

# Neurohistology I: Cells and General Features

*Overall Objectives:* to understand the histological components of nervous tissue; to recognize the morphological features of neurons; and to differentiate myelinated from non-myelinated axons

## I. Basic Organization:

A. **Central Nervous System (CNS)**—brain and spinal cord

B. **Peripheral Nervous System (PNS)**—all cranial and spinal nerves and their associated roots and ganglia

Functional PNS Divisions:

A. Somatic Nervous System—a one neuron system that innervates (voluntary) skeletal muscle or somatosensory receptors of the skin, muscle & joints.

B. Autonomic Nervous System—a two neuron visceral efferent system that innervates cardiac and smooth muscle and glands. It is involuntary and has two major subdivisions:

- 1) Sympathetic (thoracolumbar)
- 2) Parasympathetic (craniosacral)

## II. Histological Components:

A. **Supporting (non-neuronal) Cells**— Glial cells provide support and protection for neurons and outnumber neurons 10:1. The CNS has three types and the PNS has one:

1. **Astrocytes**—star-shaped cells that play an active role in brain function by influencing the activity of neurons. They are critical for 1) recycling neurotransmitters; 2) secreting neurotrophic factors (e.g., neural growth factor) that stimulate the growth and maintenance of neurons; 3) dictating the number of synapses formed on neuronal surfaces and modulating synapses in adult brain; and 4) maintaining the appropriate ionic composition of extracellular fluid surrounding neurons, by absorbing excess potassium and other larger molecules.
2. **Oligodendrocytes**— The oligodendrocyte is the analog of the Schwann cell in the central nervous system and is responsible for forming myelin sheaths around brain and spinal cord axons. Myelin is an electrical insulator.
3. **Microglia**—are the smallest of glial cells. They represent the intrinsic immune effector cells of the CNS and underlie the inflammation response that occurs following damage to the central nervous system and the invasion of microorganisms.
4. **Lemmocytes (Schwann Cells)**— Schwann cells are glia cells of the PNS. They wrap individually around the shaft of peripheral axons, forming a layer or myelin sheath along segments of the axon. The Schwann cell membrane, which forms the myelin sheath, is composed primarily of lipids; the lipid serves as an insulator thereby speeding the transmission rate of action potentials along the axon.

CNS

PNS

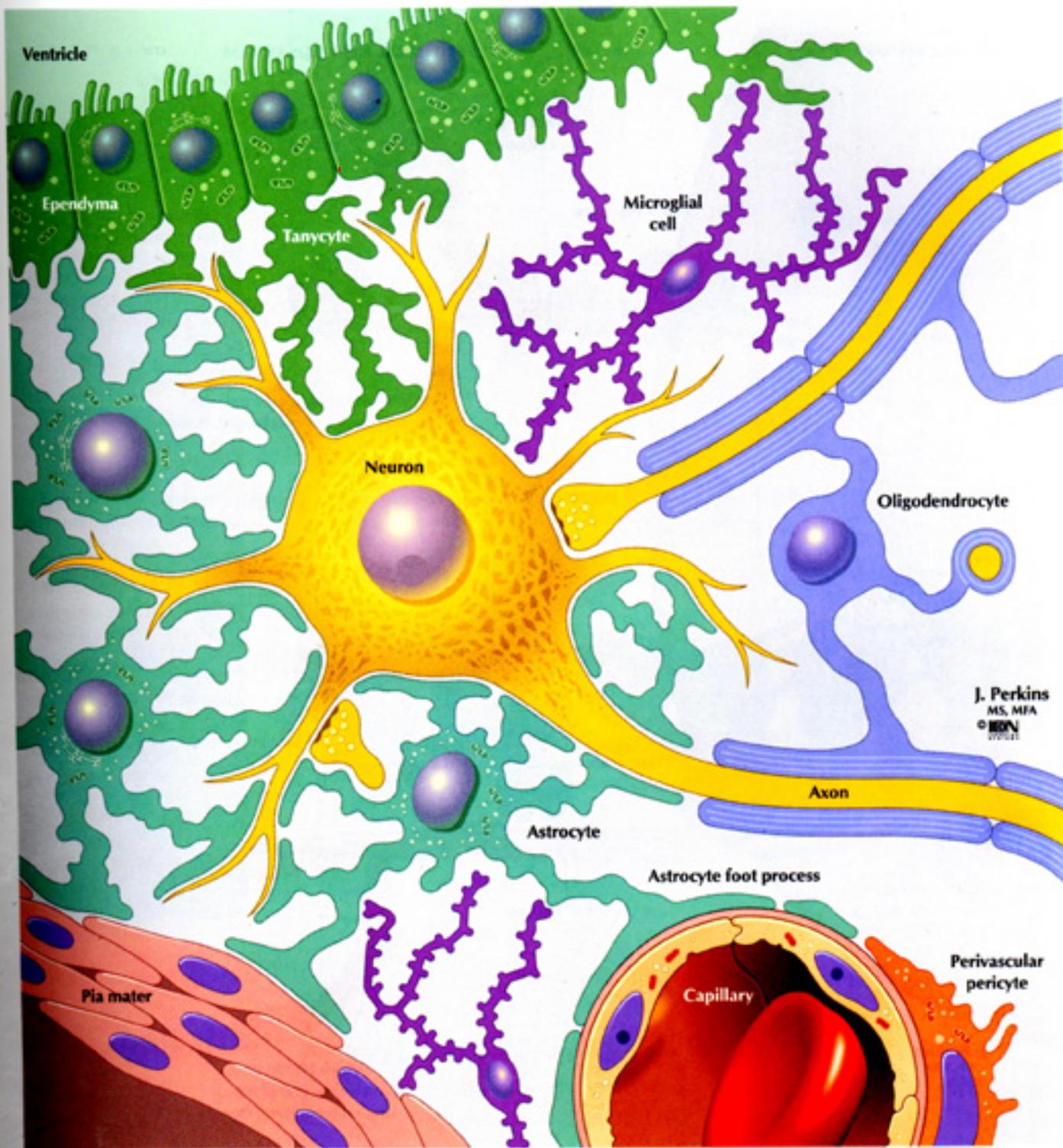


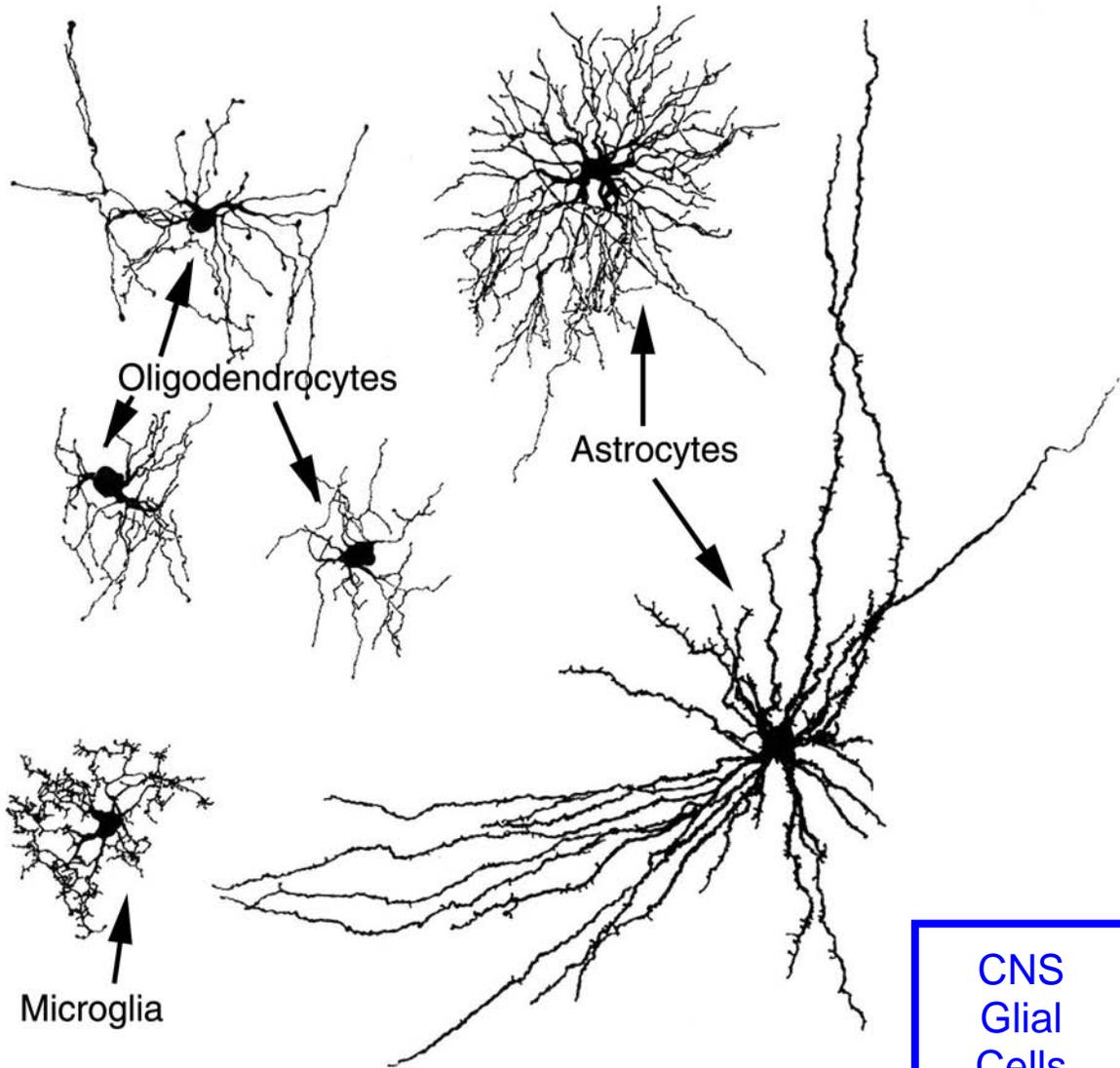
FIGURE I.4: GLIAL CELL TYPES

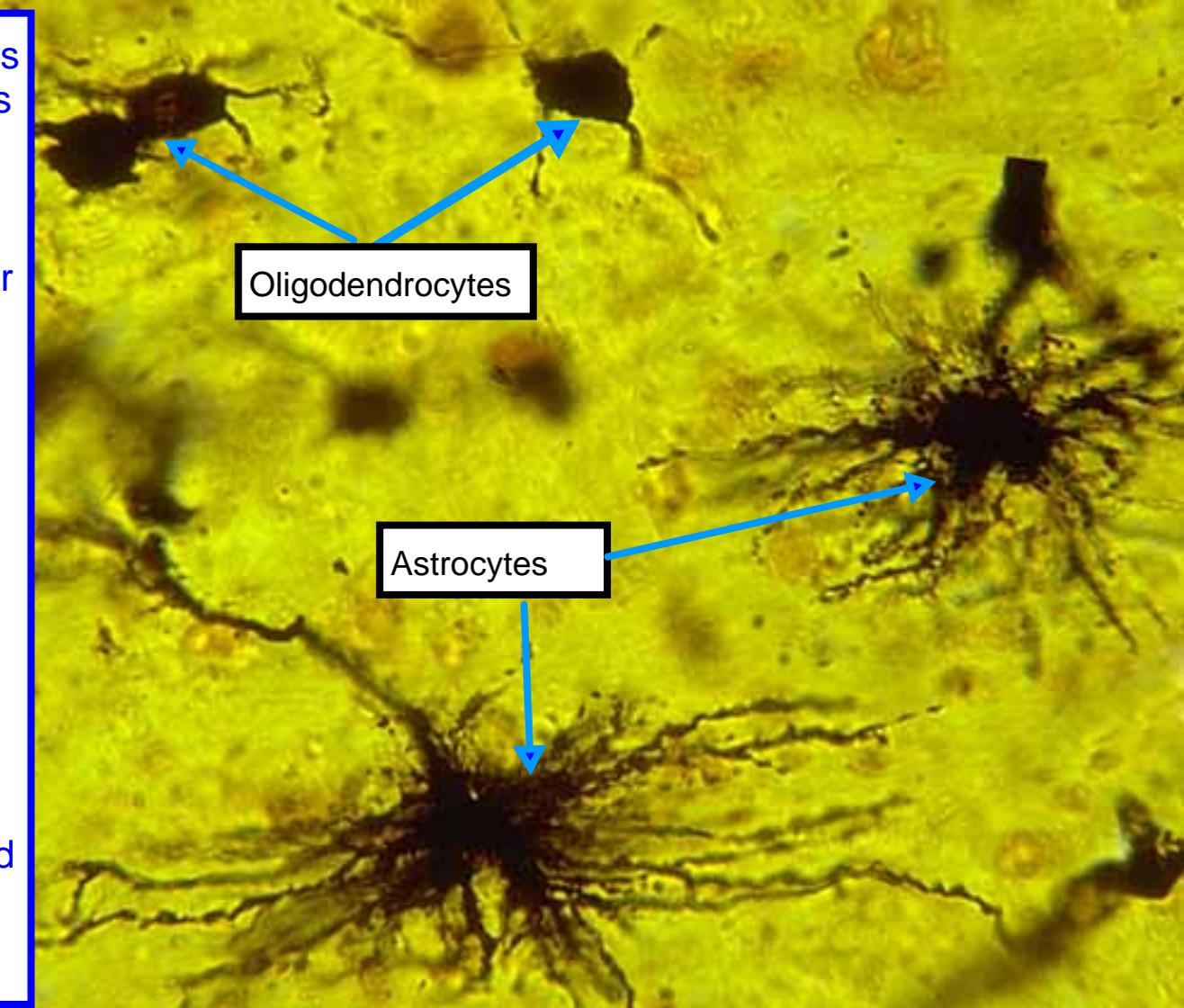


Neuron

Oligodendrocytes

Astrocyte





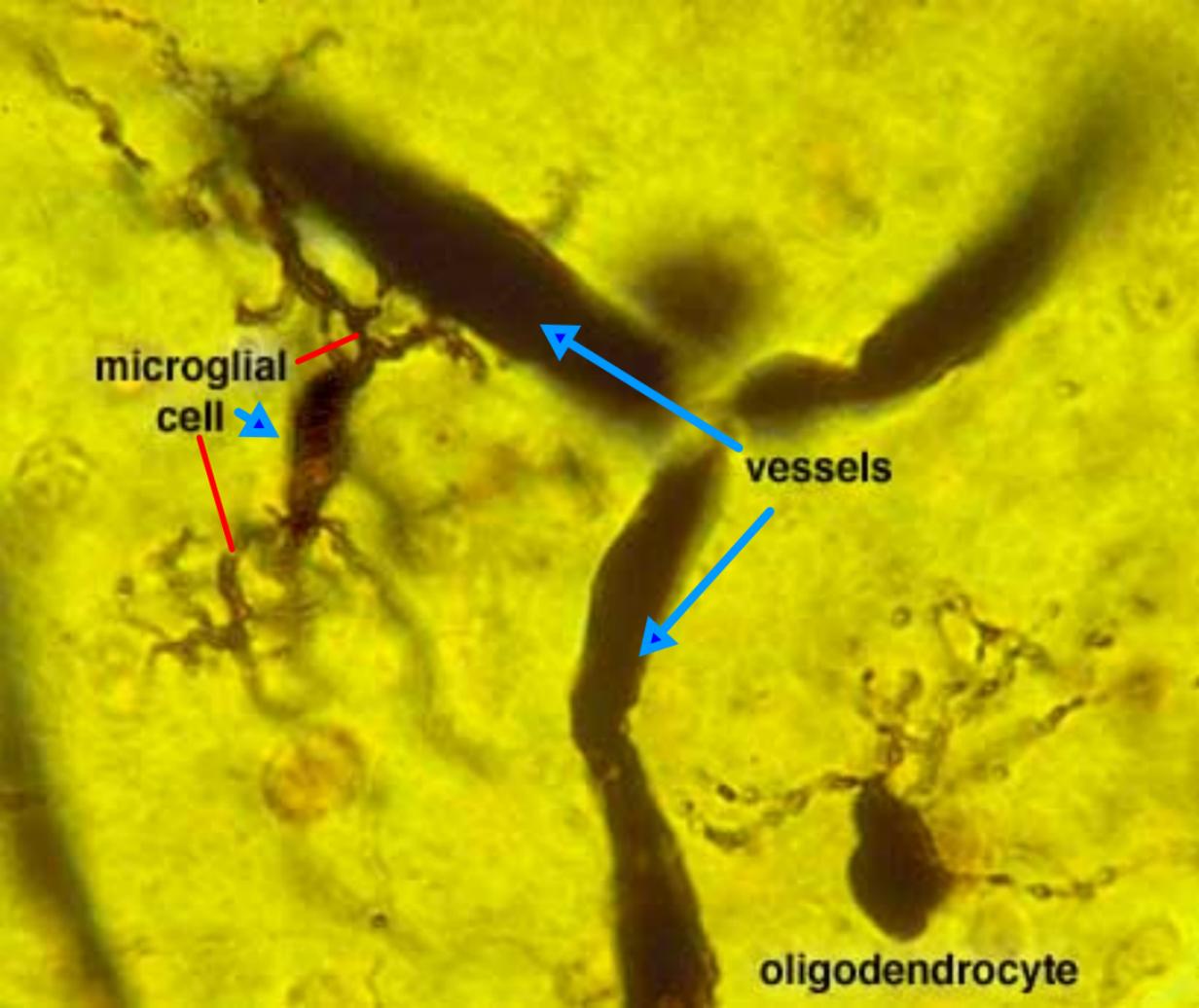
Oligodendrocytes

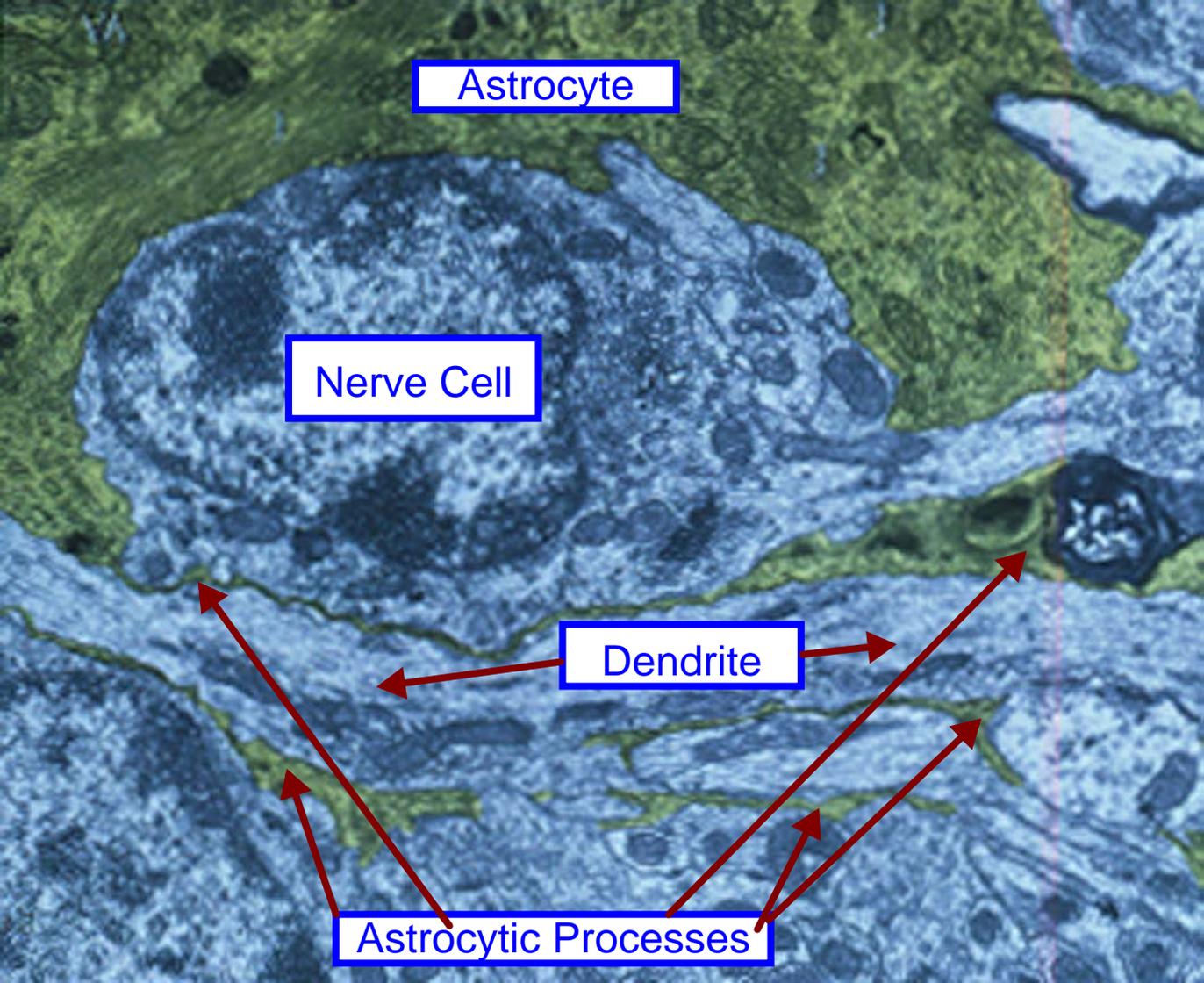
Astrocytes

microglial  
cell

vessels

oligodendrocyte





Astrocyte

Nerve Cell

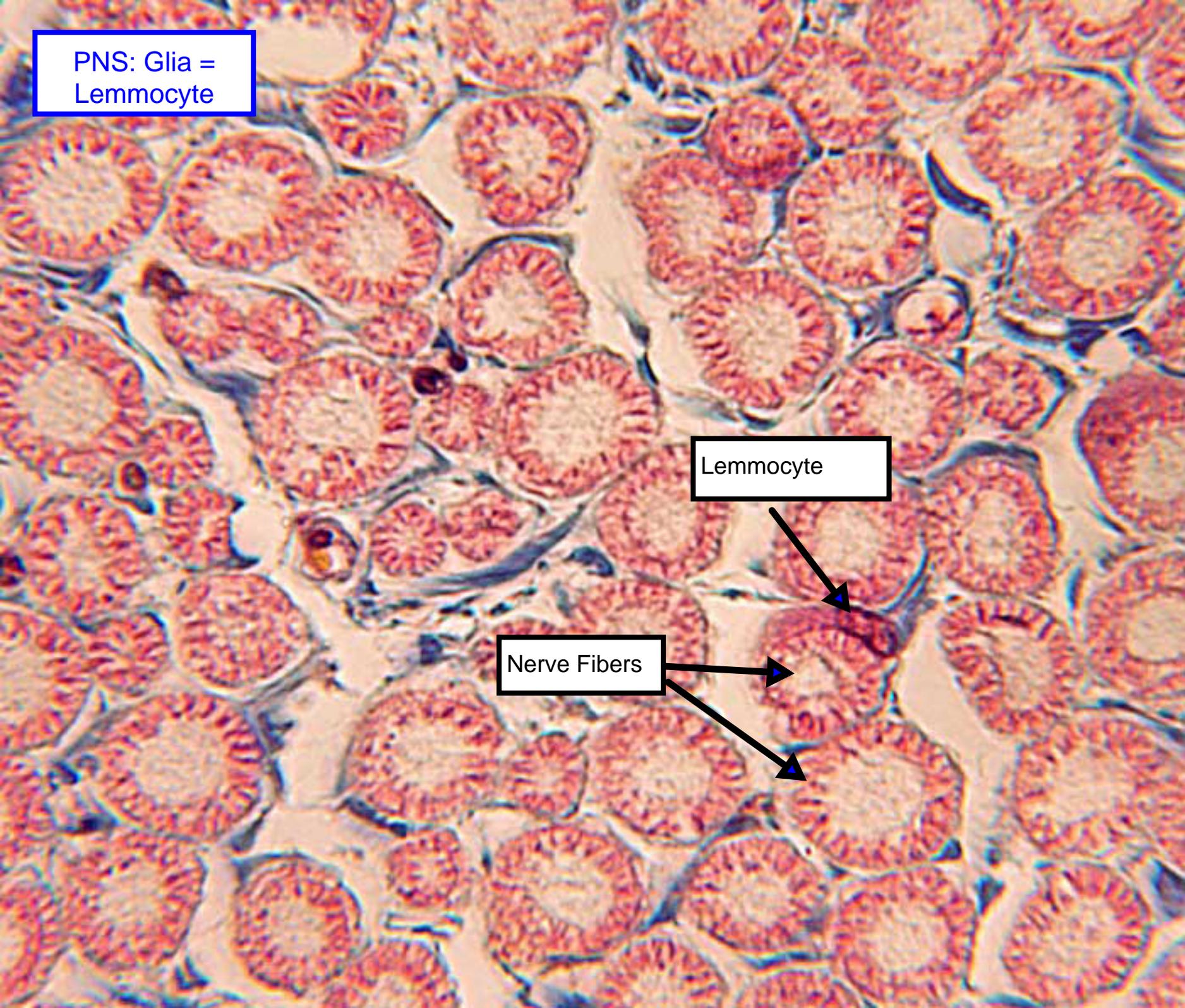
Dendrite

Astrocytic Processes

PNS: Glia =  
Lemmocyte

Lemmocyte

Nerve Fibers



## 5. Ependyma

in addition to the above glial cells, the CNS has epithelial-like cells that line the ventricles of the brain and the central canal of the spinal cord.

*Note:* Glial cells are capable of reproduction, and when control over this capacity is lost primary brain tumors result. Astrocytomas and glioblastomas are amongst the most deadly or malignant forms of cancer.

**B. Neurons** (nerve cells)—neurons are the structural and functional units of the nervous system; they are specialized to conduct electrical signals.

*Note:* The plasma membrane of the neuron contains both voltage gated ion channels (involved in generation and conduction of electrical signals) and receptors (which bind neurotransmitters and hormones and use distinct molecular mechanisms for transmembrane signaling; examples include ligand-gated ion channels and G protein coupled receptors).

**1. Morphological Features of neurons** (3 component parts; see Fig.1 below):

**A. Cell body** — the expanded portion of the neuron that contains the nucleus;  
— stains basophilically due to the abundance of RER and polyribosomes;  
— the clumps of RER & polyribosomes are referred to as **Nissl Bodies**.

**B. Dendrites** — one to many extensions of the cell body;  
— specialized to receive input from other neurons or from receptors;  
— contain Nissl bodies in their proximal parts and thus the initial portions of dendrites stain basophilically;  
— often have small protrusions, called dendritic spines, that expand the dendritic surface area and serve as sites of synaptic contact.

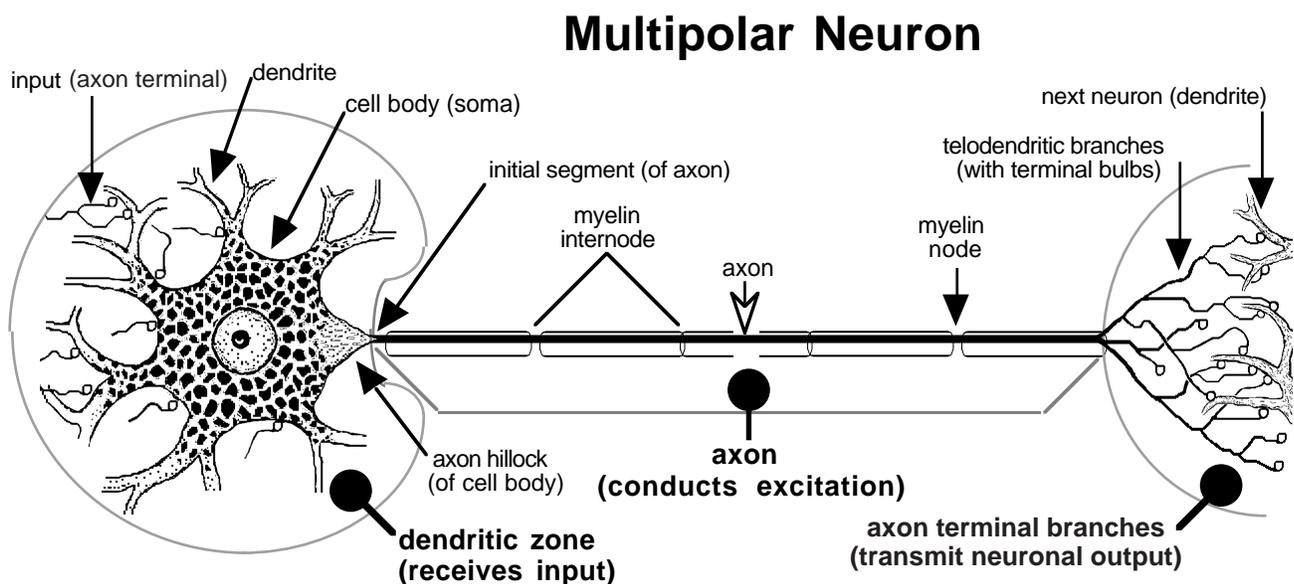


Figure 1: Diagram of a neuron illustrating its component parts



Ependymal  
cells

5. **Ependyma** — in addition to the above glial cells, the CNS has epithelial-like cells that line the ventricles of the brain and the central canal of the spinal cord.

**Clinical Note:**

*Note:* Glial cells are capable of reproduction, and when control over this capacity is lost primary brain tumors result. Astrocytomas and glioblastomas are amongst the most deadly or malignant forms of cancer.

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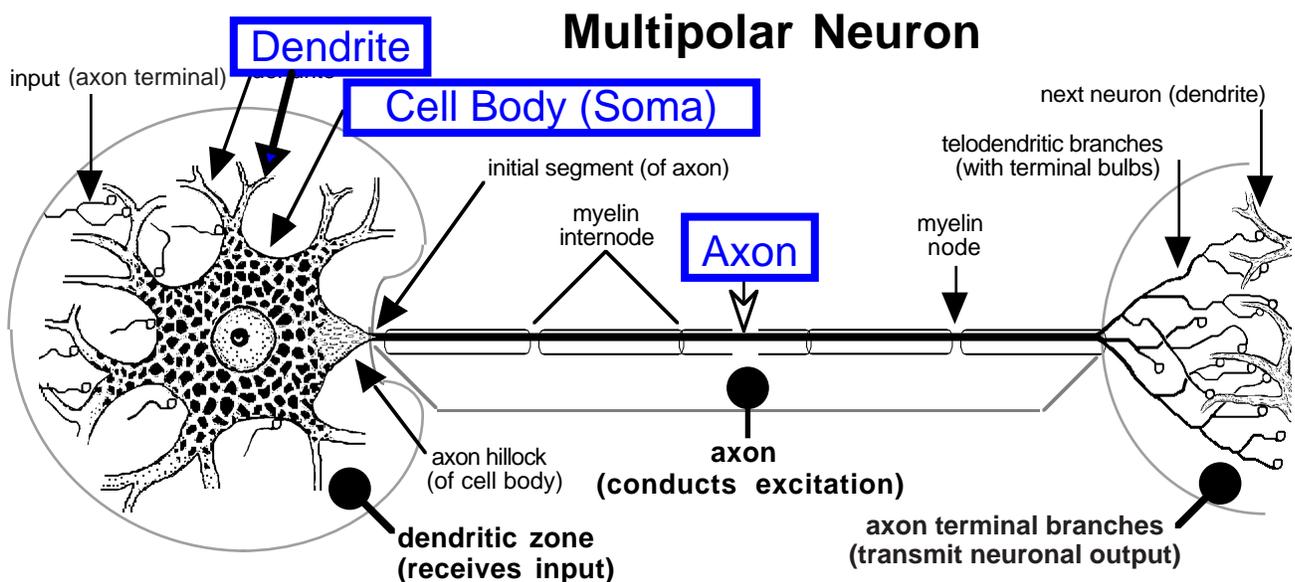
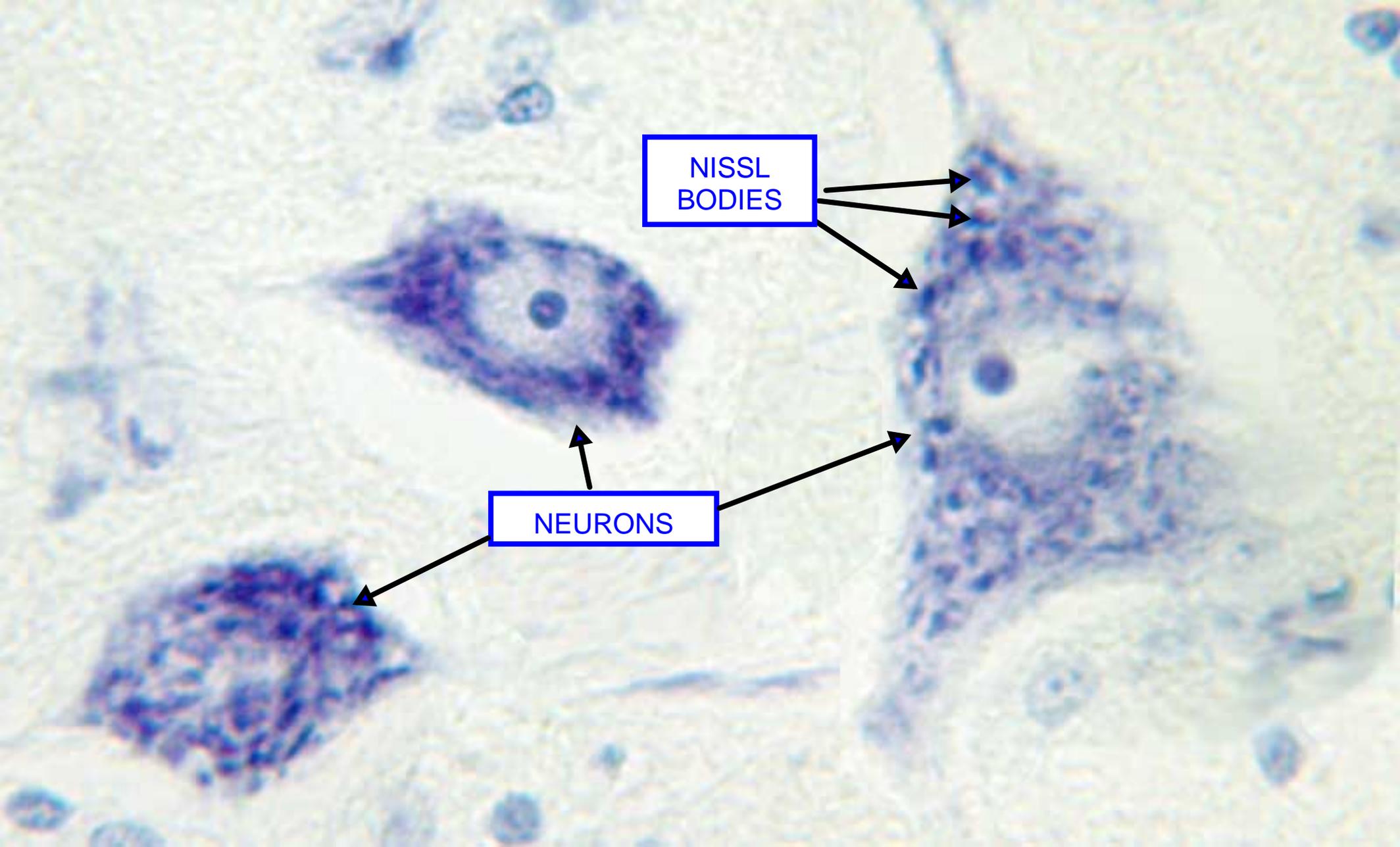
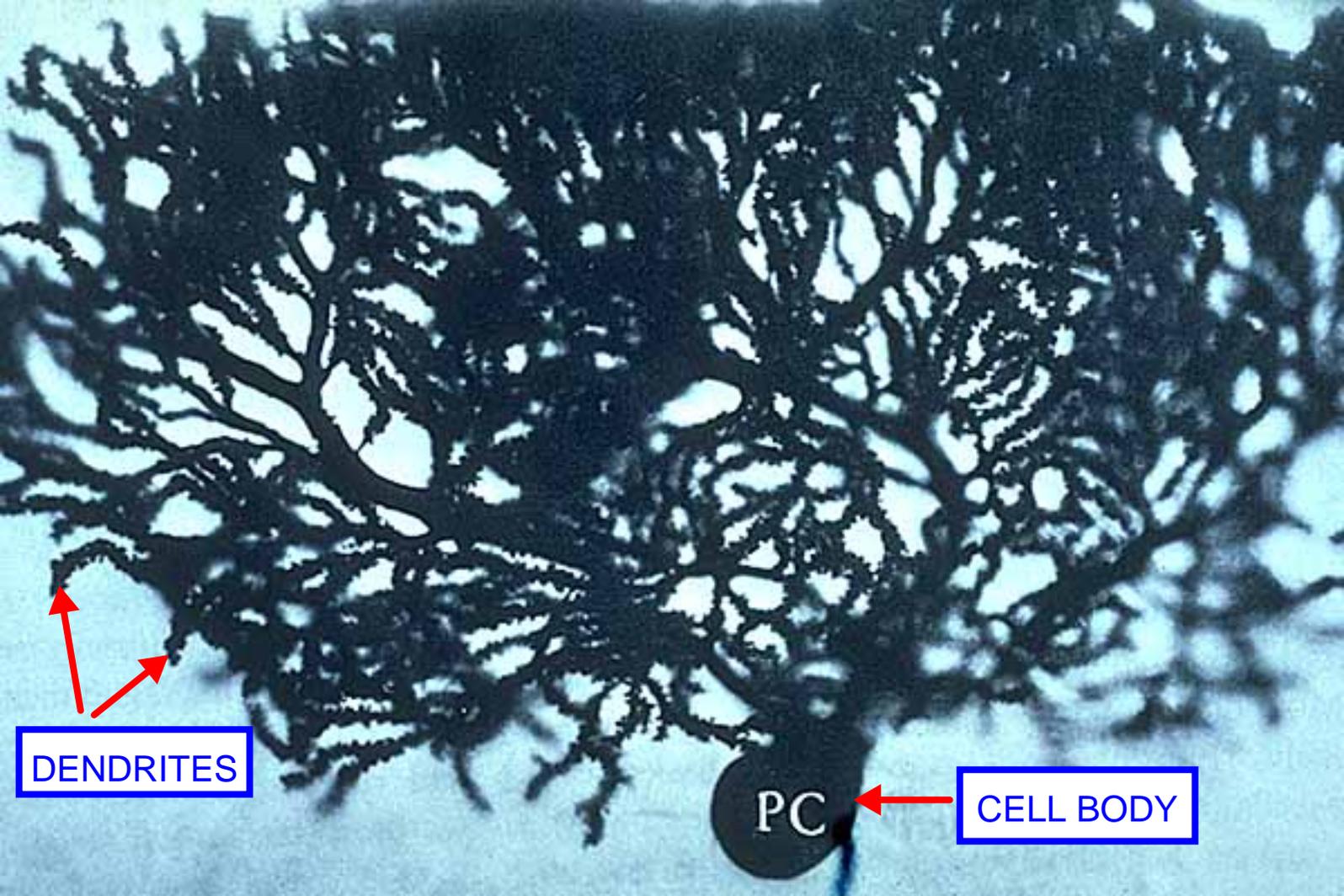


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NISL BODIES

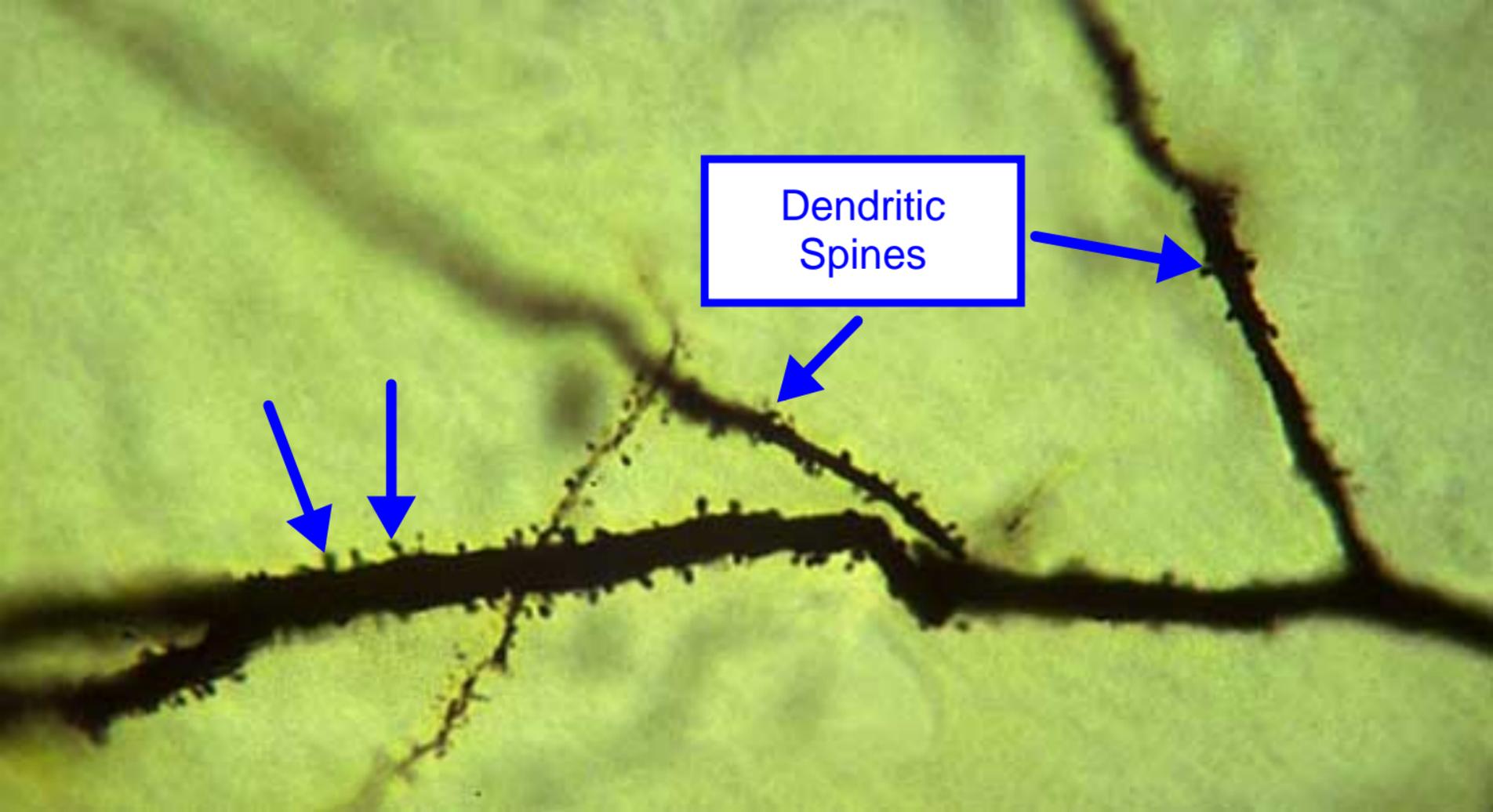
NEURONS



DENDRITES

PC

CELL BODY



A fluorescence micrograph of a neuron, showing its cell body and several branching processes. The processes are dark against a light green background. Small, dark, bulbous protrusions called dendritic spines are visible along the processes. A white box with a blue border contains the text "Dendritic Spines". Three blue arrows point from this box to specific examples of dendritic spines on different processes.

Dendritic  
Spines

## C. AXON

- typically one per neuron;
- an extension of the cell body that is specialized for conducting electrical impulses (action potentials).
- lacks Nissl bodies and does not stain with routine histological stains.

*Note:* Axons are either **myelinated** (surrounded by a fatty insulating sheath that speeds conduction of the electrical impulse) or **non-myelinated** (lacking a myelin sheath and thus conduct impulses slowly).

### 2. Definitions:

A. **Ganglion** — a collection of neuron cell bodies situated in the PNS

B. **Nucleus** — this term is used in a special sense in neurobiology to describe a collection of neuronal cell bodies in the CNS (accumulation of gray matter)

C. **Nerves** — bundles of axons that extend out from the brain as cranial nerves and from the spinal cord as spinal nerves (surrounded by connective tissue sheaths)

D. **Tract** — a bundle of axons (nerve fibers) within the CNS (connective tissue is absent)

### 3. Neuronal Classification:

A. *Anatomically*, by number of processes:

#### 1) Unipolar (pseudounipolar)

**Neuron** — has one process that bifurcates; the cell body of this neuronal type is found in spinal and cranial ganglia.

2) **Bipolar Neuron** — has 2 processes (relatively rare; retina of eye and certain cranial ganglia).

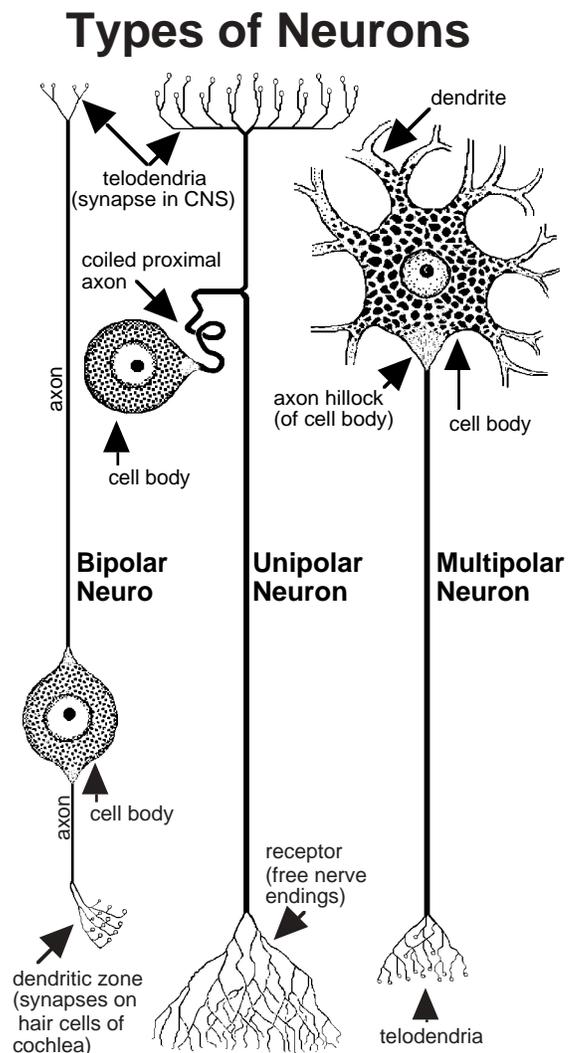
3) **Multipolar Neuron** — many processes; typically 1 axon and 2 or more dendrites (most common type of neuron).

B. *Functionally*:

1) **Motor (Efferent)** — related to innervation of muscle, glands etc.; activation of these neurons leads to some motor event (i.e., contraction of a muscle).

2) **Sensory (Afferent)** — related to the transfer of sensory information (i.e., pain, touch, pressure, etc.); e.g., neurons of spinal (dorsal root) ganglia.

3) **Interneurons** — neither motor or sensory (e.g., neurons responsible for the various spinal reflexes).



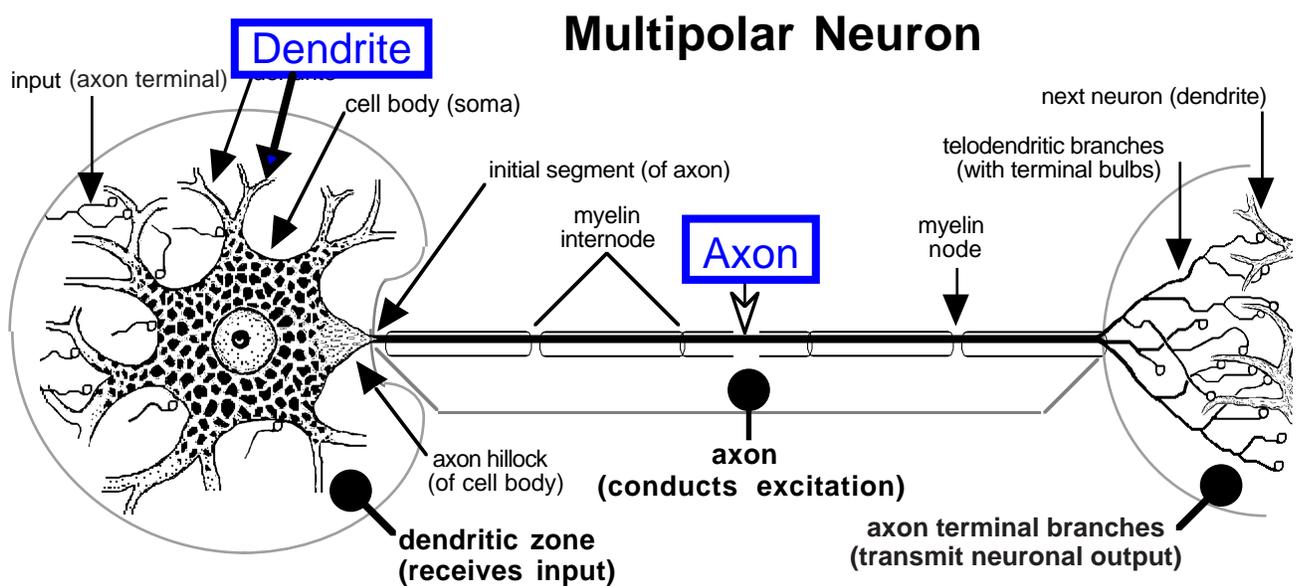
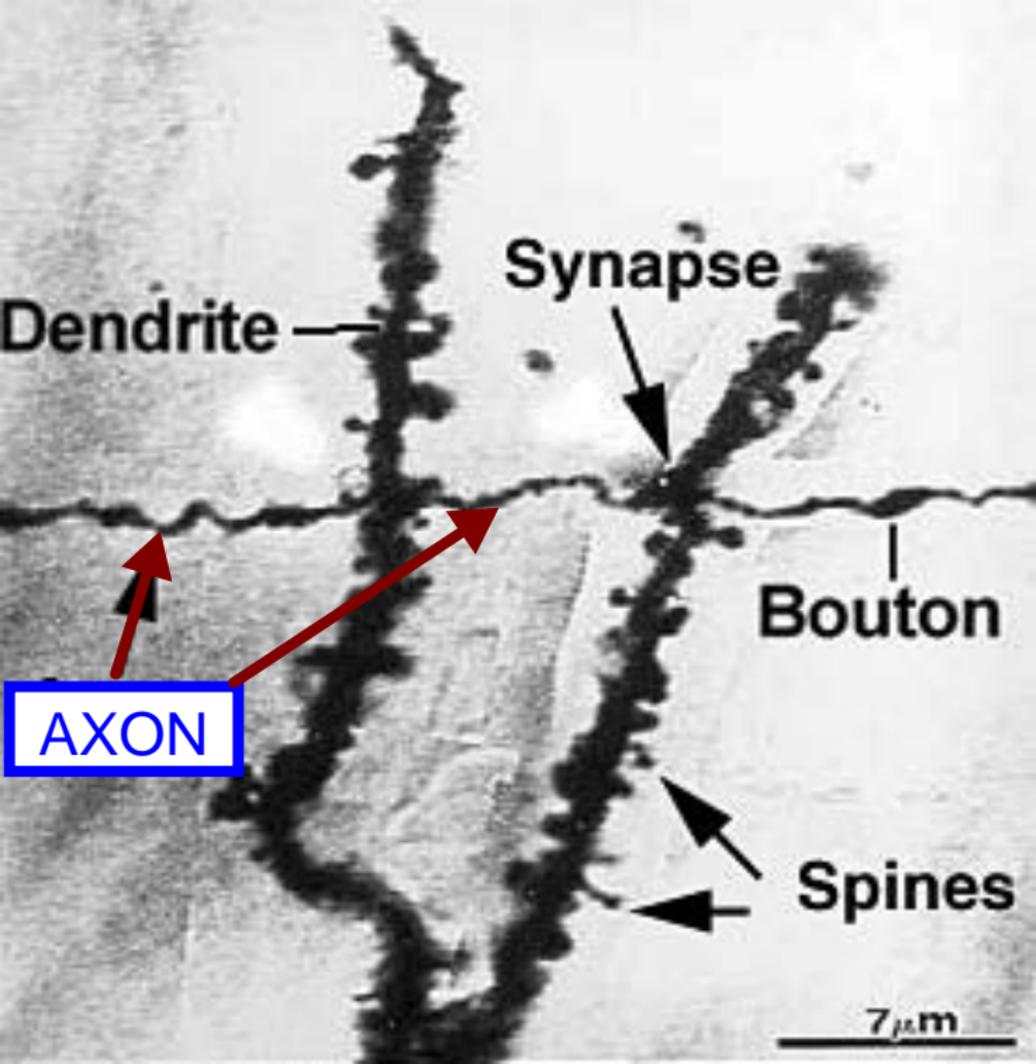
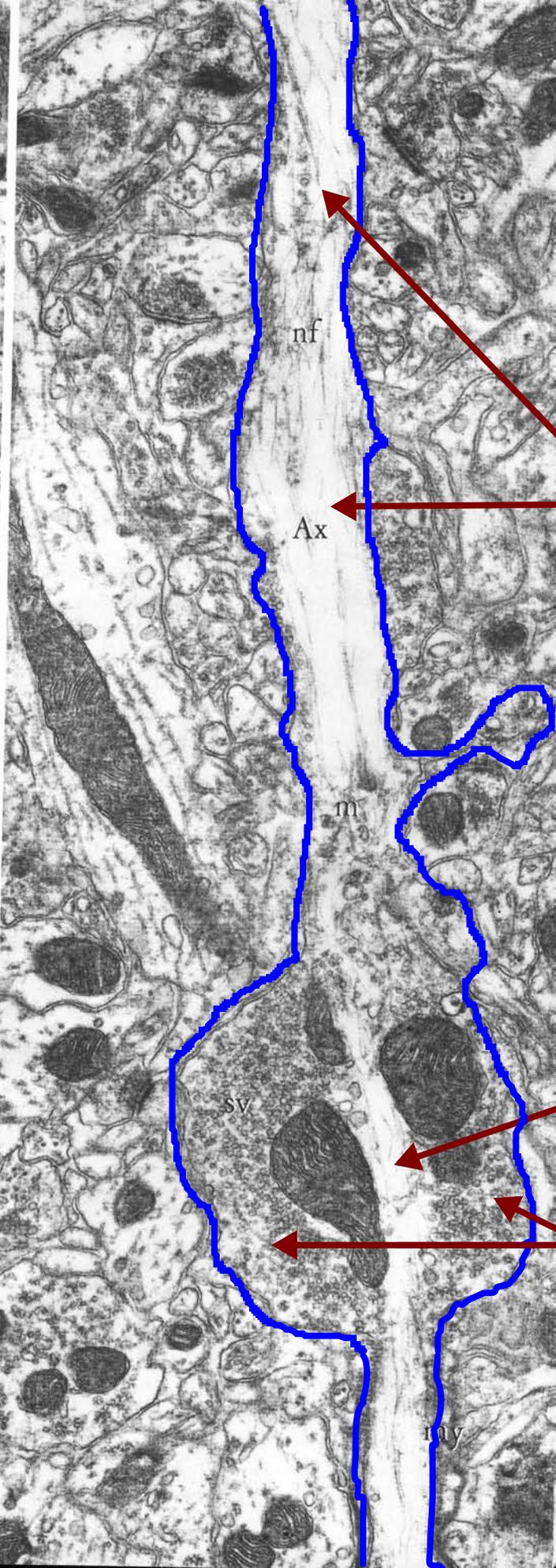


Figure 1: Diagram of a neuron illustrating its component parts





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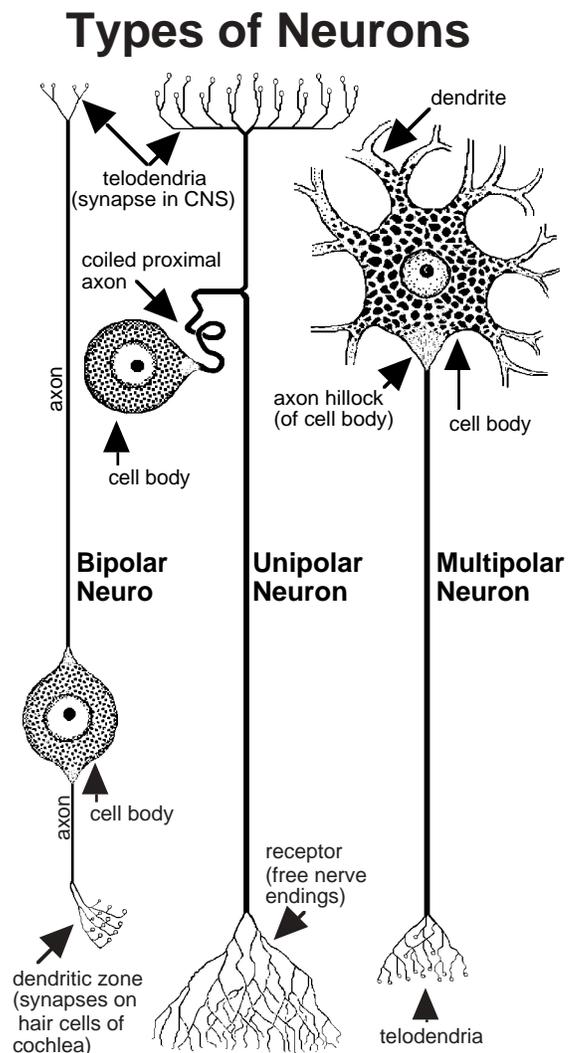
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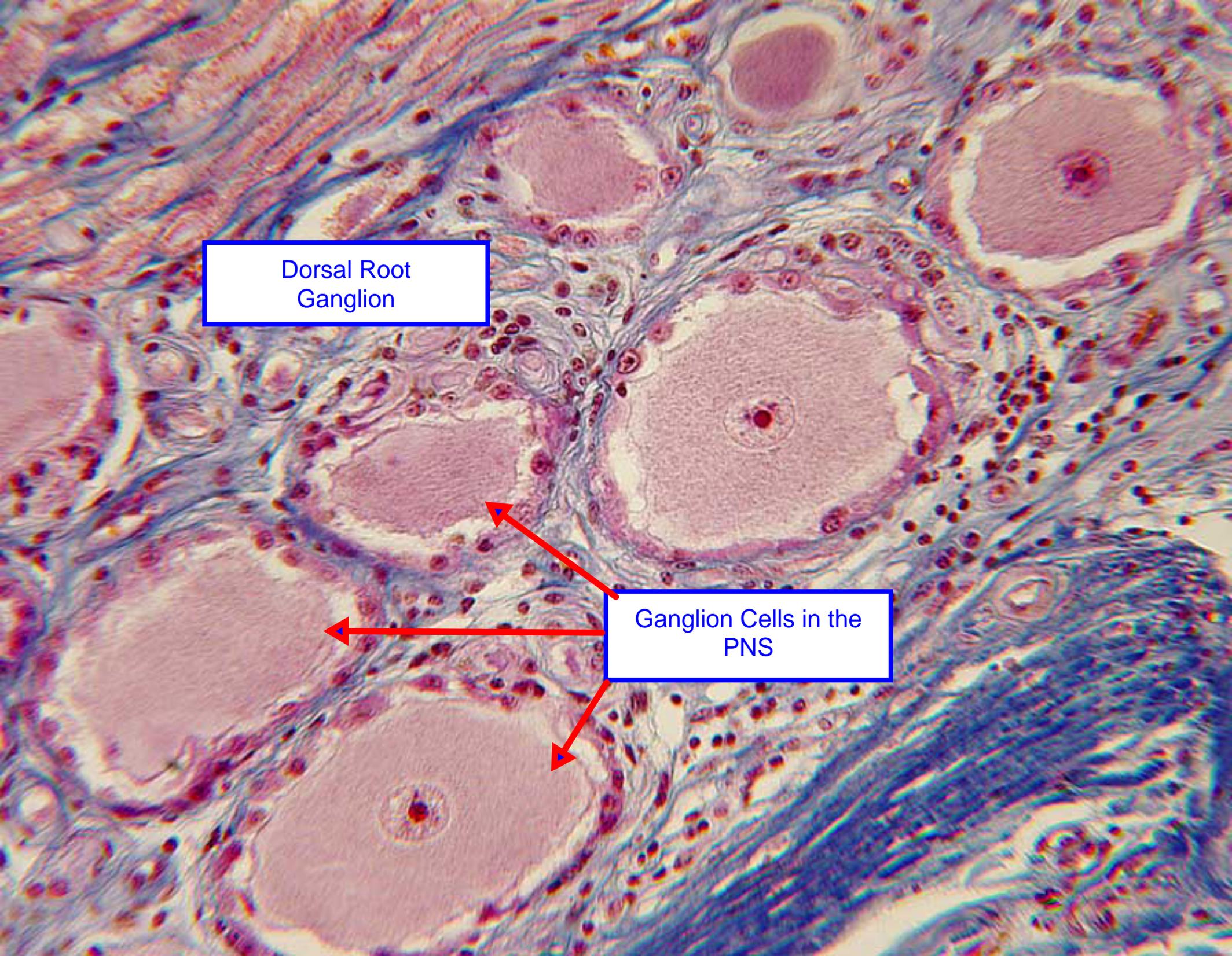
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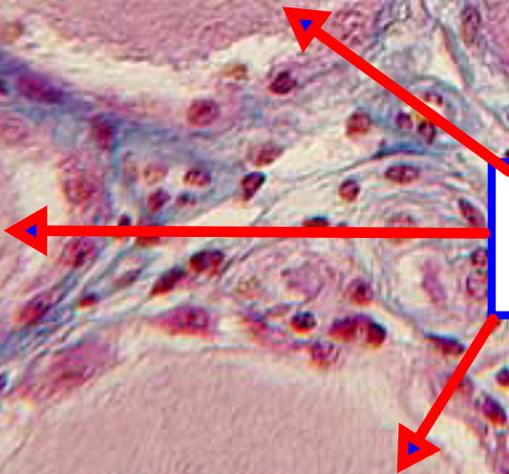
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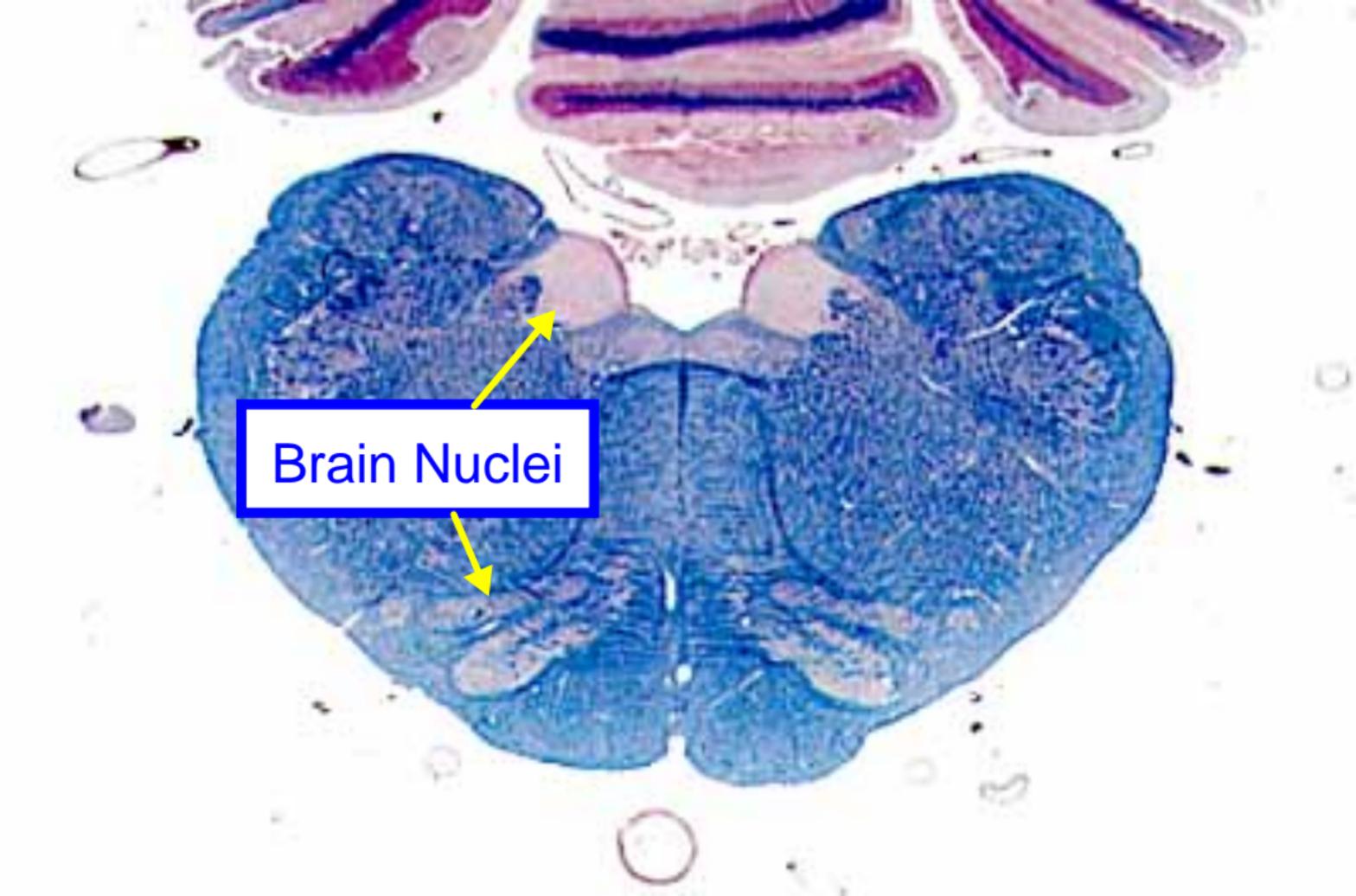




Dorsal Root  
Ganglion

Ganglion Cells in the  
PNS



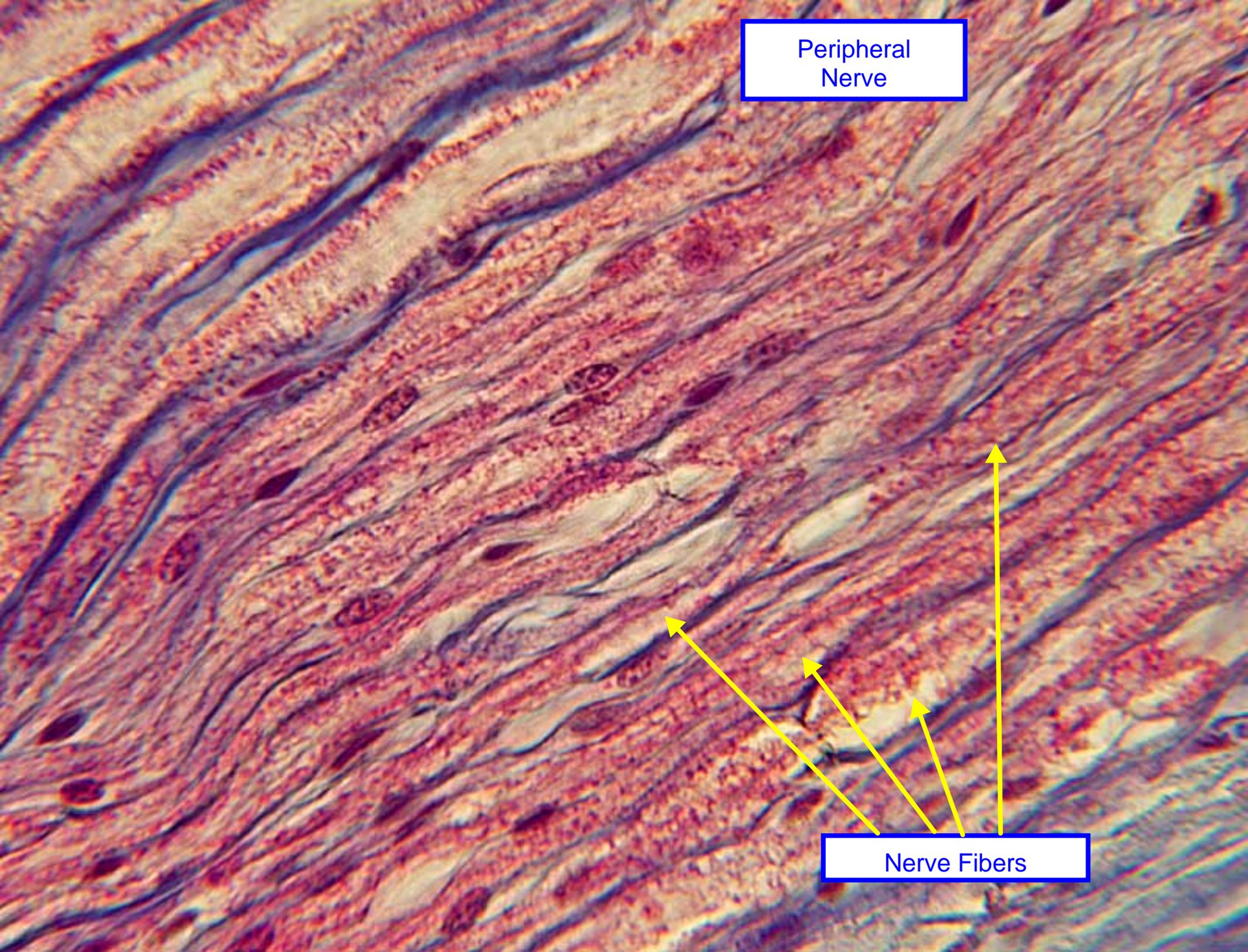


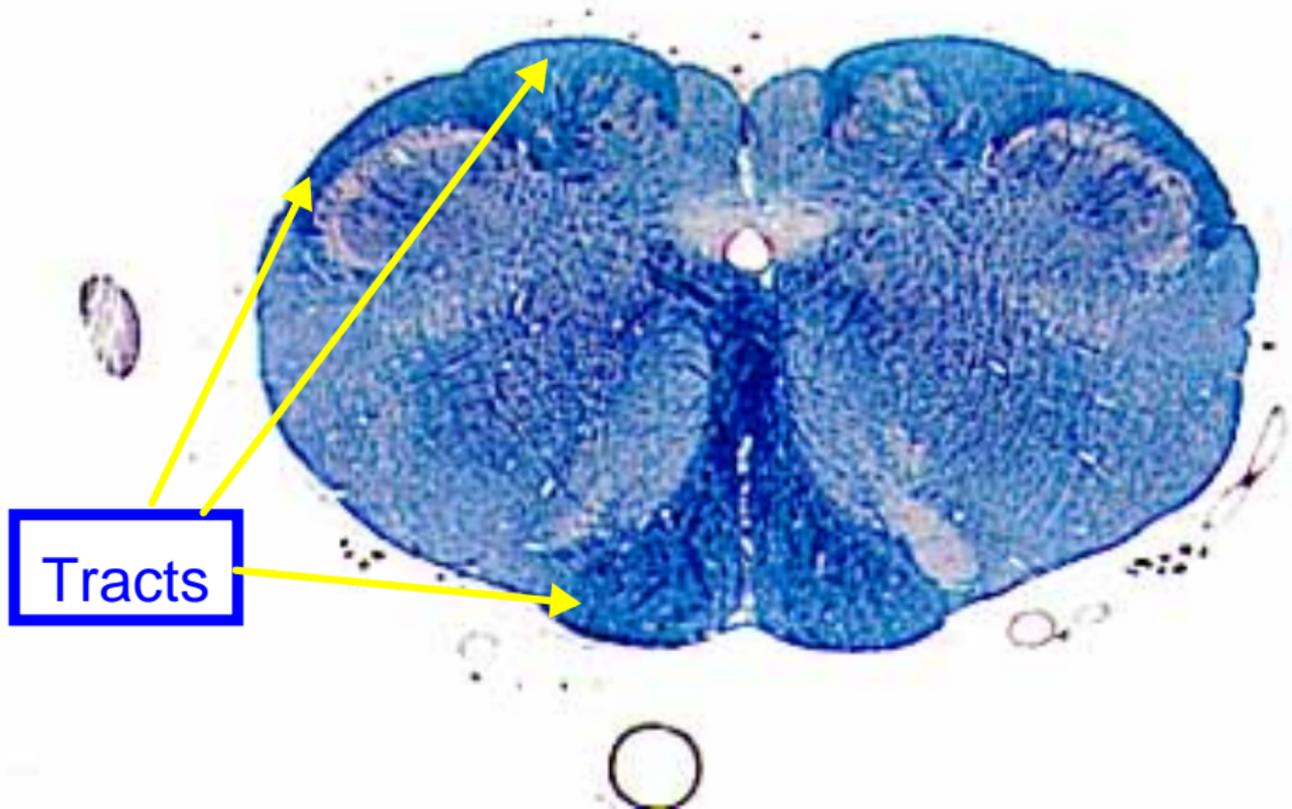
Brain Nuclei

This image shows a coronal section of a brain stained with hematoxylin and eosin (H&E). The central part of the image shows the cerebral hemispheres with their characteristic gyri and sulci. The brain nuclei, which are clusters of neurons, are visible as darker, more densely stained regions. A blue box with the text 'Brain Nuclei' is overlaid on the image, with two yellow arrows pointing to specific areas of the brain nuclei. The surrounding tissue is stained pink, and the overall structure is symmetrical.

Peripheral  
Nerve

Nerve Fibers





Tracts

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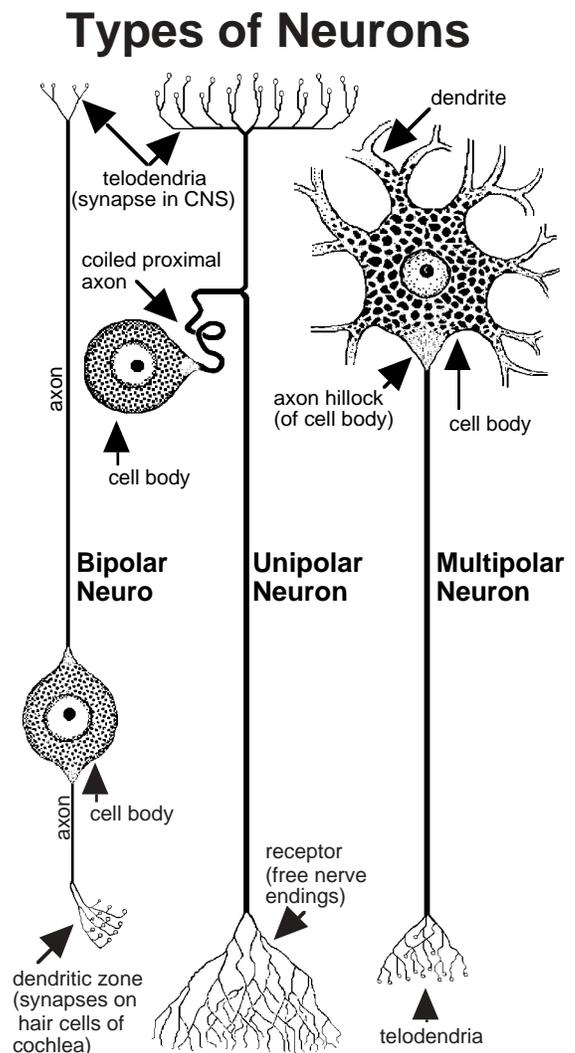
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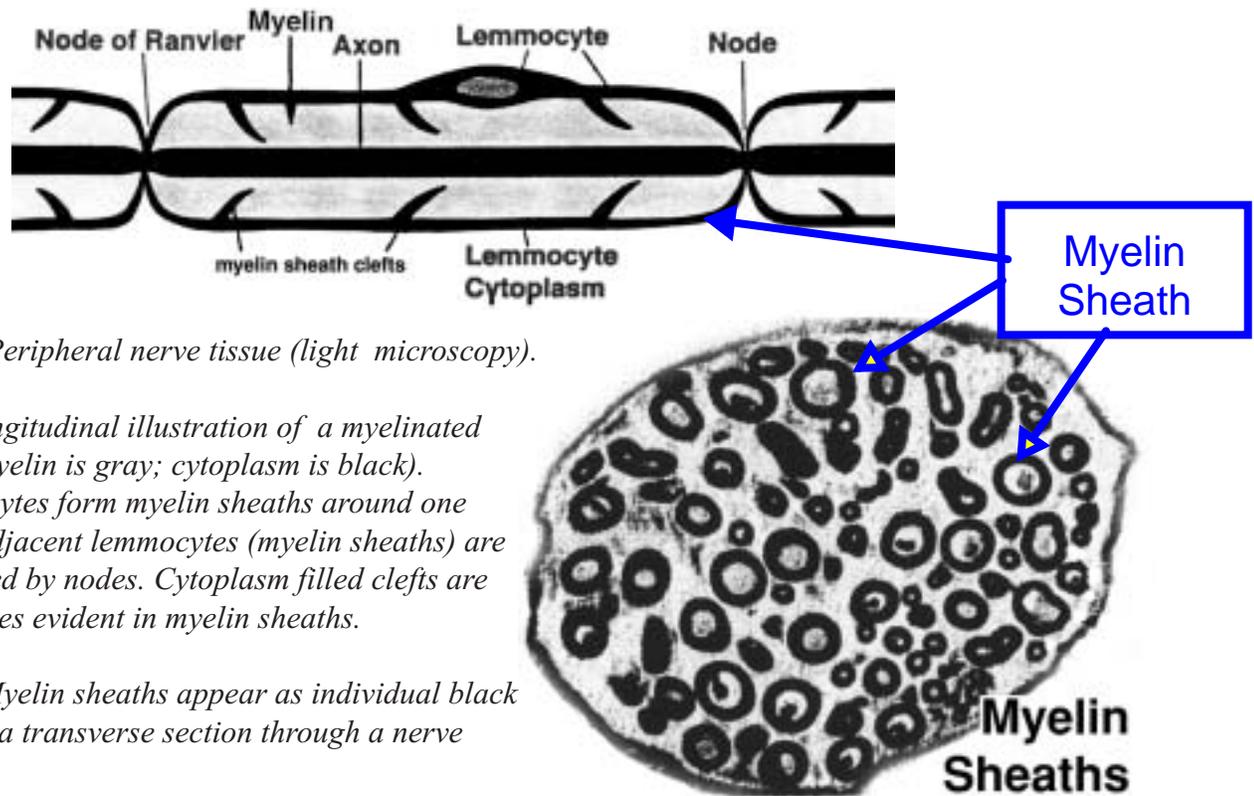


Fig. 3. Peripheral nerve tissue (light microscopy).

Top. Longitudinal illustration of a myelinated axon (myelin is gray; cytoplasm is black). Lemmocytes form myelin sheaths around one axon. Adjacent lemmocytes (myelin sheaths) are separated by nodes. Cytoplasm filled clefts are sometimes evident in myelin sheaths.

Right. Myelin sheaths appear as individual black rings in a transverse section through a nerve fascicle.

## 4. Axons:

Axons are neuron processes that project to and synapse with dendrites or cell bodies of other neurons or with non-neuronal targets (e.g. muscle). Swellings, termed **axonal varicosities/boutons**, are found along the axon or at its terminal branches and are typically the sites where synapses occur (see Neurohistology, Lecture II). Morphologically axons are divided into two types: myelinated and non-myelinated.

### A. MYELINATED AXONS (>1 $\mu\text{m}$ ; fast conducting):

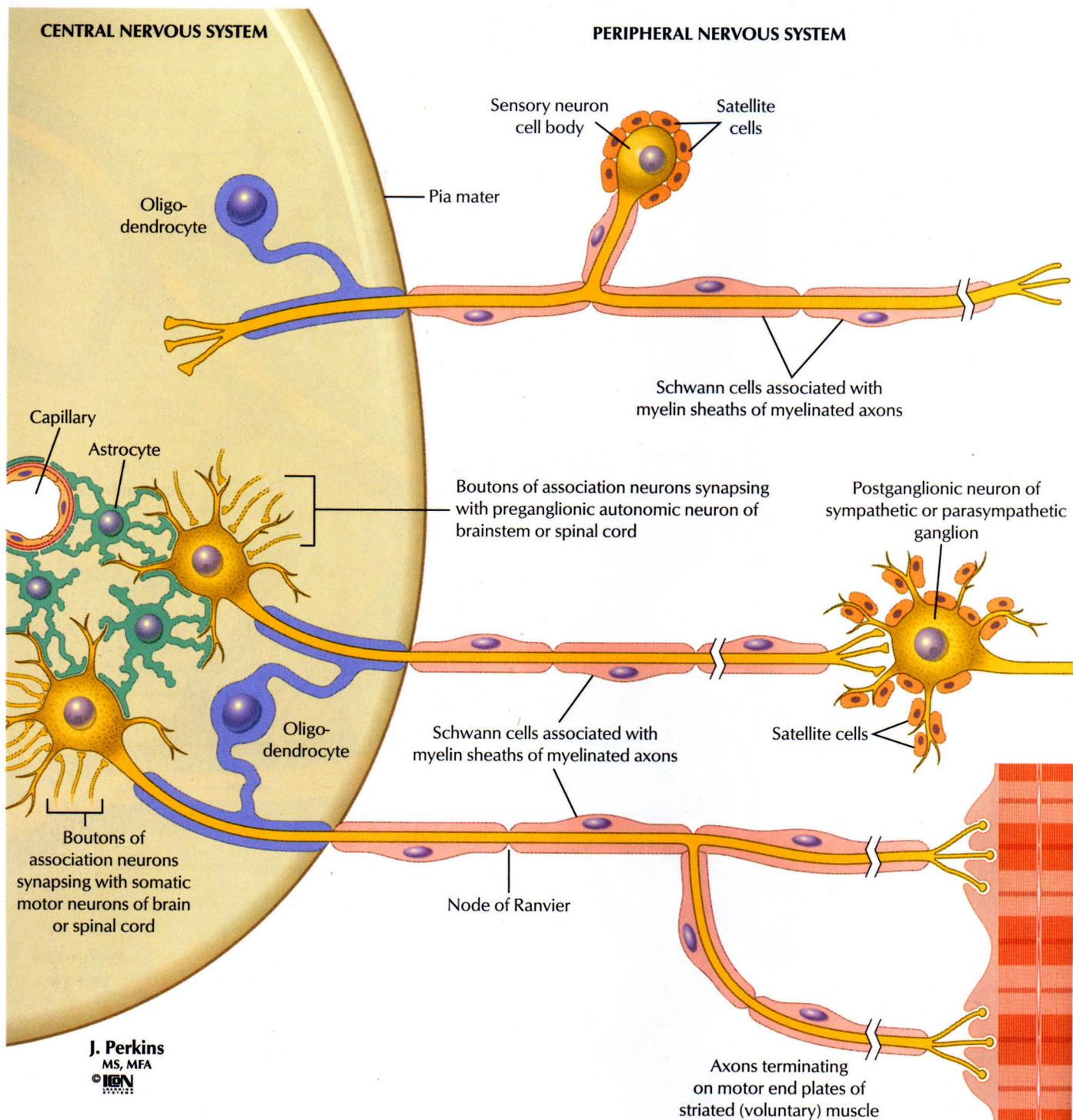
Myelinated axons are invested with a membranous, lipid sheath (making them the largest and fastest conducting nerve fibers). Myelin is a highly organized multilamellar structure formed by the plasma membrane of oligodendrocytes in the CNS and lemmocytes (Schwann cells) in the PNS. Myelin is an electrical insulator which allows increased speed of conduction along an axon. Myelinated axons located in the PNS differ from those in the CNS both in chemical composition and in the cell type that produces the myelin.

#### 1) Light microscopic appearance:

Under the light microscope, the myelin sheath appears as a tube surrounding the axon. In H & E or Triple-stained sections, myelin appears like spokes of a wheel around the axon; this appearance is actually artifactual in that tissue processing (dehydration in alcohols and clearing in xylene) dissolves lipid components of the myelin leaving nonlipid components. This remaining protein configuration is called neurokeratin.

#### 2) Nodes of Ranvier:

The nodes are breaks in the continuity of the myelin sheath which occur regularly in both the peripheral and central nervous systems. They represent the intervals between adjacent segments of myelin and occur at the junction of two lemmocytes in the PNS or two oligodendrocytes in the CNS. The nodes appear as constrictions along the nerve fiber.



**FIGURE I.5: MYELINATION OF CNS AND PNS AXONS**

# Myelin Development (PNS)

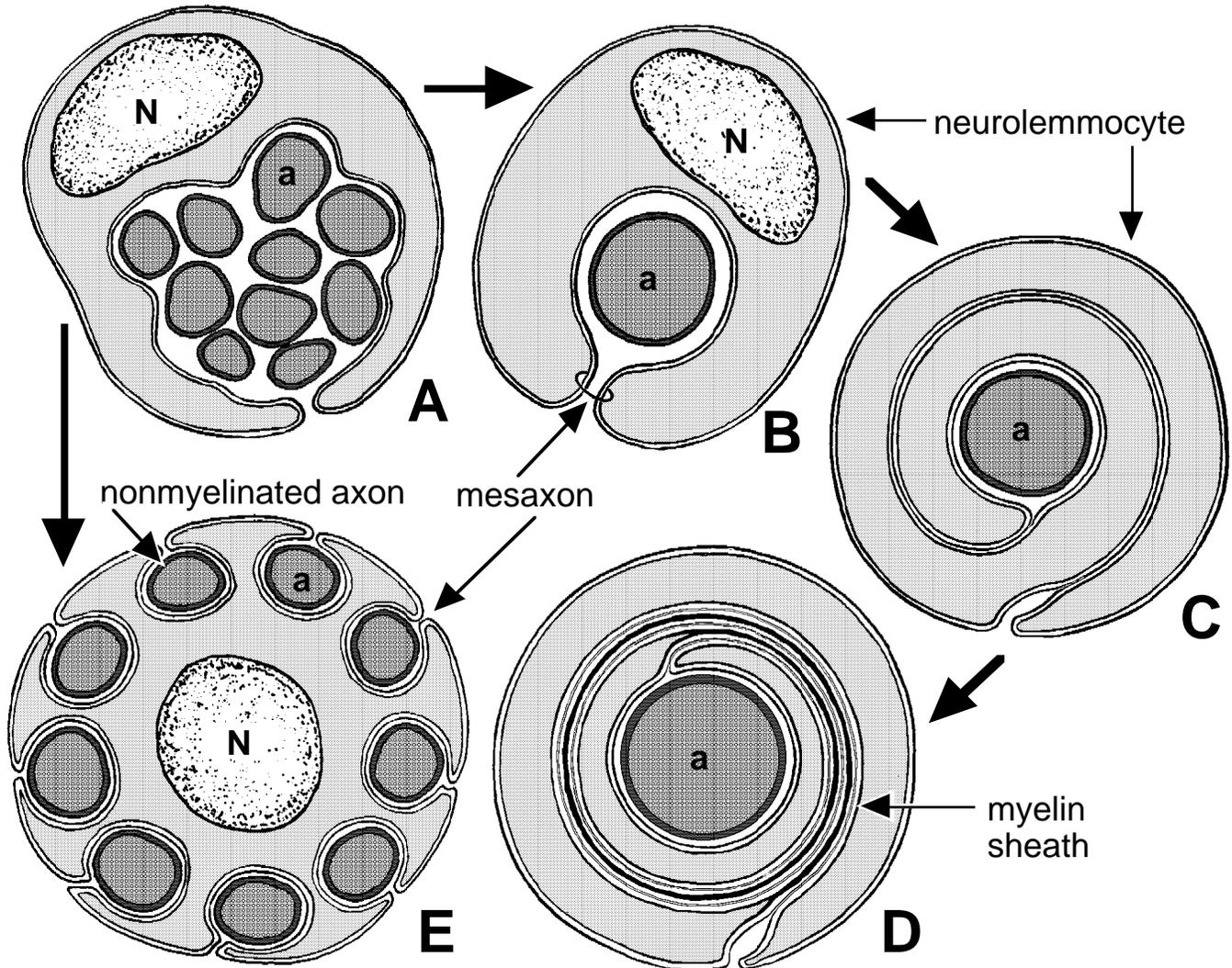
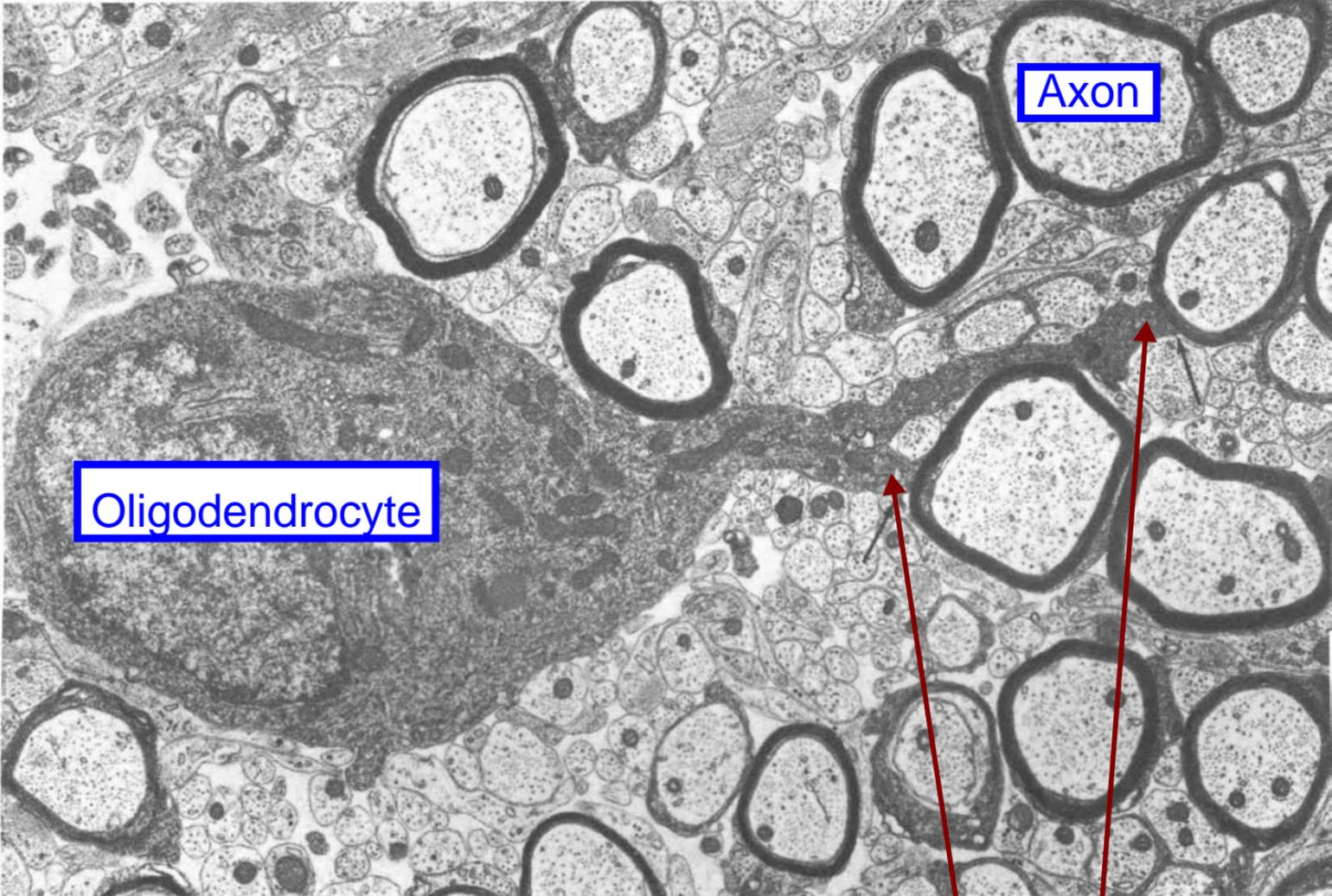


Figure 6: Diagrams showing features of myelinated and non-myelinated nerve fiber development.

## 4) CNS:

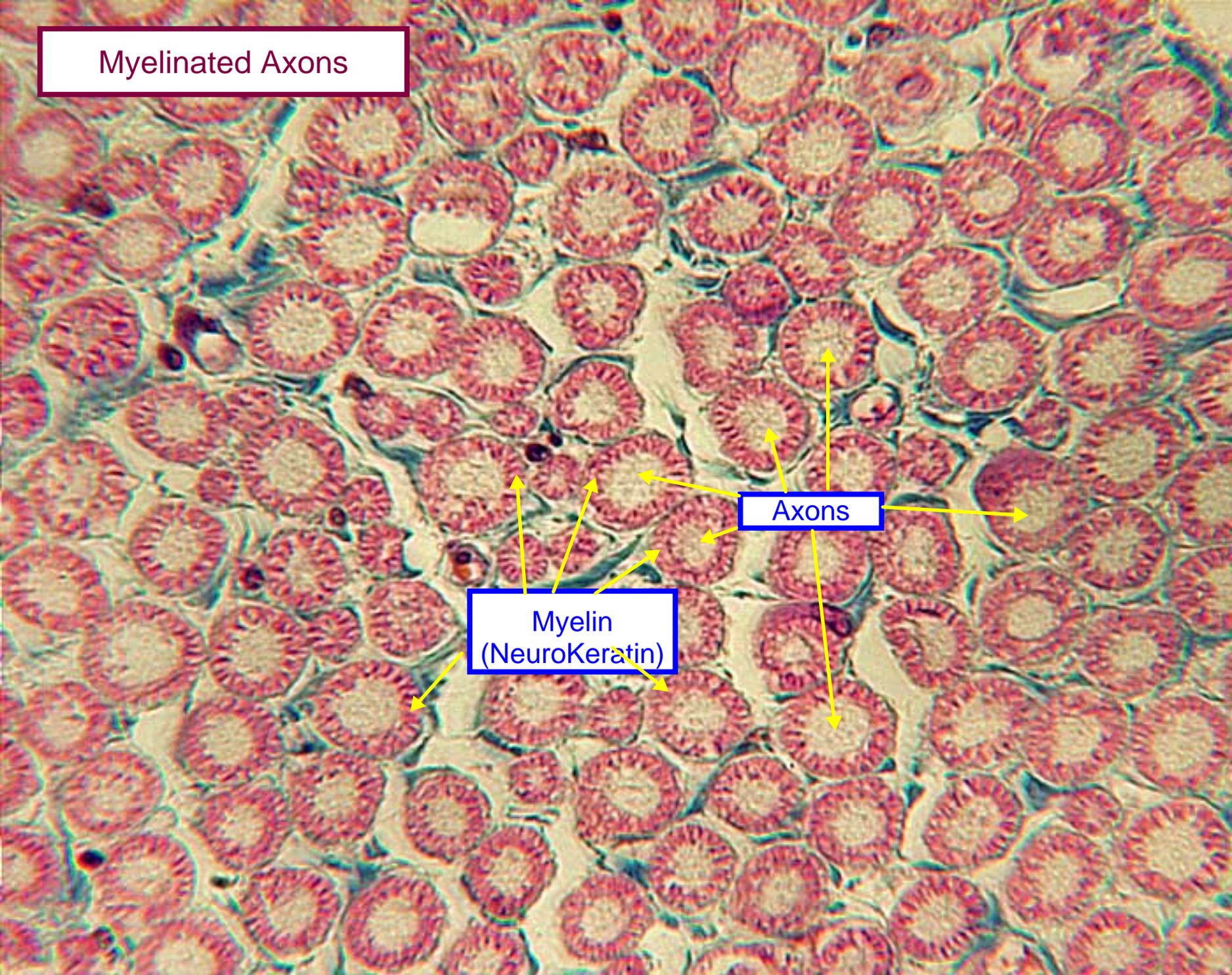
The myelin sheath is produced by **oligodendrocytes** (one of the CNS glial cells). A single oligodendrocytes will provide myelin for multiple axons. CNS myelin has more glycolipid and less phospholipid than PNS myelin. In the CNS, myelinated axons lack a basal lamina and endoneurium.



Oligodendrocyte

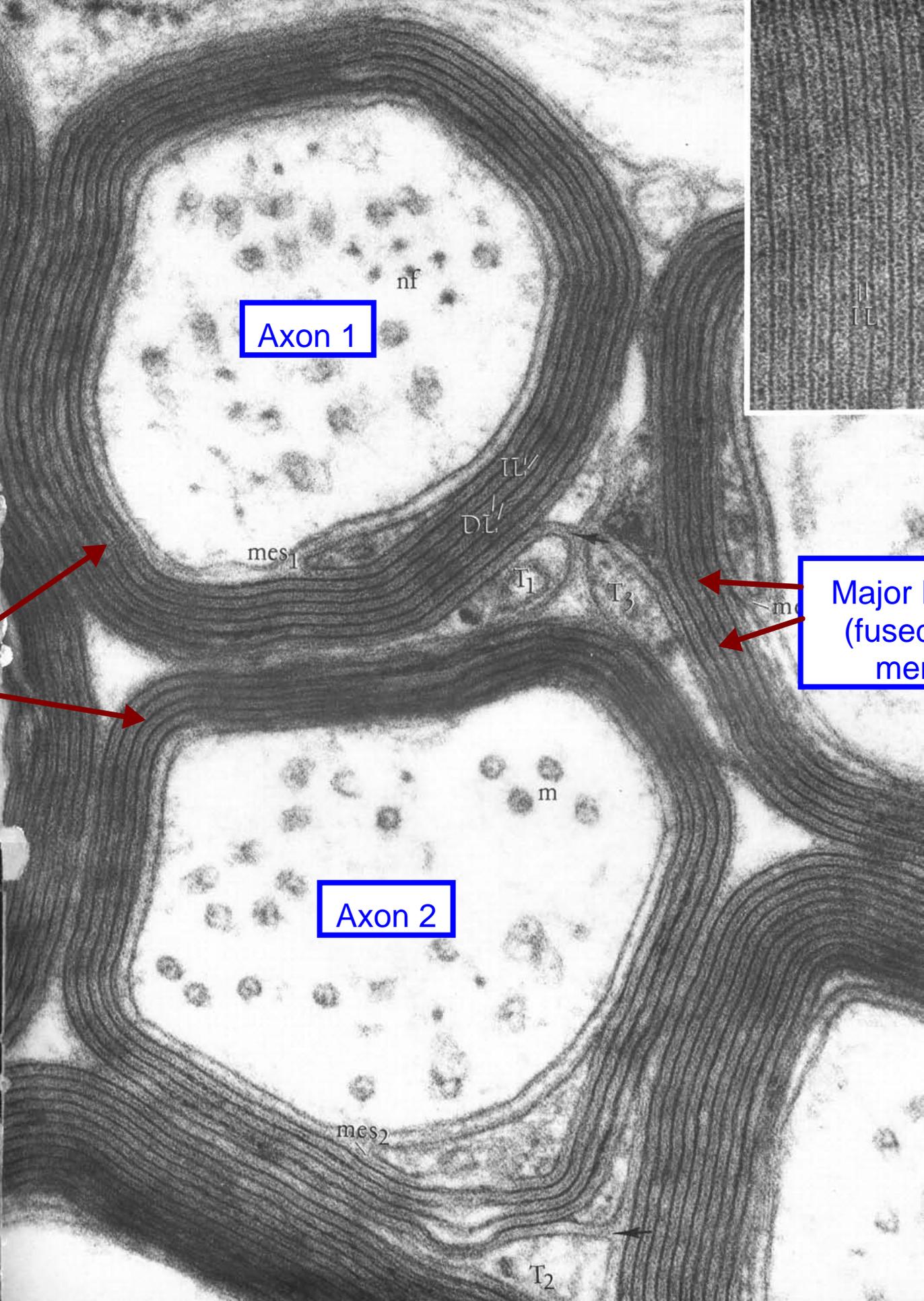
Axon

Myelinated Axons



Axons

Myelin  
(NeuroKeratin)



Axon 1

nf

mes<sub>1</sub>

T<sub>1</sub>  
T<sub>3</sub>

Major (fused) myelin

Axon 2

m

mes<sub>2</sub>

T<sub>2</sub>

### 3) PNS:

In the PNS, a typical myelinated axon has the following structure: *axon*, surrounded by *myelin sheath*, surrounded by *lemmocyte*, surrounded by *basal lamina*, surrounded by *endoneurium*.

The PNS myelin sheath is richer in phospholipid & has less glycolipid than CNS myelin. The myelin is produced by the membrane of **lemmocytes** (Schwann Cells).

**Lemmocytes**, derived from neural crest, are the supporting cells of the PNS. You will find them associated with all peripheral nerve fibers. A chain of lemmocytes is required to provide myelin for one axon in the PNS.

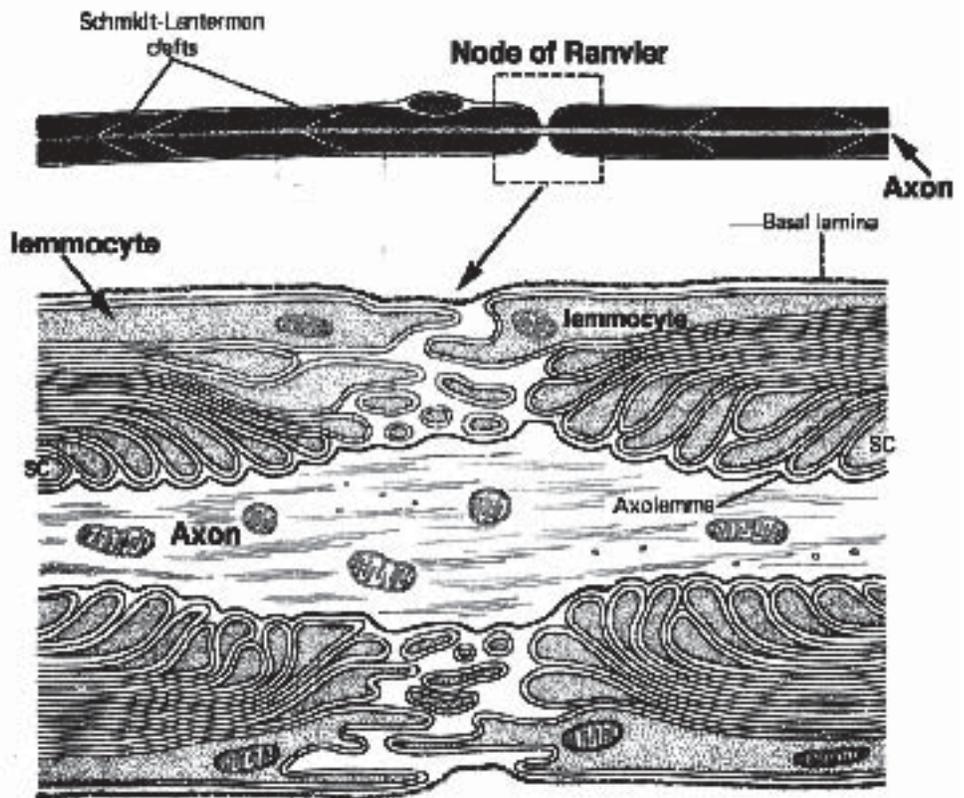


Fig. 4: Myelin Paranode—Myelin Node (of Ranvier)—Myelin Paranode chain of lemmocytes is required to provide myelin for one axon in the PNS.

**Myelin Formation**—Myelination occurs when the axon attains a diameter  $> 1 \mu\text{m}$ . The lemmocyte wraps around the nerve fiber (axon) several times producing a membranous sheath that varies in thickness depending on the number of times the lemmocyte wraps around the axon.

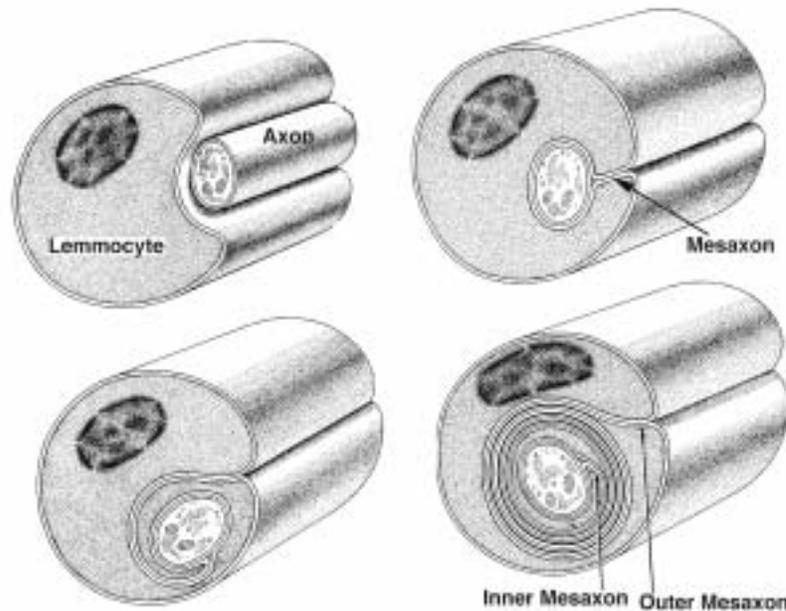
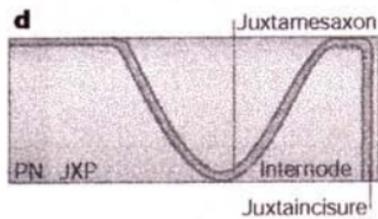
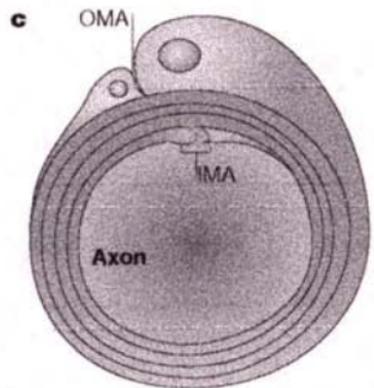
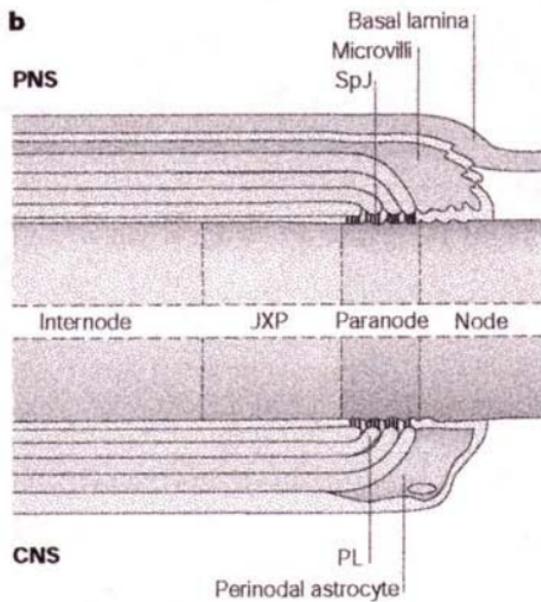
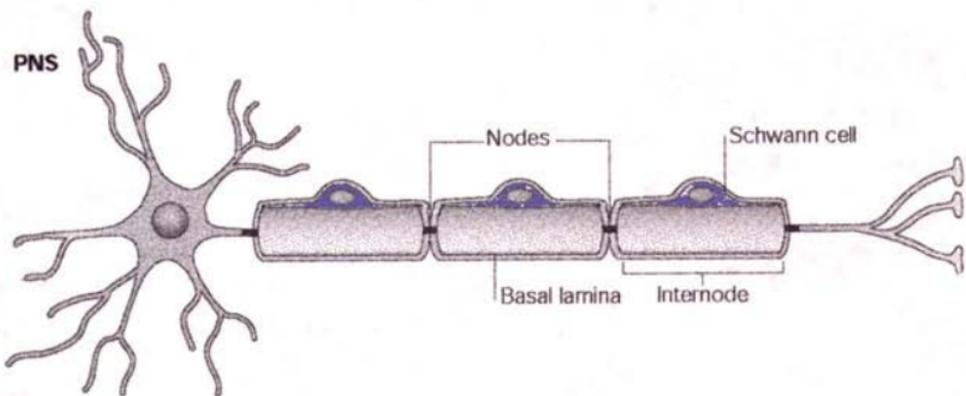
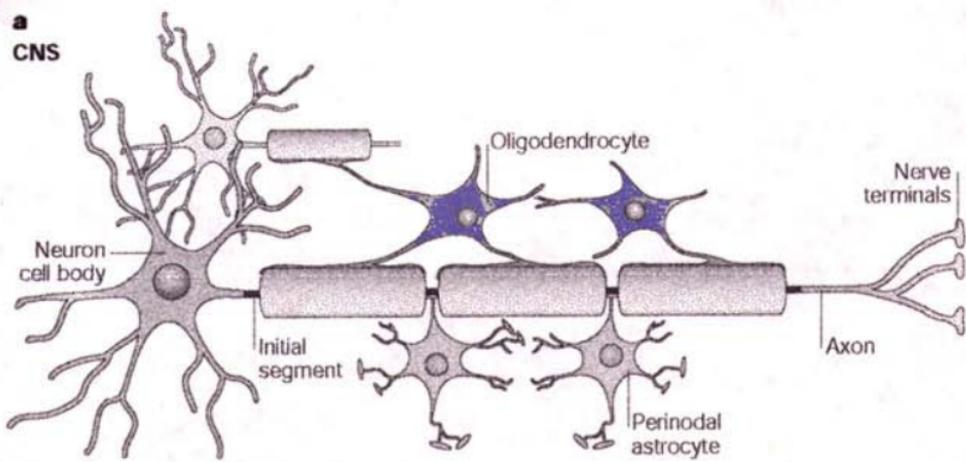
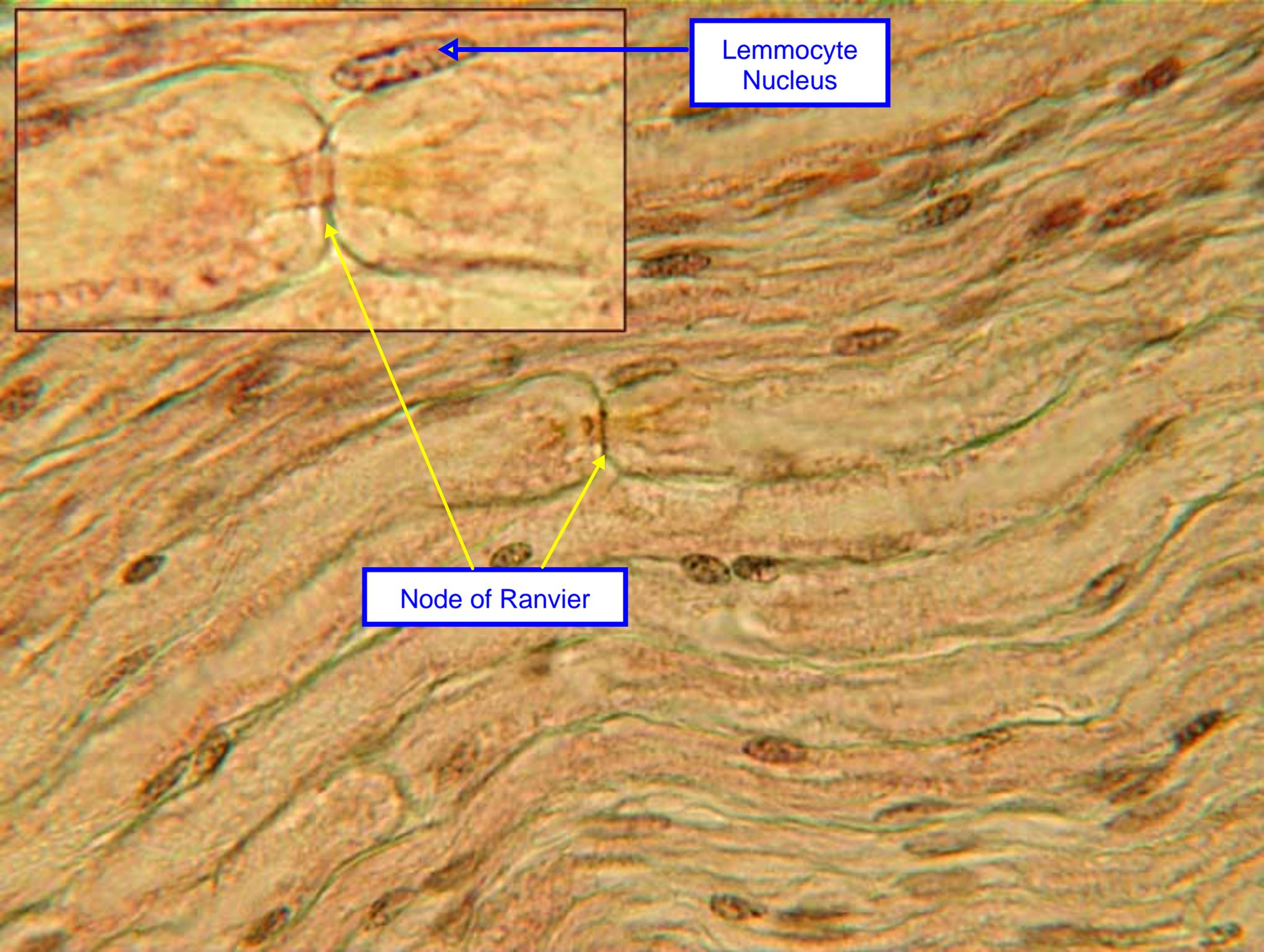


Figure 5: Schematic diagram illustrating the different phases of myelin formation in peripheral nerves.





Schwann Cell Nucleus

Node of Ranvier

## Clinical Correlation

**Demyelination** - Demyelination is the destructive removal of myelin, an insulating and protective fatty protein that sheaths nerve cell axons. When axons become demyelinated, they transmit the nerve impulses 10 times slower than normal myelinated ones and in some cases they stop transmitting action potentials altogether. There are a number of clinical diseases associated with the breakdown and destruction of the myelin sheath surrounding brain, spinal cord or peripheral nerve axons.

Degenerative myelopathy, for instance, is a progressive disease of the spinal cord in older dogs. The breeds most commonly affected include German Shepherds, Welsh Corgis, Irish Setters and Chesapeake Bay Retrievers. The disease begins in the thoracic area of the spinal cord and is associated with degeneration of the myelin sheaths of axons that comprise the spinal cord white matter. The affected dog will wobble when walking, knuckle over or drag their feet, and may cross their feet. As the disease progresses, the limbs become weak and the dog begins to buckle at the knees and have difficulty standing. The weakness gets progressively worse until the dog is unable to walk.

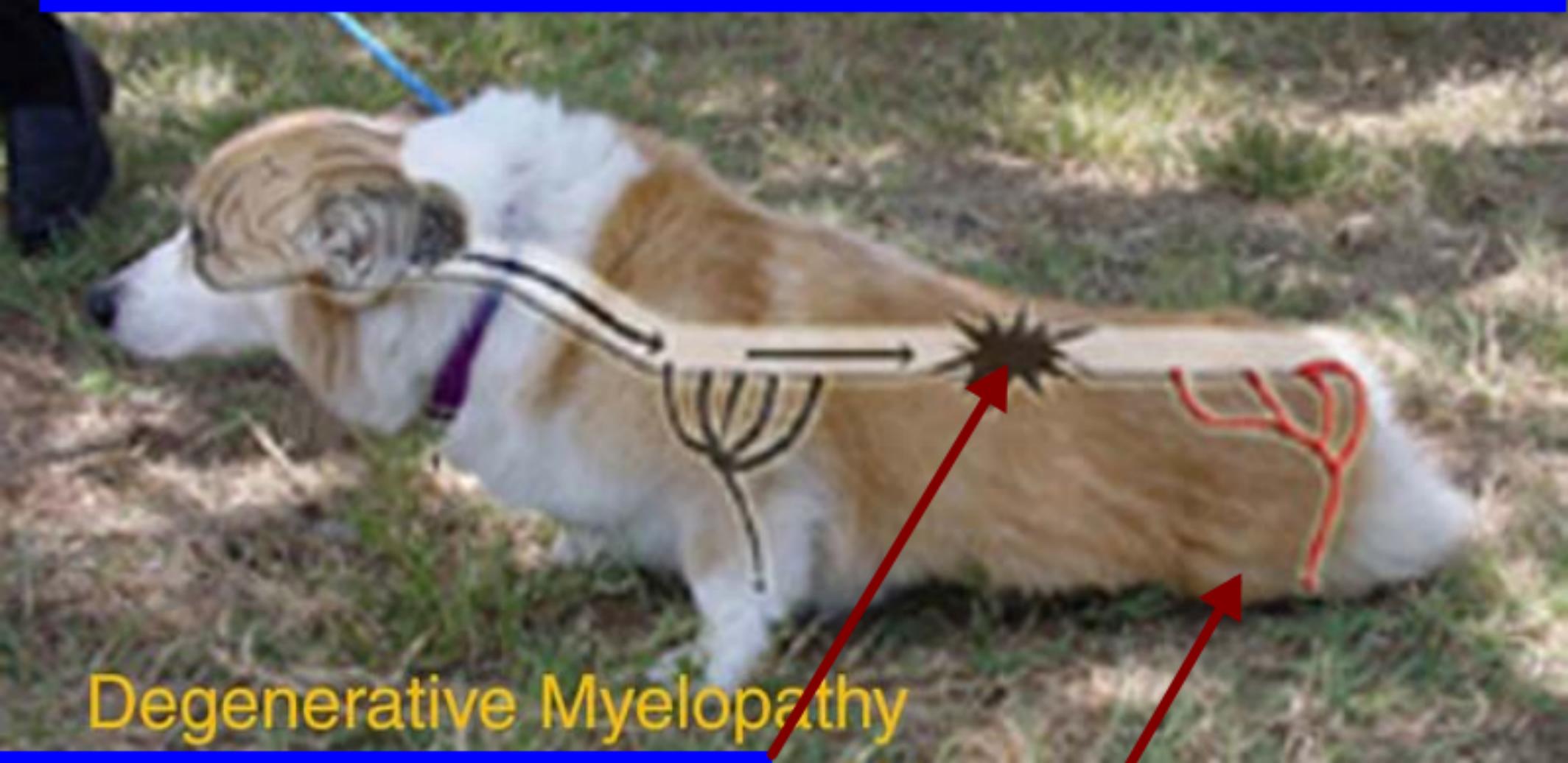
Note:

Unlike the PNS, axons in the CNS do not regenerate following injury. In part, this is due to the fact that CNS myelin contains several proteins that inhibit axonal regeneration.

### *B. NON-MYELINATED AXONS (< 1 $\mu$ m; slow conducting):*

1) **PNS** — Non-myelinated axons are embedded in infoldings of the plasma membrane of a chain of lemmocytes. Each lemmocyte typically encloses 5-20 axons (see Fig. 5, previous page). Axoplasm clumps and stains poorly with routine histological stains. A group of axons and associated lemmocytes are surrounded by basal lamina and endoneurium.

2) **CNS** — Nonmyelinated axons are **not** associated with oligodendrocytes but run free without any type of ensheathment. They are separated from one another by astrocytic processes.



Degenerative Myelopathy

Dog Carts aid in walking



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1) **PNS** — Non-myelinated axons are embedded in infoldings of the plasma membrane of a chain of lemmocytes. Each lemmocyte typically encloses 5-20 axons (see Fig. 5, previous page). Axoplasm clumps and stains poorly with routine histological stains. A group of axons and associated lemmocytes are surrounded by basal lamina and endoneurium.

2) **CNS** — Nonmyelinated axons are **not** associated with oligodendrocytes but run free without any type of ensheathment. They are separated from one another by astrocytic processes.

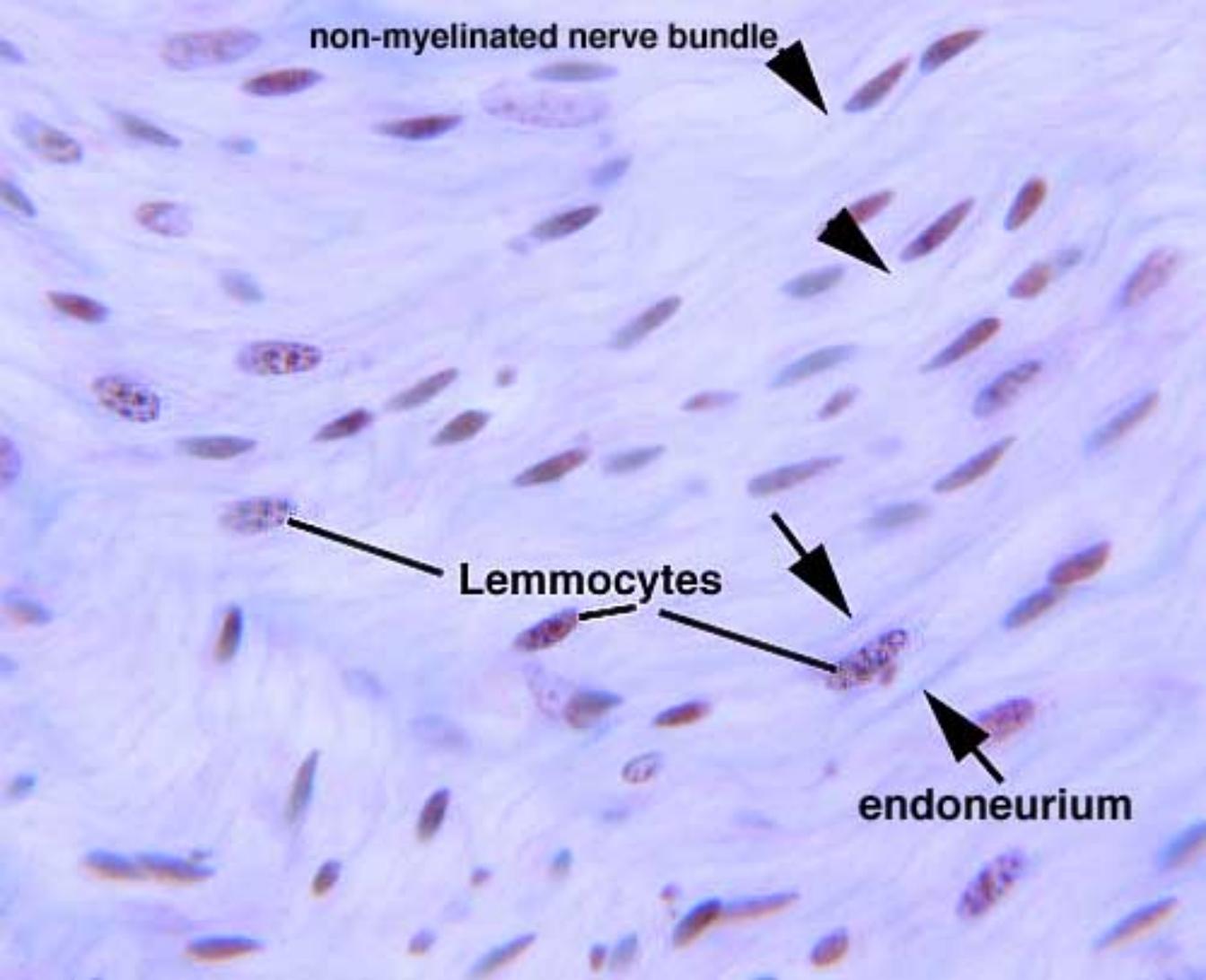
**non-myelinated nerve bundle**

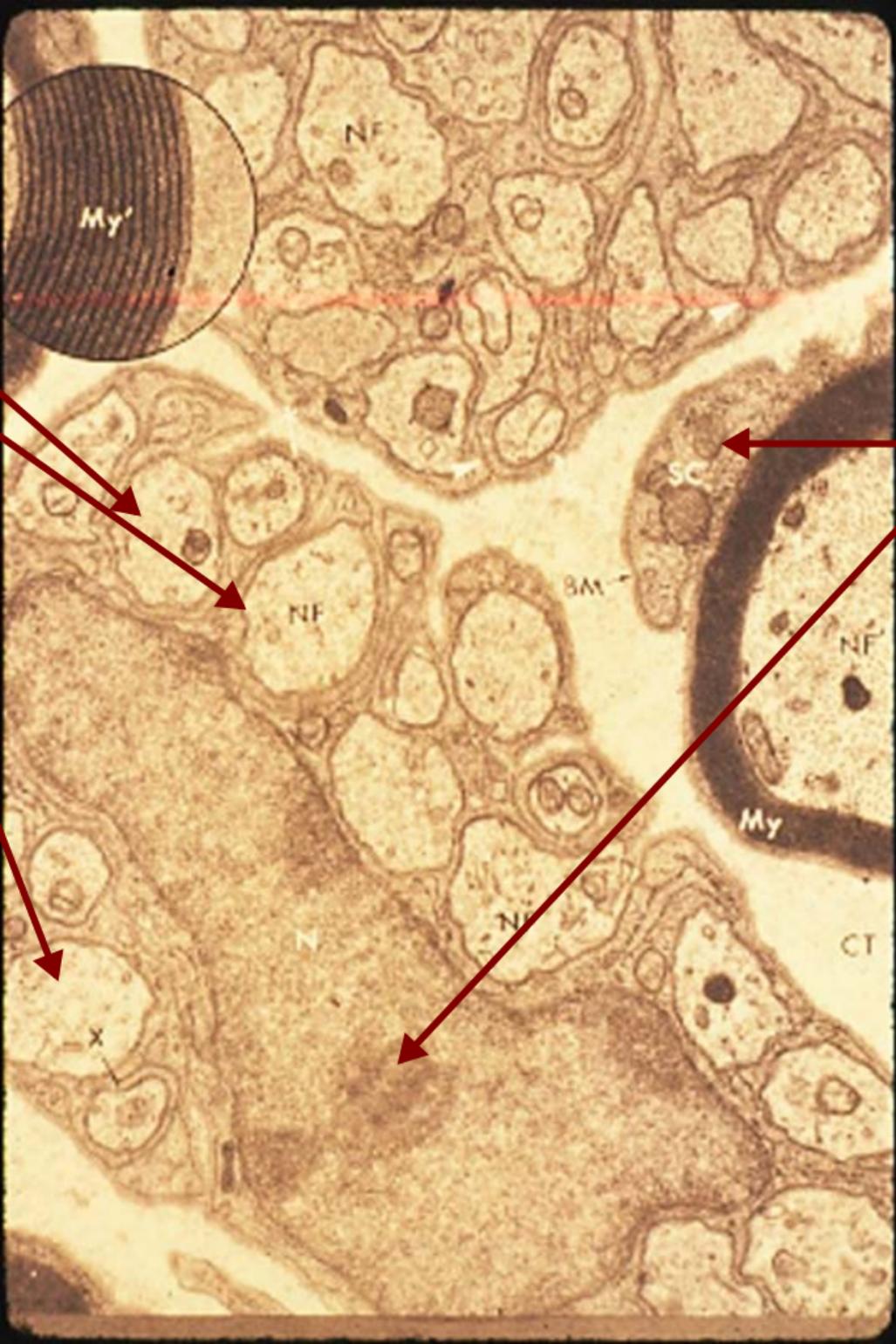


**Lemmocytes**

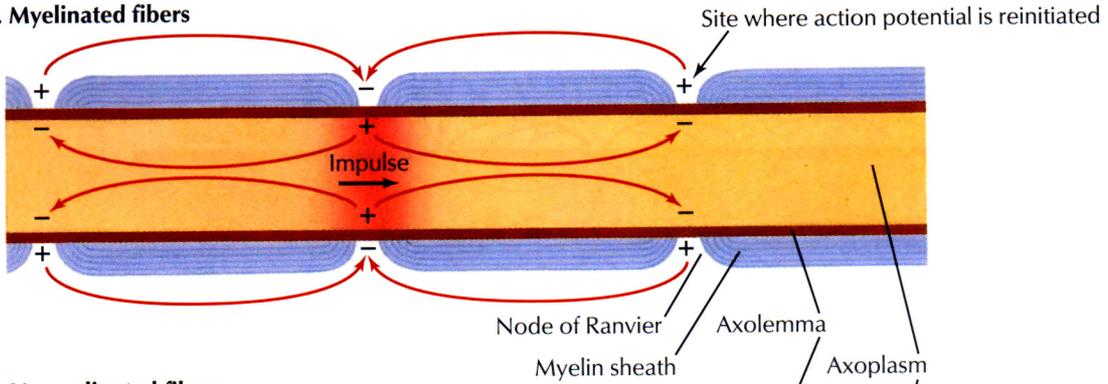


**endoneurium**

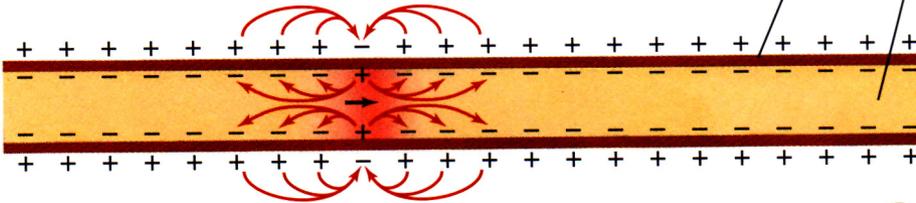




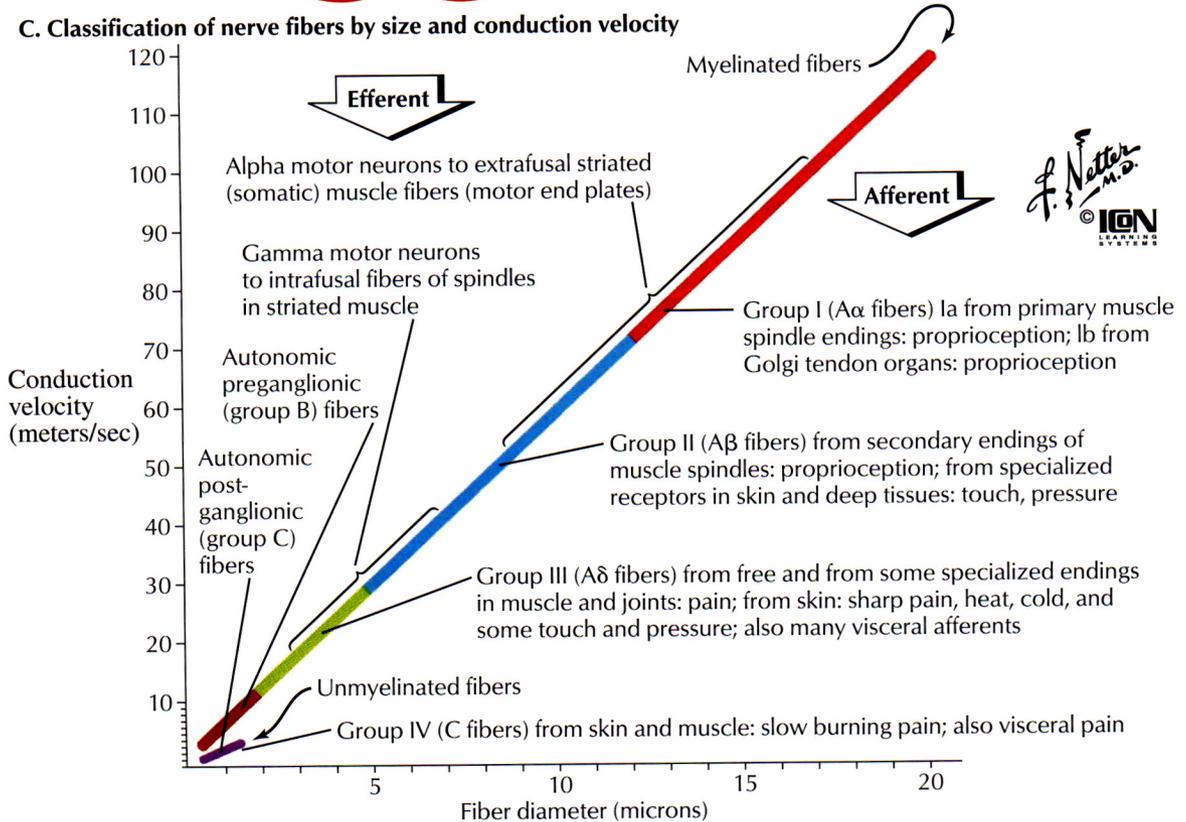
### A. Myelinated fibers

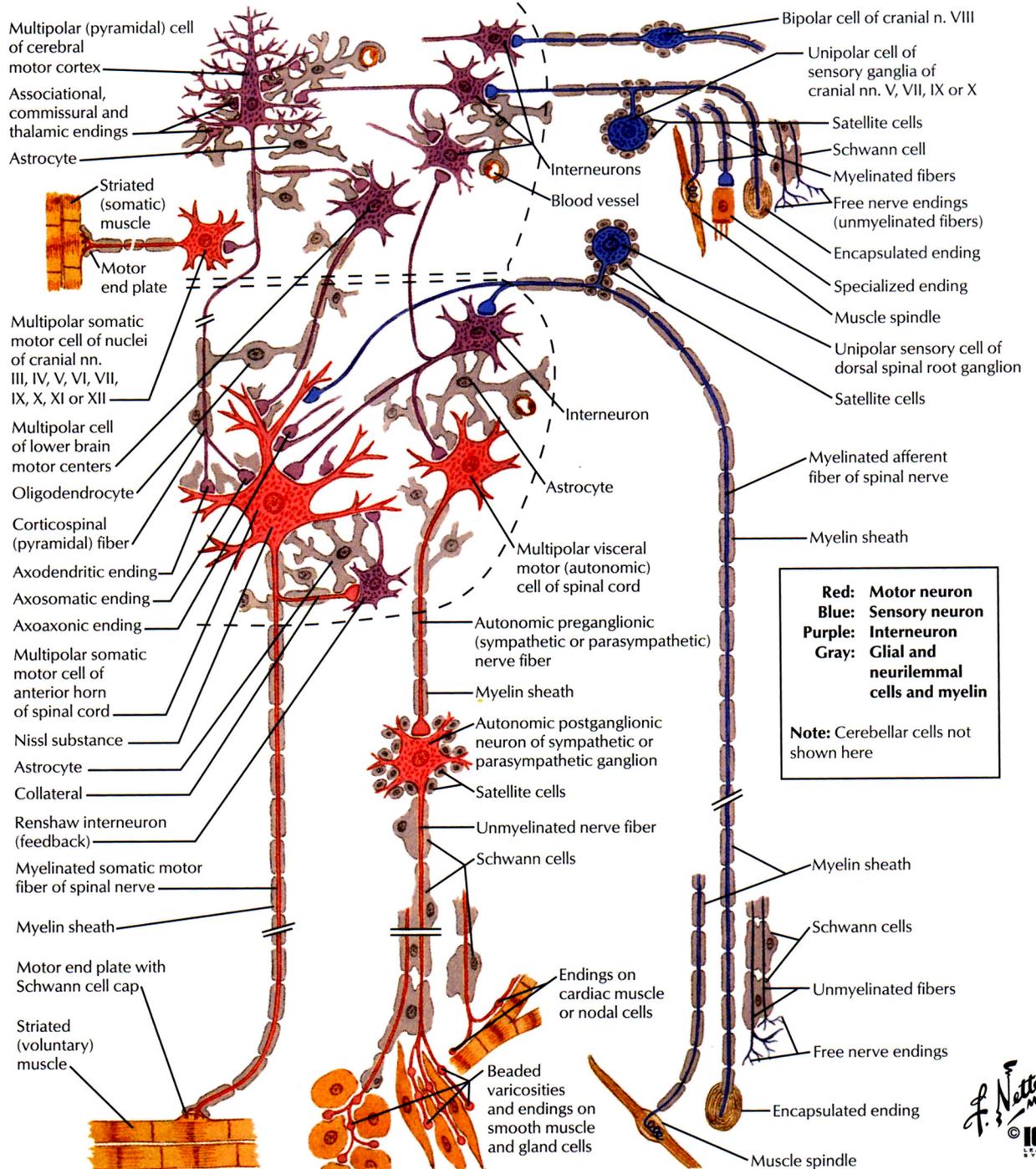


### B. Unmyelinated fibers



### C. Classification of nerve fibers by size and conduction velocity





**Red: Motor neuron**  
**Blue: Sensory neuron**  
**Purple: Interneuron**  
**Gray: Glial and neurilemmal cells and myelin**

**Note:** Cerebellar cells not shown here