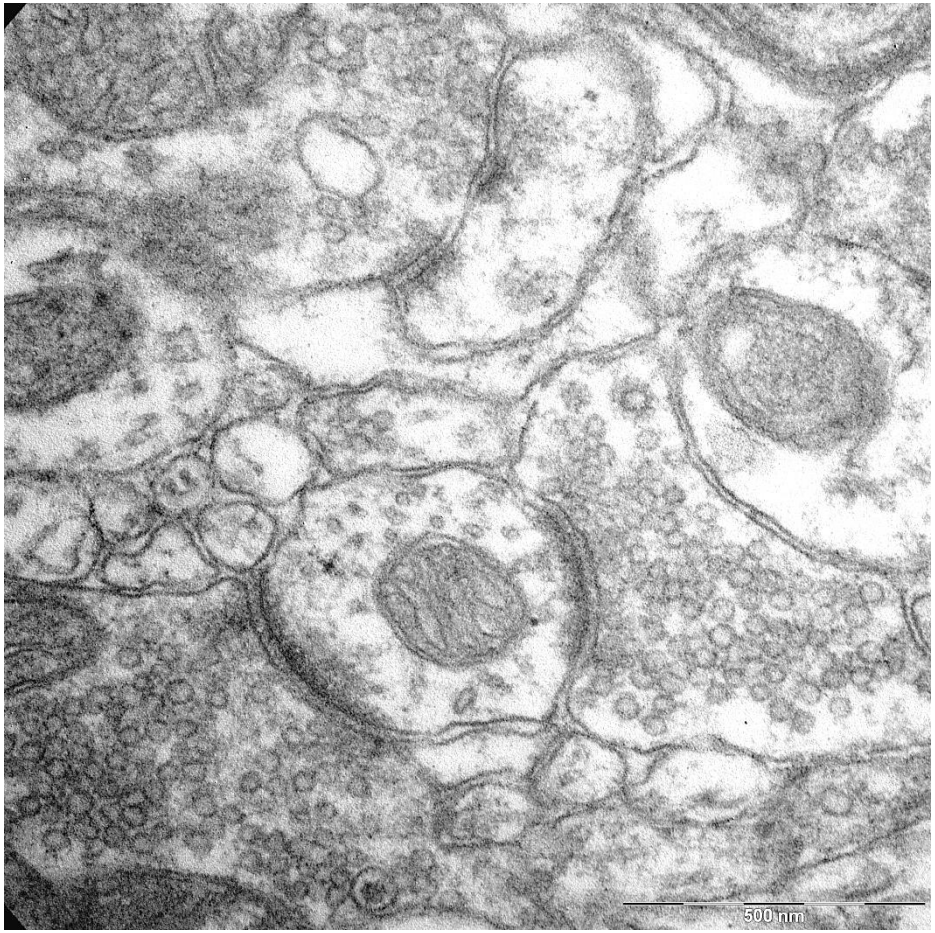
- **Acetylcholine**
- **Amioacids** – gluatamate, glycin, GABA (gamma-amminobutyric acid)
- **Monoamines** – serotonin, catecholamines, dopamine, adrenaline, …
- **Neuropeptides** – enkefalin, somatostatin, neurotensin, ….
- **Others** – adenosine, nitric oxide

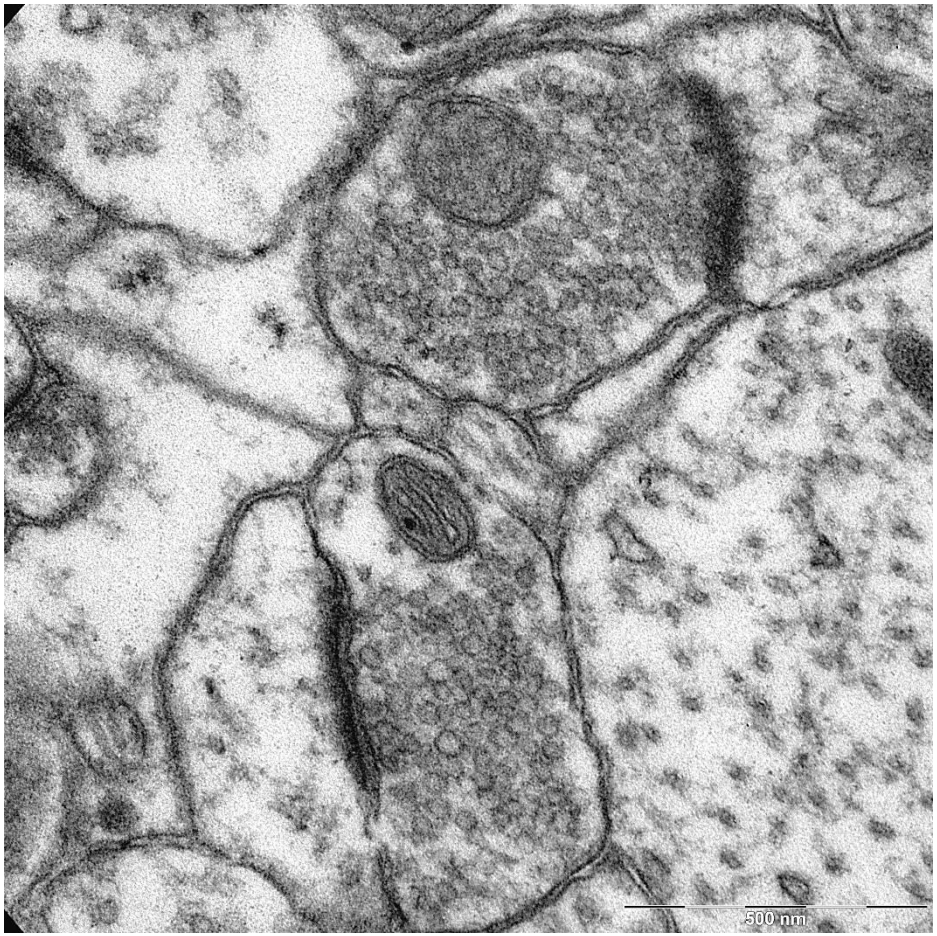
# Synapse 3


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

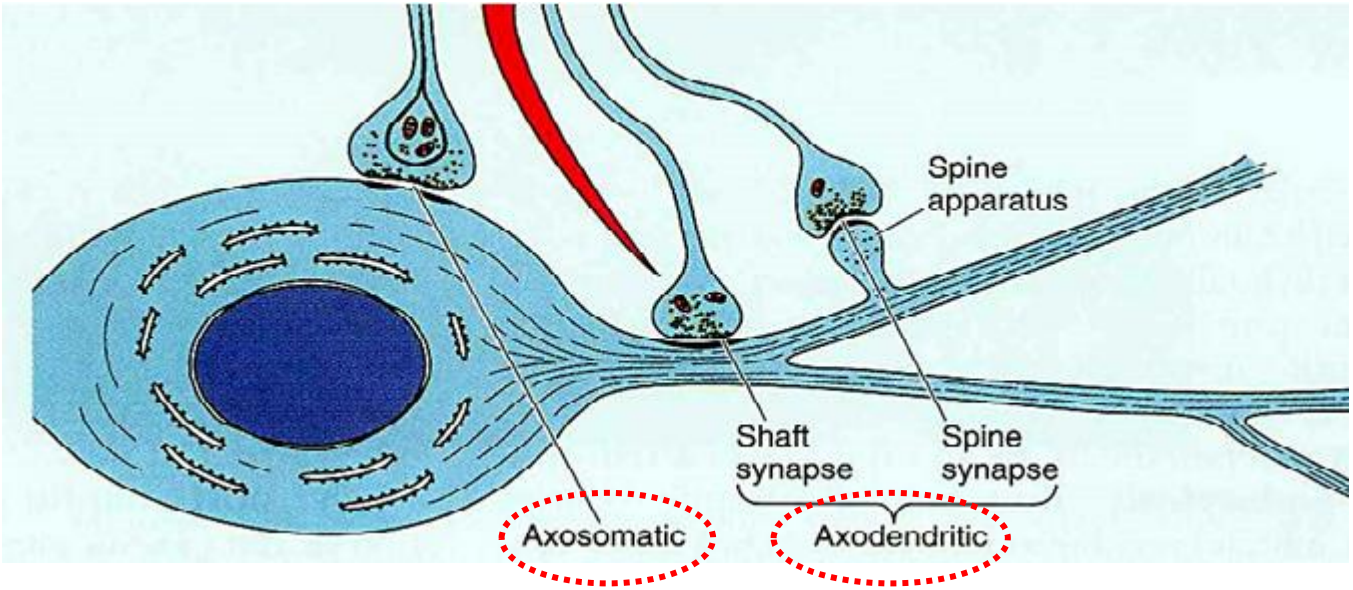
## Synapse in TEM



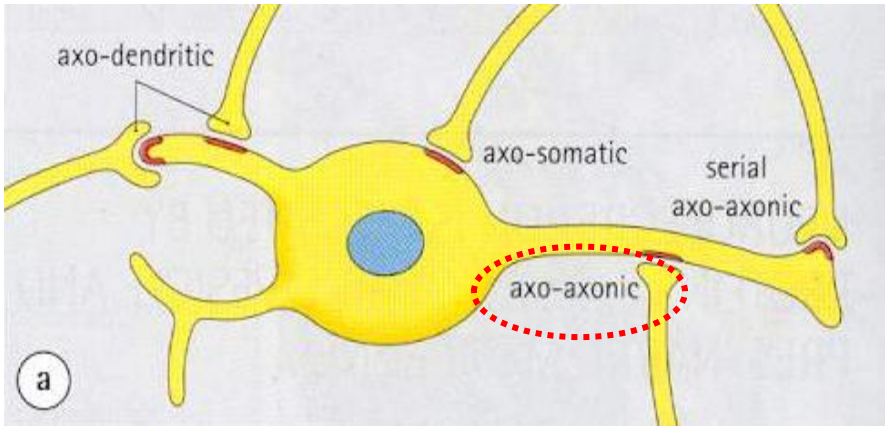
# Synapse 5

## Classification according to the constitution

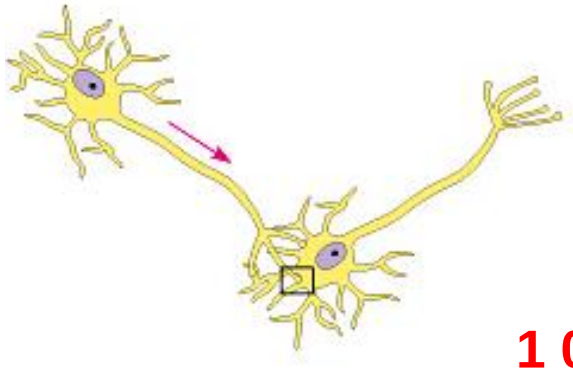



**Axodendritic**
**Axosomatic**
**Axoaxonic**

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

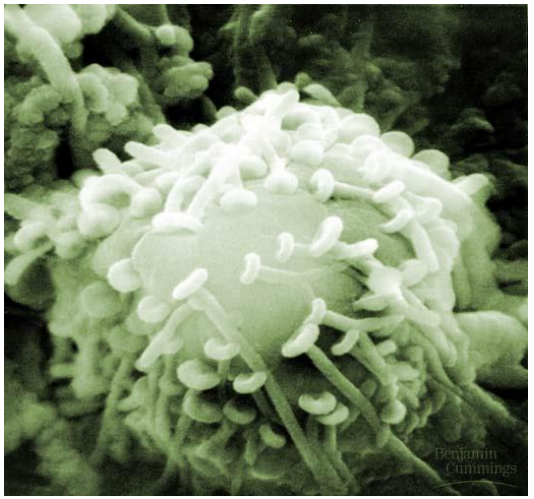


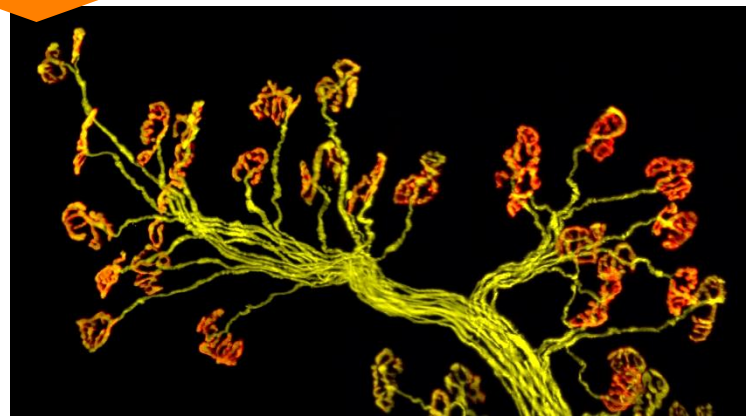
# Synapse 7



One neuron may have

**1 000 to 10 000 synapses !!!**



# Neuroglia

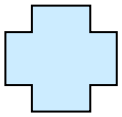
## General features

- **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

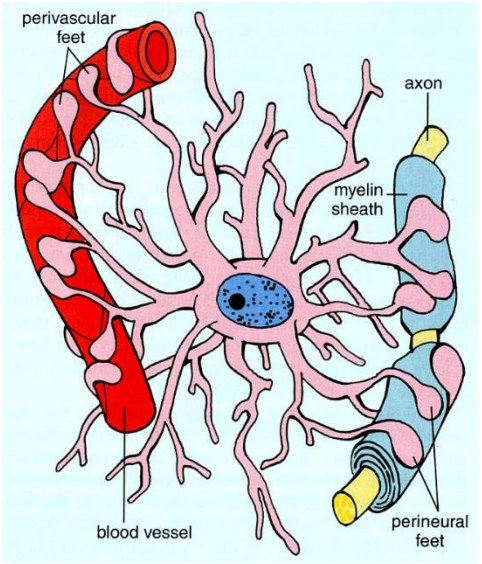
✓ **nerve growth factors** secreted by astrocytes promote neuron growth and synapse formation

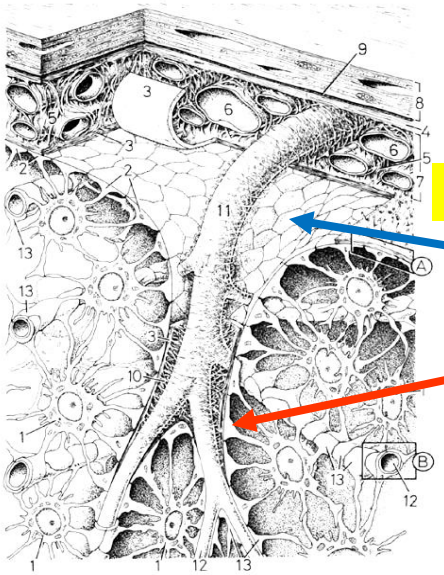
✓ communicate electrically with neurons and may **influence synaptic signaling**

✓ 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**



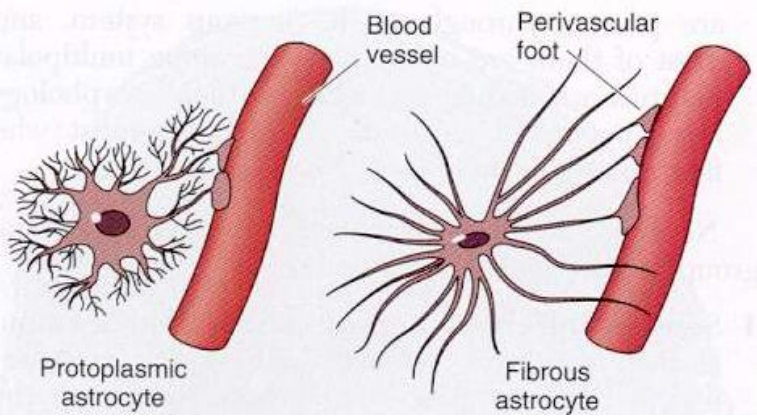



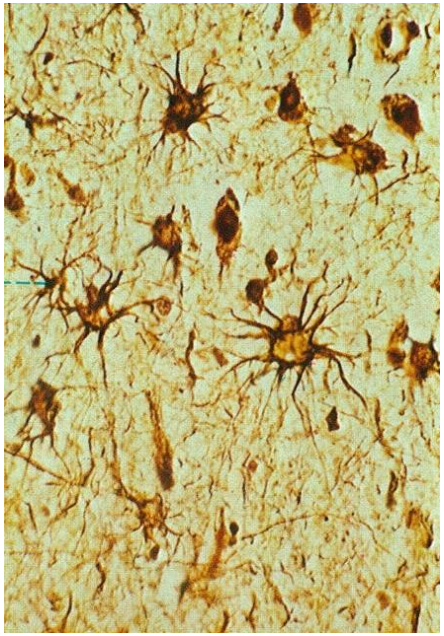
**Membrana limitans gliae…**

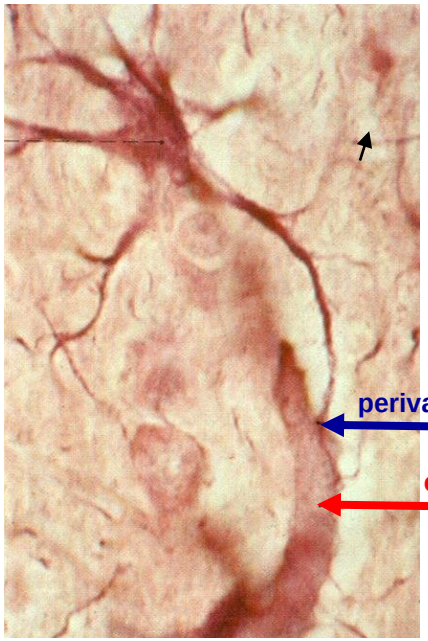
**…superficialis**

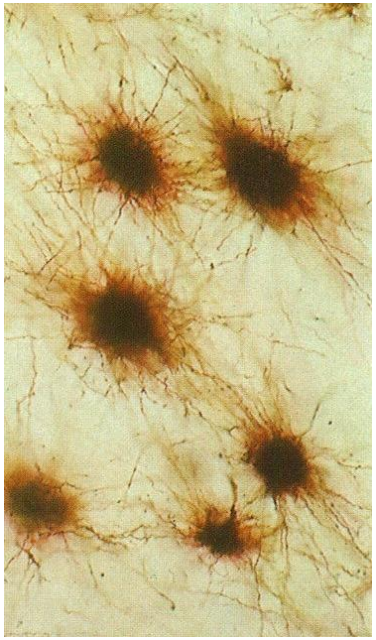
**…perivascularis**

# Neuroglia - Astrocytes





**protoplasmic astrocyte**

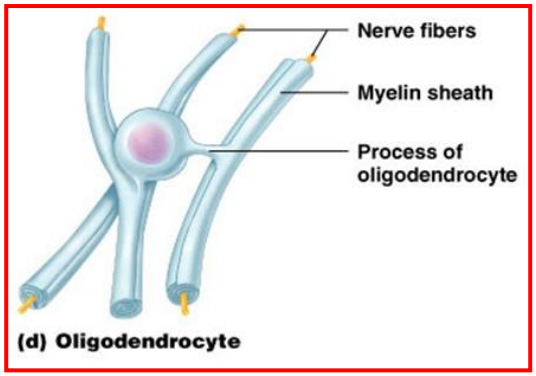
**(predominant in grey matter)**

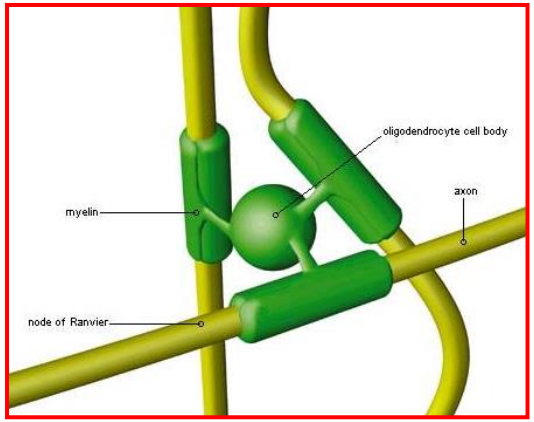
**fibrous astrocyte**

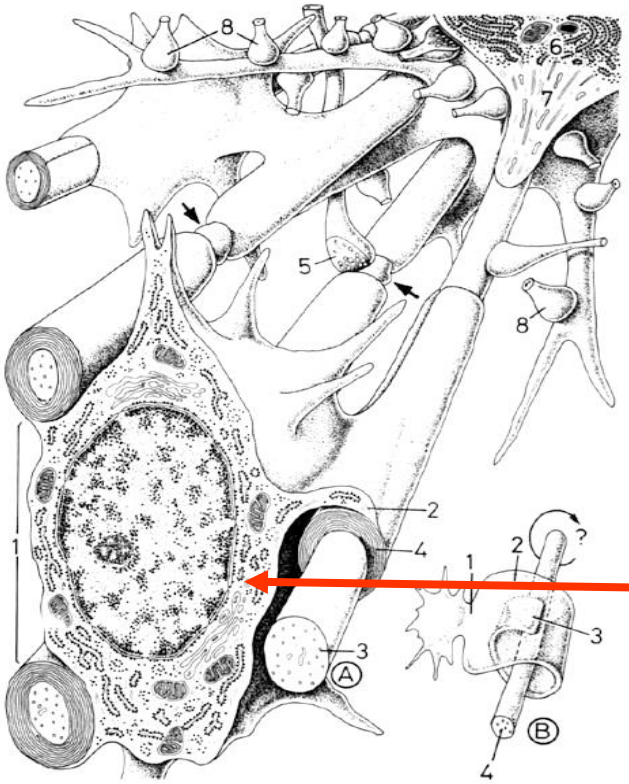
**(predominant in white matter)**

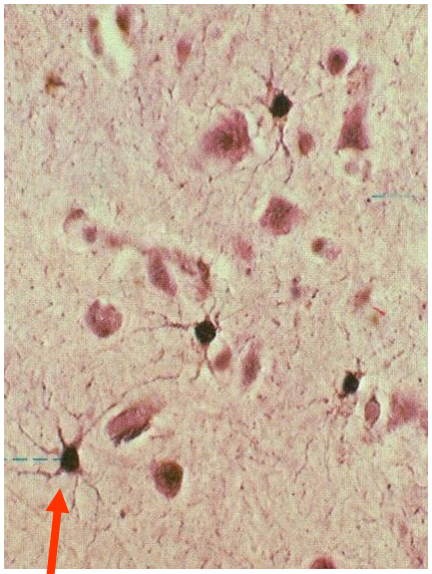
# Neuroglia - Oligodendrocytes

- ✓ 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**



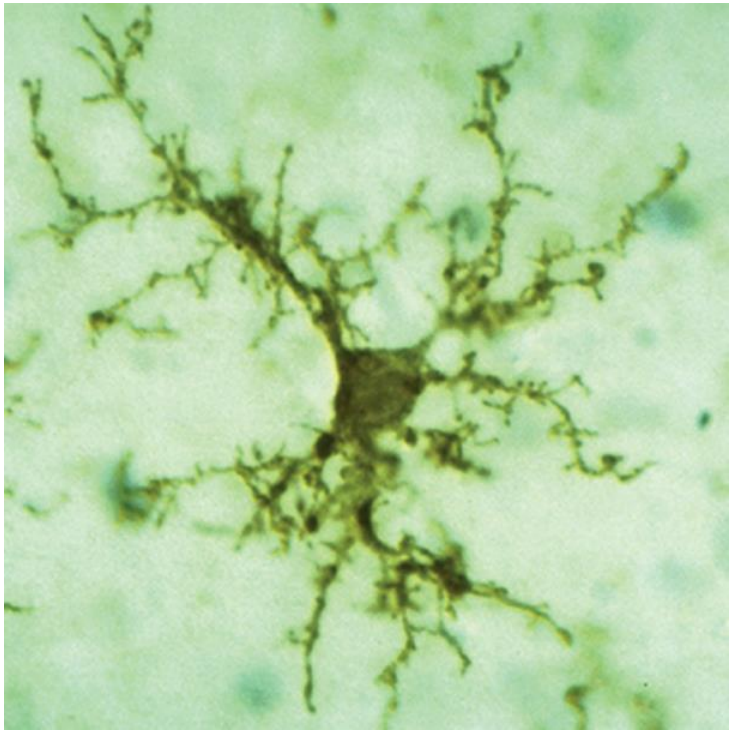



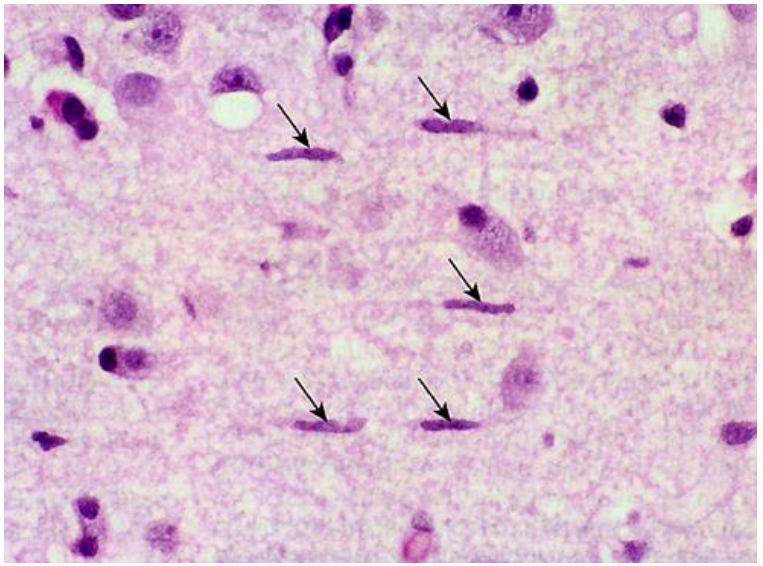



**oligodendrocyte**

# Neuroglia - Microglia

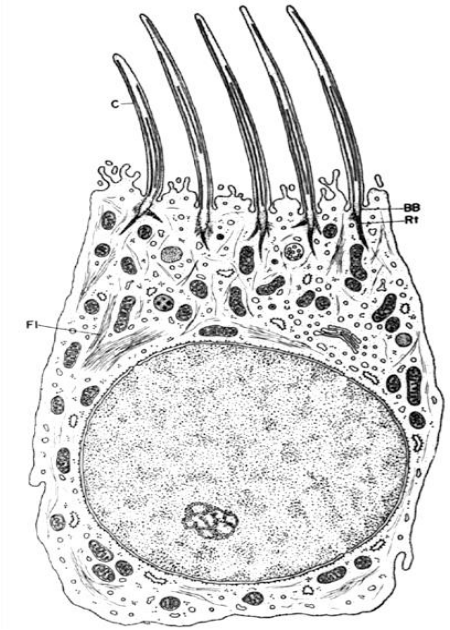
- ✓ **smallest** neuroglial cell
- ✓ small, dark, **elongated nuclei**
- ✓ possess **phagocytotic** properties
- ✓ when activated – **antigen presenting** cell
- ✓ originate in bone marrow (**mesodermal** origin)

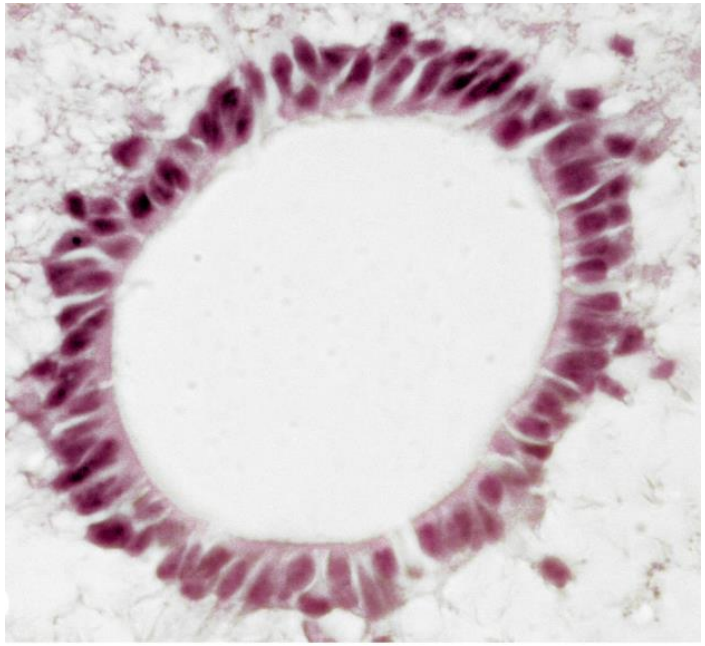




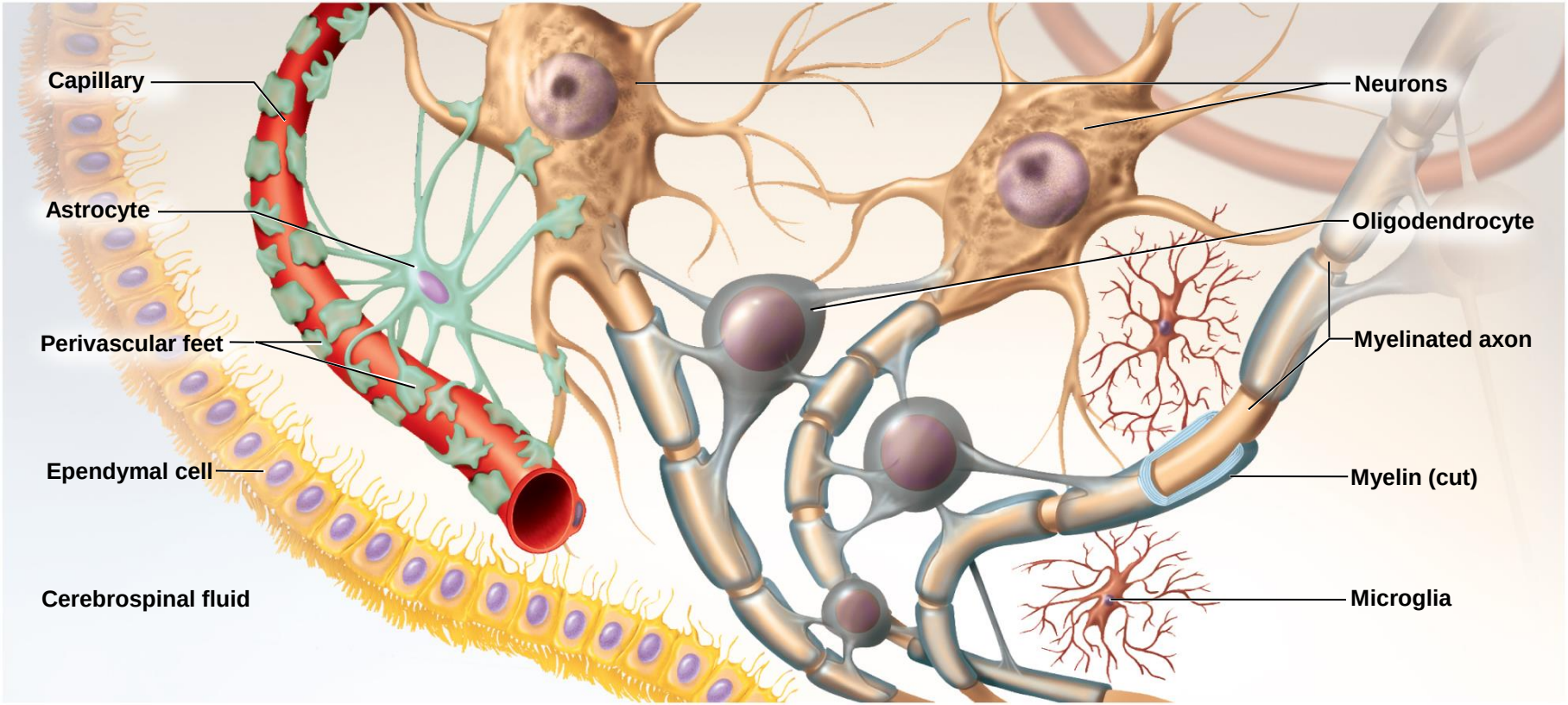
# Neuroglia – Ependymal cells

- ✓ **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

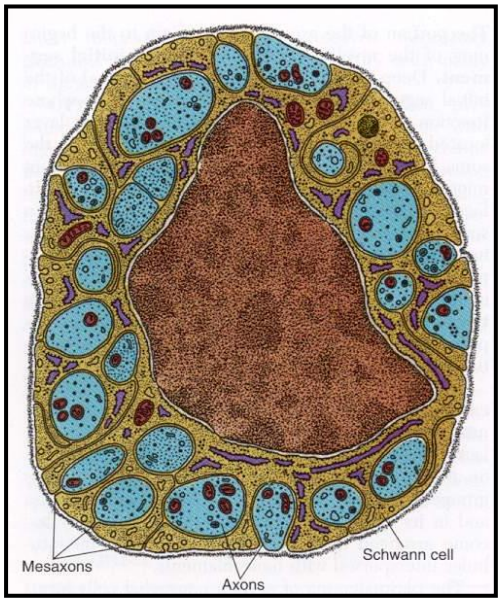


# Neuroglia in PNS – Schwann cells 1

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

## Small diameter axons

**Enveloping only by cytoplasm**

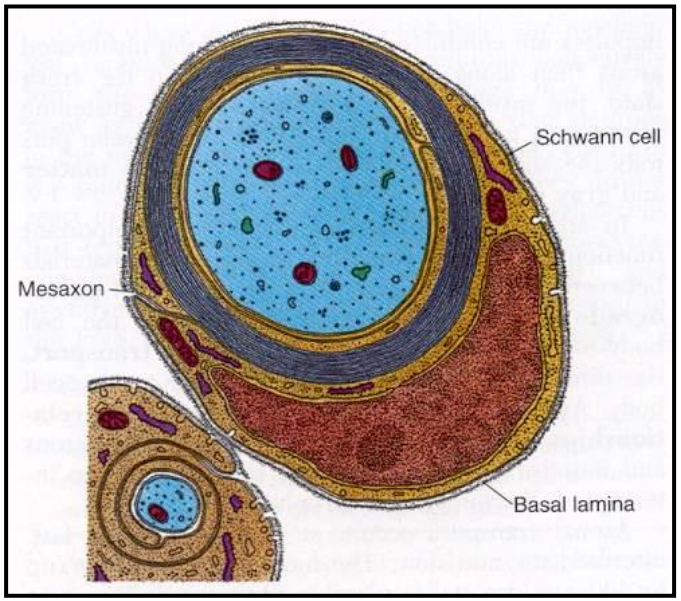



**only Schwann sheath – gray nerve fiber**

X

## Large diameter axons

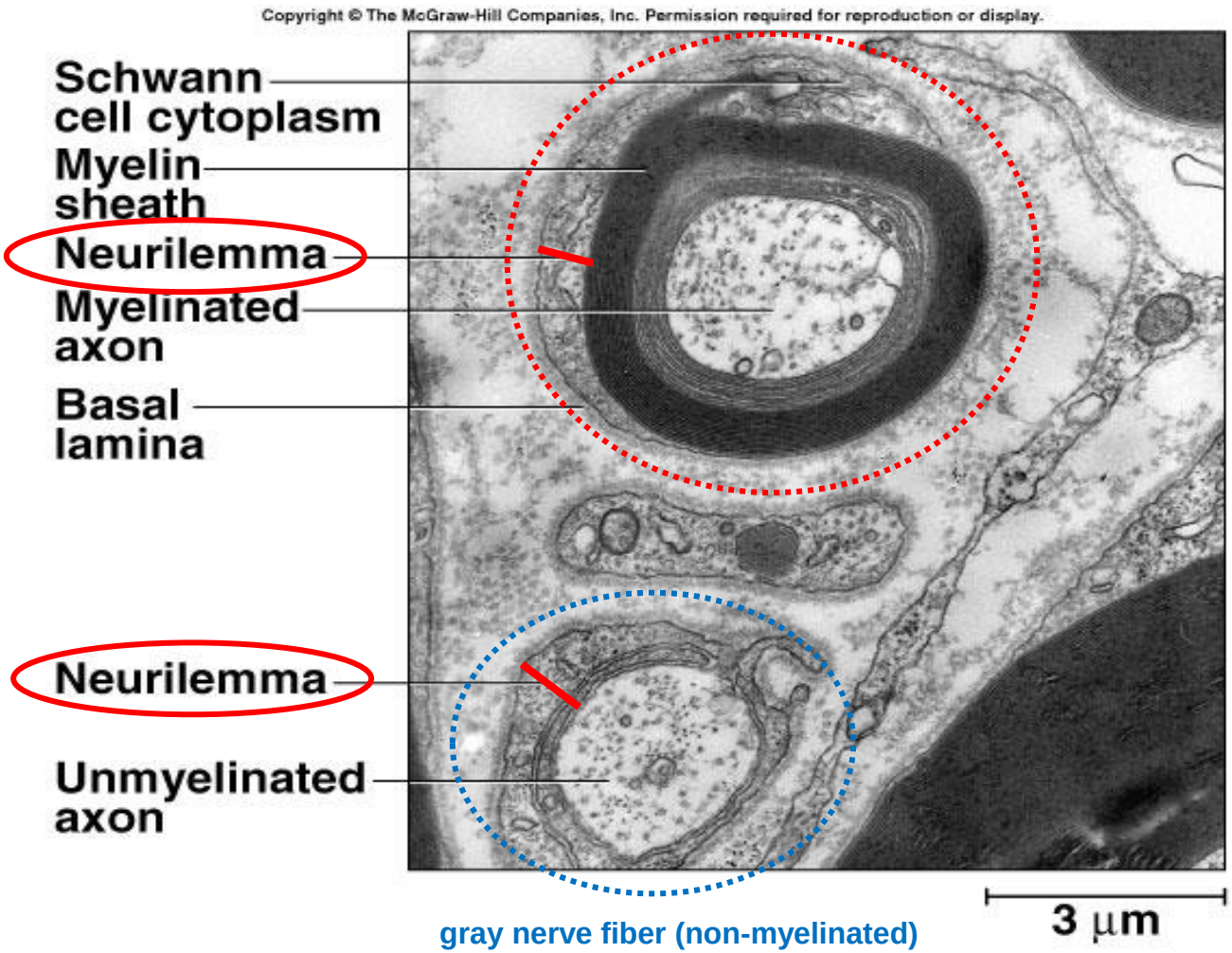
**Wrapping by myelin sheaths**




**Schwann + myelin sheath – double contoured nerve fiber**

# Neuroglia in PNS – Schwann cells 2

double contoured nerve fiber (myelinated)



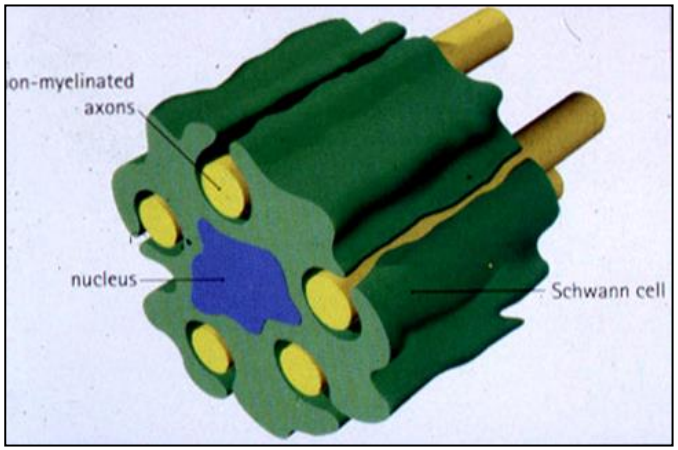

gray nerve fiber (non-myelinated)

# Neuroglia in PNS – Schwann cells 3

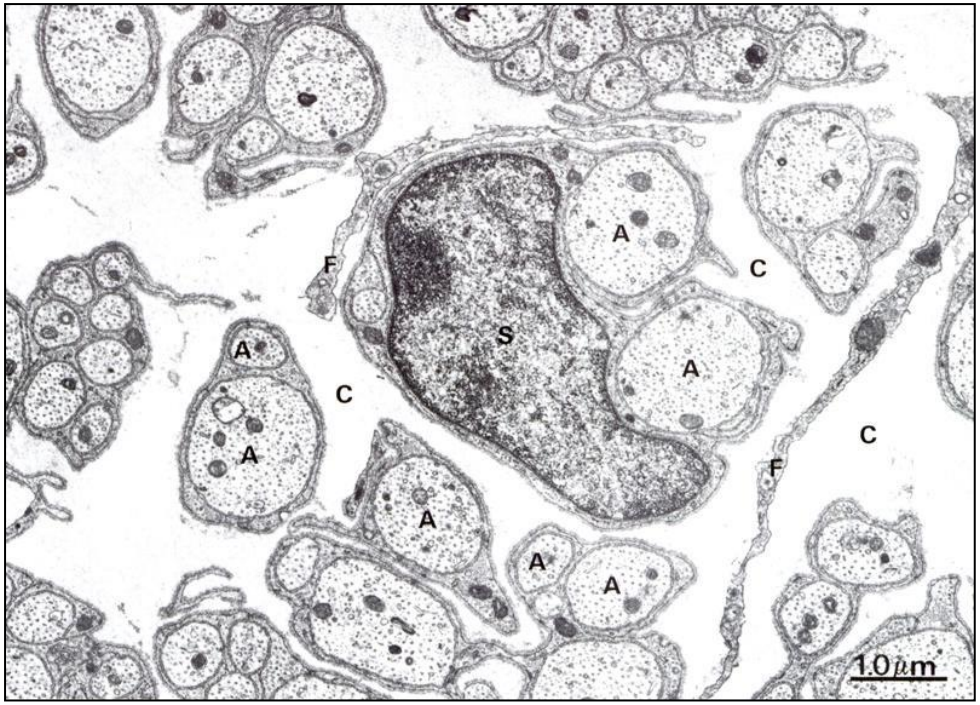
**Small diameter axons** ⇨ **Non-myelinated fibers**

(typical for autonomous nerve system)

**only Schwann sheath – gray nerve fiber**




**One Schwann cell can ensheath multiple axons**

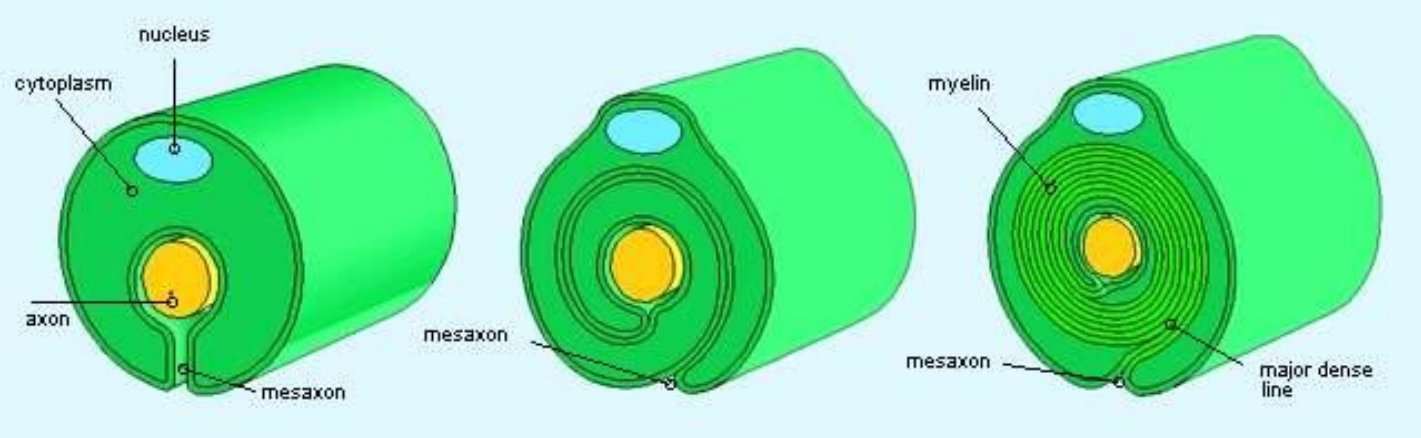


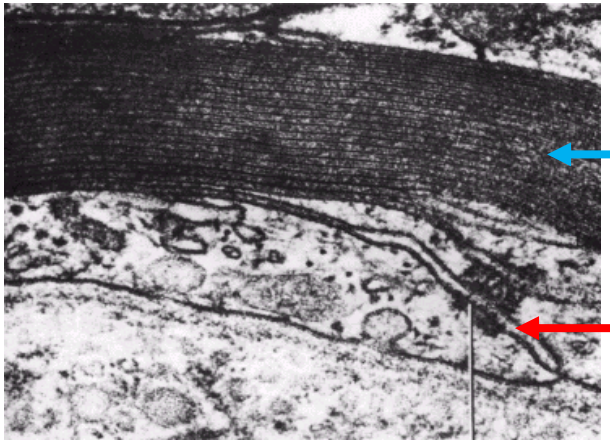
# Neuroglia in PNS – Schwann cells 4

**Large diameter axons** ⇨ **Myelinated fibers**

**Myelination**

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



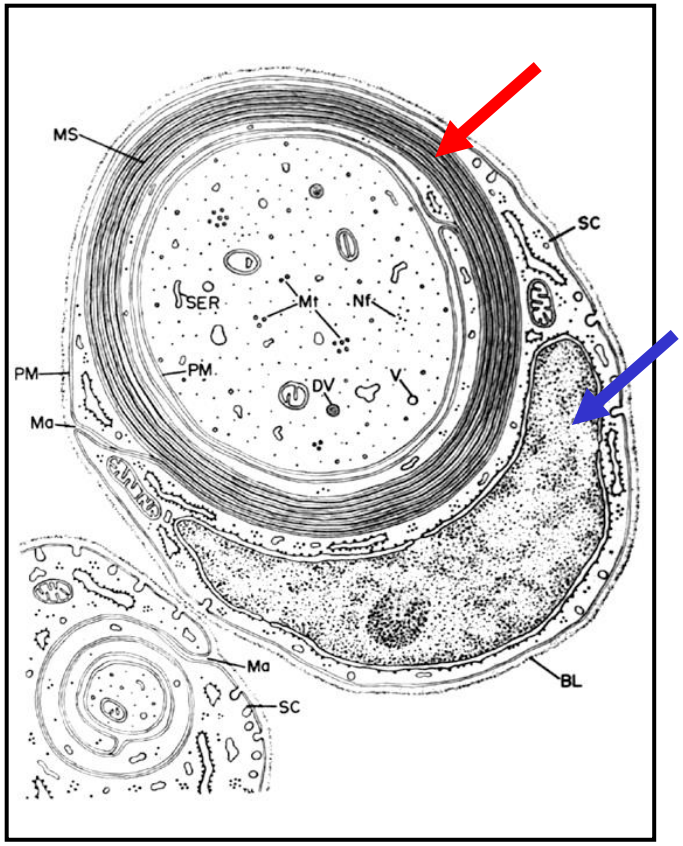



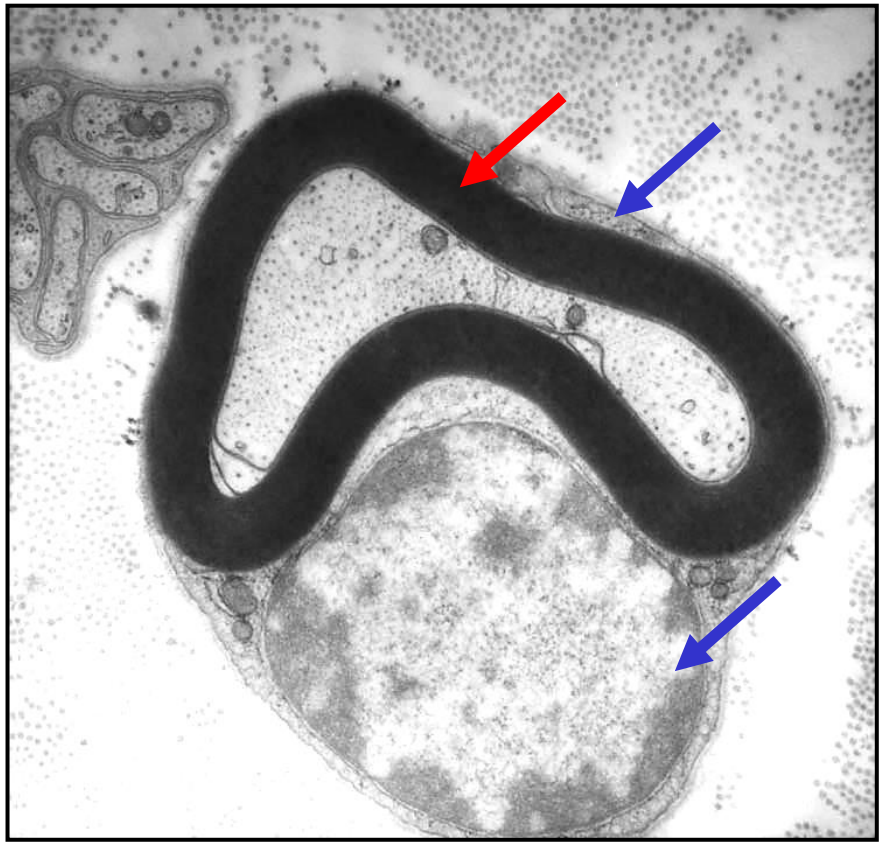
Myelin sheath

Mesaxon

# Neuroglia in PNS – Schwann cells 5

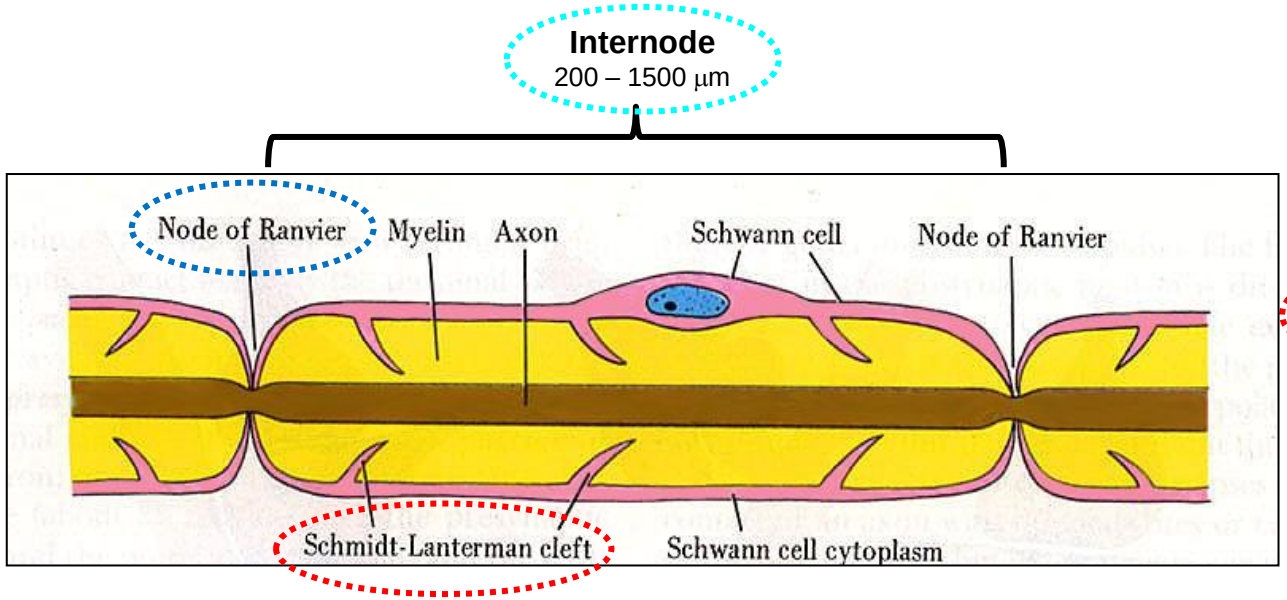
**Double contoured nerve fiber** ⇨ **Schwann sheath** **= Neurilemma**
**+**
**Myelin sheath**

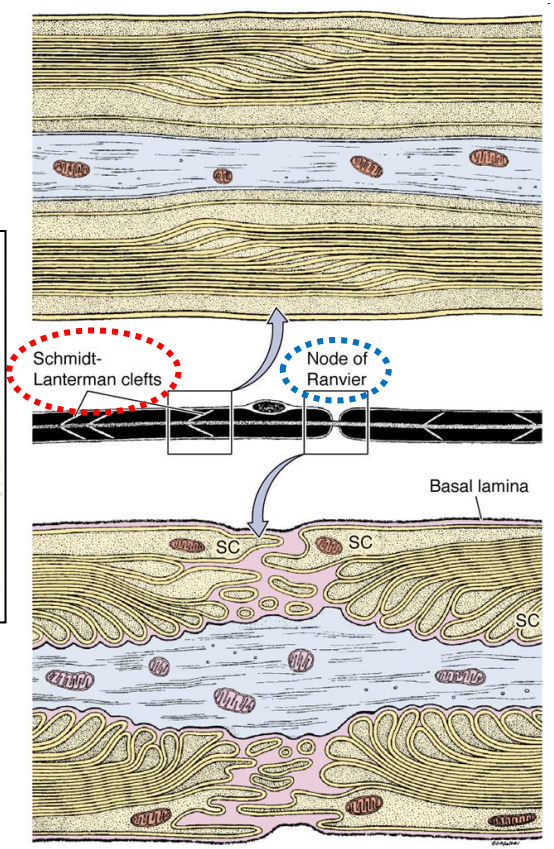


# Neuroglia in PNS – Schwann cells 6

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

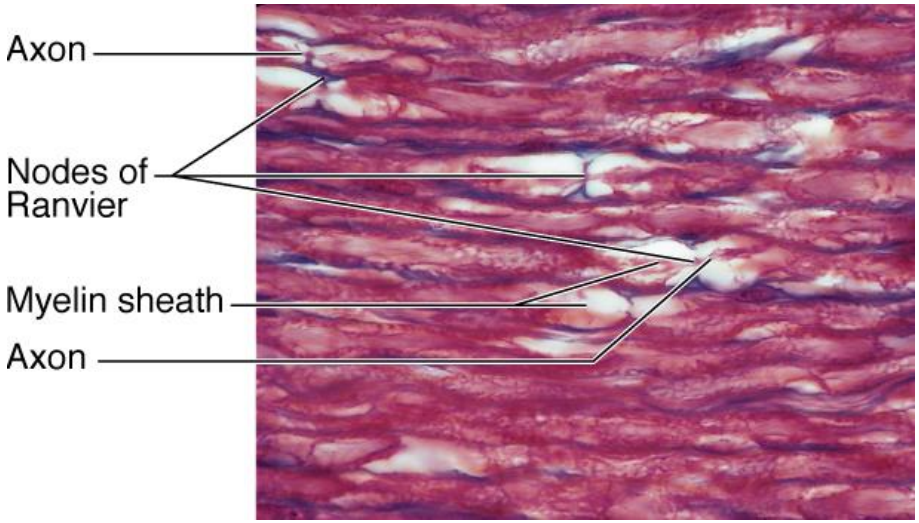


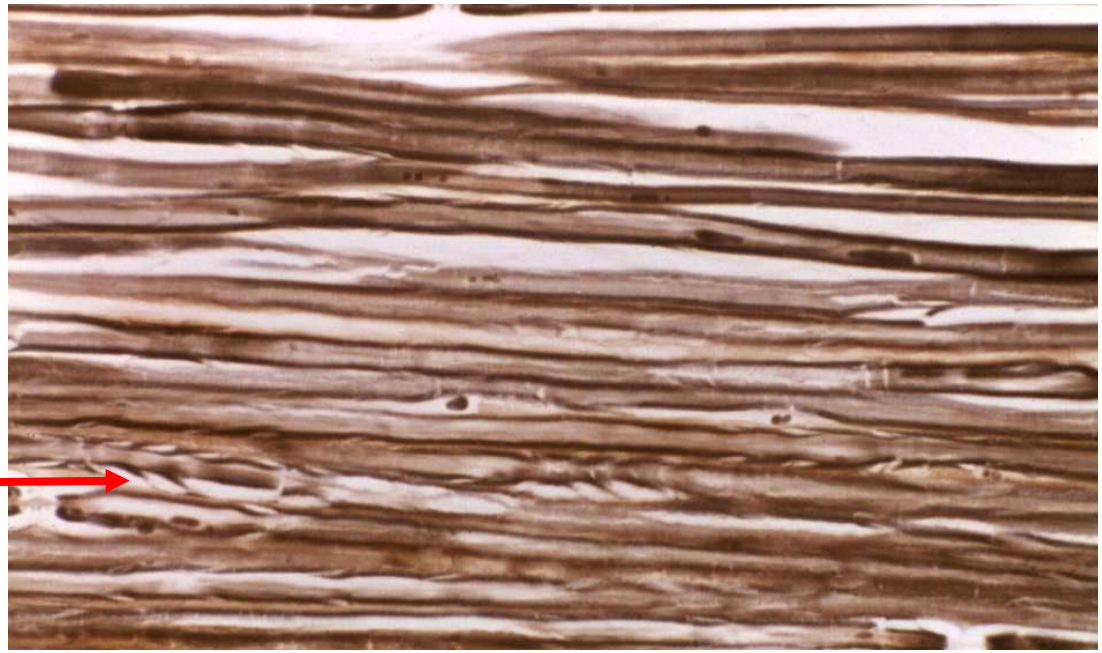




**Schmidt-Lanterman clefts**

- Schwann cell cytoplasm trapped within the lamellae of myelin

# Neuroglia in PNS – Schwann cells 7



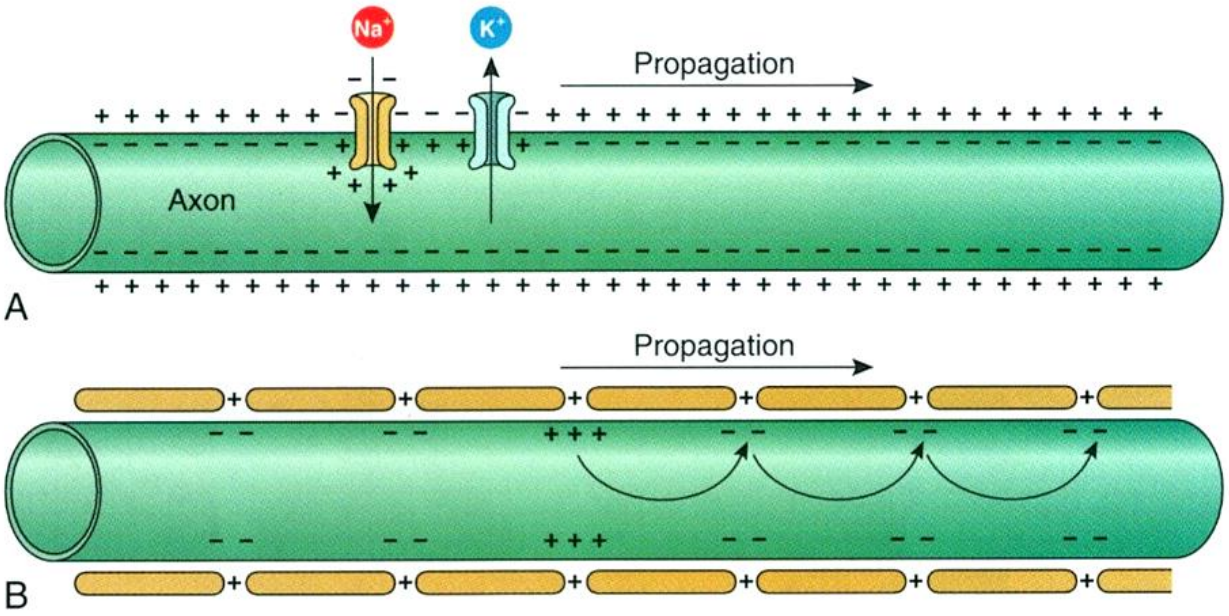



# Neuroglia – Functional effect of myelination

## Signal propagation

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

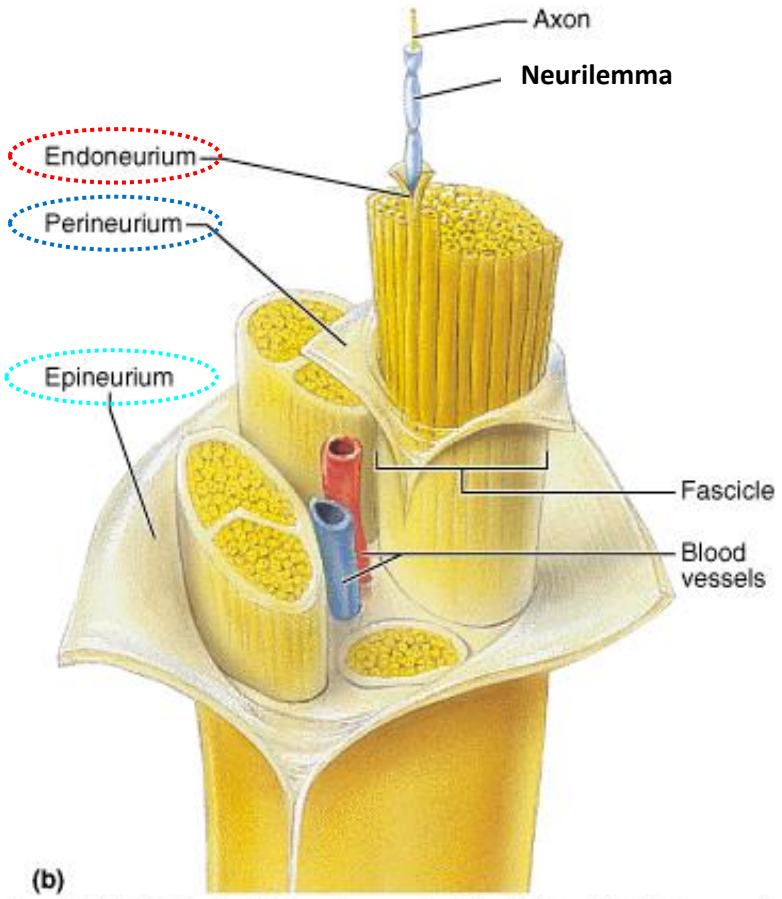
**Myelinated axons – fast** (15 – 20 m/s)




**Saltatory** (salta=jump)

# Peripheral nerve – Organization 1

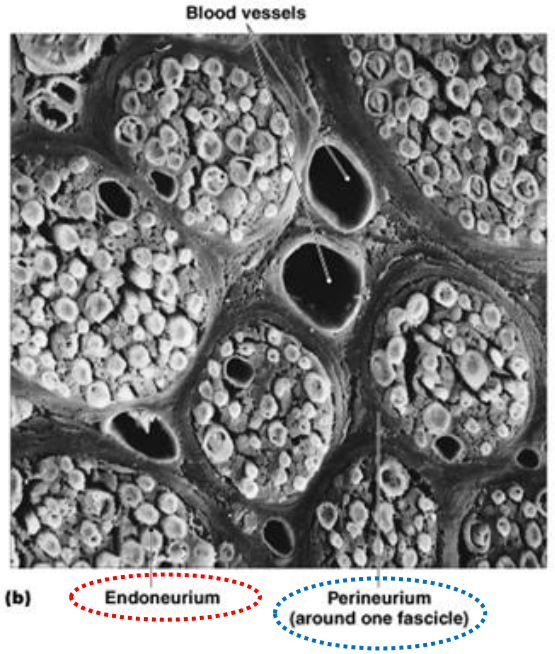
**Consists of 100's to 100,000's of myelinated and unmyelinated axons (nerve fibers).**



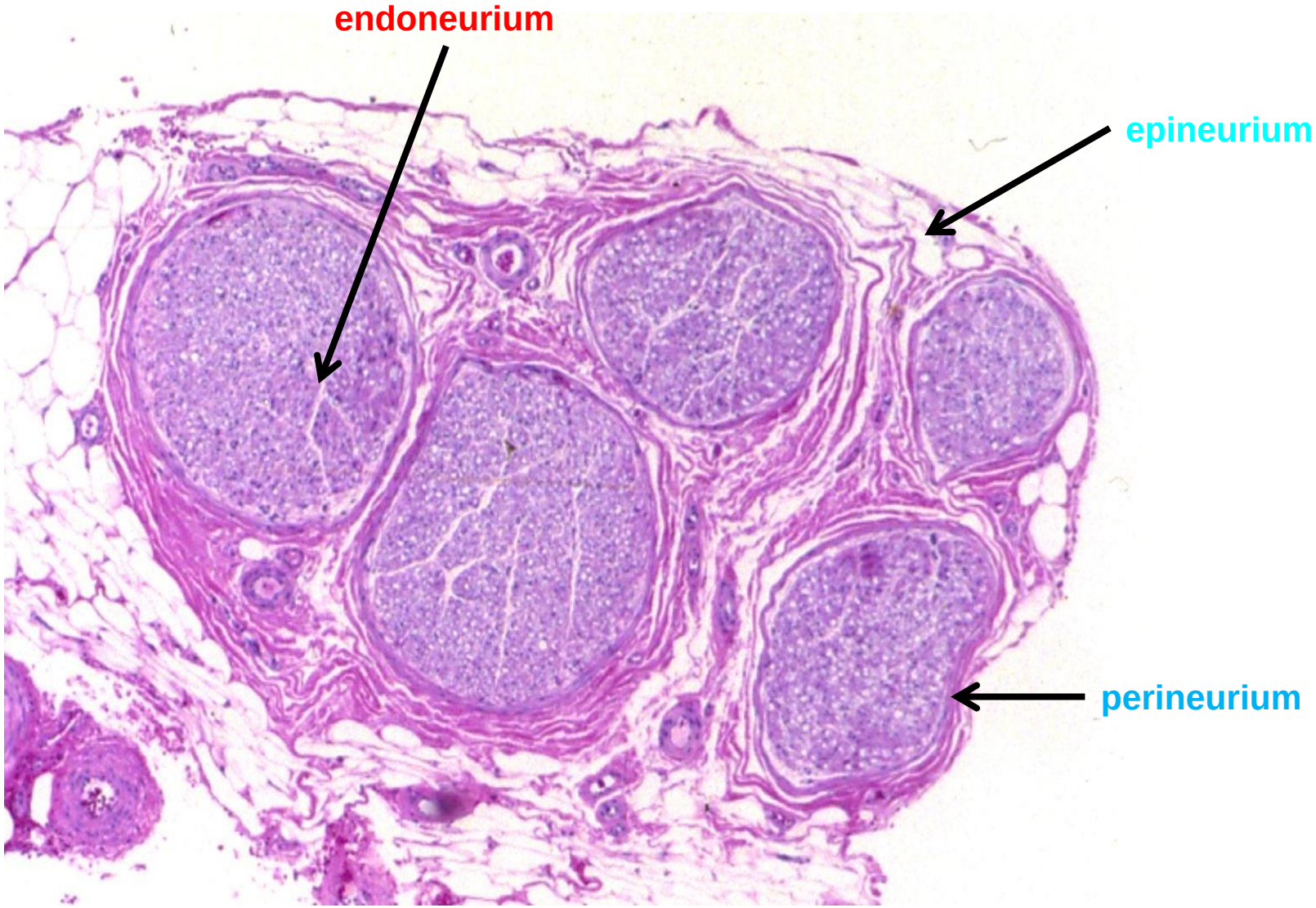



**Connective tissue layers composing nerves:**

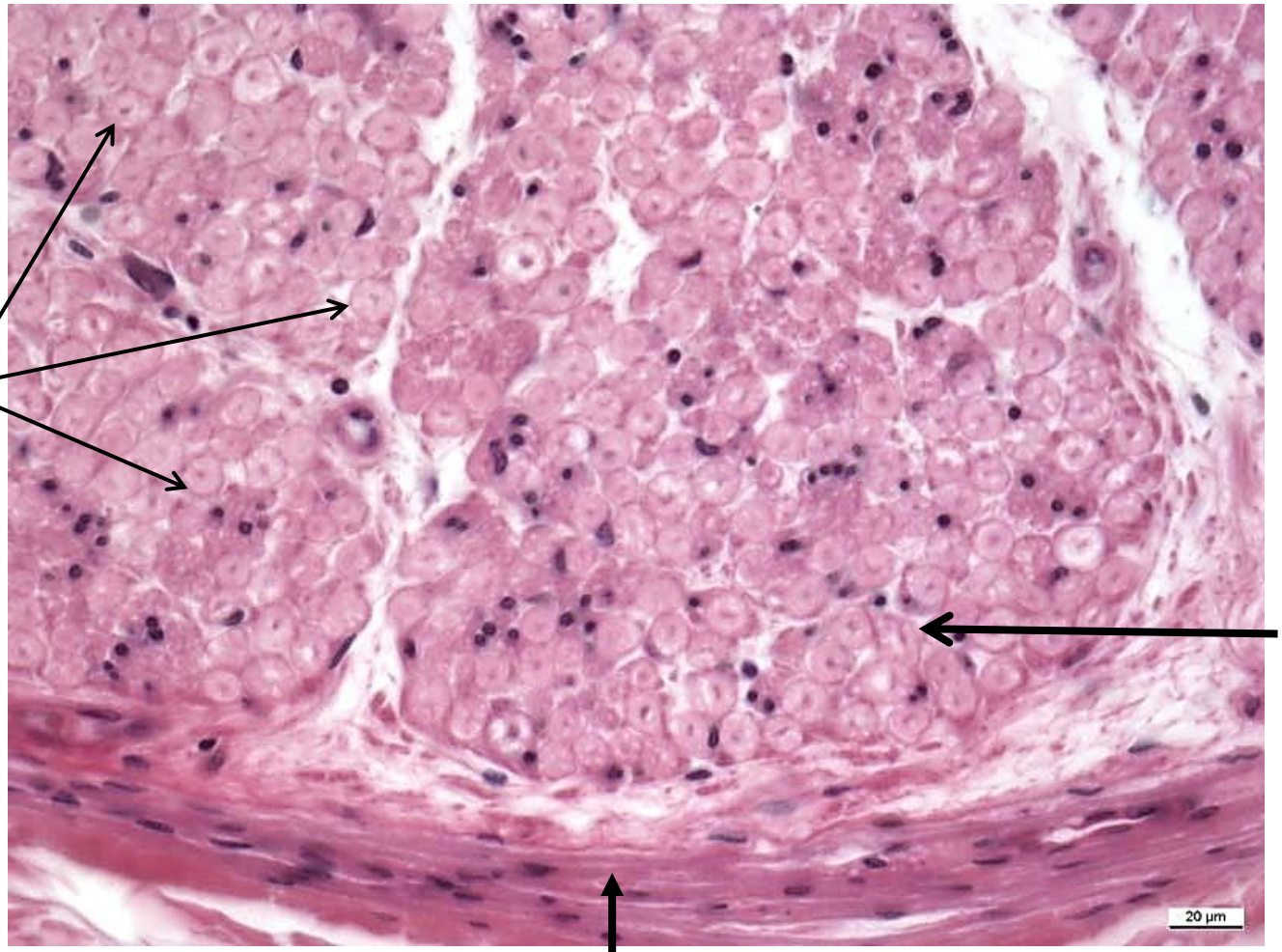
- **Endoneurium** - surrounds axons
- **Perineurium** - surrounds fascicles
- **Epineurium** - surrounds the entire nerve



# Peripheral nerve – Organization 2



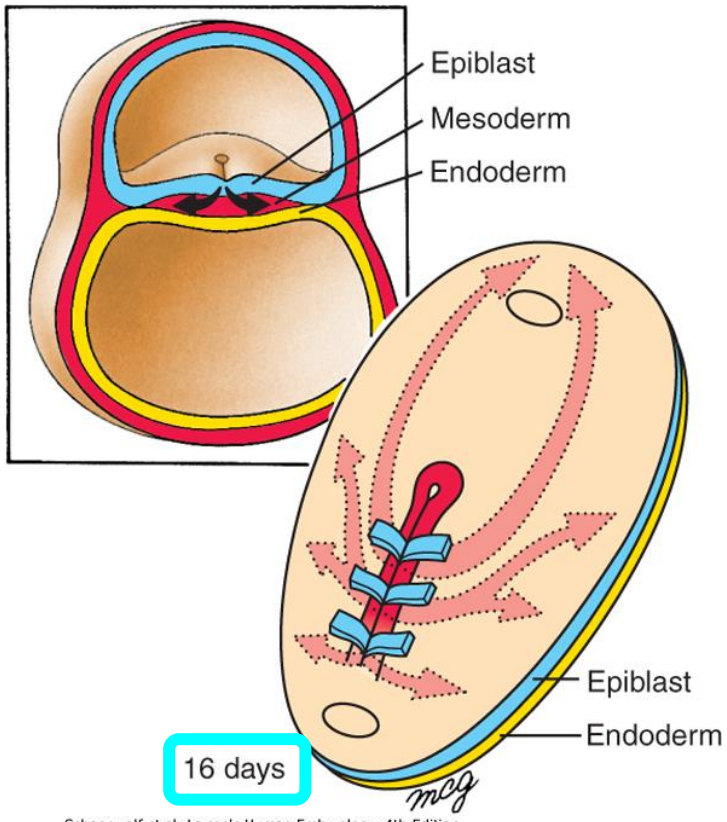
# Peripheral nerve – Organization 3



# Nerve tissue – Development 1

## Gastrulation

Formation of the three germ layers






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

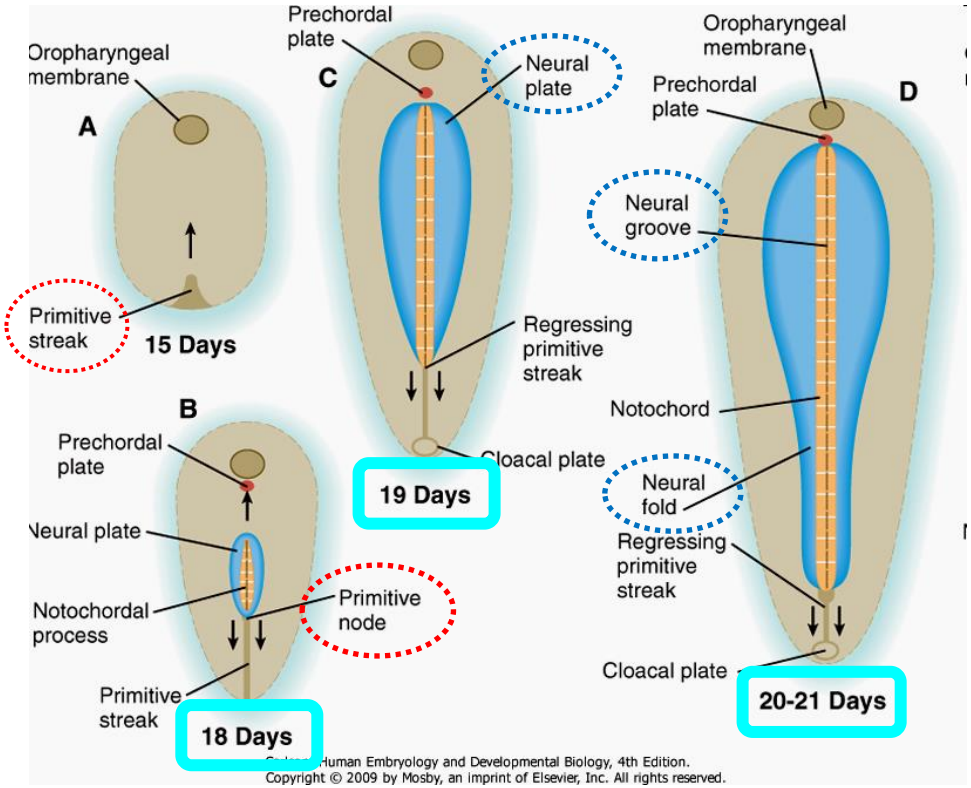
Mesoderm: middle layer, generates most of the **muscle, blood** and **connective tissues** of the body and placenta.

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

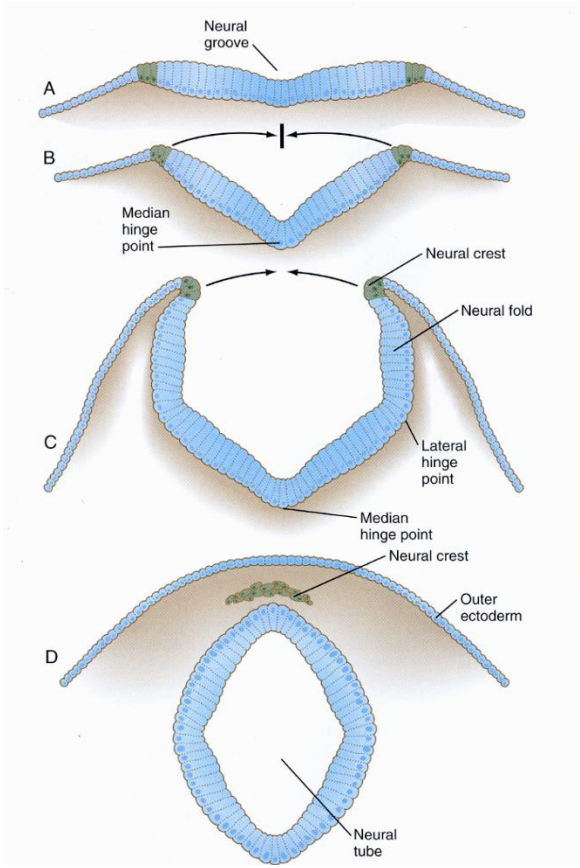
**BMP-4 antagonists**

**Ectoderm to Nerve tissue**

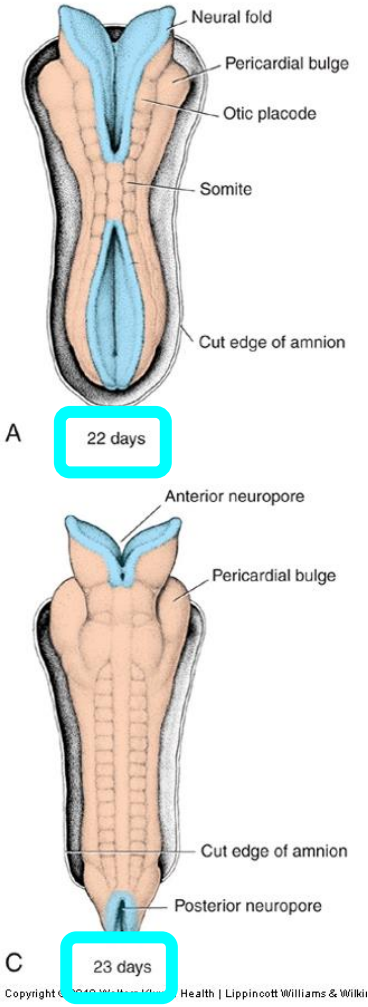
# Nerve tissue – Development 3

## Neurulation

Folding and closure of the neural plate



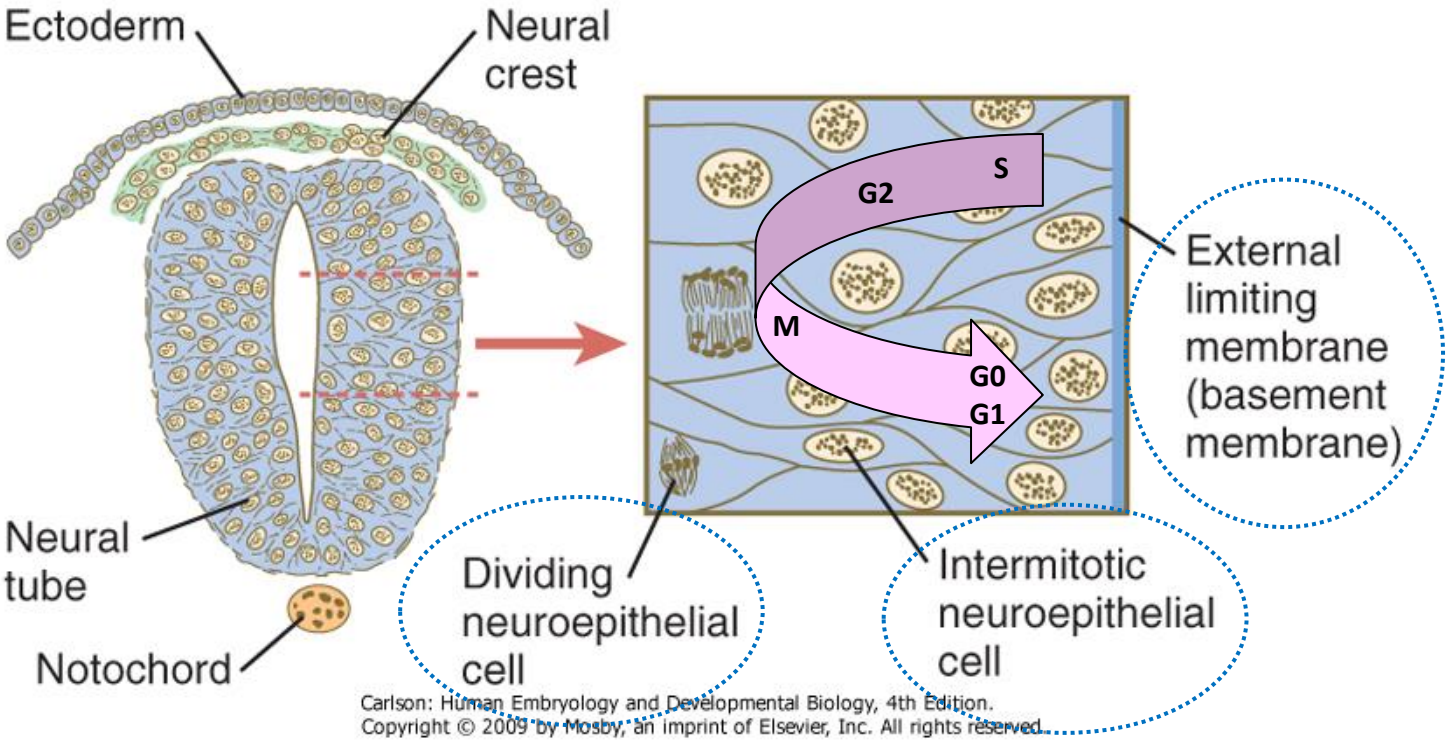

- **neural folds close**
- **neural crest delaminates** and migrates away
- **closure** happens **first in middle** of the tube and then **zips rostrally and caudally**
- **anterior neuropore closes** around **day 25**
- **posterior neuropore closes around day 28**



# Nerve tissue – Development 4

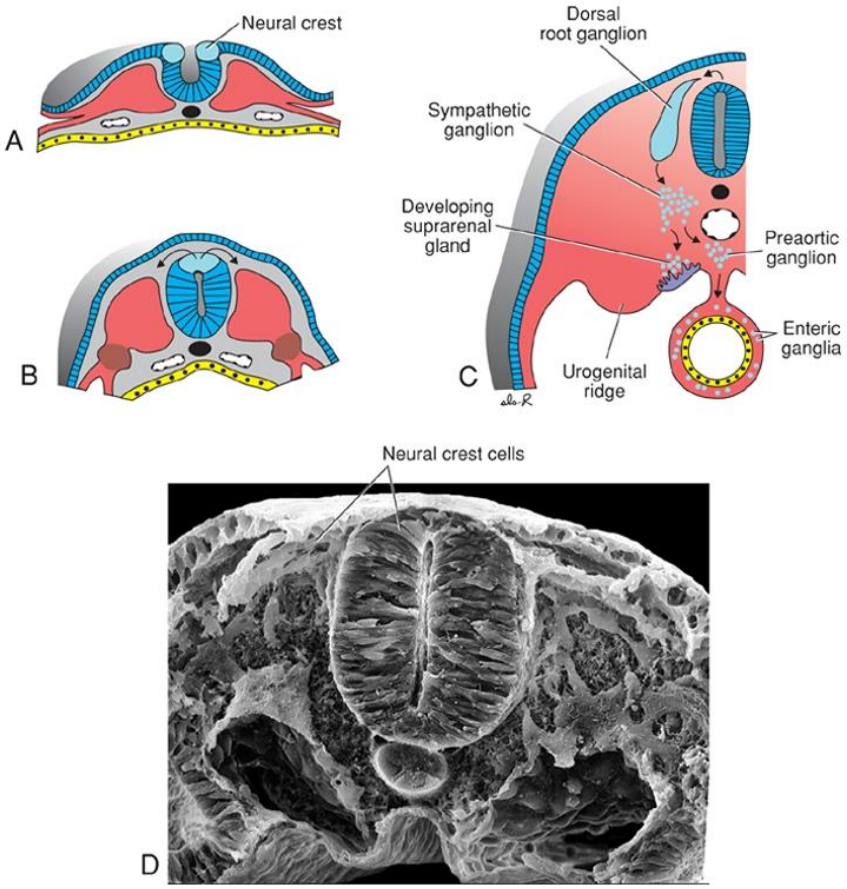
The **early neural tube** is a pseudostratified epithelium

- 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"





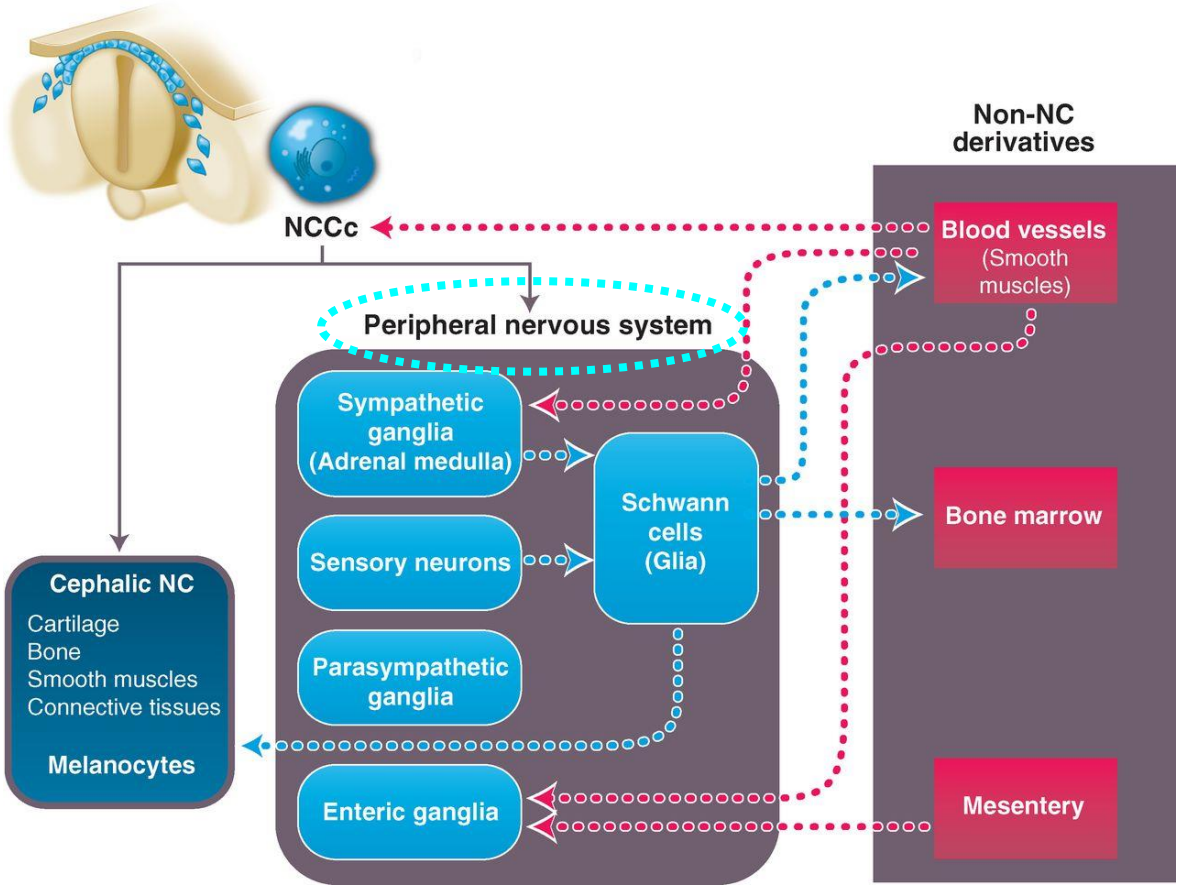

**Signals from:**
- Mesoderm
- Adjacent skin
- Neural plate

## 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

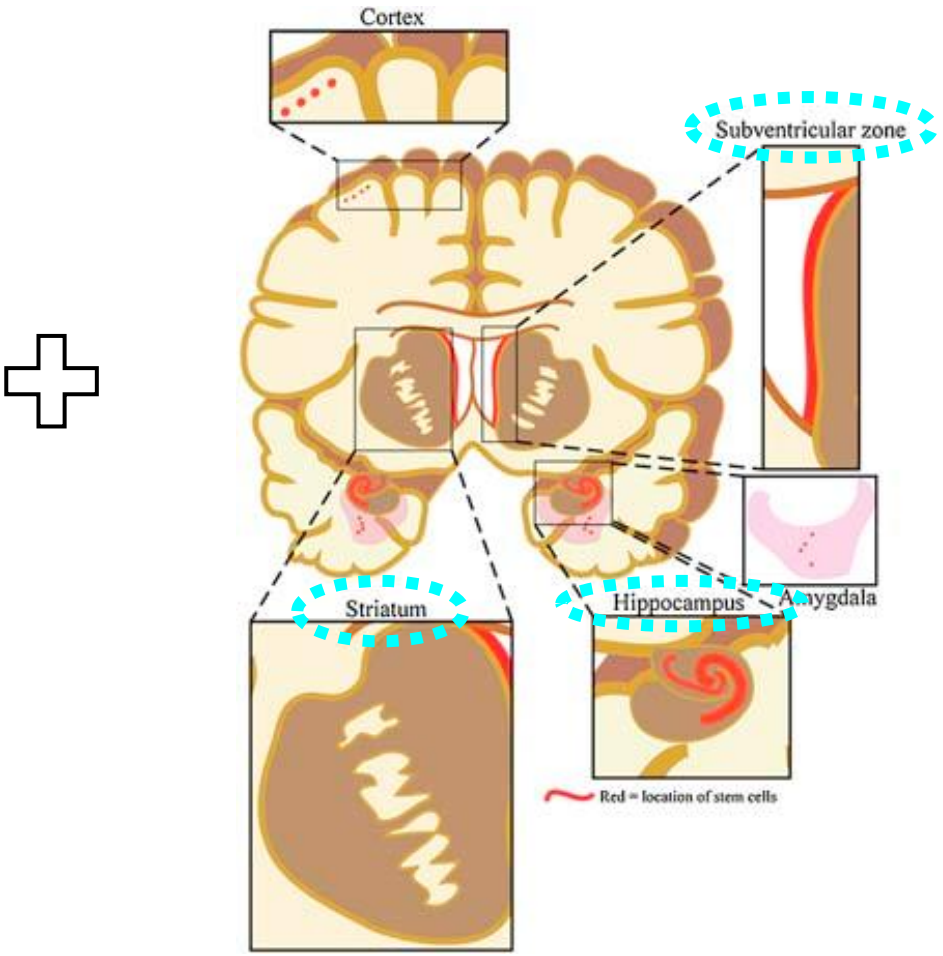


# Nerve tissue regeneration - CNS

**Stem / progenitor cells resiging in some areas of adult brain**

**Life-long plasticity of CNS**

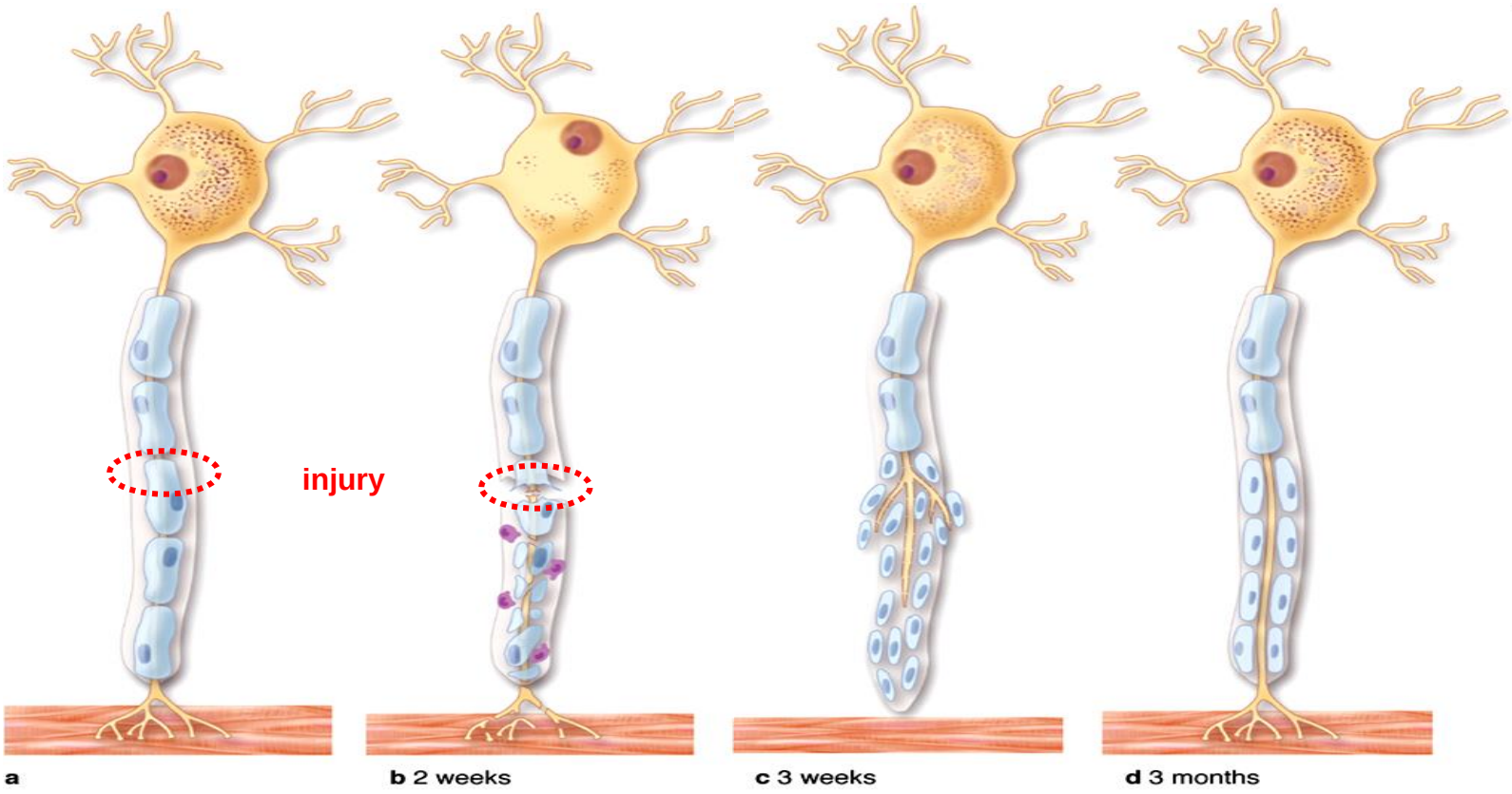
- Sprouting new dendrites
- Synthesis of new proteins
- Changes of synaptic contacts



# 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**