THE NERVOUS SYSTEM

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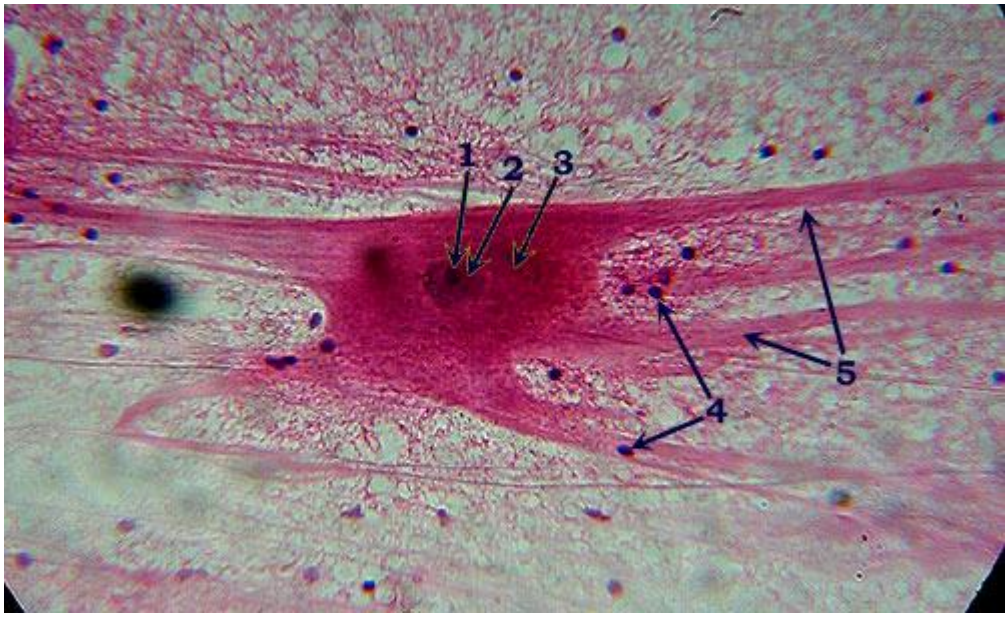


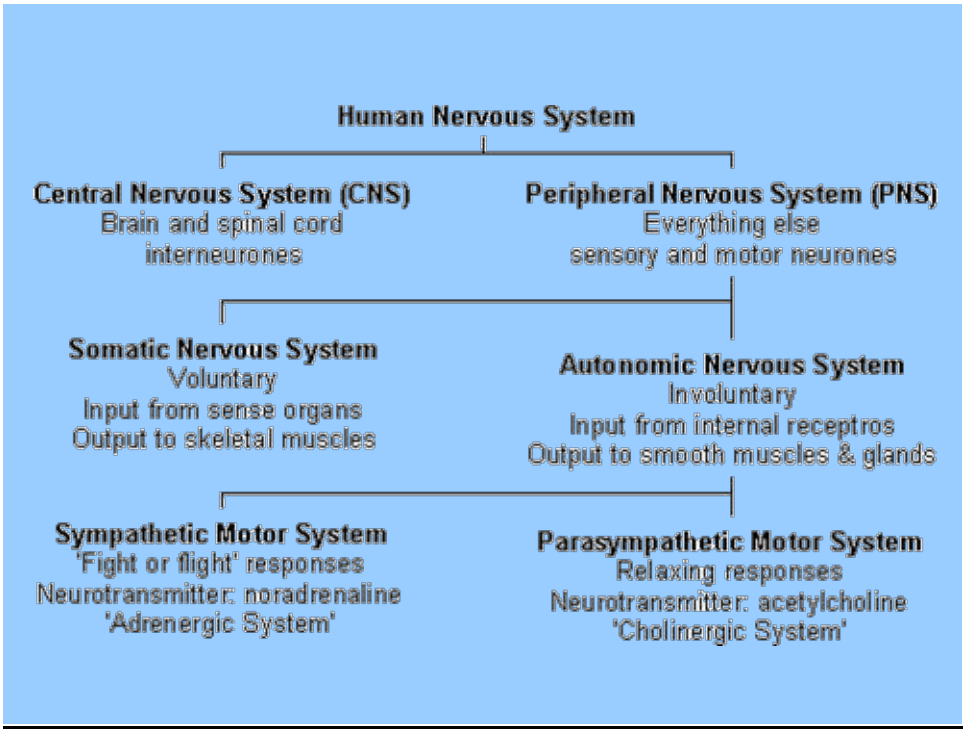
The large, irregularly shaped cell body (3) contains a darker nucleus (2), which contains an even darker-staining nucleolus (1). There are also numerous supporting glial cells, though only their small dark nuclei (4) are easily seen.

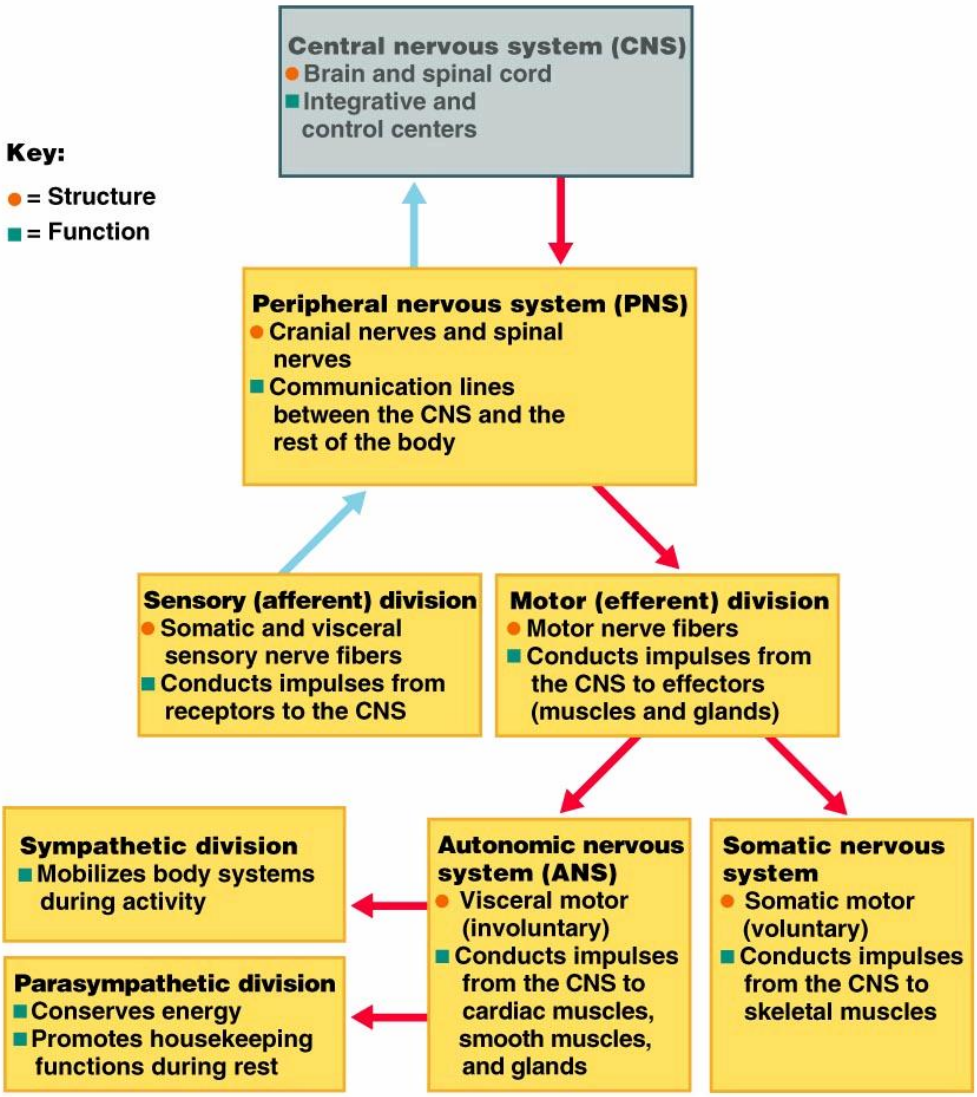
Generality and introduction:

The human nervous system consists of around a hundred billion nerve cells - or neurons. Roughly and based on anatomical features the nervous systems can be divided into two parts –

- the central nervous system (CNS)
- the peripheral (PNS).

While the brain and the spinal cord constitute the central nervous system, the so-called cranial- and spinal nerves form parts of the peripheral.
The peripheral nerves connect the central nervous system with the sense organs, i.e. the organs for vision, hearing, smell, taste and perceptional touch, and other effector organs like muscles and glands.


Human Nervous System
Central Nervous System (CNS)
Brain and spinal cord
interneurones
Peripheral Nervous System (PNS)
Everything else
sensory and motor neurones
Somatic Nervous System
Voluntary
Input from sense organs
Output to skeletal muscles
Autonomic Nervous System
Involuntary
Input from internal receptros
Output to smooth muscles & glands
Sympathetic Motor System
'Fight or flight' responses
Neurotransmitter: noradrenaline
'Adrenergic System'
Parasympathetic Motor System
Relaxing responses
Neurotransmitter: acetylcholine
'Cholinergic System'


Key:
= Structure
= Function
Central nervous system (CNS)
Brain and spinal cord
Integrative and control centers
Peripheral nervous system (PNS)
Cranial nerves and spinal nerves
Communication lines between the CNS and the rest of the body
Sensory (afferent) division
Somatic and visceral sensory nerve fibers
Conducts impulses from receptors to the CNS
Motor (efferent) division
Motor nerve fibers
Conducts impulses from the CNS to effectors (muscles and glands)
Sympathetic division
Mobilizes body systems during activity
Parasympathetic division
Conserves energy
Promotes housekeeping functions during rest
Autonomic nervous system (ANS)
Visceral motor (involuntary)
Conducts impulses from the CNS to cardiac muscles, smooth muscles, and glands
Somatic nervous system
Somatic motor (voluntary)
Conducts impulses from the CNS to skeletal muscles

Central Nervous System (CNS)

The CNS consists of the brain (encephalon), which is enclosed in the skull, and the spinal cord, which is contained within the vertebral canal.

Nervous tissue of the CNS does not contain connective tissue other than that in the meninges and in the walls of large blood vessels.

Collagenous fibers or fibrocytes/blasts are consequently not observed, which is quite unlike other tissues.

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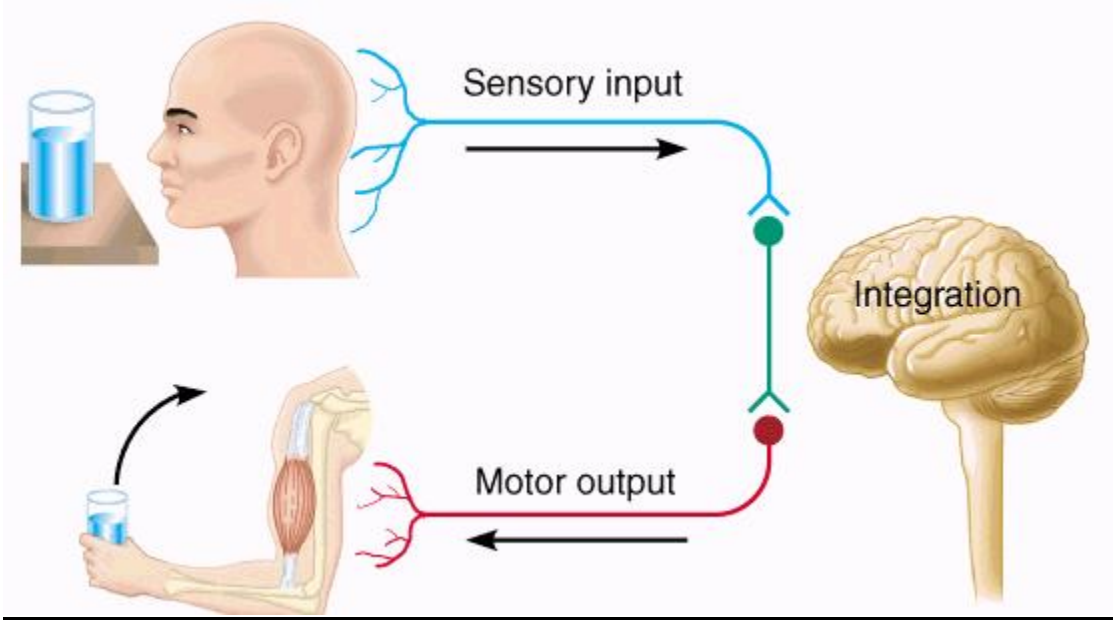
Because of the absence of connective tissue, fresh CNS tissue has a very soft, somewhat jelly-like consistency.

The two major classes of cells that make up the nervous tissue are nerve cells, neurons, and supporting cells, glia

- ***The master controlling and communicating system of the body***
- ***Functions***
  - **Sensory input – monitoring stimuli**
  - **Integration – interpretation of sensory input**
  - **Motor output – response to stimuli**

- ***Central nervous system (CNS)***
  - **Brain and spinal cord**
  - **Integration and command center**

- ***Peripheral nervous system (PNS)***
  - **Paired spinal and cranial nerves**
  - **Carries messages to and from the spinal cord and brain**



Peripheral Nervous System (PNS): Two Functional Divisions

- ***Sensory (afferent) division***
  - **Sensory afferent fibers – carry impulses from skin, skeletal muscles, and joints to the brain**
  - **Visceral afferent fibers – transmit impulses from visceral organs to the brain**
- ***Motor (efferent) division***

- **Transmits impulses from the CNS to effector organs**

Motor Division: Two Main Parts

- ***Somatic nervous system***
  - **Conscious control of skeletal muscles**
- ***Autonomic nervous system (ANS)***
  - **Regulates smooth muscle, cardiac muscle, and glands**
  - **Divisions – sympathetic and parasympathetic**

Anatomical division of nervous system:

<u>*CNS*</u> devoid of collagen except in vicinity of blood vessels and **meninges;** contains no lymphocytes

blood-brain barrier: CNS capillaries impermeable to certain plasma constituents especially larger molecules; absent in choroid plexus, pituitary and pineal glands and vomiting center of hypothalamus

capillary endothelium: junctions btwn endothelial cells are sealed; little or no pinocytosis in endothelium; luminal surface membranes contain enzymes which destroy neurotoxic metabolites (neuroactive humoral substanes)

astrocyte foot processes: maintain barrier

- **White matter** (myelin): tracts of nerve fibers; substantial numbers myelinated

- **Gray (grey) matter:** almost all neuron cell bodies (**perikarya**) and axons and **neuropil**: feltwork of axons and dendrites surrounding neurons and neuroglia; esosinophilic; generally devoid of myelin

- **non-myelinated nerve fibers:** note: in PNS when neurolemmocyte only investment: small diameter axons (autonomic nervous system and small pain fibres)

- **myelinated nerve fibers:** increased velocity of action potential; Myelin sheath formation begins in the CNS of the human embryo at about 4 months gestational age with the formation of most sheaths at least commenced by about the age of one year. From this time, successive layers continue to be laid down with final myelin sheath thickness being achieved by the time of physical maturity.

CT: endoneurium (loose, vascular ct surrounds neurolemmocytes) **; perineurium** (dense ct surrounds fascicles)**; epineurium** (loose ct [condensed peripherally] around peripheral nerves with more than one fascicle)

peripheral nerves: one or more bundles = **fascicles** of nerve fibers;

fascicle: surrounded by **perineurium**

each **fiber** contained in neurolemmocyte; surrounded by **endoneurium**

neurolemmocyte (Schwann cell): invest all axons in PNS; variable number of axons per neurolemmocyte

external lamina: neurolemmocytes (i.e., individual cells) have external lamina but neurons do not

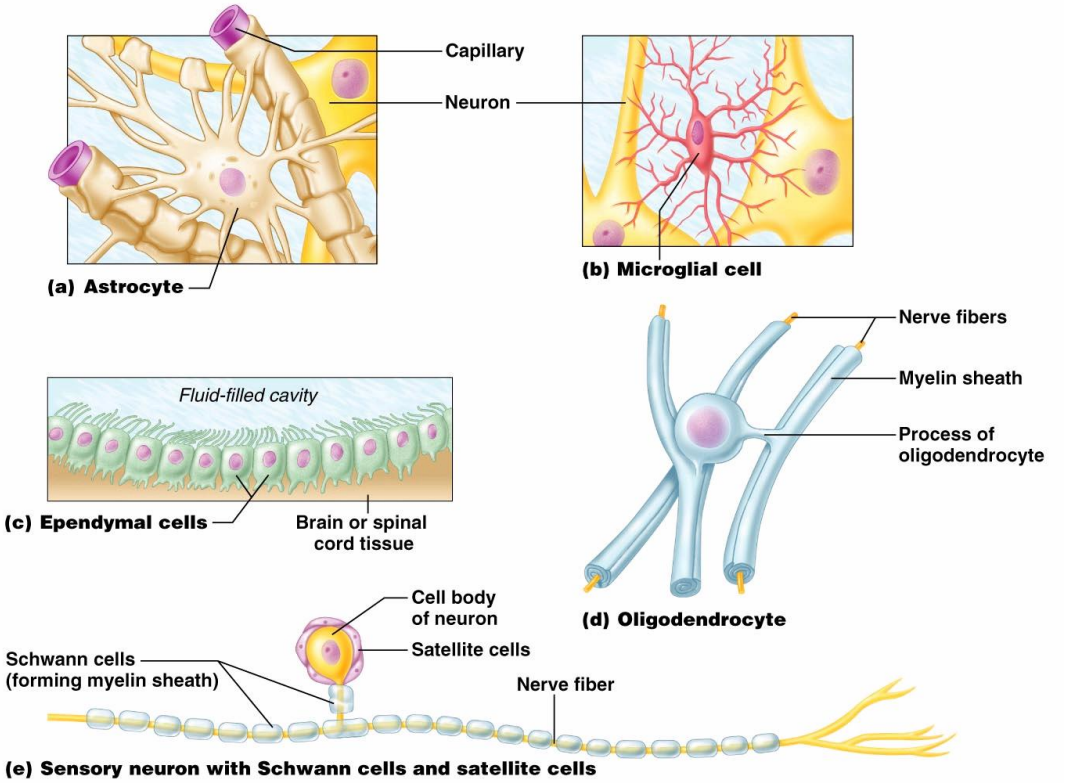
Non-myelinated Nerve Fibers:

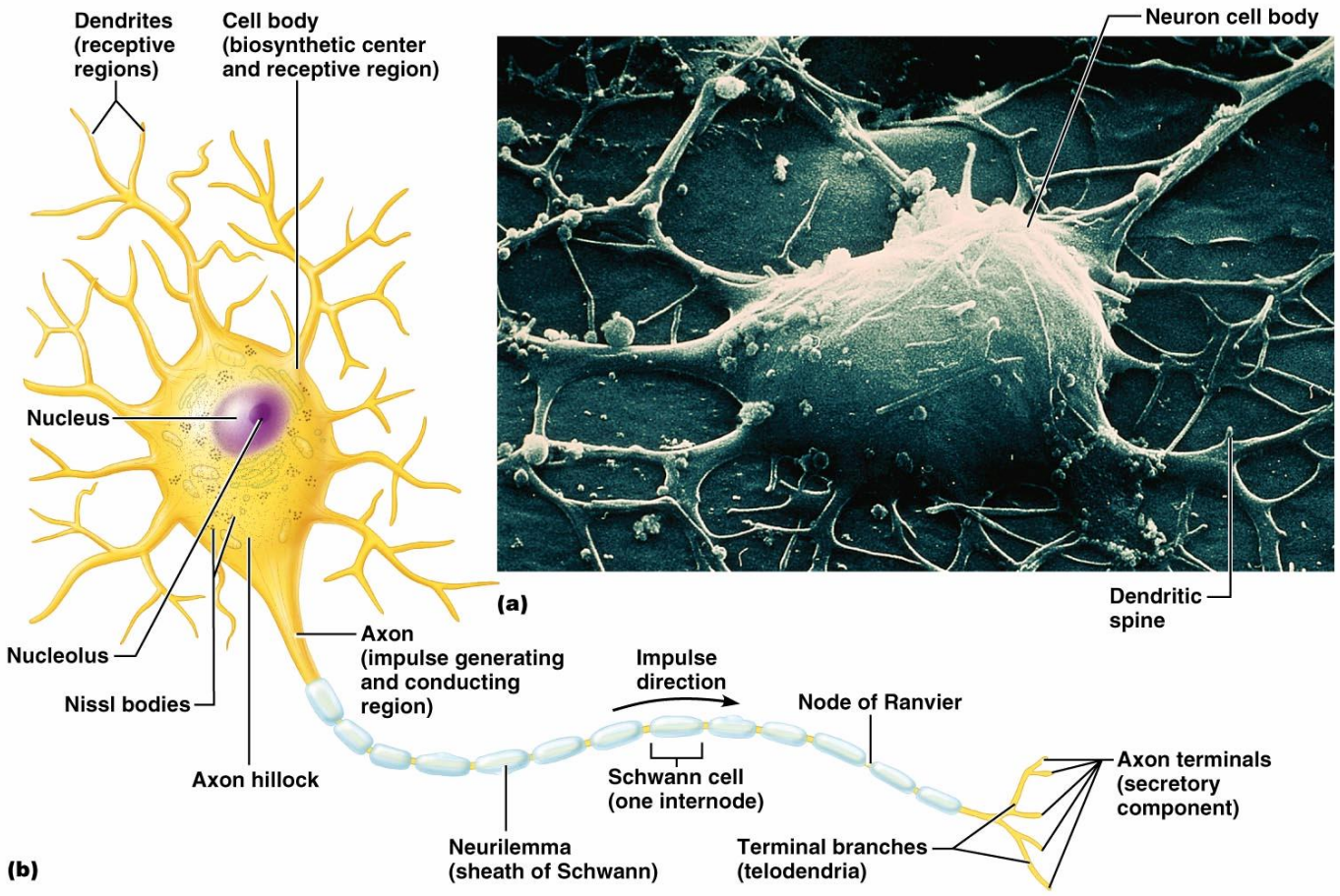
when neurolemmocyte only investment: small diameter axons (autonomic nervous system and small pain fibres)

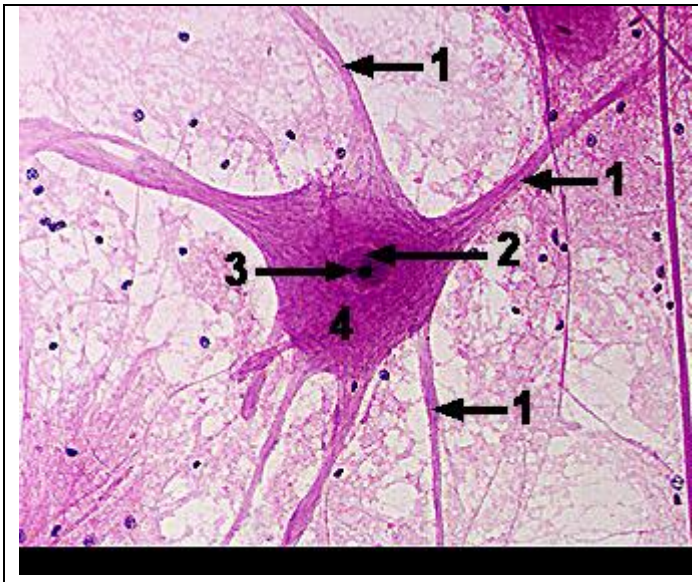
- **neurolemmocytes:** extend short distance along axons; abutt each other end to end.
- **mesaxon:** zone of apposition of neurolemmocyte cell membrane
- **channel within neurolemmocyte:** may be occupied by more than one axon

Myelinated Nerve Fibers: increased velocity of action potential

- **ensheathing neurolemmocyte** forms myelin sheath; large diameter fibers


Capillary
Neuron
(a) Astrocyte
(b) Microglial cell
Fluid-filled cavity
(c) Ependymal cells
Brain or spinal cord tissue
Nerve fibers
Myelin sheath
Process of oligodendrocyte
(d) Oligodendrocyte
Cell body of neuron
Satellite cells
Schwann cells (forming myelin sheath)
Nerve fiber
(e) Sensory neuron with Schwann cells and satellite cells


Dendrites (receptive regions)
Cell body (biosynthetic center and receptive region)
Nucleus
Nucleolus
Nissl bodies
Axon hillock
Axon (impulse generating and conducting region)
Neurilemma (sheath of Schwann)
Impulse direction
Schwann cell (one internode)
Node of Ranvier
Terminal branches (telodendria)
Axon terminals (secretory component)
(b)
Neuron cell body
Dendritic spine
(a)



1. Cell processes 2. Nucleus 3. Nucleolus 4. Cell body

Part I nervous system histology:

Development of Neurons

- ***The nervous system originates from the neural tube and neural crest***
- ***The neural tube becomes the CNS***
- ***There is a three-phase process of differentiation:***
  - **Proliferation of cells needed for development**
  - **Migration – cells become amitotic and move externally**
  - **Differentiation into neuroblasts**

Axonal Growth

- ***Guided by:***
  - **Scaffold laid down by older neurons**
  - **Orienting glial fibers**
  - **Release of nerve growth factor by astrocytes**
  - **Neurotropins released by other neurons**
  - **Repulsion guiding molecules**
  - **Attractants released by target cells**

N-CAMs

- ***N-CAM – nerve cell adhesion molecule***
- ***Important in establishing neural pathways***
- ***Without N-CAM, neural function is impaired***

Found in the membrane of the growth cone

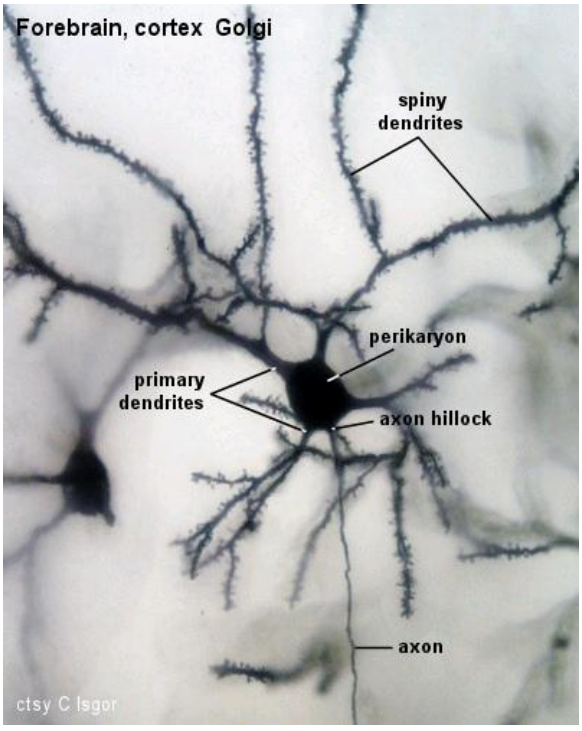
Neurons types

Nervous tissue is composed of two main cell types:

- neurons
- glial cells.

Neurons transmit nerve messages.

Glial cells are in direct contact with neurons and often surround them.

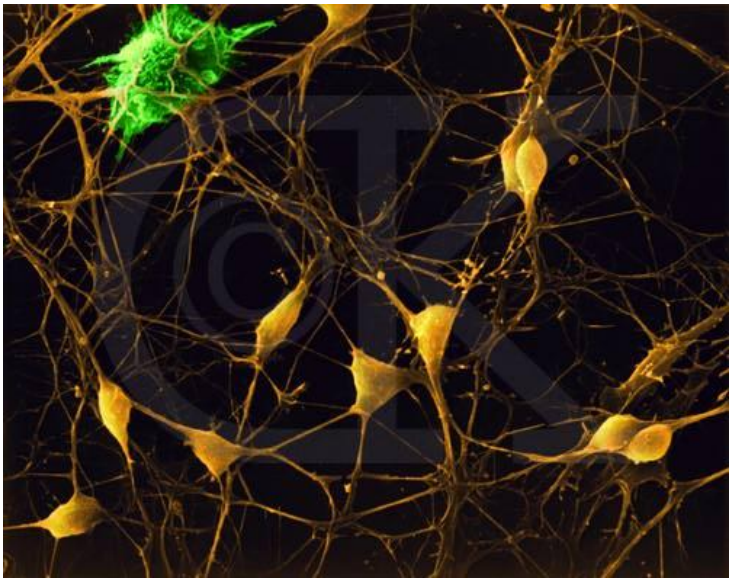


neurons (nerve cells) and neuroglia (glial cells) with all their processes and external laminae plus connective tissue sheaths

Neurons: specialized cells: sensory receptors, conducting pathways, sites of integration and analysis; lg cell body; perikaryon - nucleus and surrounding cytoplasm; **terminally differentiated**

- **nucleus**: chromatin dispersed; nucleolus conspicuous
- **chromatophilic substance** (nissl substance [bodies])
- **neurofilaments**: intermediate filaments (provide structural support?)

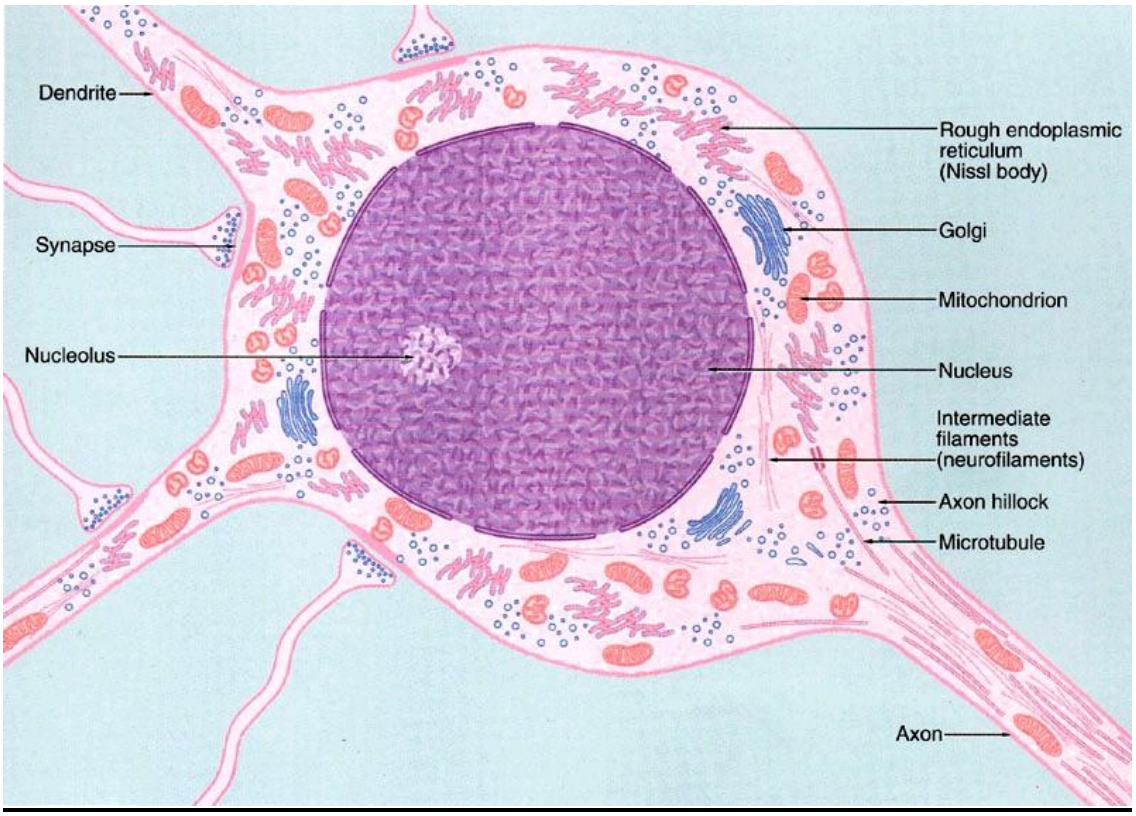
- **microtubules**: axonal transport of neurotransmitter substances, enzymes, membrane and cellular constituents
- **golgi**: diffuse
- **multivesicular bodies**: transport to organelles

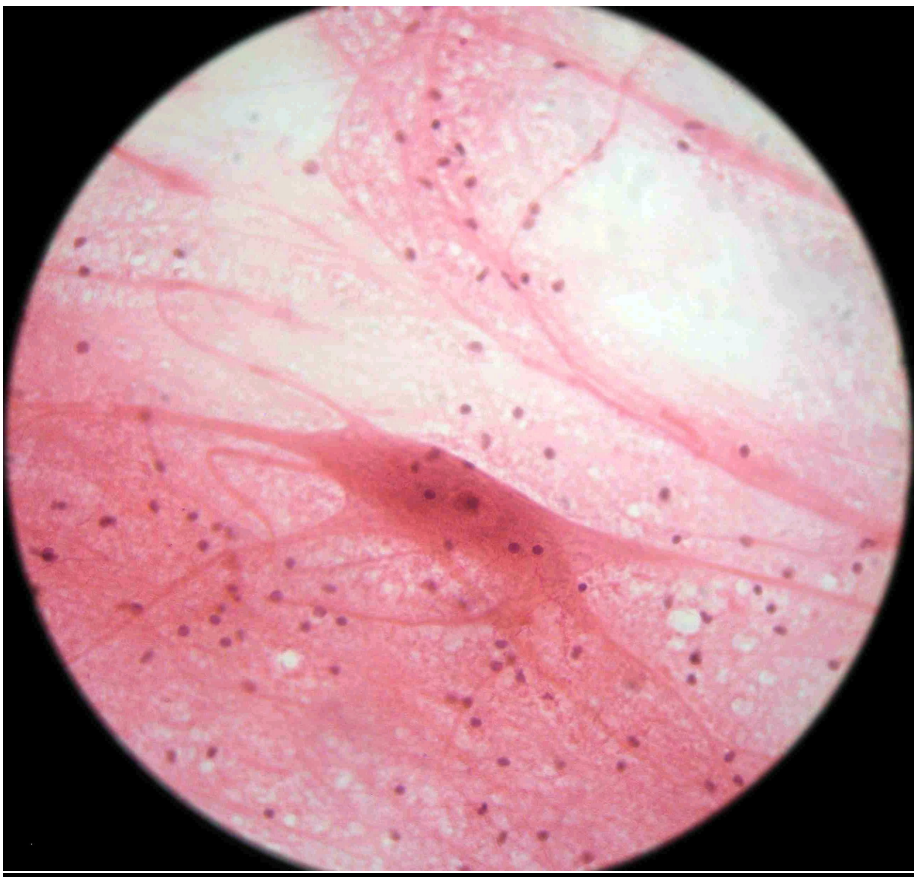


Nerve Cells and Astrocyte (SEM x2,250).

The neuron is the functional unit of the nervous system.

- Humans have about 100 billion neurons in their brain alone! While variable in size and shape, all neurons have three parts.
- Dendrites receive information from another cell and transmit the message to the cell body.
- The cell body contains the nucleus, mitochondria and other organelles typical of eukaryotic cells.
- The axon conducts messages away from the cell body.



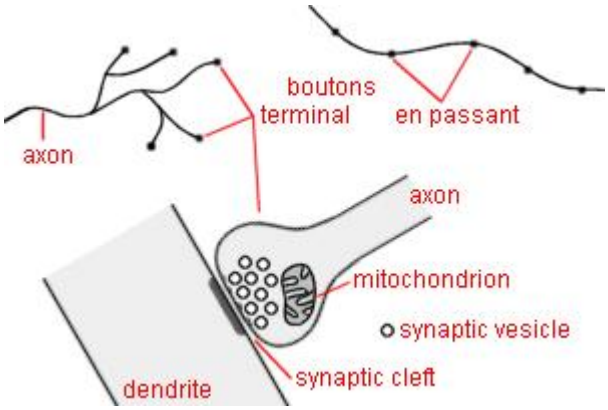


The shape of the neurone and its processes

- Neurons have long processes, which extend from the part of the cell body around the nucleus, the perikaryon or soma.
- The processes can be divided into two functionally and morphologically different groups, dendrites and axons.

- Dendrites are part of the receptive surface of the neuron.
- As a rule neurones have one to several primary dendrites, which emerge from the perikaryon.
- Primary dendrites may divide into secondary, tertiary etc. dendrites.
- Dendrites can be smooth, or they can be studded with small, mushroom-shaped appendages, which are called spines.
- Each neuron has as a rule one axon, and never more than one axon which emerges from the perikaryon or close to the trunks of one of the primary dendrites.
- The point of origin of the axon from the perikaryon is the axon hillock.
- The axon may, like the dendrites, branch as it travels through the nervous tissue to its destination(s).
- The axon is the "transmitting" process of the neuron

The axon forms small, bulb-shaped swellings called boutons at the ends (terminal boutons) or along the course (boutons en passant) of its branches. Synapses are morphologically specialised contacts between a bouton formed by one neuron, the presynaptic neurone, and the cell surface of another neurone, the postsynaptic neurone. Synaptic vesicles contain the neurotransmitters. Synaptic vesicles typically accumulate close to the site of contact between the bouton and the postsynaptic neurone. The release of the neurotransmitter from the synaptic vesicles into the synaptic cleft, i.e. the space between the bouton and the postsynaptic neuron, mediates the transfer of information from the pre- to the postsynaptic neuron.



- The shape and orientation of the dendritic tree of the neurone determines the amount and type of information that may reach the neurone.
- The course of its axon determines to which neurones this information may be passed on.
- The location of the neurone within the CNS determines to which major system the neurone belongs.
- There are several hundred functionally different areas, i.e. groups of neurones, in the CNS.
- Based on their location, the shape of their dendritic tree and the course of their axon, several thousand types of neurones can be distinguished in the CNS.

Neurons (Nerve Cells)

- *Structural units of the nervous system*
  - Composed of a body, axon, and dendrites
  - Long-lived, amitotic, and have a high metabolic rate
- *Their plasma membrane function in:*
  - Electrical signaling
  - Cell-to-cell signaling during development

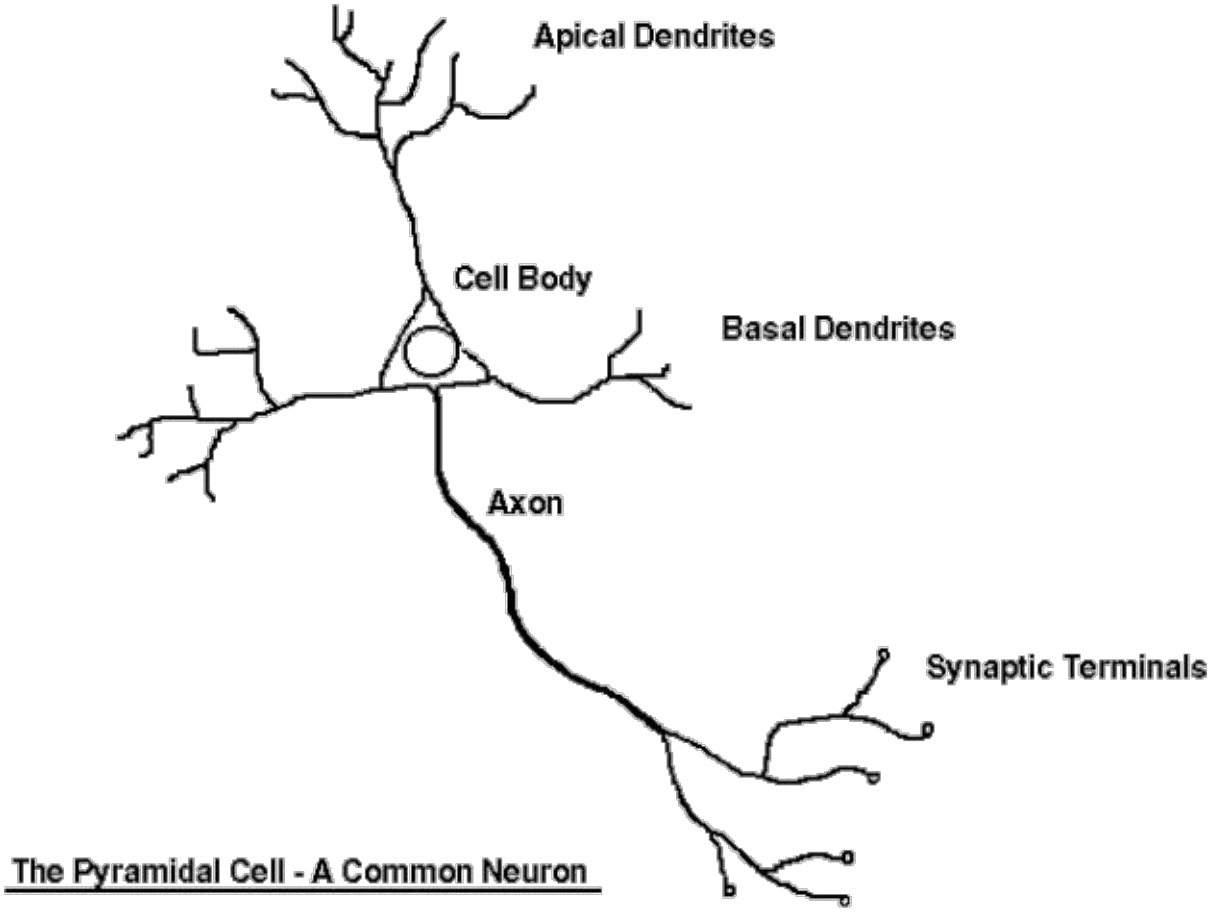
A ELEMENTS OF NERVOUS SYSTEM

I Nerve cells/neurons

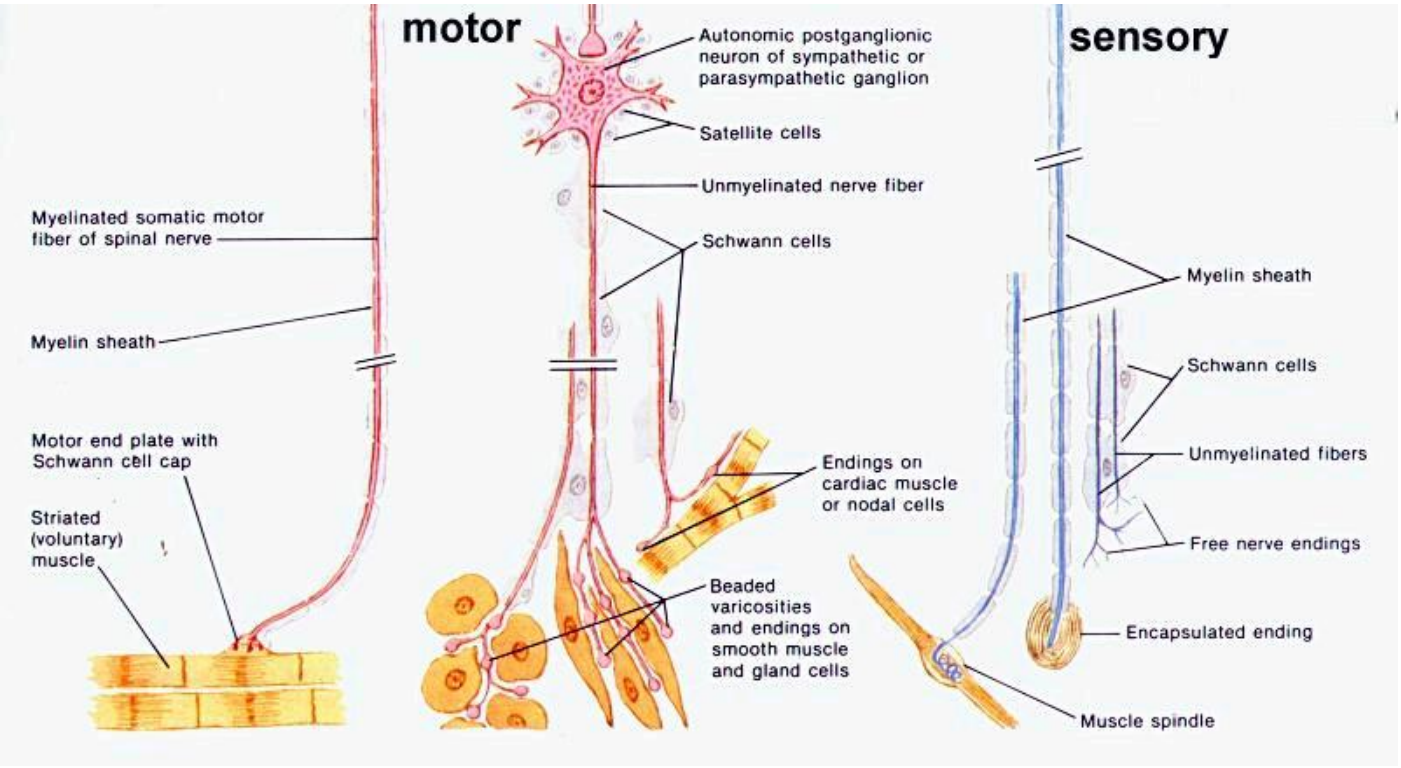
| Oligodendrocytes, Astrocytes, Ependymal cells,
| Microglia, Special glial cells - (CNS)

2 Glial cells ---|
| Schwann cells, Satellite/Capsule cells,
|_Enteric (gut) glia - (PNS)

3 Blood vessels
4 Connective tissue enclosing sheaths



Structure of a typical neuron. The above image is from http://eleceng.ukc.ac.uk/~sd5/pics/research/big/neuron.gif.

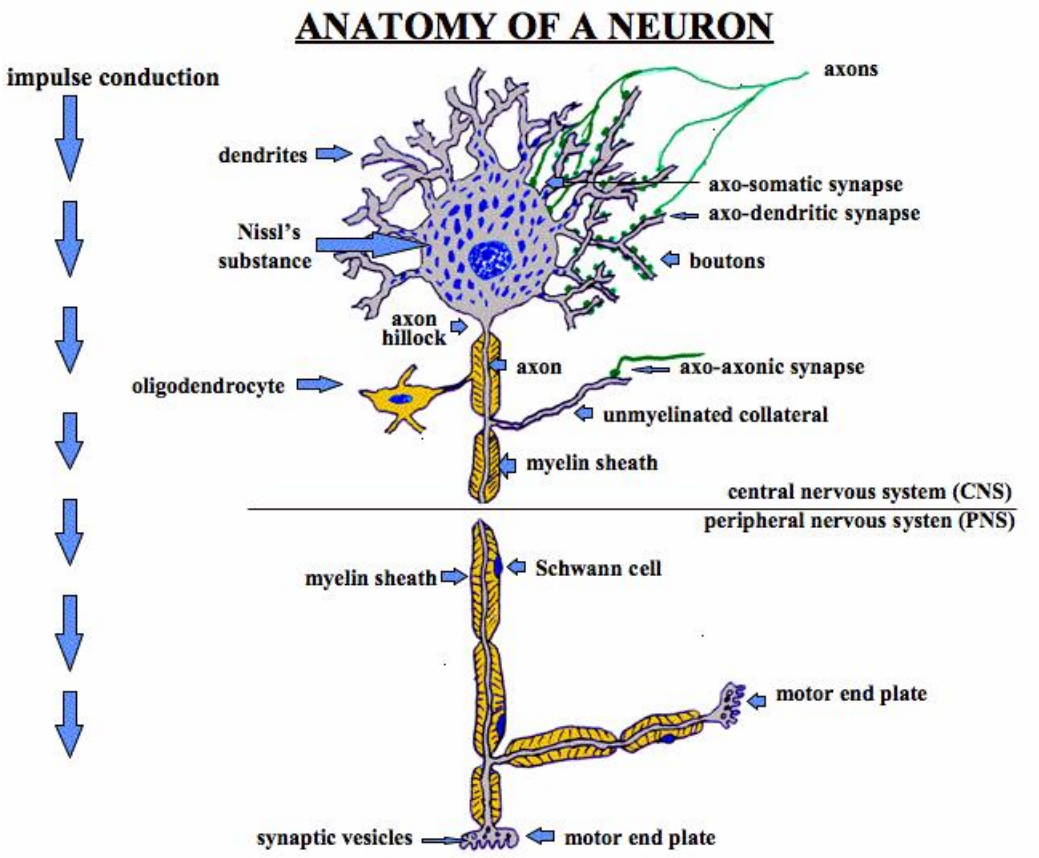


Three types of neurons occur.

- **Sensory neurons** typically have a long dendrite and short axon, and carry messages from sensory receptors to the central nervous system.

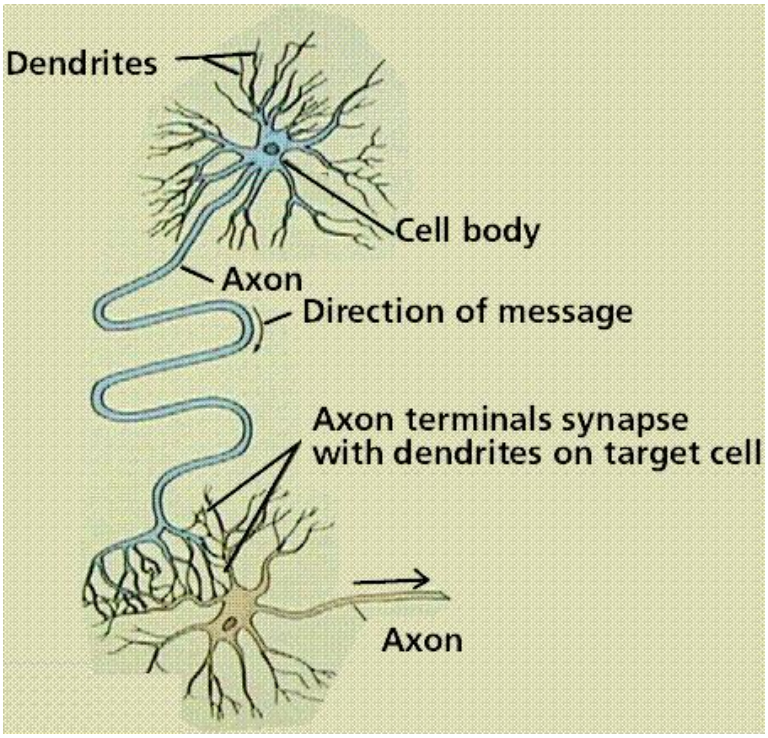
- **Motor neurons** have a long axon and short dendrites and transmit messages from the central nervous system to the muscles (or to glands).

- **Interneurons** are found only in the central nervous system where they connect neuron to neuron.

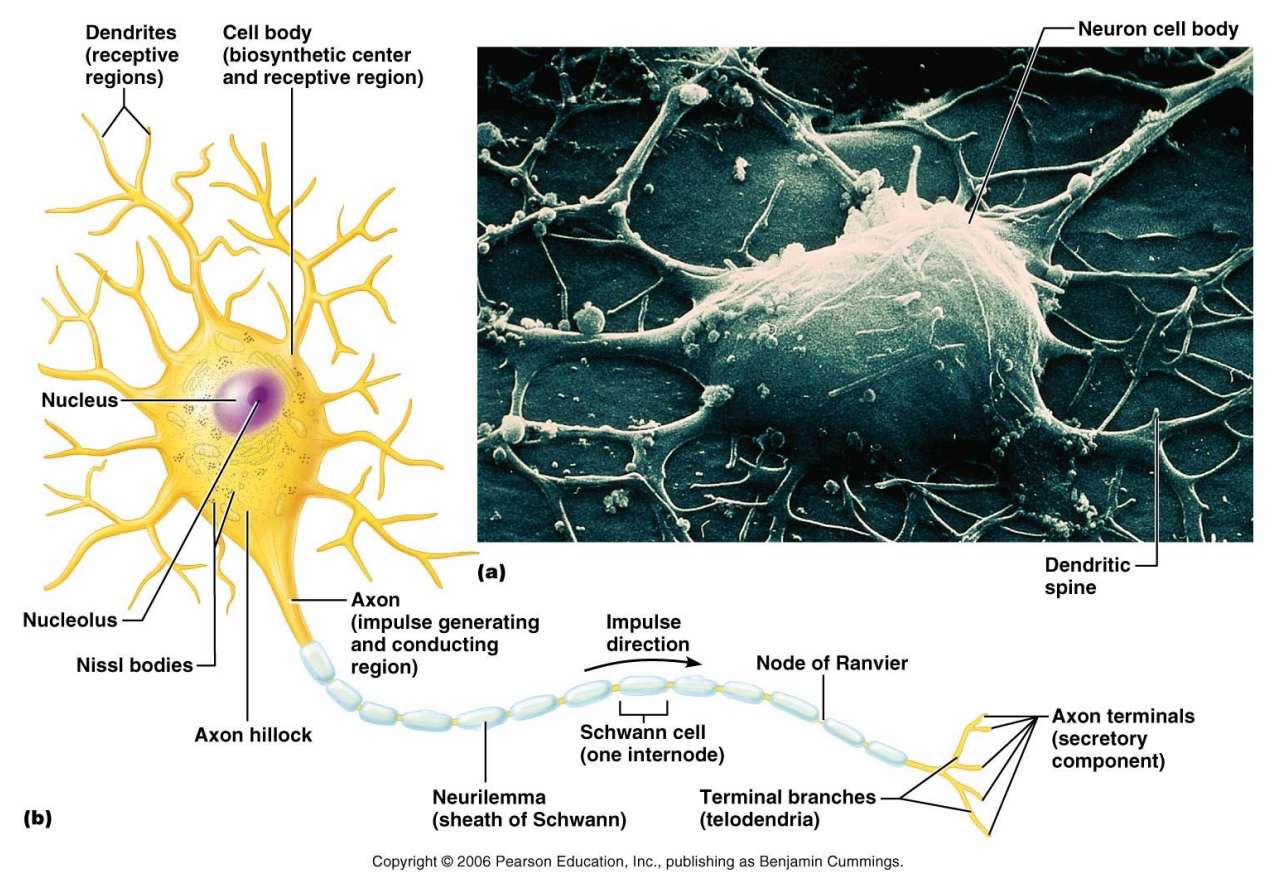


Processes: **Note: may regenerate if neuron cell body is intact**

- **dendrites**: drawn out extensions of cell; highly branched, tapering, either end in specialized sensory receptors (primary sensory neurons) or form synapses with neighboring neurons; receive stimuli; information input; generally convey impulse toward nerve cell body (afferent); contains rER; sER prominent;
- **axon** (commonly: nerve fibers): differentiated (specialized) extension of cell; single; arises from axon hillock; cylindrical process (may be one meter long); terminates on other neurons or effector organs through branches ending in terminal boutons; generally convey impulse away from nerve cell body (efferent); **has no rER (Nissl bodies) beyond hillock** except in motor end plate with striated muscle**;** sER prominent; extremely slender and elongate mitochondria



Structure of a neuron and the direction of nerve message transmission. Image from Purves et al., Life: The Science of Biology, 4th Edition, by Sinauer Associates (www.sinauer.com) and WH Freeman (www.whfreeman.com), used with permission.



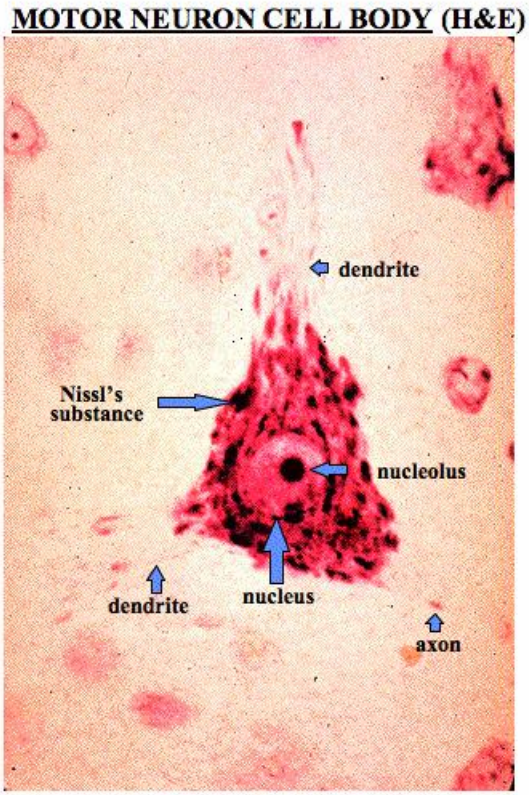
Nerve Cell Body (Perikaryon or Soma)

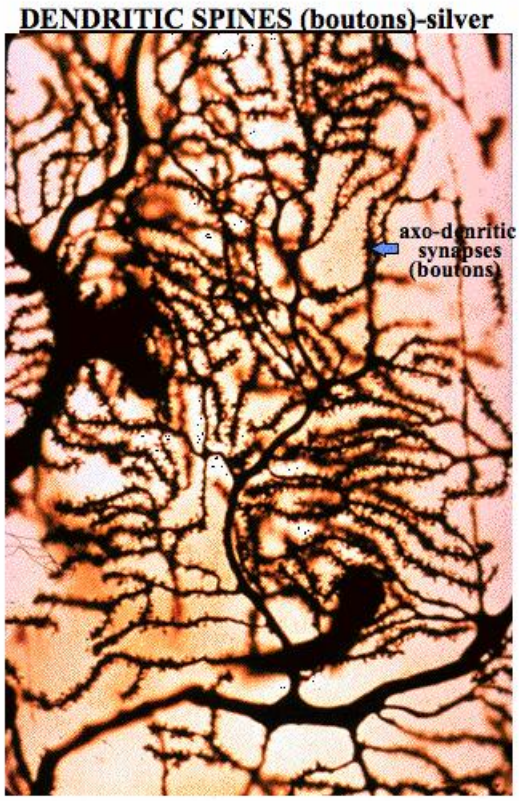
- *Contains the nucleus and a nucleolus*
- *Is the major biosynthetic center*
- *Is the focal point for the outgrowth of neuronal processes*
- *Has no centrioles (hence its amitotic nature)*
- *Has well-developed Nissl bodies (rough ER)*
- *Contains an axon hillock – cone-shaped area from which axons arise*

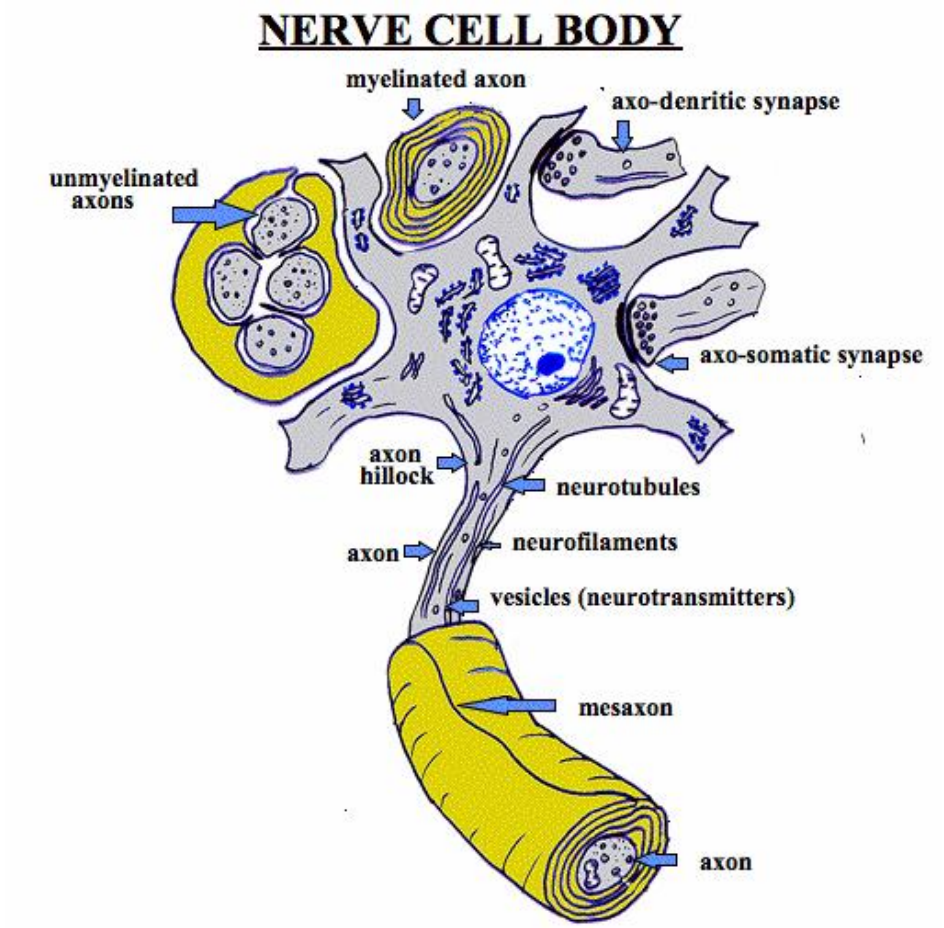
Cell body

a. cytoplasm – includes everything inside the cell membrane, including the various organelles. Cytosol, the internal fluid of the cell, is gel-like, mostly water with a high concentration of protein. Highly organized at the molecular level.
b. nucleus – location of genetic material, the chromosomes. Genes are transcribed in the nucleus to RNA, the RNA is processed and exits the nucleus as mRNA (Bear Fig 2.8)
c. ribosomes – found either free or attached to the surface of endoplasmic reticulum, hence rough ER. Responsible for translating mRNA into protein, which may be modified and sorted in the Golgi.
d. mitochondria – powerhouse of the cell, responsible for generating ATP

cytoskeleton – microtubules and various filaments. Provides structural support and a "highway" for movement of organelles and protein. Dynamically regulated.





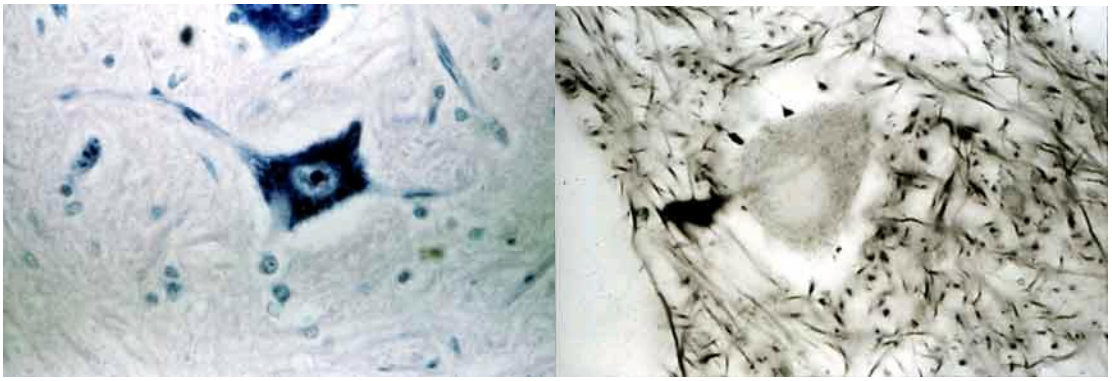


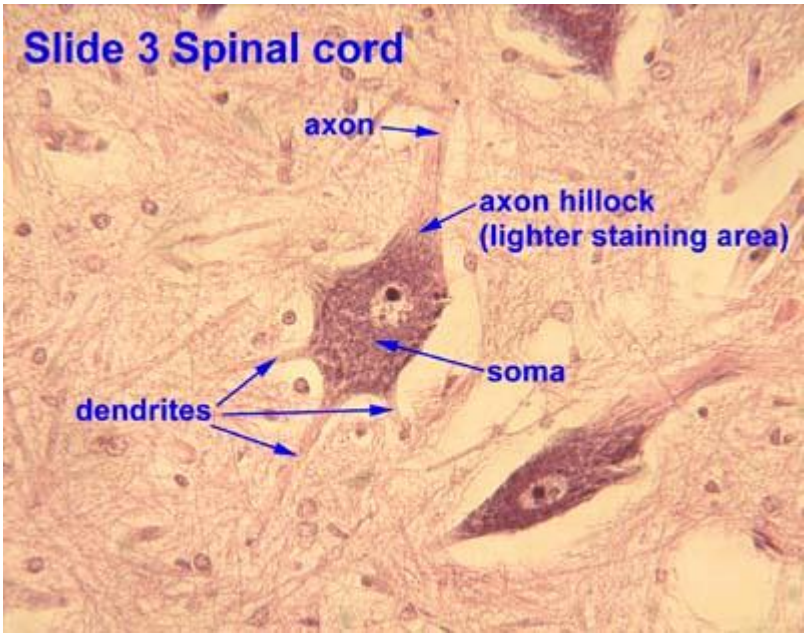
Processes

- *Armlike extensions from the soma*
- *Called tracts in the CNS and nerves in the PNS*
- *There are two types: axons and dendrites*

Dendrites of Motor Neurons

- *Short, tapering, and diffusely branched processes*
- *They are the receptive, or input, regions of the neuron*
- *Electrical signals are conveyed as graded potentials (not action potentials)*





Axons: Structure

- *Slender processes of uniform diameter arising from the hillock*
- *Long axons are called nerve fibers*
- *Usually there is only one unbranched axon per neuron*
- *Rare branches, if present, are called axon collaterals*
- *Axonal terminal – branched terminus of an axon*

- The **axolemma** is the membrane of a neuron's axon. It is responsible for maintaining the cell's membrane potential, and it contains channels through which ions can flow. This changes the voltage inside the axon and can depolarize or hyperpolarize the cell. Adequate depolarization will lead to an action potential, which will travel down the axon in a self-propagating manner, as more ion channels open due to stimulation by the influx of positive ions.

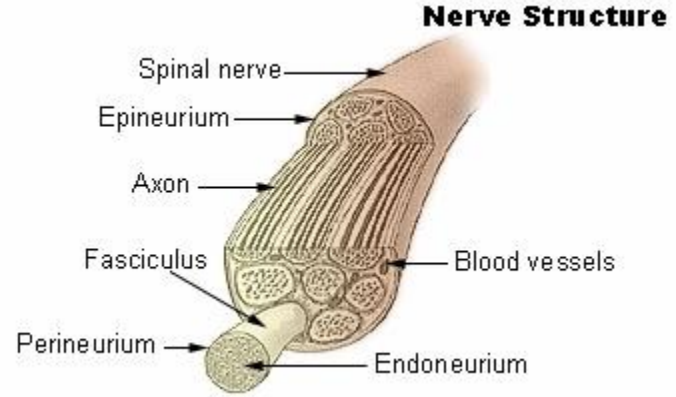
If the axolemma is damaged, it becomes unable to perform its vital role of maintaining the concentration gradient of ions on the outside of the cell. When these ions rush down their gradient into the cell, they can cause a number of different cellular processes that lead to cellular damage and sometimes death.

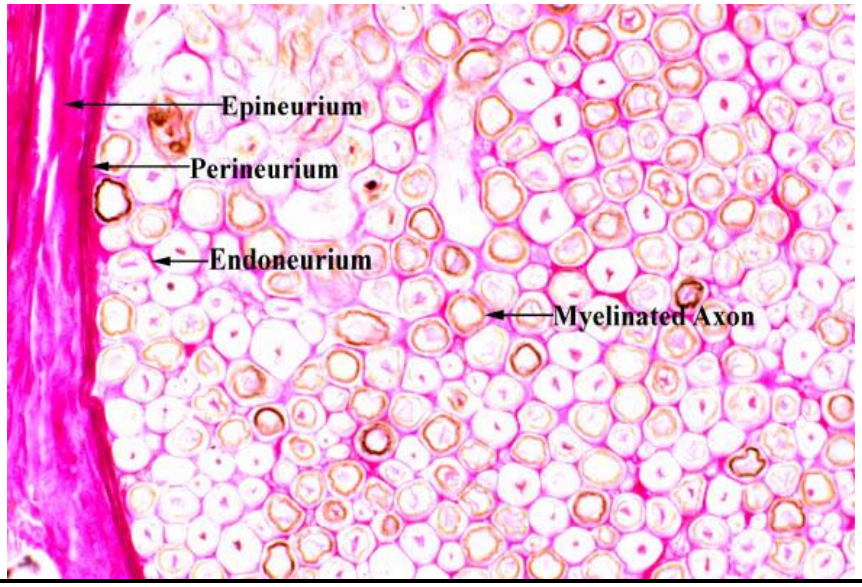
- **Endoneurium**

The nerve fibers are held together and supported within the funiculus by delicate connective tissue, called the **endoneurium**.

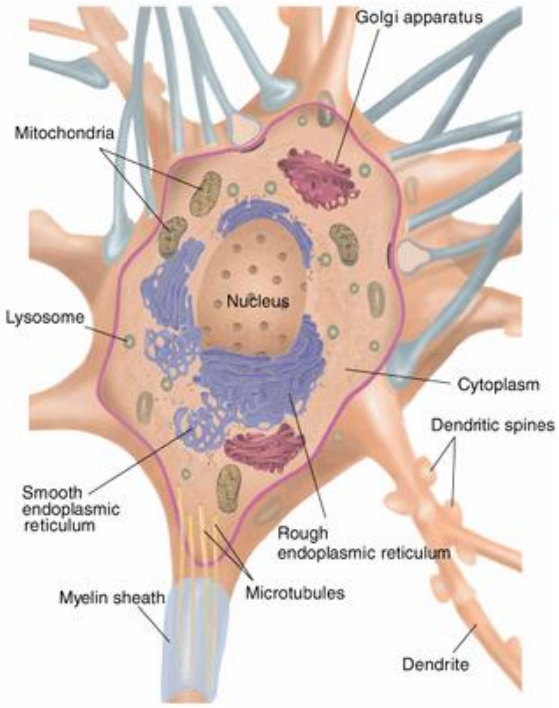
It is continuous with septa which pass inward from the innermost layer of the perineurium, and shows a ground substance in which are imbedded fine bundles of fibrous connective tissue, primarily collagen, running for the most part longitudinally.

It serves to support capillary vessels, arranged so as to form a net-work with elongated meshes.


Nerve Structure
Spinal nerve
Epineurium
Axon
Fasciculus
Blood vessels
Perineurium
Endoneurium


Epineurium
Perineurium
Endoneurium
Myelinated Axon

Principal Internal Structures of a Multipolar Neuron



Axons: Function

- *Generate and transmit action potentials*
- *Secrete neurotransmitters from the axonal terminals*
- *Movement along axons occurs in two ways*
  - Anterograde — toward axonal terminal
  - Retrograde — away from axonal terminal

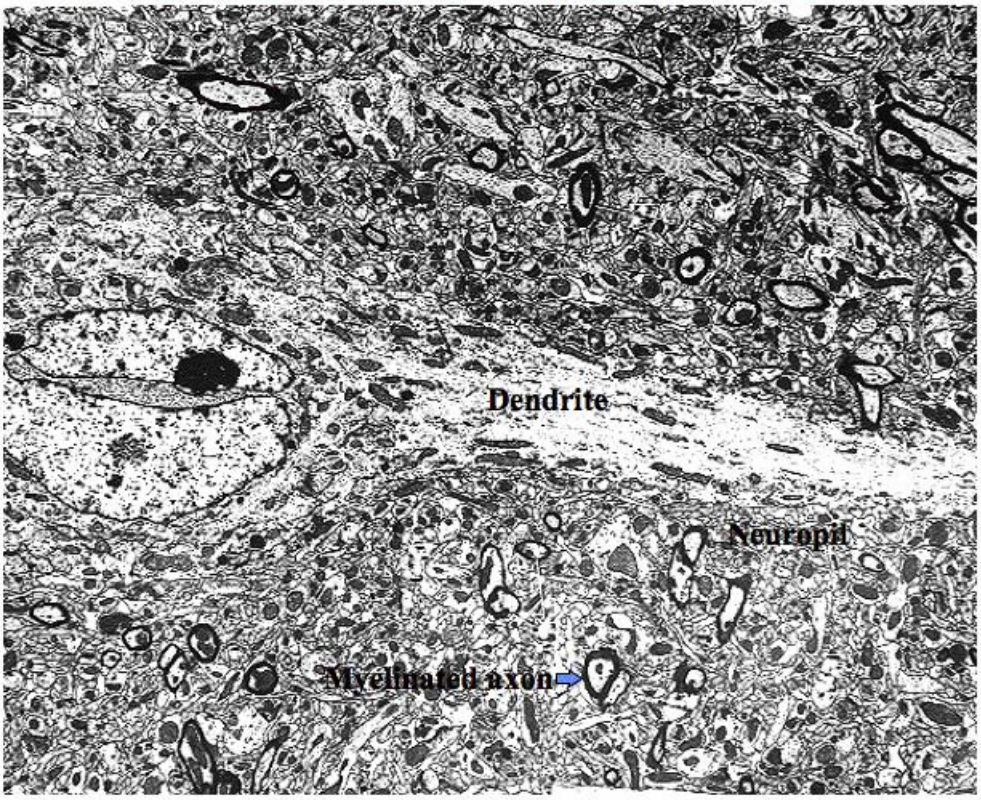
Neurons are similar to other cells in the body because:

1.Neurons are surrounded by a cell membrane.
2.Neurons have a nucleus that contains genes.
3.Neurons contain cytoplasm, mitochondria and other organelles.
4.Neurons carry out basic cellular processes such as protein synthesis and energy production.

Neurons differ from other cells in the body because:

1.Neurons have specialised extensions called dendrites and axons. Dendrites bring information to the cell body and axons take information away from the cell body.
2.Neurons communicate with each other through an electrochemical process.
3.Neurons contain some specialized structures (for example, synapses) and chemicals (for example, neurotransmitters).

NEURON CELL BODY, DENDRITE AND NEUROPIL

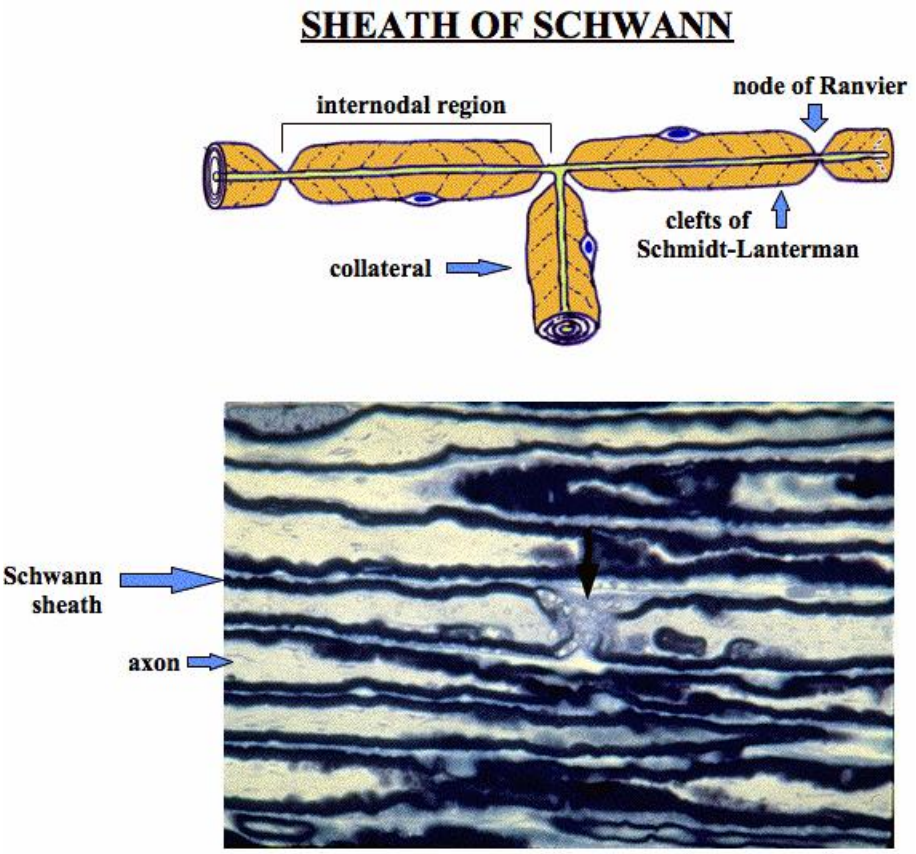


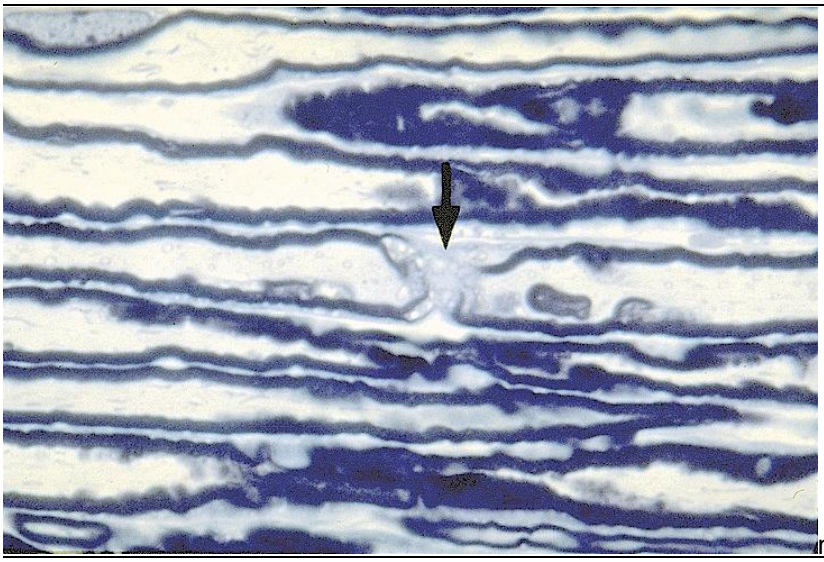
Myelin Sheath

- *Whitish, fatty (protein-lipoid), segmented sheath around most long axons*
- *It functions to:*
  - Protect the axon
  - Electrically insulate fibers from one another
  - Increase the speed of nerve impulse transmission

Myelin Sheath and Neurilemma: Formation

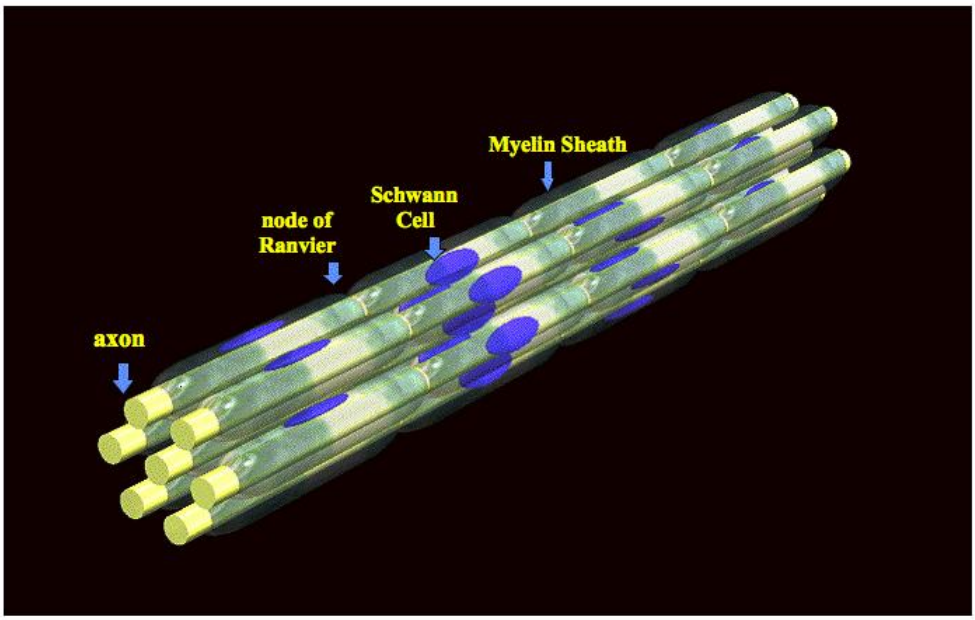
- *Formed by Schwann cells in the PNS*
- ***A Schwann cell:***
  - Envelopes an axon in a trough
  - Encloses the axon with its plasma membrane
  - Has concentric layers of membrane that make up the myelin sheath
- ***Neurilemma*** *– remaining nucleus and cytoplasm of a Schwann cell*





node of ranvier the arrow

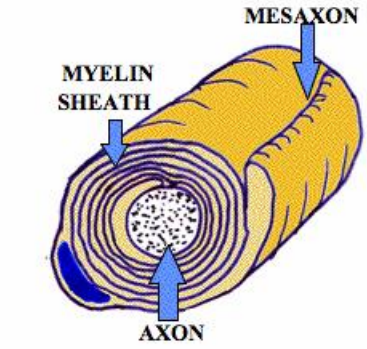
MYELINATED AXONS

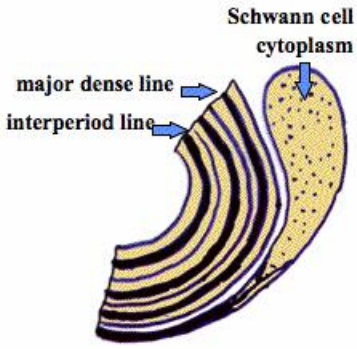


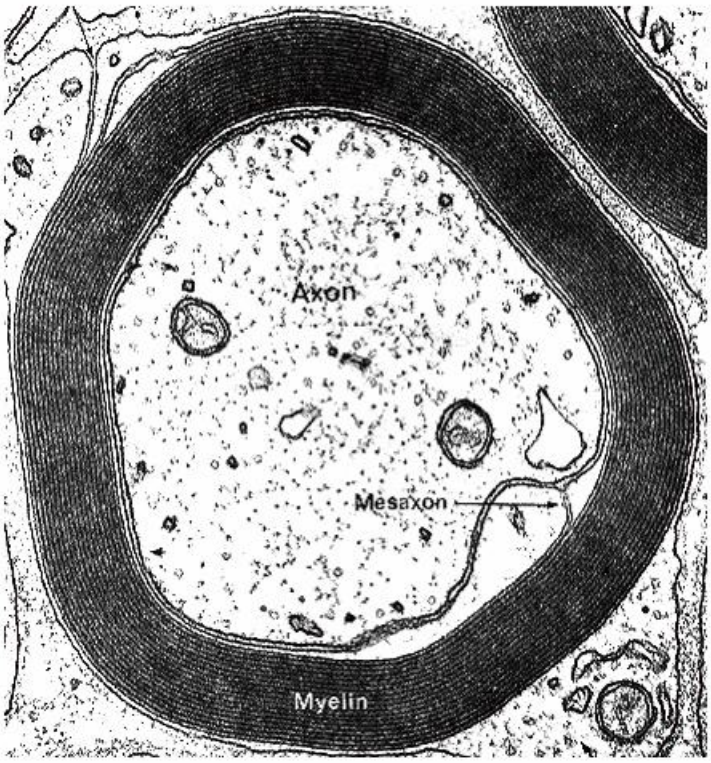
Nodes of Ranvier (Neurofibral Nodes)

- ***Gaps in the myelin sheath between adjacent Schwann cells***
- ***They are the sites where axon collaterals can emerge***

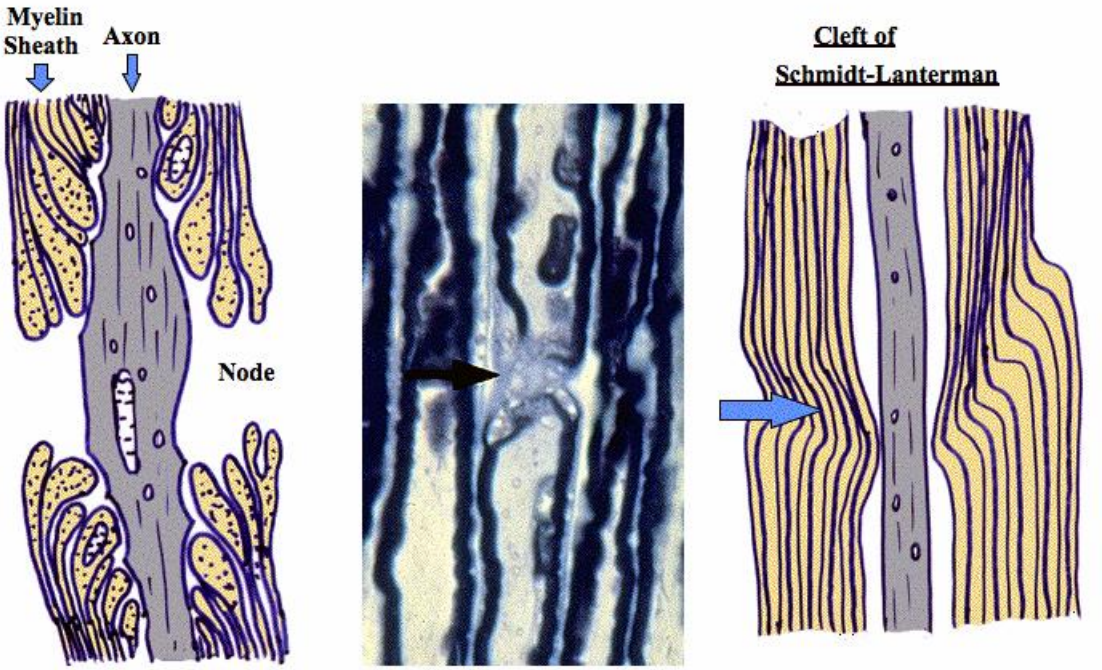
MYELIN







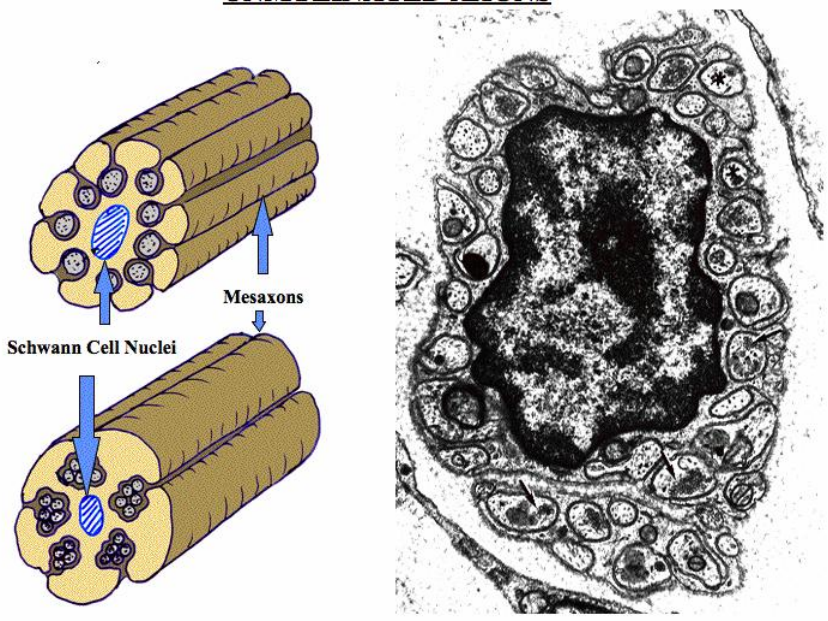
NODE OF RANVIER AND CLEFTS OF SCHMIT-LANTERMAN



Unmyelinated Axons

- ***A Schwann cell surrounds nerve fibers but coiling does not take place***
- ***Schwann cells partially enclose 15 or more axons***

UNMYLINATED AXONS

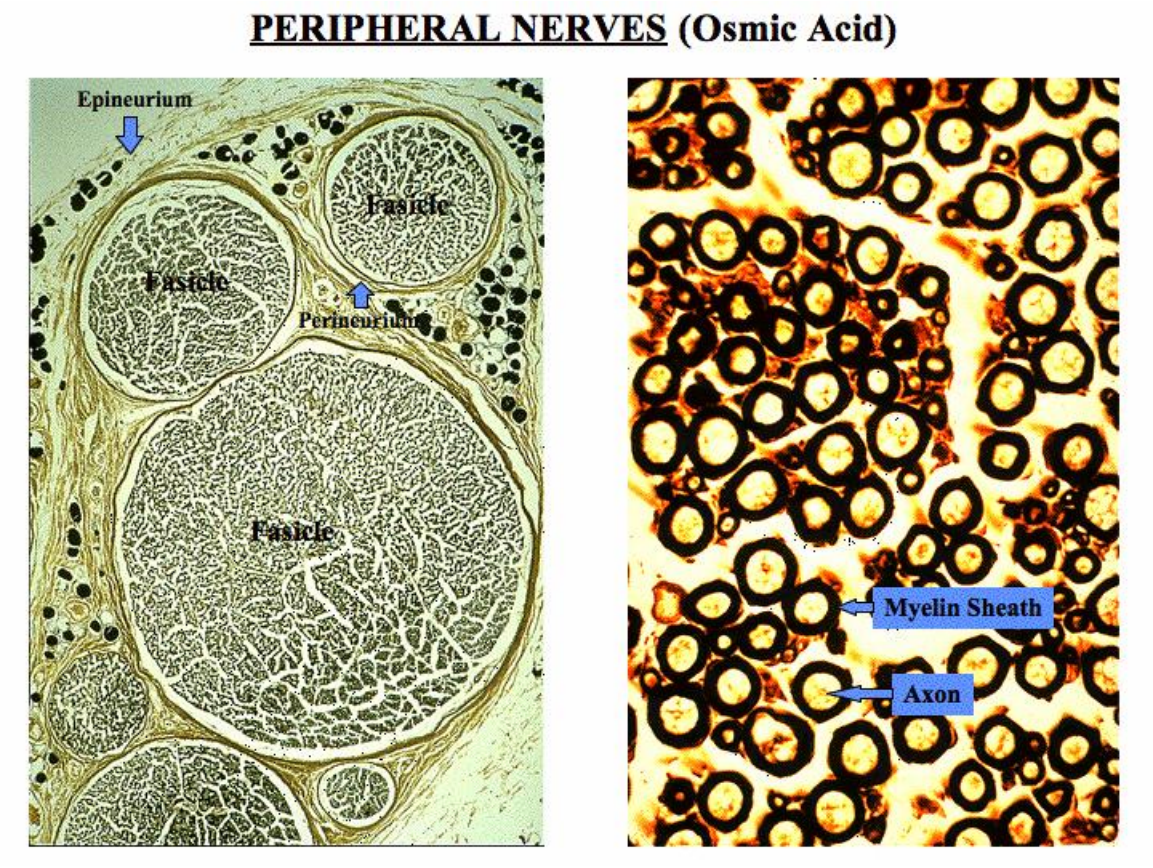


Axons of the CNS

- ***Both myelinated and unmyelinated fibers are present***
- ***Myelin sheaths are formed by oligodendrocytes***
- ***Nodes of Ranvier are widely spaced***
- ***There is no neurilemma***

Regions of the Brain and Spinal Cord

- ***White matter – dense collections of myelinated fibers***
- ***Gray matter – mostly soma and unmyelinated fibers***



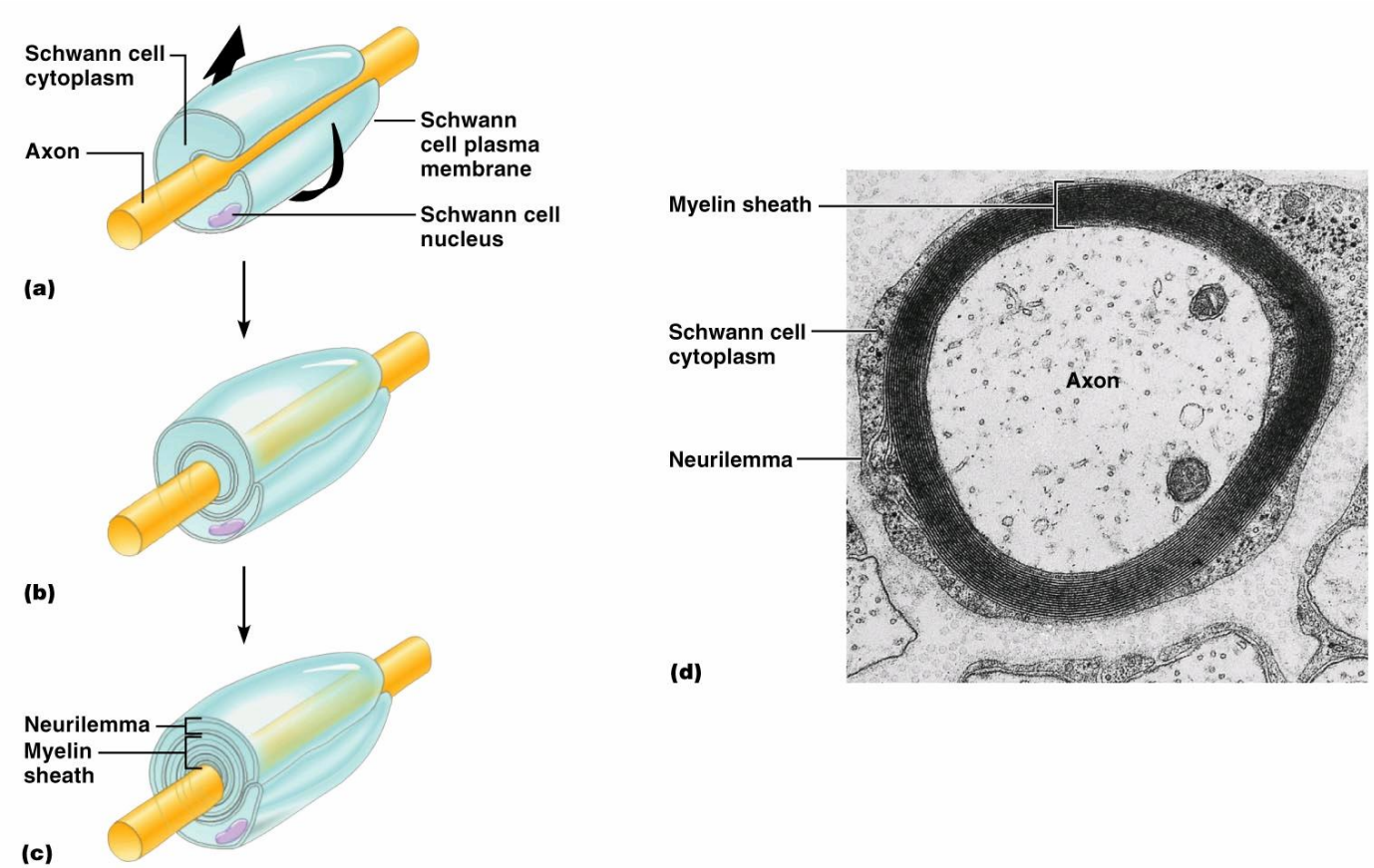
Some axons are wrapped in a myelin sheath formed from the plasma membranes of specialized glial cells known as **Schwann cells**. \

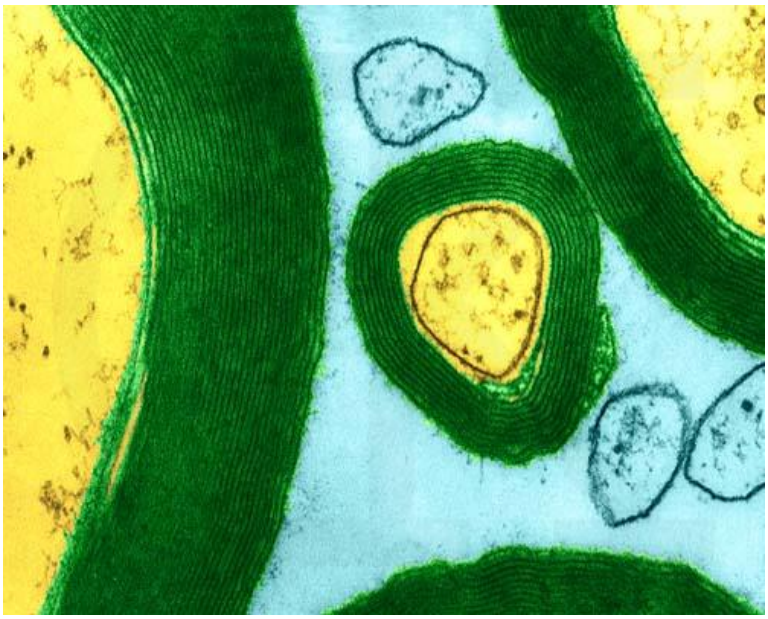
Schwann cells serve as supportive, nutritive, and service facilities for neurons.

The gap between Schwann cells is known as the **node of Ranvier,** and serves as points along the neuron for generating a signal.

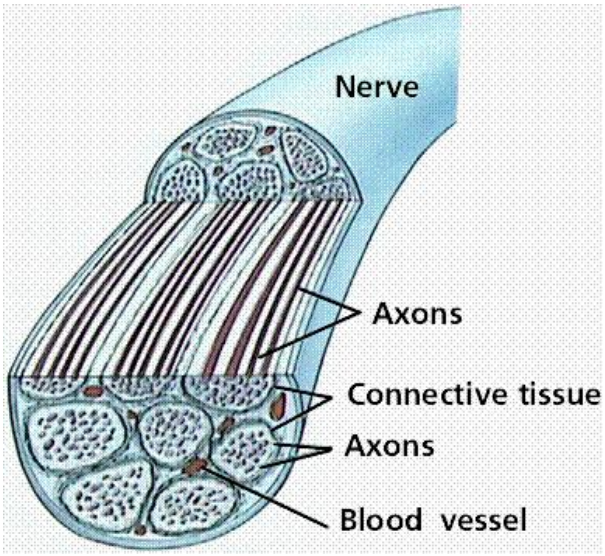
Signals jumping from node to node travel hundreds of times faster than signals traveling along the surface of the axon.

This allows your brain to communicate with your toes in a few thousandths of a second.

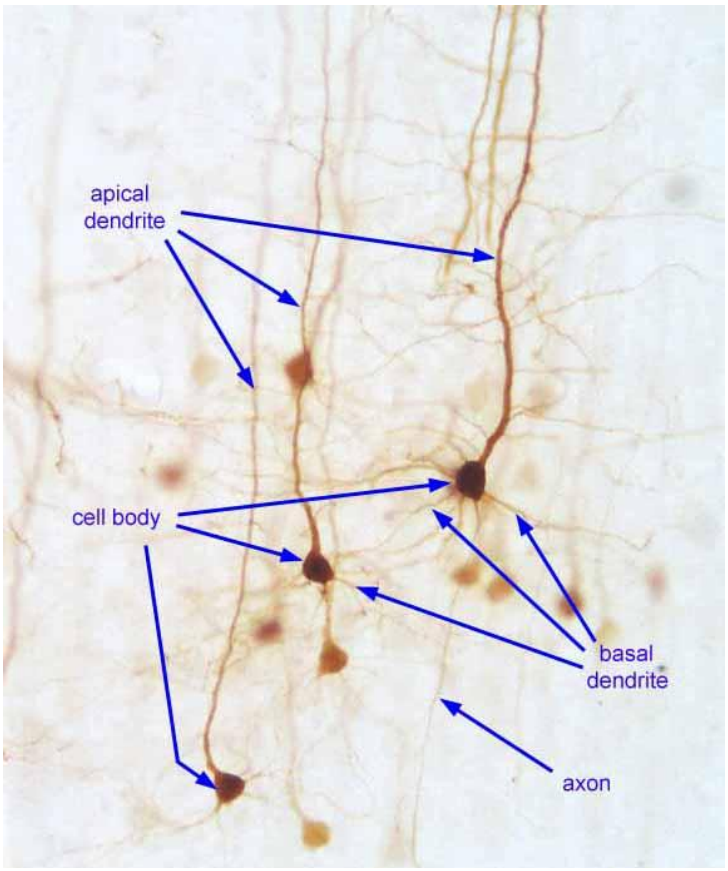




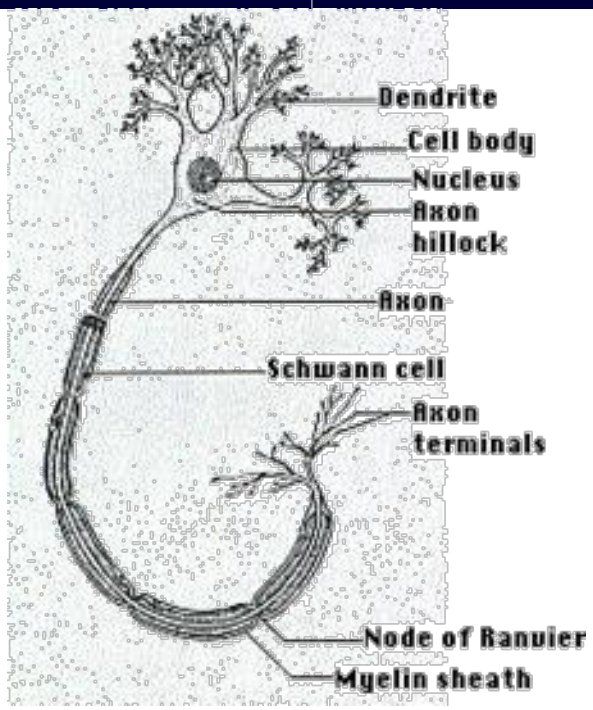
Cross section of **myelin sheaths** that surround **axons** (TEM x191,175). This image is copyright Dennis Kunkel at www.DennisKunkel.com, used with permission.

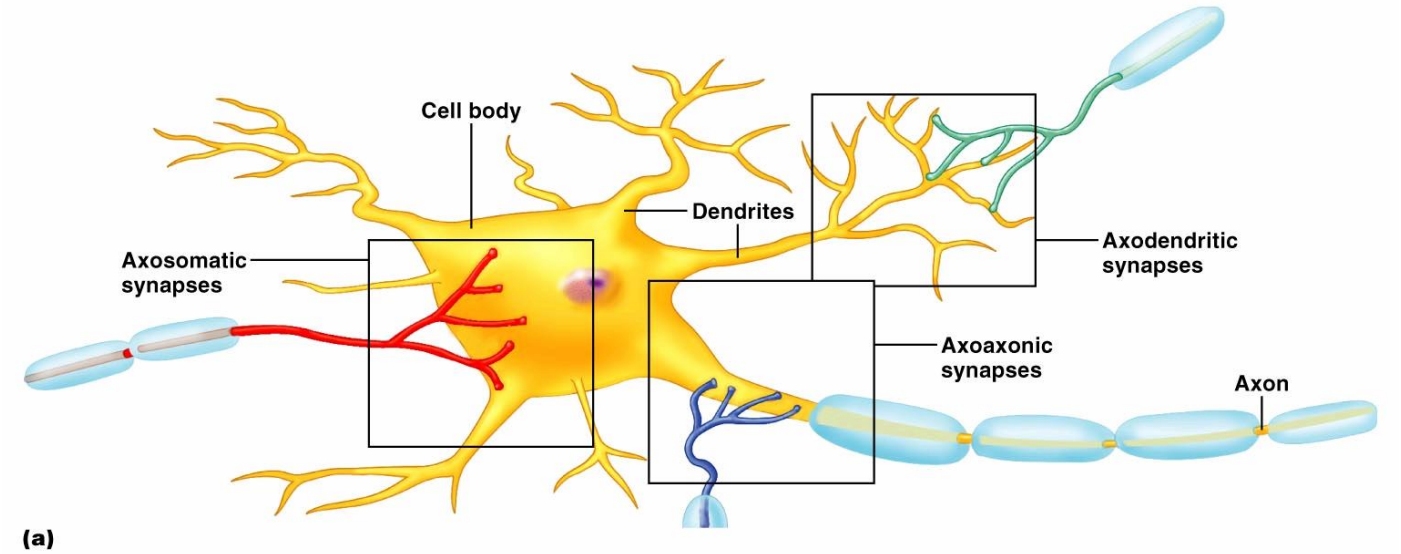


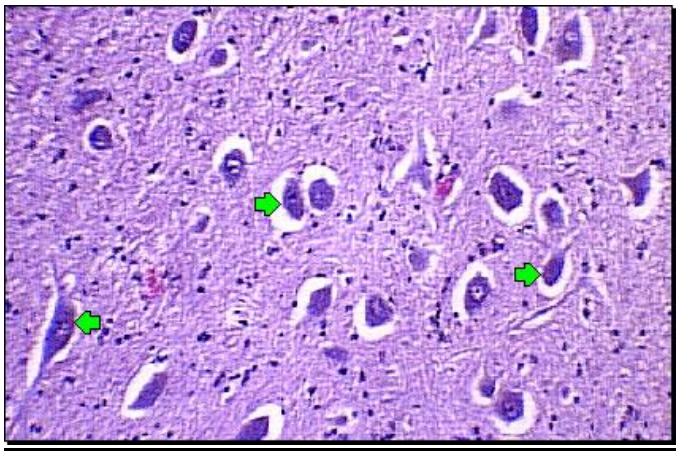
Structure of a nerve bundle. Image from Purves et al., Life: The Science of Biology, 4th Edition, by Sinauer Associates (www.sinauer.com) and WH Freeman (www.whfreeman.com), used with permission.

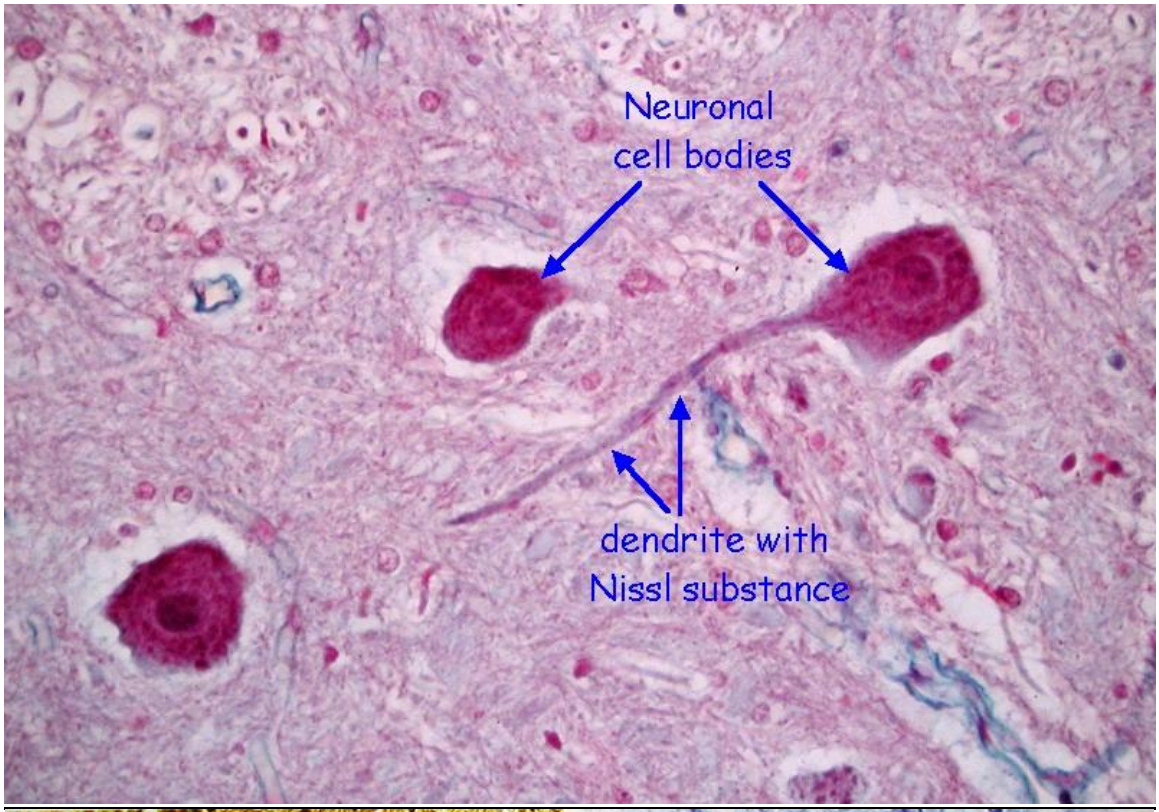


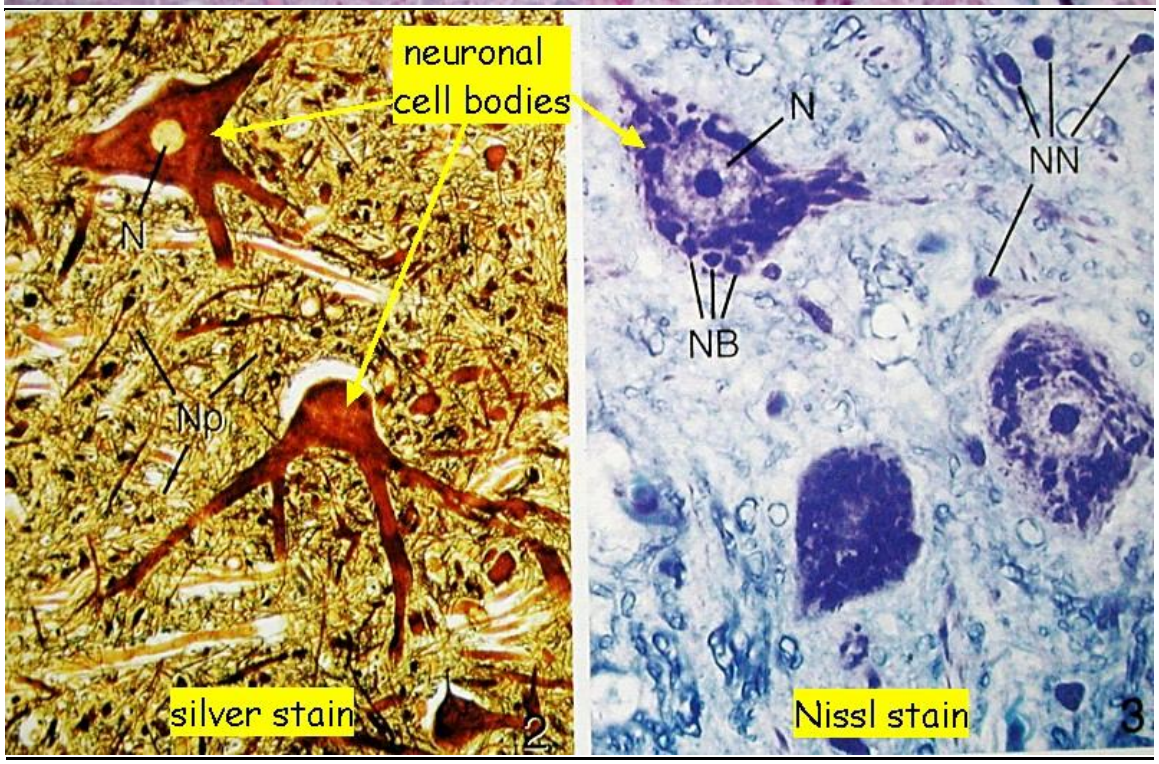
Axons	Dendrites
•Take information away from the cell body •Smooth Surface •Generally only 1 axon per cell •No ribosomes •Can have myelin •Branch further from the cell body	•Bring information to the cell body •Rough Surface (dendritic spines) •Usually many dendrites per cell •Have ribosomes •No myelin insulation •Branch near the cell body

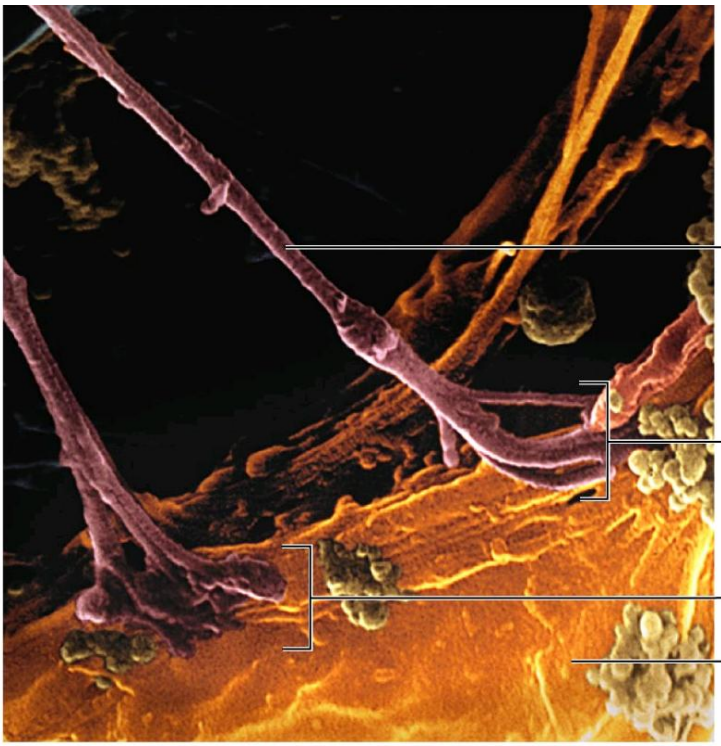


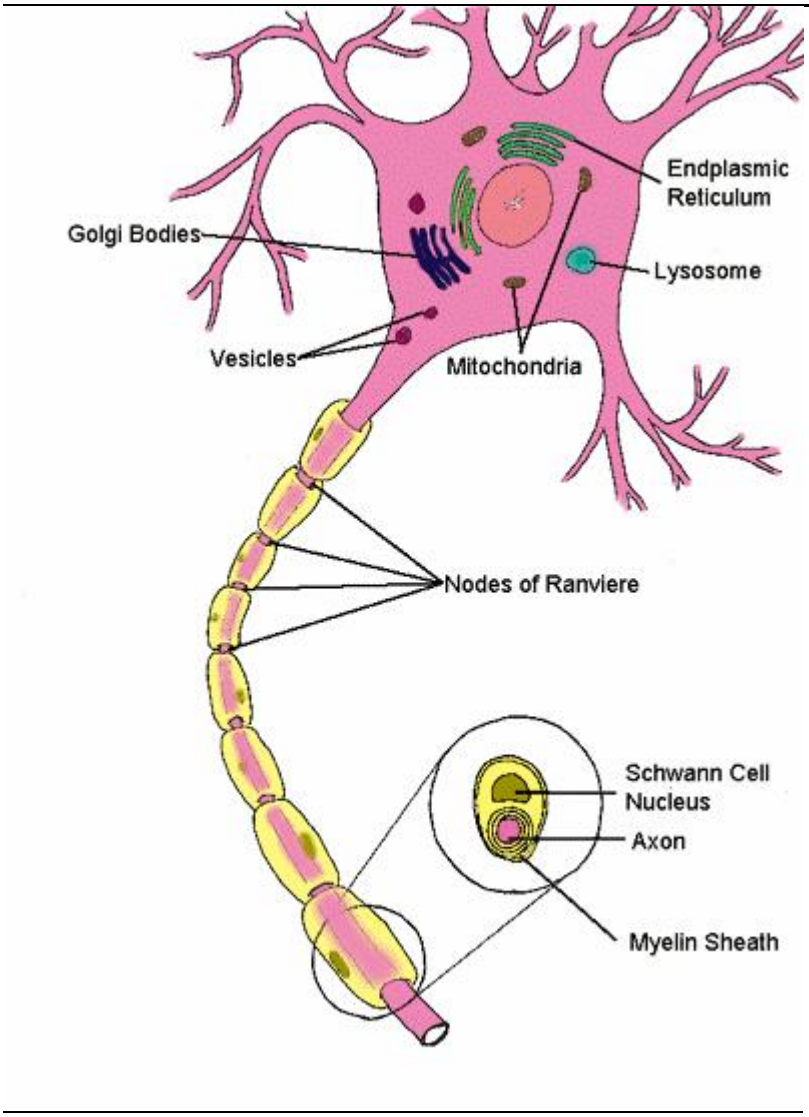





Neuronal
cell bodies
dendrite with
Nissl substance


neuronal
cell bodies
N
NO
silver stain
N
NN
NB
Nissl stain
3


Axon
Axosomatic synapses
Soma of postsynaptic neuron


Endplasmic Reticulum
Golgi Bodies
Lysosome
Vesicles
Mitochondria
Nodes of Ranviere
Schwann Cell Nucleus
Axon
Myelin Sheath

Neuron Classification

- *Structural:*
  - **Multipolar** — three or more processes
  - **Bipolar** — two processes (axon and dendrite)
  - **Unipolar** — single, short process
- *Functional:*
  - **Sensory (afferent)** — transmit impulses toward the CNS
  - **Motor (efferent)** — carry impulses away from the CNS
  - **Interneurons (association neurons)** — shuttle signals through CNS pathways

	Sensory neuron	Interneuron	Motor Neuron
Length of Fibers	Long dendrites and short axon	Short dendrites and short or long anxon	Short dendrites and long axons
Location	Cell body and dendrite are outside of the spinal cord; the cell body is located in a dorsal root ganglion	Entirely within the spinal cord or CNS	Dendrites and the cell body are located in the spinal cord; the axon is outside of the spinal cord
Function	Conduct impulse to the spinal cord	Interconnect the sensory neuron with appropriate motor neuron	Conduct impulse to an effector (muscle or gland)

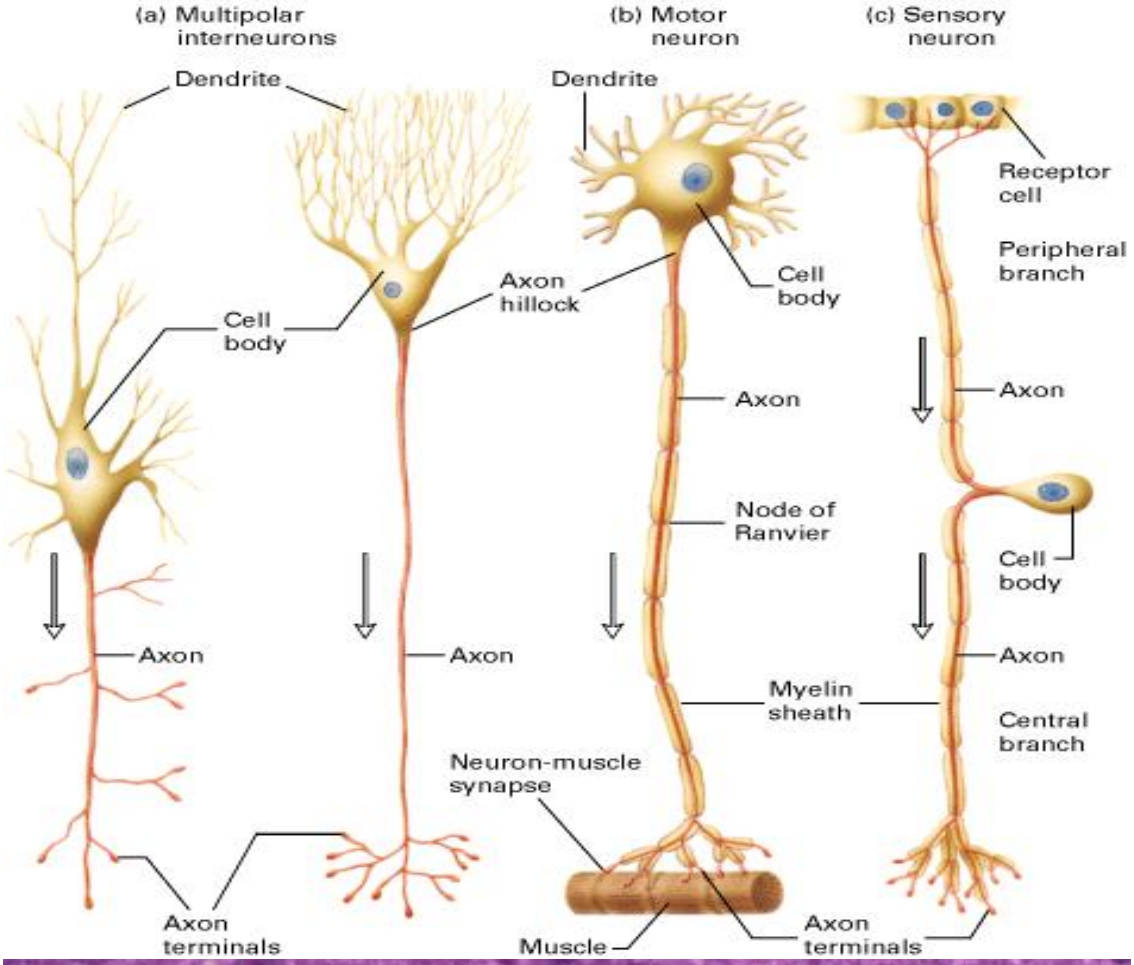
Structural classification

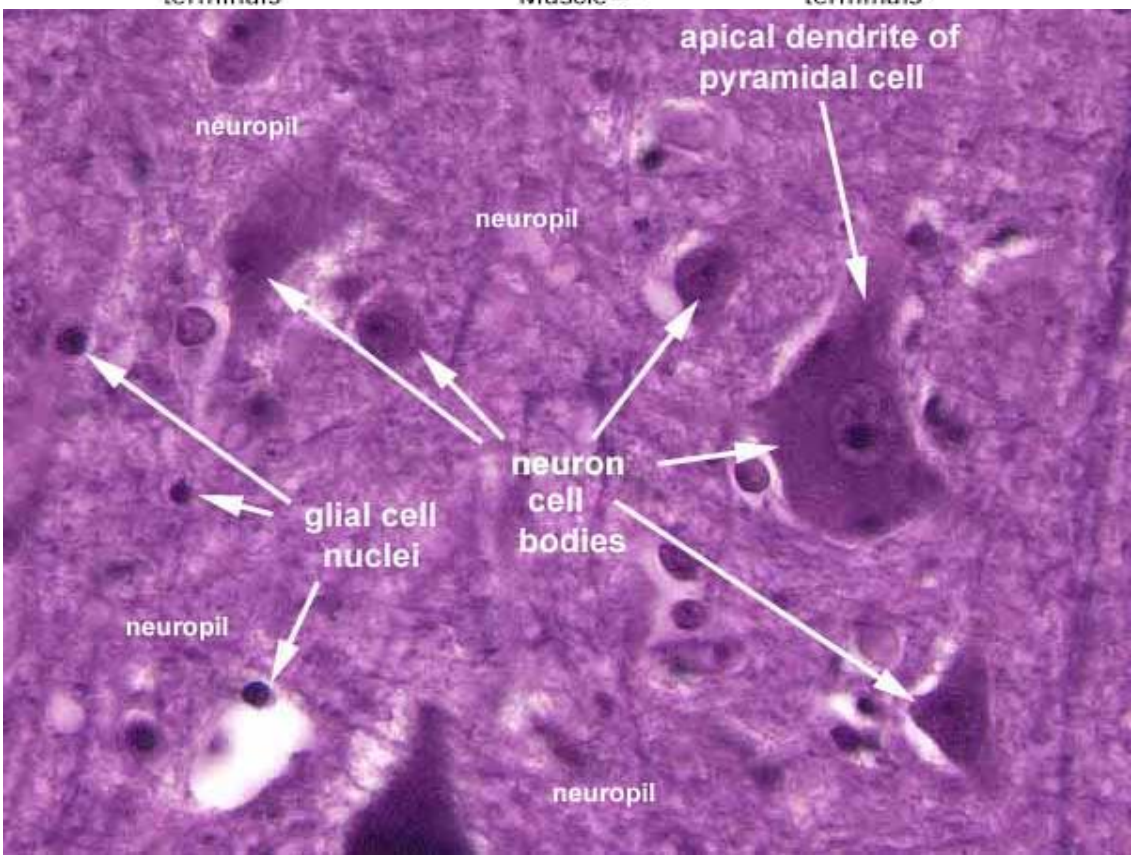
Most neurons can be anatomically characterized as:

- •Unipolar or Pseudounipolar- dendrite and axon emerging from same process.
- •Bipolar - single axon and single dendrite on opposite ends of the soma.
- •Multipolar - more than two dendrites
  - •Golgi I- neurons with long-projecting axonal processes.
  - •Golgi II- neurons whose axonal process projects locally.

Some unique neuronal types can be identified according to their location in the nervous system and distinct shape.

Some examples are basket, Betz, medium spiny, Purkinje, pyramidal and Renshaw cells.


(a) Multipolar interneurons
(b) Motor neuron
(c) Sensory neuron
Dendrite
Dendrite
Receptor cell
Peripheral branch
Axon hillock
Cell body
Cell body
Axon
Axon
Node of Ranvier
Cell body
Axon
Axon
Myelin sheath
Central branch
Neuron-muscle synapse
Axon terminals
Muscle
Axon terminals

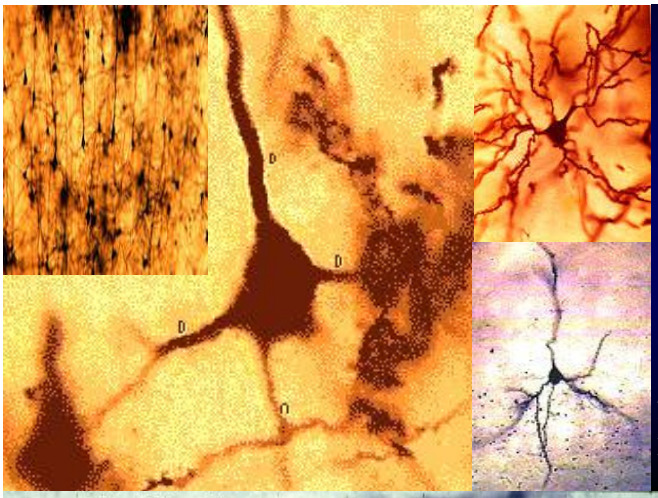

apical dendrite of pyramidal cell
neuropil
neuropil
neuron cell bodies
glial cell nuclei
neuropil
neuropil

Classification by action on other neurons

- **Excitatory neurons** evoke excitation of their target neurons. Excitatory neurons in the brain are often glutamatergic. Spinal motoneurons use acetylcholine as their neurotransmitter.

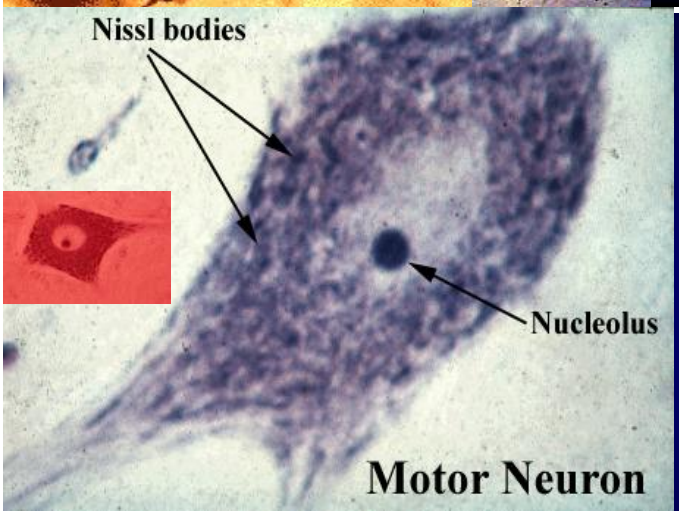
- **Inhibitory neurons** evoke inhibition of their target neurons. Inhibitory neurons are often interneurons. The output of some brain structures (neostriatum, globus pallidus, cerebellum) are inhibitory. The primary inhibitory neurotransmitters are GABA and glycine.

- **Modulatory neurons** evoke more complex effects termed neuromodulation. These neurons use such neurotransmitters as dopamine, acetylcholine, serotonin and others.



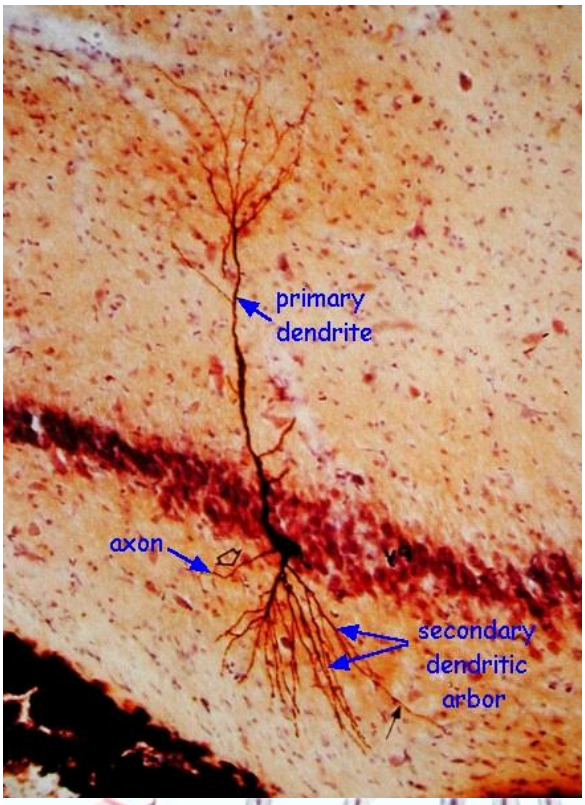
A **Nissl body** (or **Nissl granule** or **tigroid body**) is a large granular body found in nerve cells.

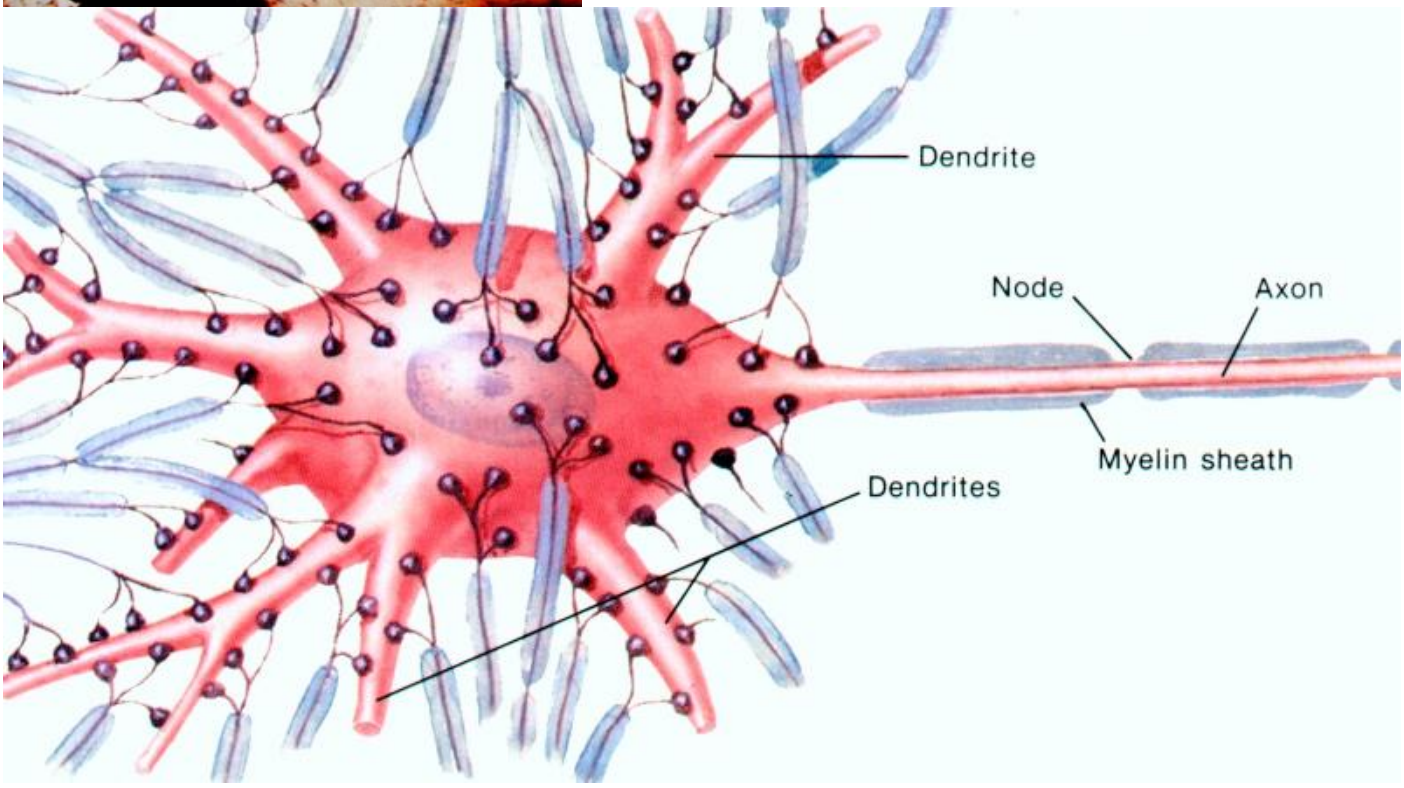
These granules are rough endoplasmic reticulum (with ribosomes) and are the site of protein synthesis.
Nissl bodies show changes under various physiological conditions and in pathological conditions they may dissolve and disappear (karyolysis).



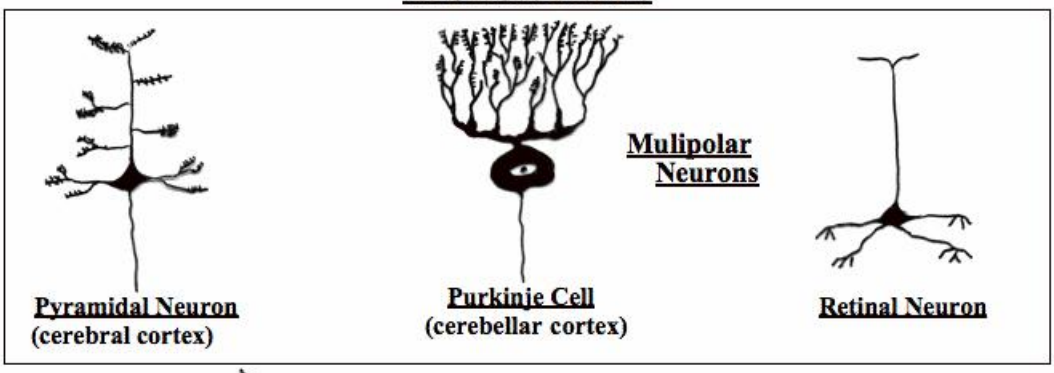
The **axolemma** is the membrane of a neuron's axon.

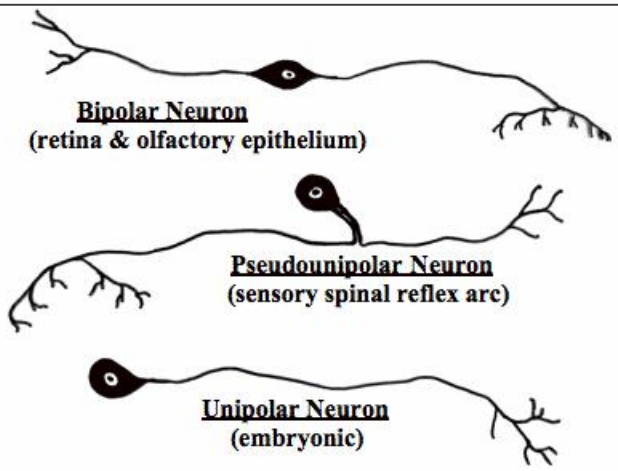
It is responsible for maintaining the cell's membrane potential, and it contains channels through which ions can flow.

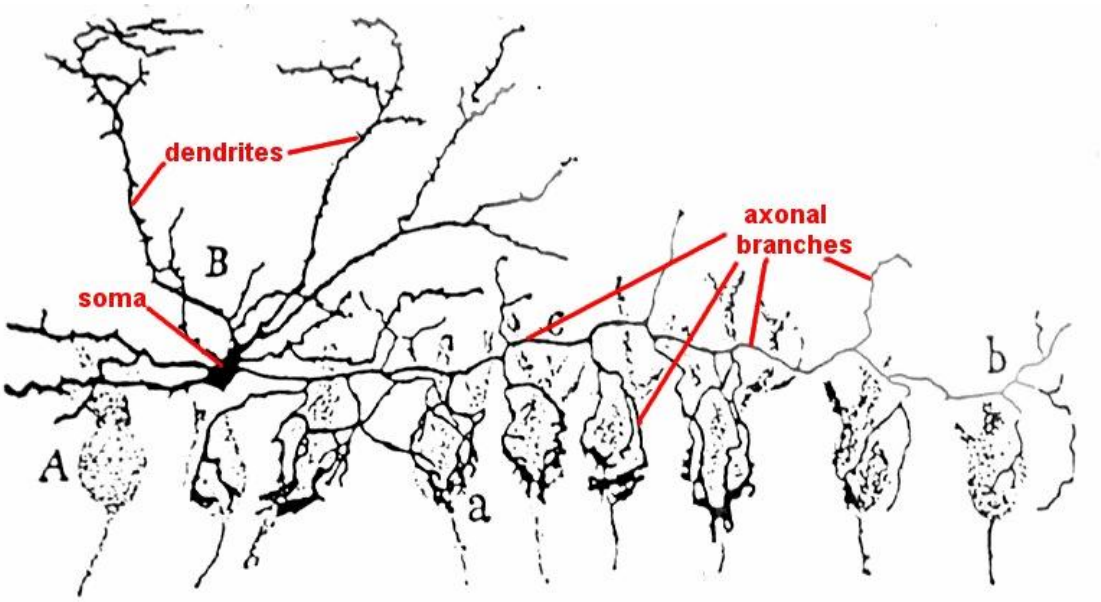

primary
dendrite
axon
secondary
dendritic
arbor

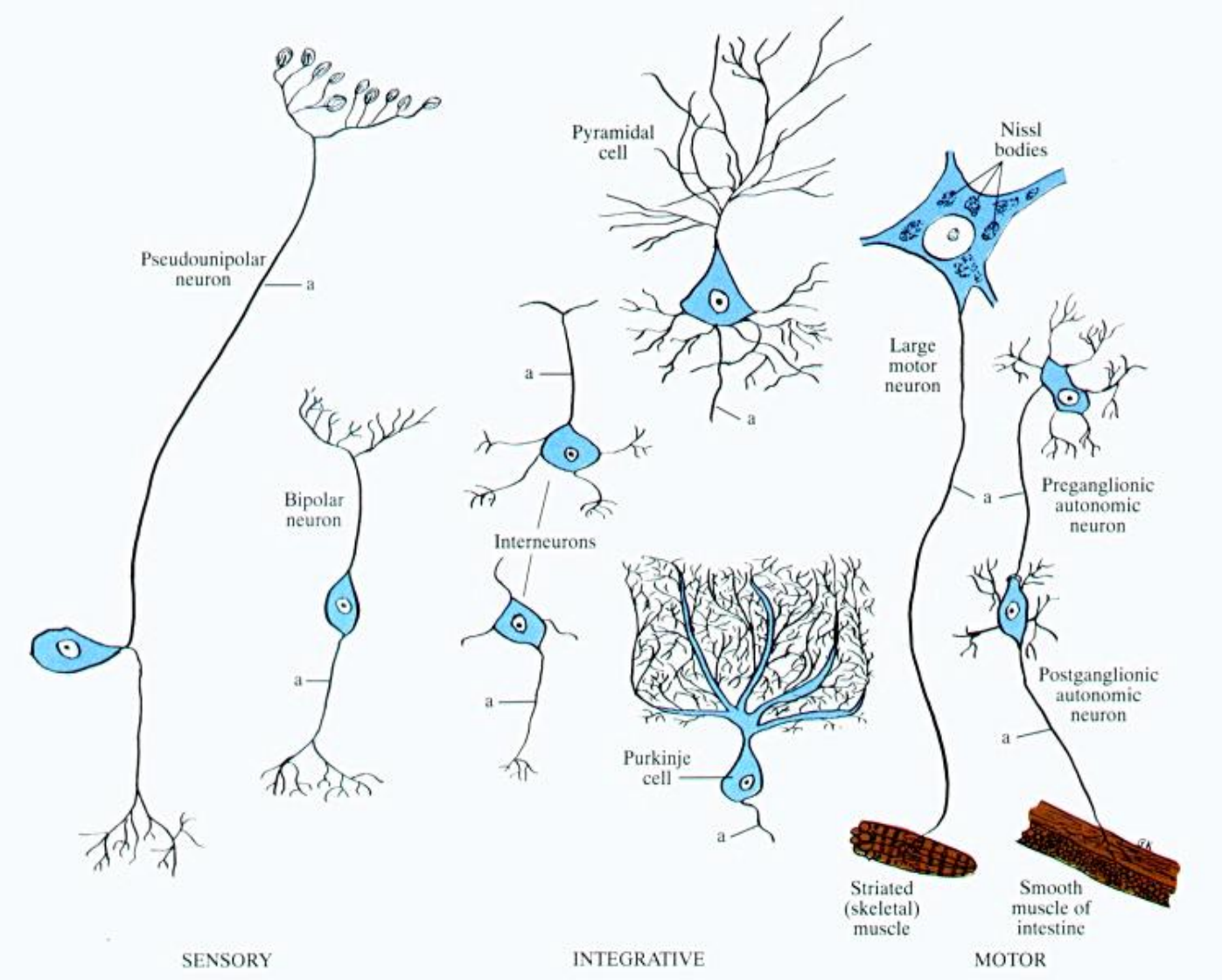

Dendrite
Node
Axon
Myelin sheath
Dendrites

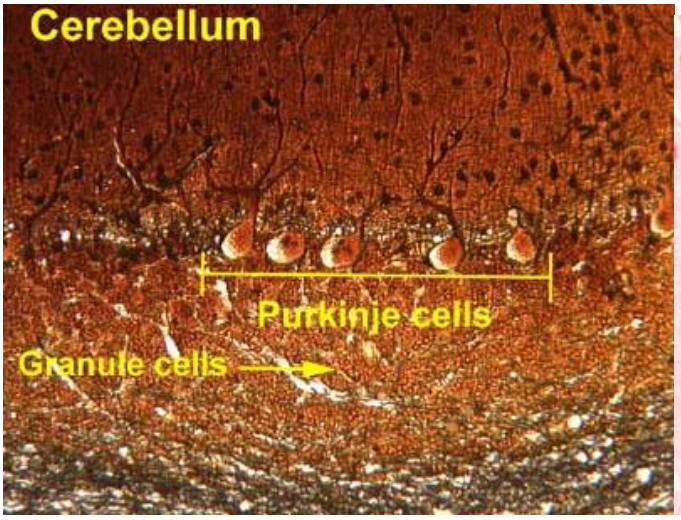
NEURON TYPES

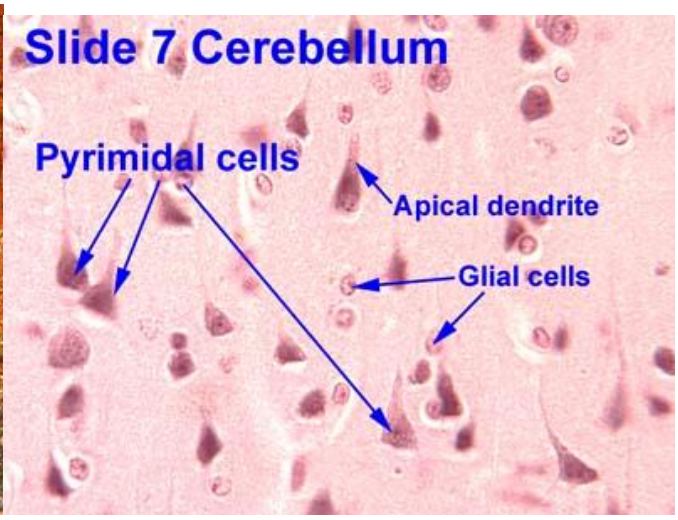












Basic neuron types: **arrangement of axon and dendrites with respect to cell body.**

multipolar neuron: most common; numerous dendrites project from cell body; intermediate, integratory and motor neurons

bipolar neuron: single dendrite arises opposite origin of axon; receptor neurons for senses of smell, sight and balance

pseudo-unipolar neuron: primary sensory neurons; single dendrite and axon arise from common stem formed by fusion;

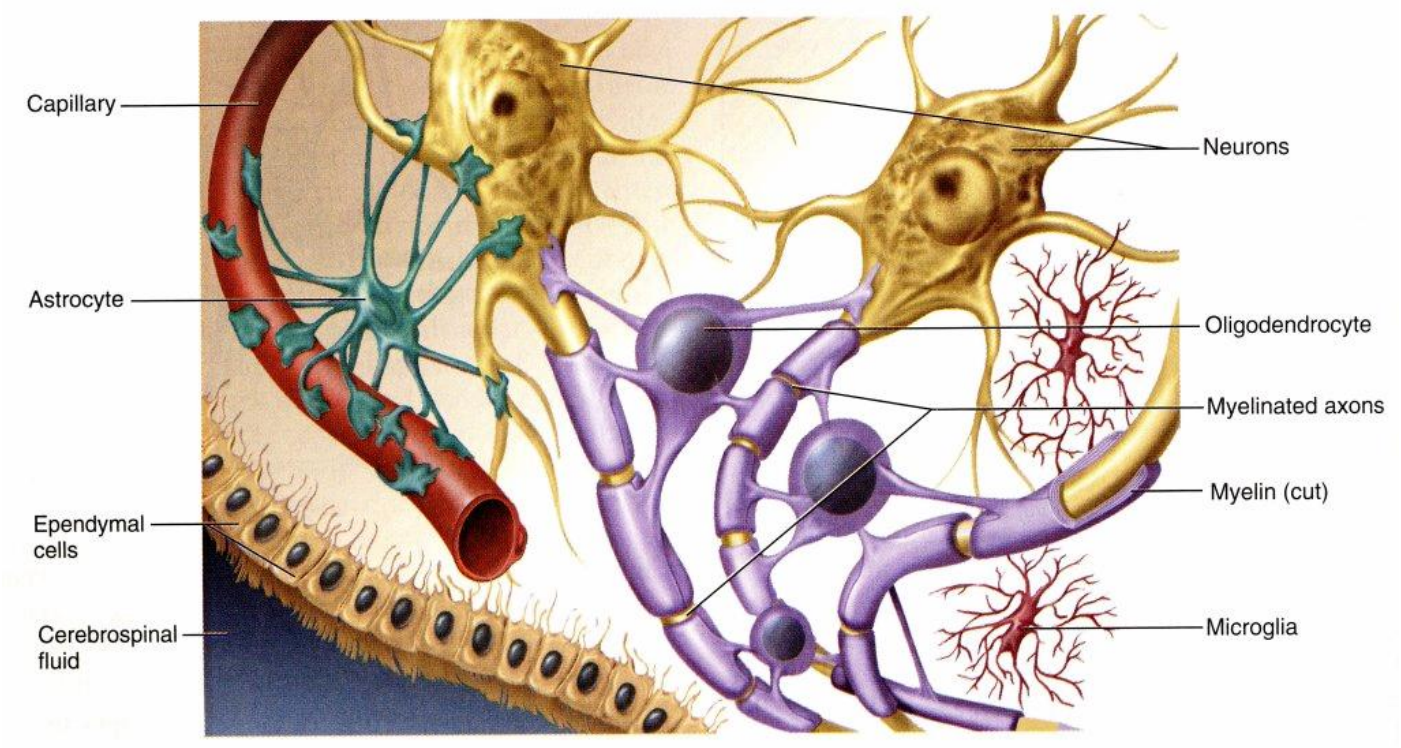
- ***The two principal cell types of the nervous system are:***
  - **Neurons** – excitable cells that transmit electrical signals
  - **Supporting cells** – cells that surround and wrap neurons

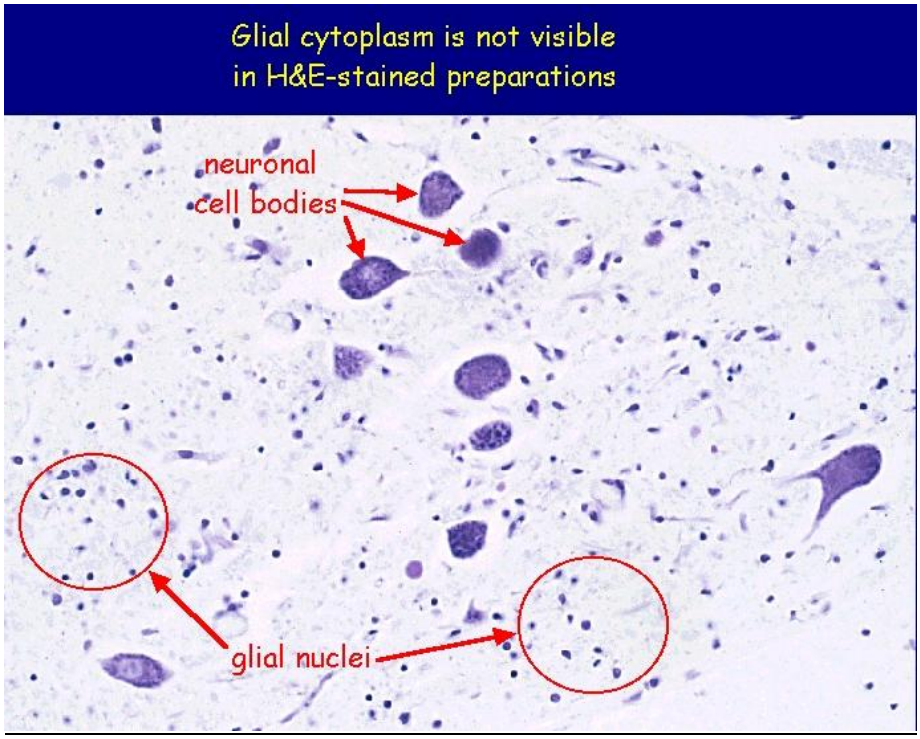
NEUROGLIA OR GLIA

- **Glial cells**, commonly called **neuroglia** or simply **glia**, are non-neuronal cells that provide
  - support and nutrition,
  - maintain homeostasis,
  - form myelin,
  - participate in signal transmission in the nervous system.

TYPE OF NEUROGLIA

- **Microglia [Microglia are specialized macrophages capable of phagocytosis that protect neurons of the CNS.]**
- **Macroglia FOR CNS**
  - **Astrocytes: The most abundant type of glial cell, astrocytes (also called *astroglia*)**
  - **Oligodendrocytes**
  - **Ependymal cells**
  - **Radial glia**
- **FOR PNS [PERIPHERIC NERVOUS SYSTEM**
  - **Schwann cells**
  - **Satellite cells**



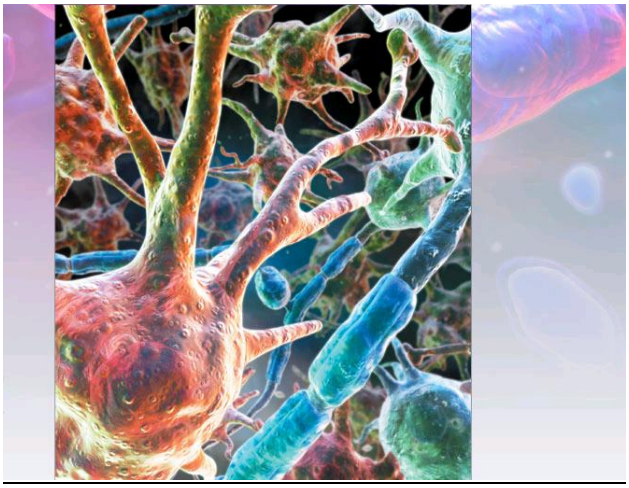


Supporting Cells: Neuroglia

- *The supporting cells (neuroglia or glial cells):*
  - Provide a supportive scaffolding for neurons
  - Segregate and insulate neurons
  - Guide young neurons to the proper connections
  - Promote health and growth
  - **Are very important -Are not neurons Have no action potentials - But have threshold charges -Act as a support function**

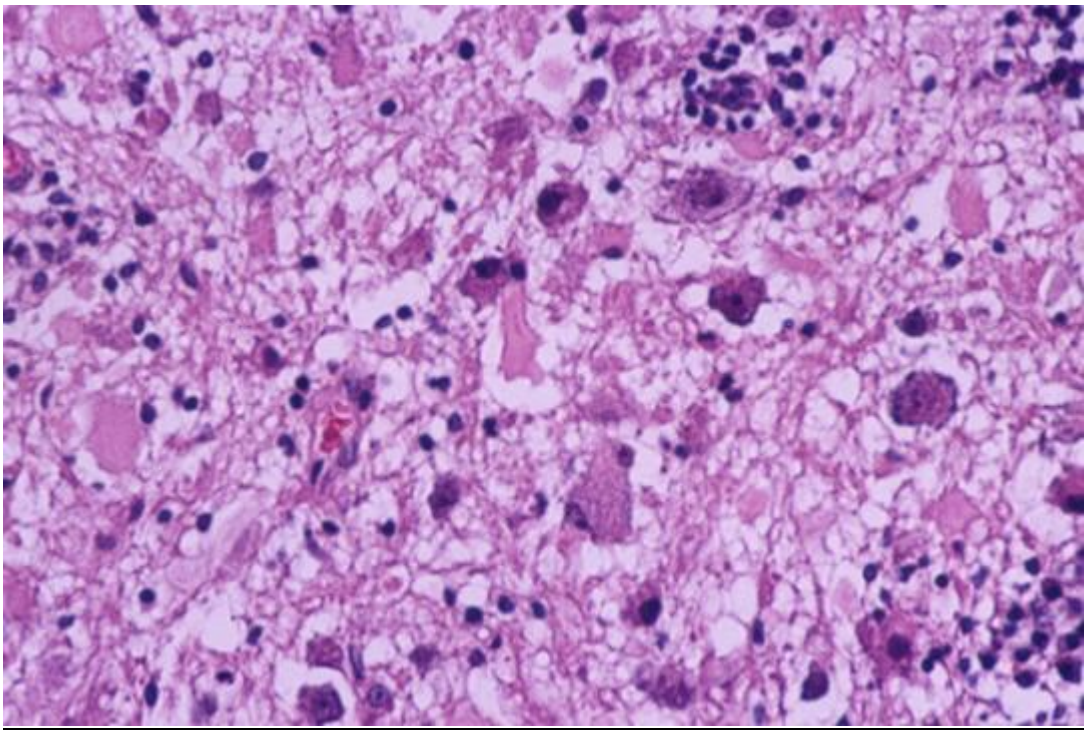
Glial Functions

Myelination - Salutatory Functions
NT uptake
Ion uptake
Glue
Nutritive



Two Major Groups

- **Microglia**
- **Macroglia**

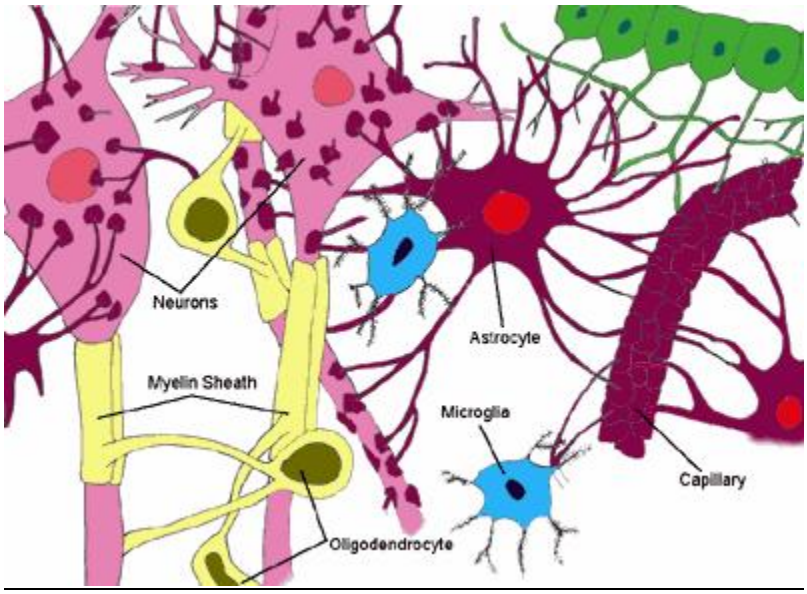


- **Microglia**
  - **Are phagocytes**
  - **Eat up dead material and things**
  - **Will migrate to damaged areas**
  - **With Lesions get Gliosis Concentrate and clean up material**
  - **Forms scar tissue**
  - **Serve as part of the immune system**
- **Macroglia**

Types

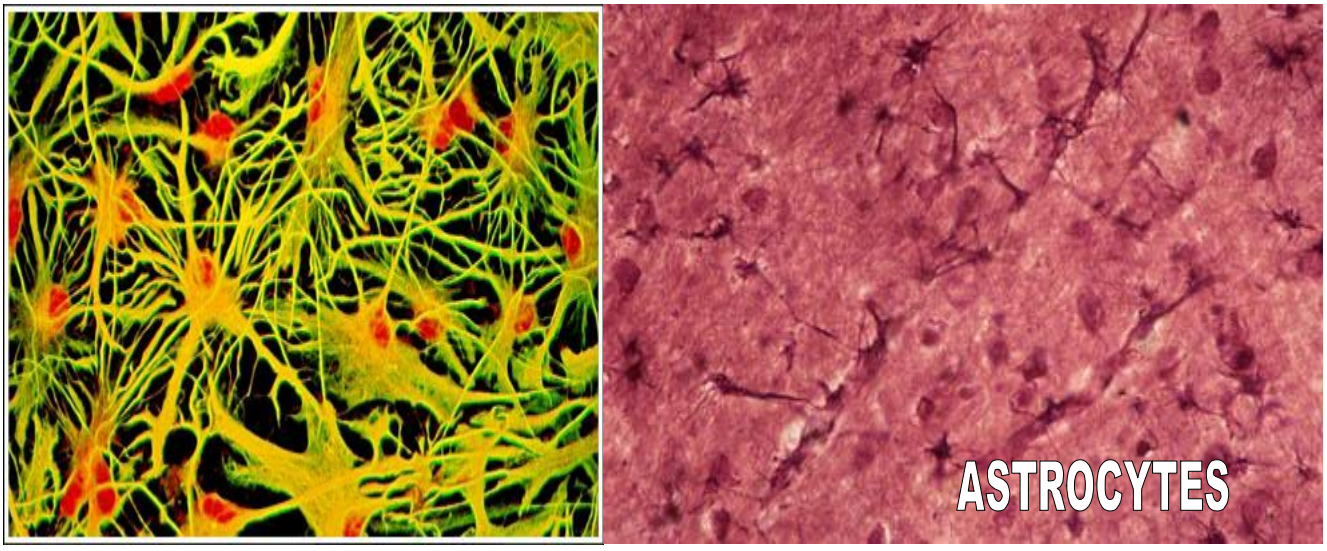
- **Astrocytes**
- **Oligodendrocytes**
- **Ependymal**
- **Schwann**

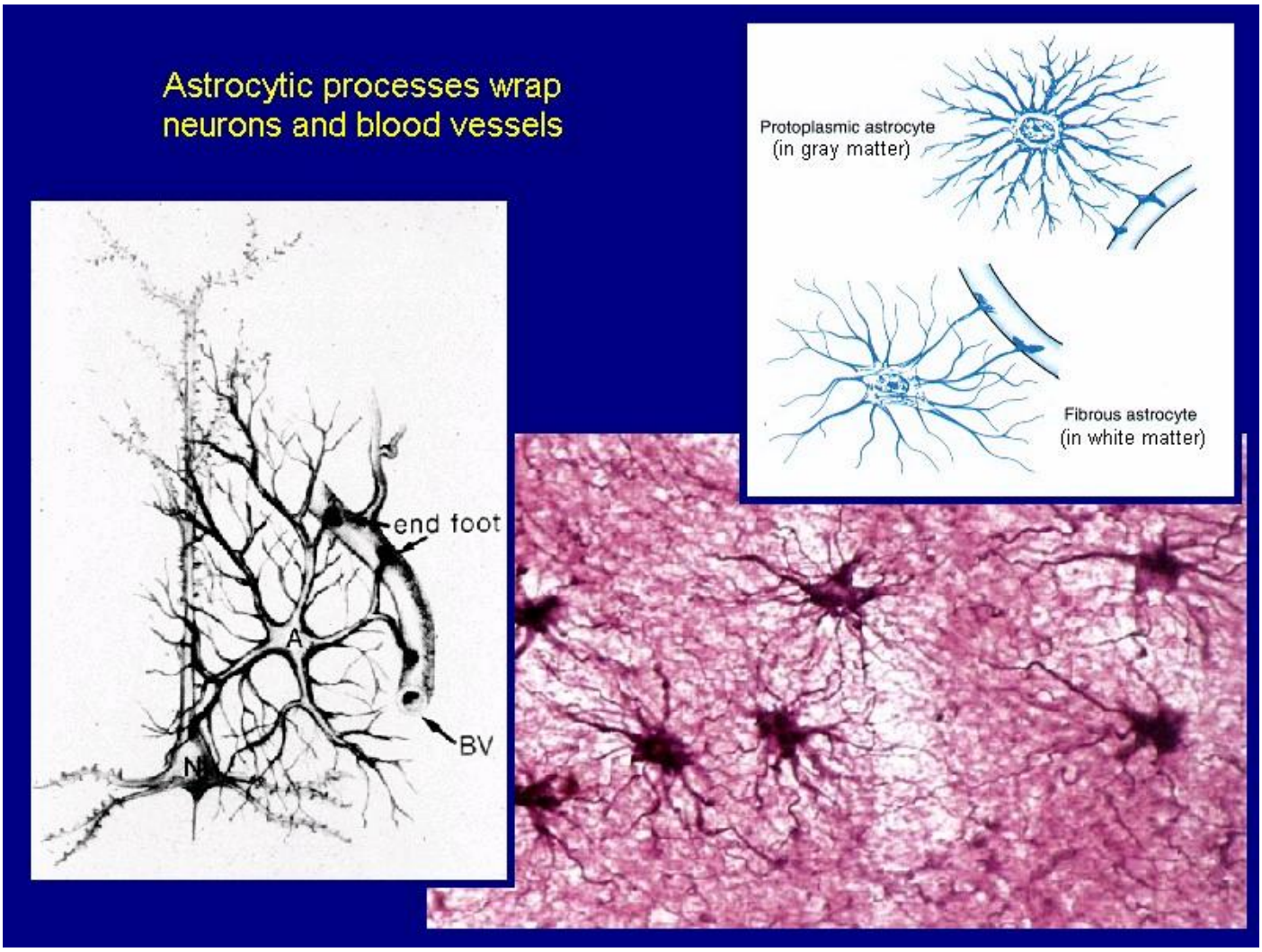
- **Astrocyte - provides physical and nutritional support for neurons; digests part of dead neurons as well as regulates the extracelullar fluid around the neuron.**
- **Microglia - digests part of dead neurons**
- **Oligodendroglia - provides insulation for neurons (myelin)**
- **Satellate cell - provides physical support for neurons in PNS**
- **Schwann cell - provides insulation for neurons (myelin)**



Astrocytes

- *Most abundant, versatile, and highly branched glial cells*
- *They cling to neurons and their synaptic endings, and cover capillaries*
- *Functionally, they:*
  - Support and brace neurons
  - Anchor neurons to their nutrient supplies
  - Guide migration of young neurons
  - Control the chemical environment





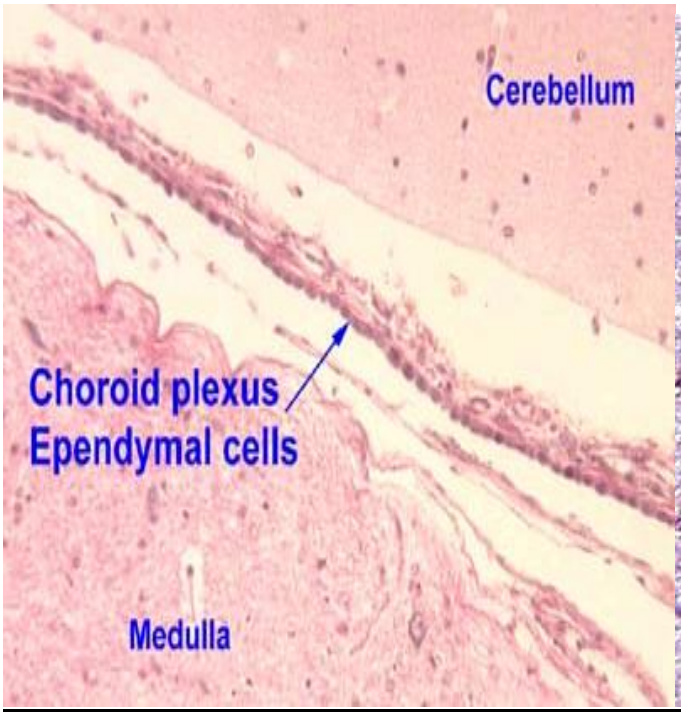
Hallow stars
Appear transparent and look like stars
Make contact with both white and gray matter
Do not migrate much

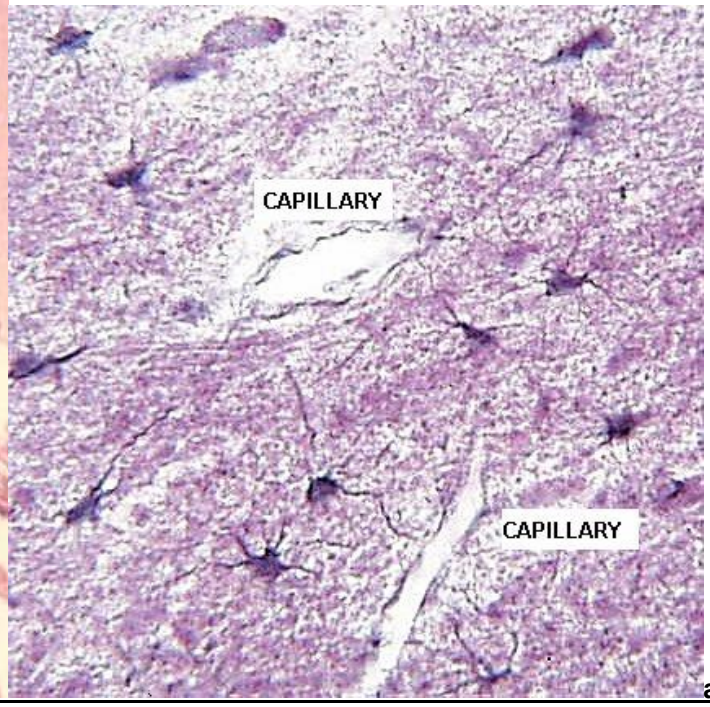
Fibrous Astrocytes

- **Find in Myelinated Tissue (but don't make myelin)**

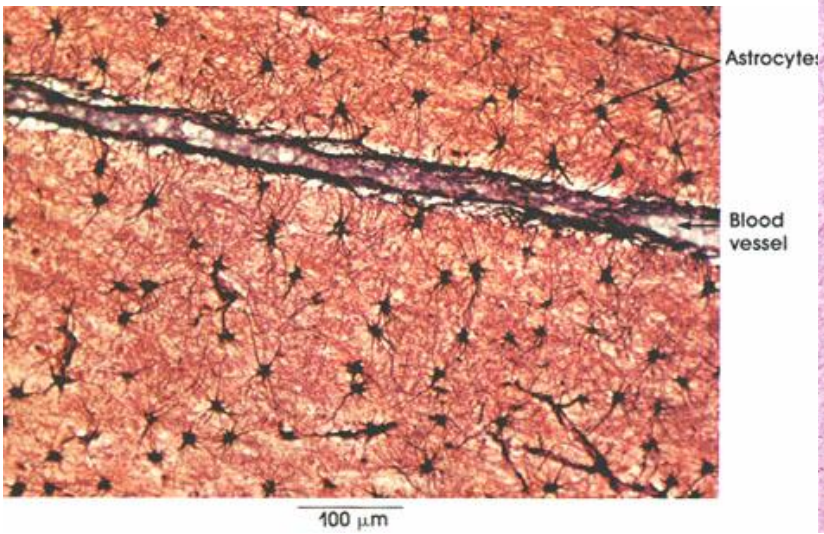
Protoplasmic

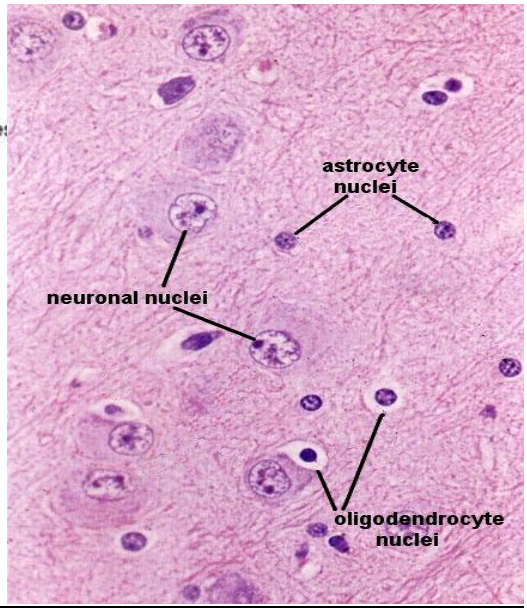
- **Are star-shaped and have lots of cytoplasm**
- **Make function with capillaries**
- **Are phagocytotic.**





as trocytes





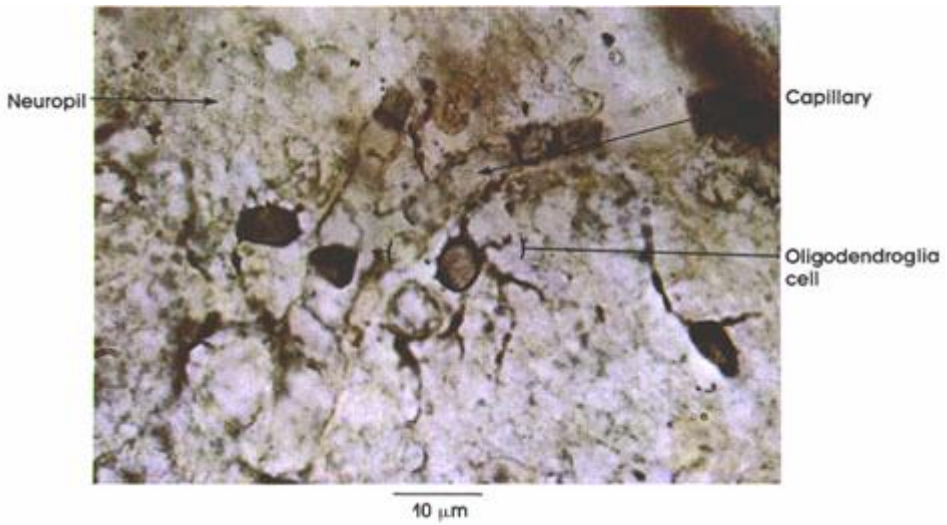
Microglia and Ependymal Cells

- ***Microglia*** *– small, ovoid cells with spiny processes*
  - Phagocytes that monitor the health of neuron

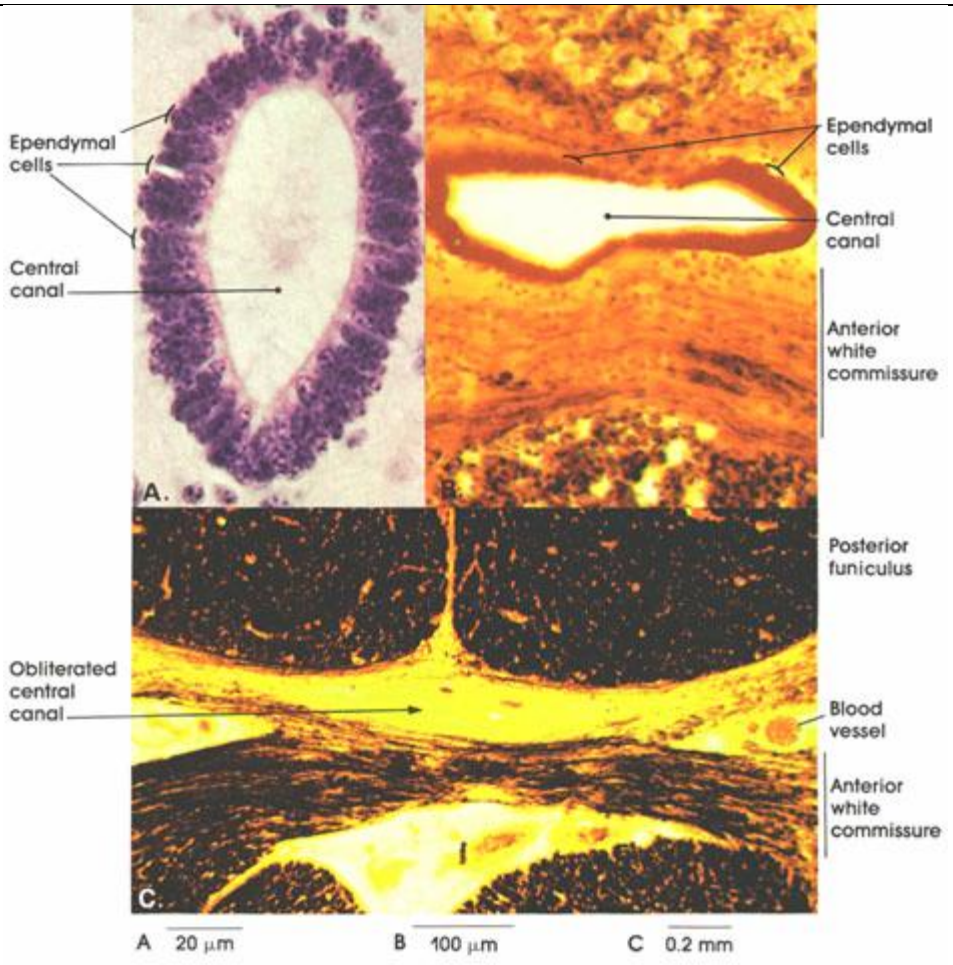
- ***Ependymal cells*** *– range in shape from squamous to columnar*
  - They line the central cavities of the brain and spinal column

Oligodendrocytes, Schwann Cells, and Satellite Cells

- ***Oligodendrocytes –*** *branched cells that wrap CNS nerve fibers*
- ***Schwann cells (neurolemmocytes) –*** *surround fibers of the PNS*
- ***Satellite cells*** *surround neuron cell bodies with ganglia*



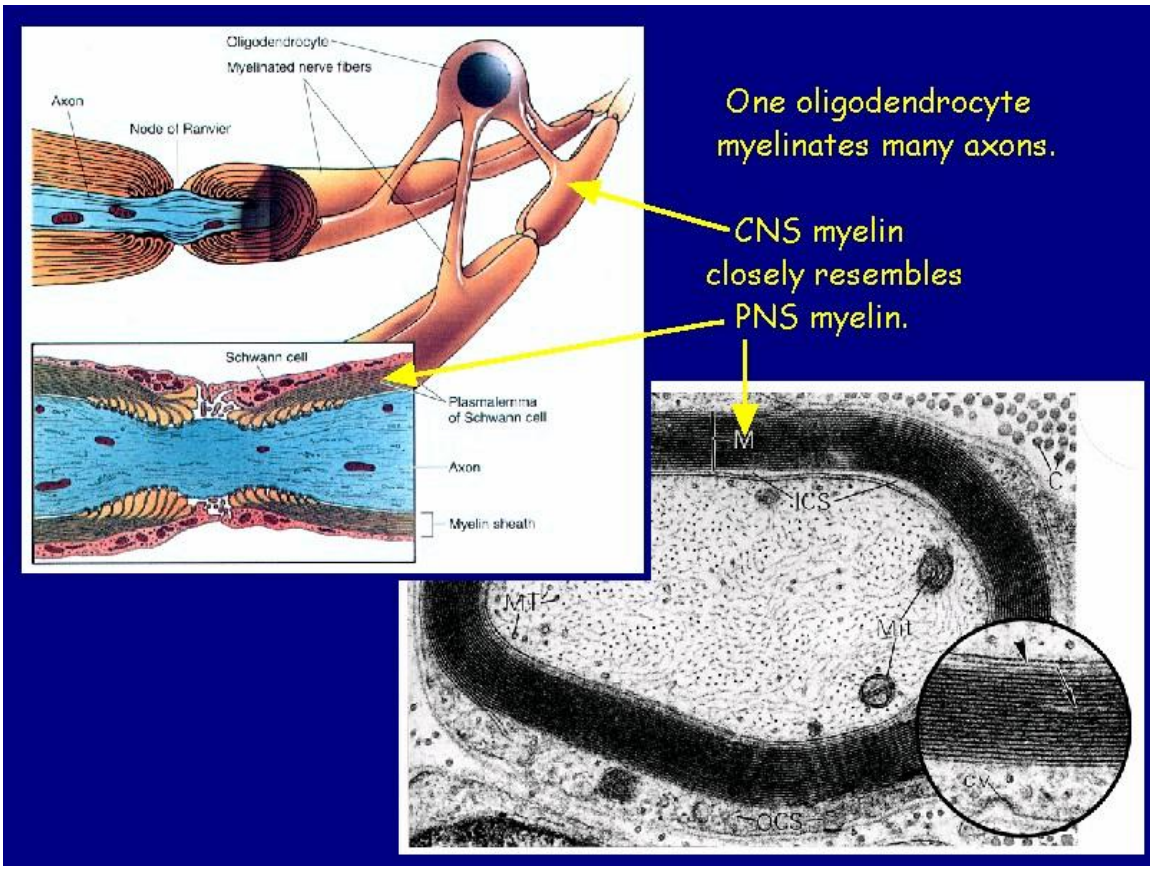
Oligodendrocytes Are located in the CNS
Is a many branching cell
In CNS, will myelinate 30-40 axons
Prob.- Do not regenerate well

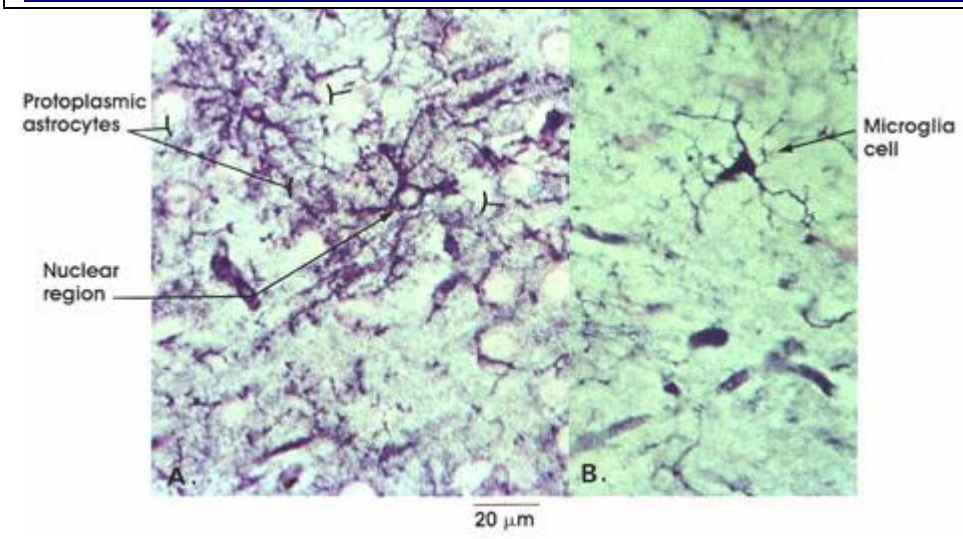


Schwann Cell

Are found in the PNS
Also make myelin
One cell makes one myelin sheath
Regenerate faster than Oligodendrocytes.
Provide conduits for an axon to follow.
Hypothesized why you get better neural regeneration when damage occurs.

In CNS
When oligodendrocytes are destroyed, axon distribution becomes confused
No conduits
Growth cones are random





Ependymal

Forms the lining of ventricles
Has cilia
Appears to aid in the movement of CSF through ventricles
CSF is made very fast and is very dynamic.
Diffusion cannot explain the speed of CSF

Neuroglia: non-neural cells of CNS; neurolemmocytes of PNS; ependyma lining ventricles and canal of CNS

astrocytes: star-shaped with heavy metal impregnation; most numerous glial cells in gray matter; highly branched packing cells; form mass surrounding nerve cells processes; rounded, nuclei closely enmeshed in neuropil; mediate metabolic exchange btwn neurons and blood; regulate composition of intercellular environment in CNS.

- **Glial fibrillary acidic protein (GFAP):** unique intermediate filament; demonstrated by immunoperoxidase method

fibrous astrocytes: astrocytes of white matter with relatively straight cytoplasmic processes
protoplasmic astrocytes: astrocytes of gray matter with numerous short highly branched cytoplasmic processes

- **glial limitans:** relatively impermeable; foot processes invest basement membrane CNS and innermost layer of meninges (pia mater)
- **perivascular feet:** terminate upon basement membranes of capillaries; cover most of surface of capillary in CNS

oligodendrocytes: invest axons in myelin; form multiple myelin internodes; contribute to ensheathment of as many as 50 individual axons; small rounded condensed nuclei; cytoplasm unstained by H&E; tend to be aggregated around neuron cell bodies; most numerous glial cell in **white matter;** analogous to satellite cells in ganglia; analogous to neurolemmocytes in PNS nerves

- **light oligodendrocytes**: capable of cell division; highly active in myelin sheath formation (predominant in fetus and neonate)
- **dark oligodendrocytes:** main form in mature CNS
- **medium oligodendrocytes:** immature form involved in myelination and maturation; capacity for remyelination after demyelinating disease such as **multiple sclerosis**

ependymal cells: cuboidal or low columnar; luminal junctional complexes; **no basement membrane**; bases taper and break up into fine branches that ramify into underlying layer with astrocytes; luminal: variable number of cilia; microvilli also present; lining epithelium of ventricles and spinal canal

microglia: monocyte-macrophage cells; invade CNS during fetal period; small irregular nuclei; relatively little cytoplasm forms fine, highly-branched processes; transform into large amoeboid phagocytic cells.

- **Myelination:** formation **myelin sheath:** formed by oligodendrocytes in CNS and neurolemmocytes in PNS
- **mesaxon**: zone of apposition of neurolemmocyte (oligodendrocyte) cell membrane that extends into jellyroll;
- **major dense lines**: inner leaflets of plasma membrane fuse with each other; expands to form **membrane loop** containing cytoplasm as it approaches neurofibral node
- **intraperiod lines**: represent closely applied outer membrane leaflets; multiple layers of membranes constitute myelin sheath; **peripheral neurolemmocyte cytoplasm:** main bulk of neurolemmocyte cytoplasm encircles myelin sheath; **periaxonal neurolemmocyte cytoplasm:** thin layer persists immediately surrounding axon
- **internode**: single segment of myelin produced by each neurolemmocyte; **internodal length** function of diameter of axon; may be up to 1.5 mm in largest fibers

neurofibral node = node of Ranvier: interval at which axon not covered by myelin sheath; between neurolemmocytes; **external lamina (basal lamina)** continues across node

myelin fissure = Schmidt Lantermann cleft (incisures);

narrow channels of uncompacted cytoplasm;

- **Functional division:**

***Somatic nervous system:* voluntary functions**

***Autonomic nervous system:* controls involuntary functions**

- **Sensory receptors**

functional classification:

- **exteroceptors:** stimuli from outside: touch, light pressure, deep pressure, cutaneous pain, temperaure, smell, taste, sight and hearing
- **proprioceptors:** located within skeletal muscle; conscious and unconscious information about orientation, skeletal position, tension and movement; vestibular apparatus of ear, tendon organs and neuromucsular spindles
- **interoceptors:** viscera; chemoreceptors of blood, vascular (pressure) baroreceptors, receptors for state of distension of hollow viscera (gastrointestinal tract and urinary bladder; visceral pain, hunger, thirst, wellbeing and malaise

morphological classification

- **simple**
  - **free nerve endings:** branched or unbranched nerve endings of affarent fibers; small diameters; slow rates of conduction; devoid of myelin even where arising from myelinated nerves (e.g., nerves servicing tactile epitheliocytes); responsible for cutaneous pain and temperature;
    tactile epitheliocyte = Merkel's cell; sensation of touch
    - **compound**
  - **tactile body:** corpuscle of touch; Meissner's corpuscle; reception of light discriminatory touch; oval shape; located in dermal papillae immediately beneath epidermis; delicate collagenous capsule surrounding mass of plump oval cells arranged transversely (specialized neurolemmocytes); non-myelinated branches of large myelinated sensory fibers ramify throughoug cell mass in helical manner
    - **lamellated corpuscle**
      - (Vater) **Pacinian corpuscles**; large encapsulated sensory receptors responsive to pressure or coarse touch, vibration and tension; in deeper layers of skin ligaments and joint capsules, some serous membranes, mesenteries, some viscera and erogenous areas; 1 to 4 mm in length; appearance of an onion; delicate capsule enclosing concentric lamellae of flattened (neurolemmocytes) cells separated by interstitial fluid space and delicate collage fibers; core contains single, unbranced non-myelinated nerve fibre with several club-like terminals; becomes myelinated upon leaving corpuscle
        Ruffini corpuscles: robust spindle-shaped structures in soles of feet
        Krause end bulbs: delicate receptors in lining of oropharynx and conunctiva of eye
  - **neuromuscular spindle:** stretch receptor organs within skeletal muscle; regulate muscle tone via spinal stretch reflex; encapsulated, lymph filled fusiform up to 6 mm long by 1 mm in diameter; parallel to muscle fibers; embedded in endomysium or perimysium; 2 to 10 modified skeletal muscle fibers; evokes motor response from large, alpha motor neurons
    - **intrafusal fibers** smaller than skeletal muscle fibers (= encapsulated extrafusal fibers); nuclei concentrated in central, nonstriated area

nuclear bag: central area dilated

nuclear chain nuclei arranged in row

annulo-spiral endings: branched, non-myelinated endings of large, myelinated sensory fibers wrapped around central area

flower-spray endings: smaller, myelinated sensory fibers located on striated portions of intrafusal fibers; from Gamma motor fiber; increase sensitivity by causing contraction of striated portions of infrafusal fibers

organs of special sense: eye, ear and receptors for senses of smell and taste

Glial cell types

l ***Protoplasmic astrocytes*****:** large, star-shaped with many processes, some of which attach pedicels/pedicles/sucker-feet to blood vessels or the basal lamina under the pia mater; have cytoplasmic filaments and microtubules; are common in grey matter.

2 ***Fibrous astrocytes***: similar to protoplasmic astrocytes, but have more filaments and glycogen, and lie in the white matter.

3 ***Oligodendrocytes*****/oligodendroglia**: plump cell body with fairly dense cytoplasm and a darker nucleus and fewer, shorter processes than an astrocyte; common in white matter, but some are perineuronal.

4 ***Microglia*****:** - (a) derived from mesenchyme via bone marrow; (b) potentially phagocytic; (c) dispersed throughout the brain; (d) a small elongated cell with many short processes and a dark nucleus.
This is the ramified or resting microglial cell, which becomes round and phagocytic as a *reactive microglial cell* (Gitter cell), when responding to damage.

5 ***Ependymal cells*****:** lining ventricles, and covering the choroid plexus.

6 ***Peripheral glia*****: satellite cells and Schwann cells** may be roughly equated with oligodendrocytes by function. Peripheral glia in the gut autonomic system - enteric glia - are more like astrocytes. Olfactory ensheathing cells enwrap the unmyelinated axons of the olfactory nerve bundles, and may provide favourable cues for axonal regeneration.

7 ***Specialized central glia*****:** Müller astrocytes of the retina, pituitary-gland pituicytes, and periventricular tanycytes extending away from the ventricles.
Because of the readily measured electrical activity, much is known of the neuron's physiology, but glial activities are less easily studied. Certain functions are special to the various types of glia.

2 Glial functions

l *Myelination* of myelinated axons (oligodendrocytes).

2 Augmenting the *extracellular space*, e.g., being an active compartment for ionic buffering by taking up and redistributing K^+, and metabolizing transmitters (astrocytes). The CNS has little true tissue space and no lymphatics.

3 Helping to induce endothelial cells to create the *blood-brain barrier* (astrocytes).

4 *Insulating* chemical and electrical events from nearby sensitive structures (astrocytes and oligodendrocytes).

5 *Storing glycogen* and passing on raw materials for the energetic and synthetic processes of the neuron (astrocytes).

6 *Acting as macrophages* to remove degenerating nerve cell components (microglia).

7 *Protecting* neurons by metabolising excess ammonia from liver disease (astrocytes).

8 *Mechanically supporting* the neuronal elements and keeping them properly spaced (astrocytes and oligodendrocytes).

9 Transient radial glia *guide* the migration of developing neurons.

3 Some evidence for cell types performing these functions

l Oligodendroglia contain myelin basic protein. Their membranes are connected with myelin lamella that they form.

2 Excluding myelin, insulation is a task of astrocytes whose processes enfold synapses and neural membranes.

3 Astrocyte cytoplasm also could serve as a nutritive pathway via its pedicles and processes from the blood capillary wall to the neuron, and can transfer ions and inactivated transmitters in the reverse direction.

4 Fibrous astrocytes have long processes, firm connections with one another and very little in their cytoplasm but filaments and glycogen. They would seem to be fitted for the role of mechanical support.

4 Myelination process

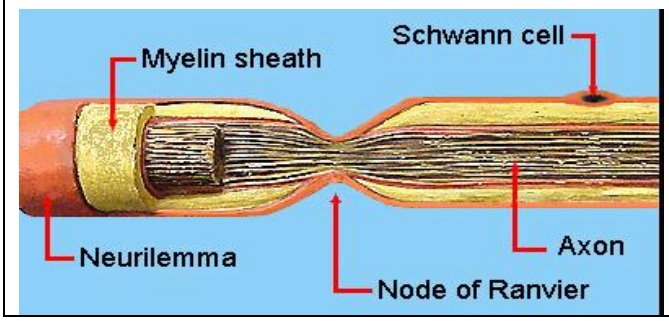
l Many axons remain unmyelinated throughout their existence. However, for rapid *saltatory* (jumping) nerve conduction a myelin sheath interrupted by *nodes* is necessary. This sheath is a modified lipoprotein membrane, rich in cerebrosides and other special lipids and proteins.

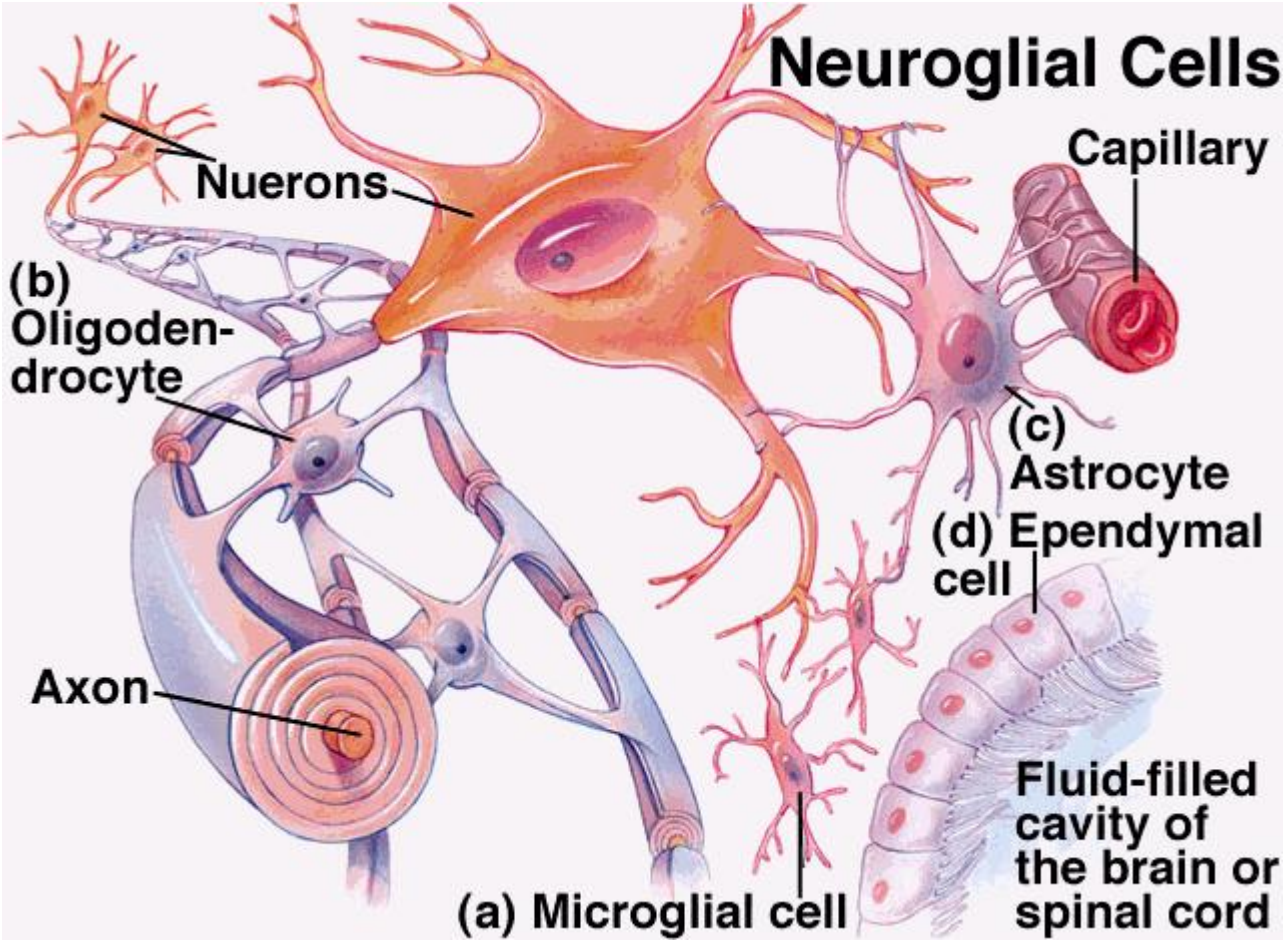
2 The process of myelination in *peripheral* fibres is by an apparent 'rotation' of the *Schwann cell* in relation to the axon that it has enfolded, thus enclosing the axon in many layers of Schwann-cell membrane. These membranes fuse together, but the lamellar structure remains visible in EM, and an outer *mesaxon* connects the last wrapping to the Schwann cell's own plasmalemma.
One Schwann cell myelinates a given length of axon, which is separated by an unmyelinated *node of Ranvier* from the next myelinated segment. Outside the Schwann-cell or neurolemmal sheath lies a *basal lamina*, beyond which are found the collagen fibrils and fibroblasts of the *endoneurium*.

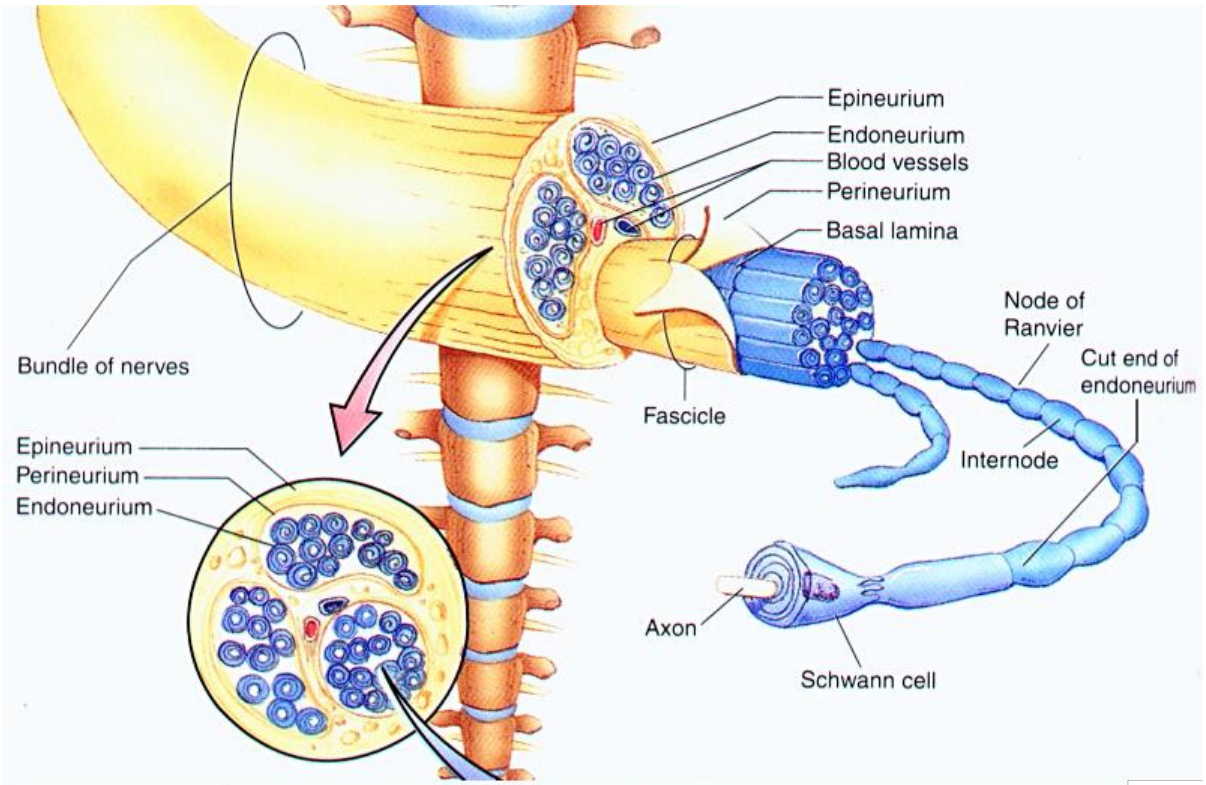
3 In the CNS, the oligodendrocyte incrementally adds membranes to several axons, and to more than one segment per axon. This myelin configuration is compatible with 'spiralling' membrane synthesis, but not actual rotation. Nodes are present, but not as distinct as in the PNS.

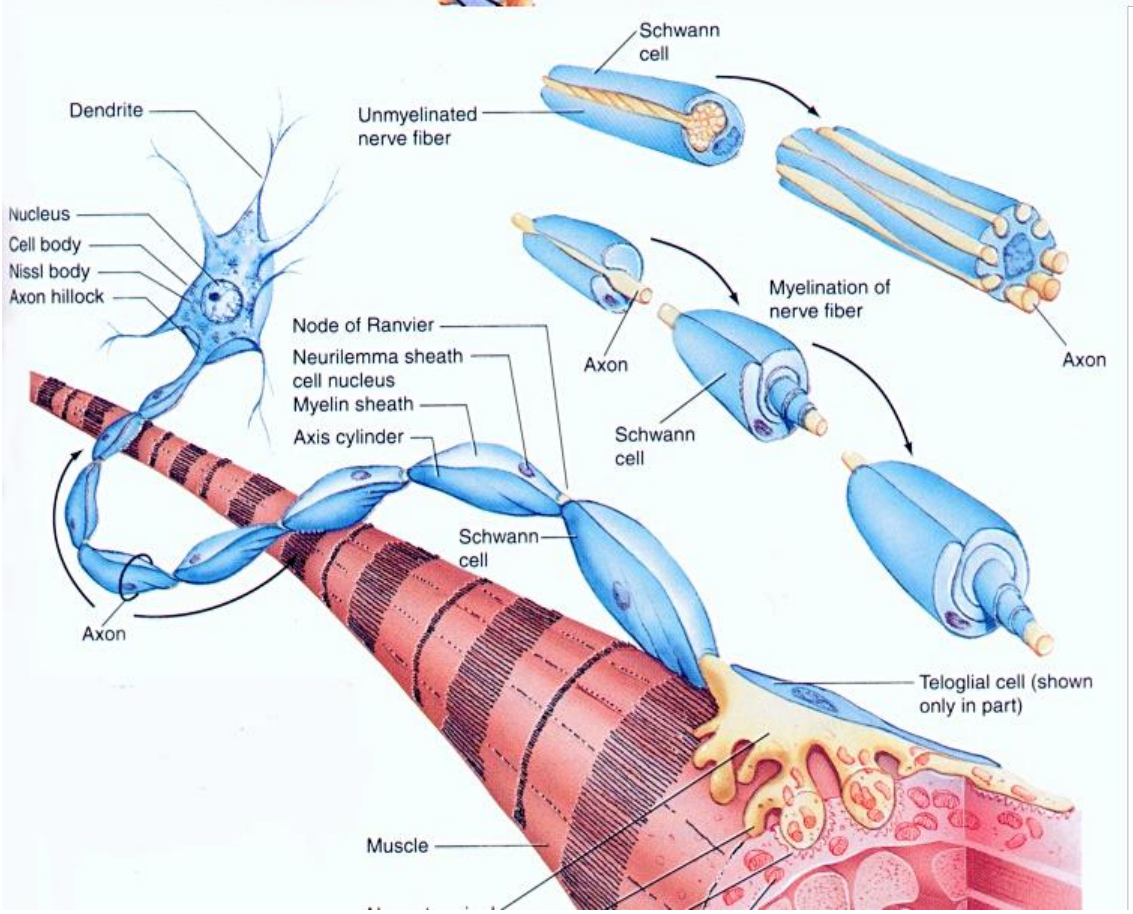
4 Myelination takes place in different tracts of the brain at different times during development. The time of myelination correlates fairly well with the development of the ability to function in that system.

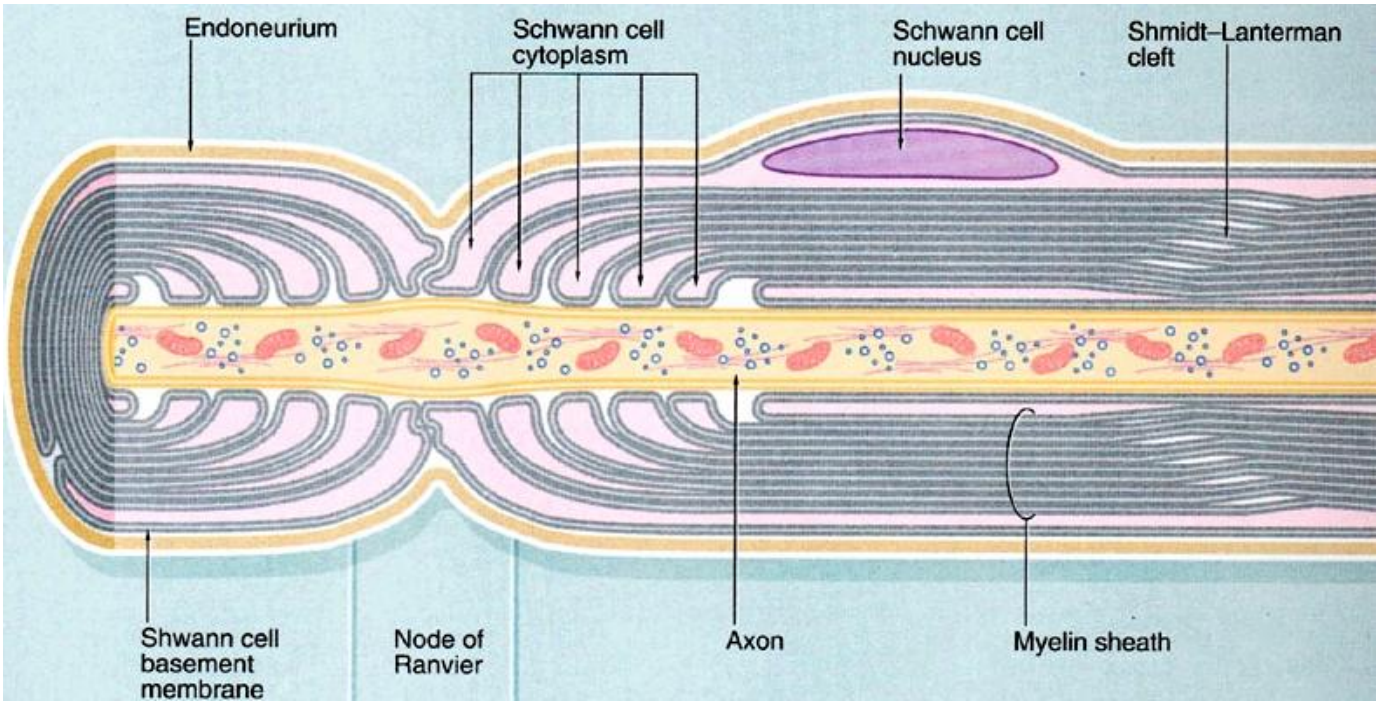
5 *Remyelination* (successful or attempted) is involved in the mature nervous system in two circumstances - the regeneration of peripheral nerve fibres, and demyelinating diseases in the CNS and peripheral NS.




Neuroglial Cells
Nuerons
Capillary
(b)
Oligoden-
drocyte
(c)
Astrocyte
(d) Ependymal
cell
Axon
Fluid-filled
cavity of
the brain or
spinal cord
(a) Microglial cell


Epineurium
Endoneurium
Blood vessels
Perineurium
Basal lamina
Node of Ranvier
Cut end of endoneurium
Bundle of nerves
Fascicle
Internode
Epineurium
Perineurium
Endoneurium
Axon
Schwann cell


Schwann cell
Dendrite
Unmyelinated nerve fiber
Nucleus
Cell body
Nissl body
Axon hillock
Myelination of nerve fiber
Axon
Axon
Node of Ranvier
Neurilemma sheath cell nucleus
Myelin sheath
Axis cylinder
Schwann cell
Schwann cell
Axon
Teloglial cell (shown only in part)
Muscle



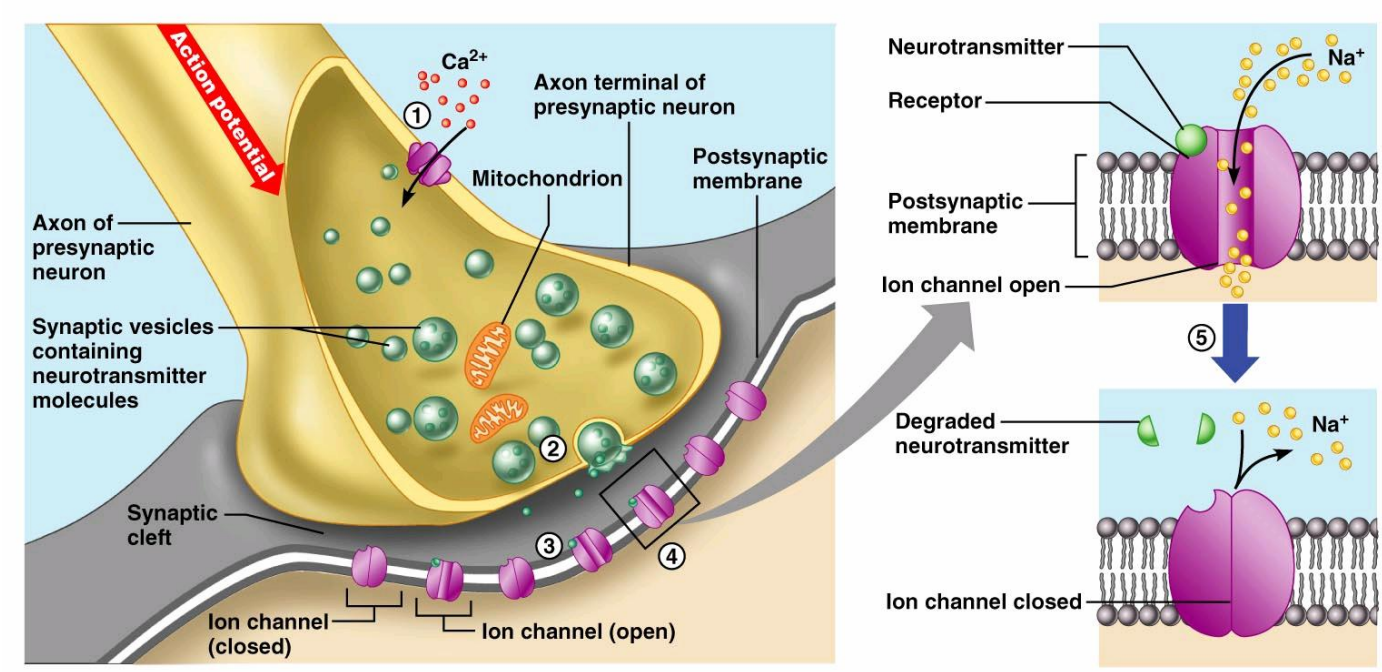
Neurophysiology [see more in the neurophysiology section]

- *Neurons are highly irritable*
- *Action potentials, or nerve impulses, are:*
  - Electrical impulses carried along the length of axons
  - Always the same regardless of stimulus
  - The underlying functional feature of the nervous system

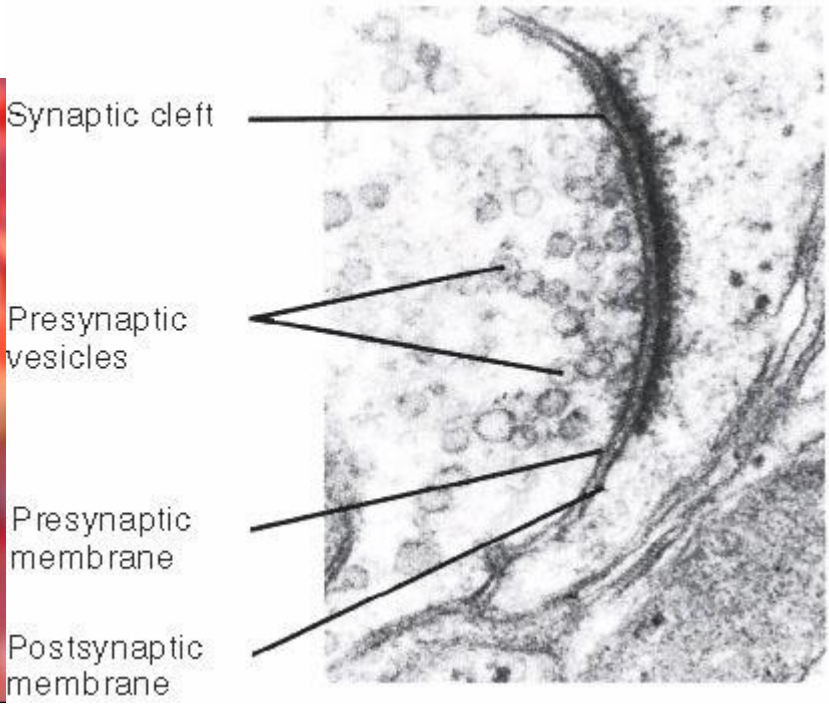
Nerve Fiber Classification

- ***Nerve fibers are classified according to:***
  - **Diameter**
  - **Degree of myelination**
  - **Speed of conduction**

Synapses



- ***A junction that mediates information transfer from one neuron:***
  - **To another neuron**
  - **To an effector cell**
- ***Presynaptic neuron – conducts impulses toward the synapse***
- ***Postsynaptic neuron – transmits impulses away from the synapse***



Synapses and neuromuscular junctions = motor end plates; unidirectional but may be stimulatory or inhitibory; **site of intercommunication btwn adjacent neurons**

main types of synapses

- **axosodendritic**
- **axosomatic**
- **axoaxonic**

anatomy of synapse

- **terminal bouton:** not myelinated; contain mitochondria etc.
  - **synaptic vesicle:** about 50 nm in diameter; derived from sER
    - **dense-cored vesicles:** autonomic synapses
  - **presynaptic membrane:** release contents of presynaptic vesicles upon arrival of action potential
- **synaptic cleft** (20 to 30 nm): uniform thickness; neurotransmitter diffuse across; contain hydrolytic and oxidative enzymes which inactivate released neurotransmitters;
- **postsynaptic membrane**
  - receptors
  - postsynaptic web

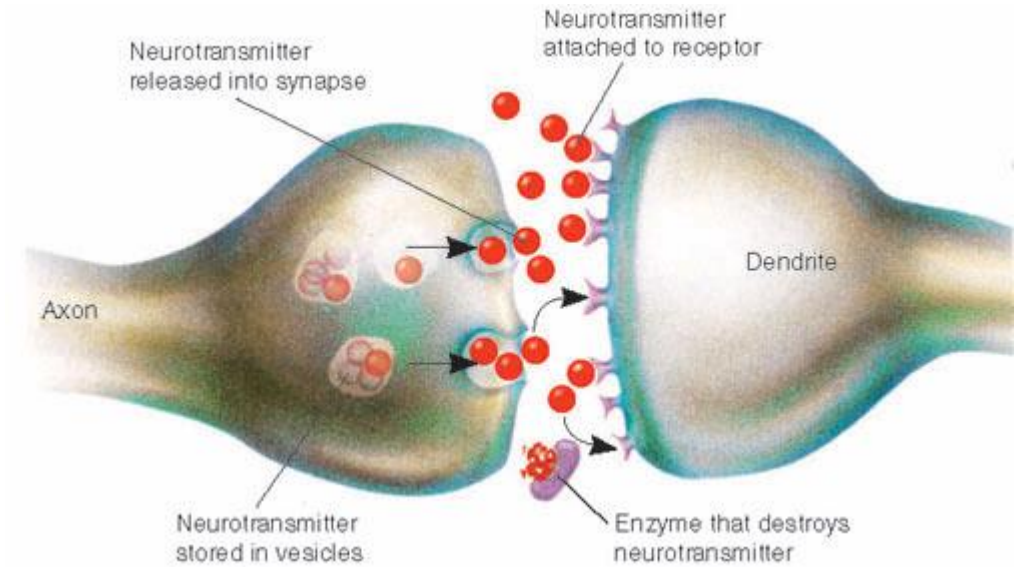
neurotransmitters: chemical transmitter substances initiate action potential in adjacent neuron or effector organ

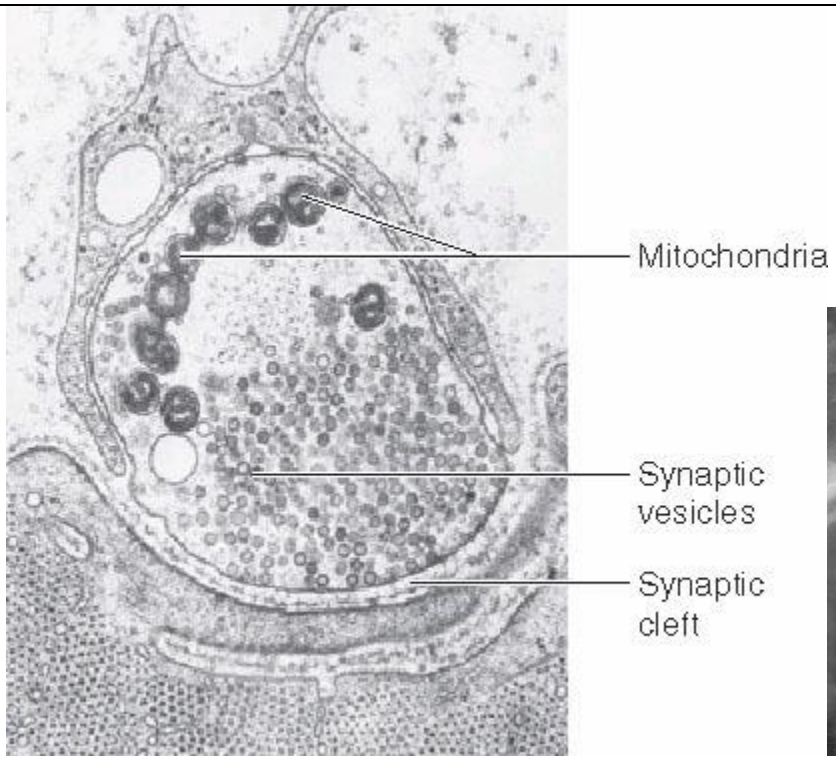
CNS: many types

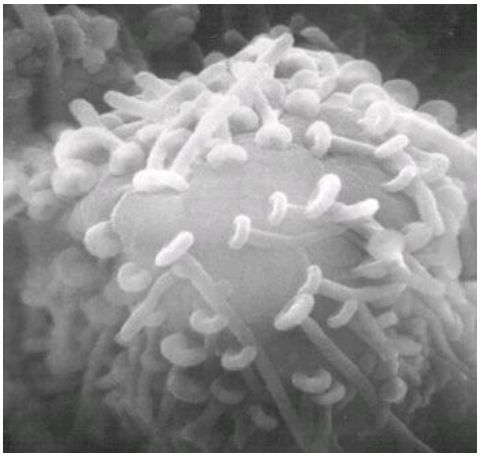
PNS: 2 types

acetylcholine: neurotransmitter of somatic neuromuscular junctions; neurotransmitter of all preganglionic fibers in autonomic nervous system; main neurotransmitter of postganglionic parasympathetic neurons

noradrenaline (norepinephrine): main neurotransmitter of postganglionic sympathetic neurons (except sweat glands)





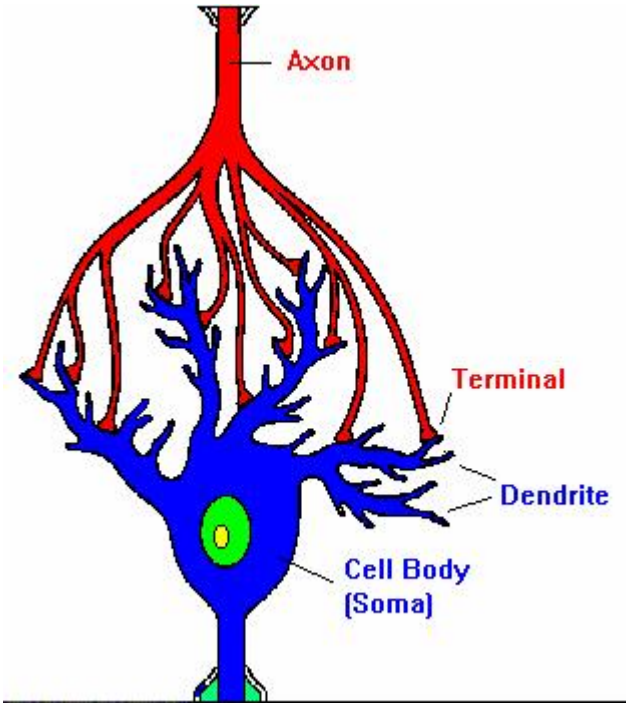


motor end plate: contains concentraton of mitochondria and rER

sole plate: recess in effector (muscle) cell surface; covered by extension of last **neurolemmocyte** (= Schwann cell)**;** external lamina of neurolemmocyte merges with that of muscle fiber; endoneureum merges with endomycium

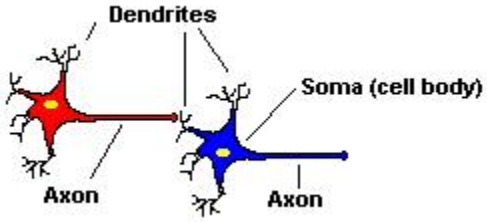
secondary synaptic clefts: deep folds in postsynaptic membrane; contain acetylacolinesterase

postsynaptic membrane: concentration of receptors for acetylcholine

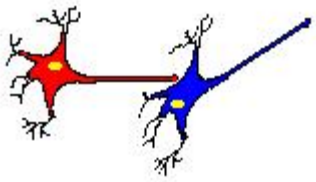


- **excitability**: change in membrane permeability in response to stimuli > reversal of ionic gradient across membrane and plasma membrane is **depolarized**
- **action potential** = wave of depolarization; depolarization spread along plasma membrane; faster in larger axons; incrased velocity with myelination
- **repolarization: membrane reestablishes** resting potential
- **saltatory conduction:** enhances conduction velocity; action potential travels by jumping from node to node
- **pathway:** arrangement of integrating neurons conducting action potential from receptor to effector organ
- **effector organ:** of voluntary nervous pathways: skeletal muscle of involuntary pathways: smooth muscle, cardiac muscle, muscle-like epithelial cells (myoepithelial cells) within some exocrine glands
- **ganglia:** aggregations of primary sensory neurons and terminal effector neurons of autonomic nervous system at peripheral sites

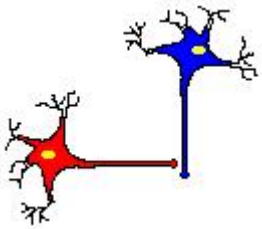
Types of Synapses



Axodendritic Synapse



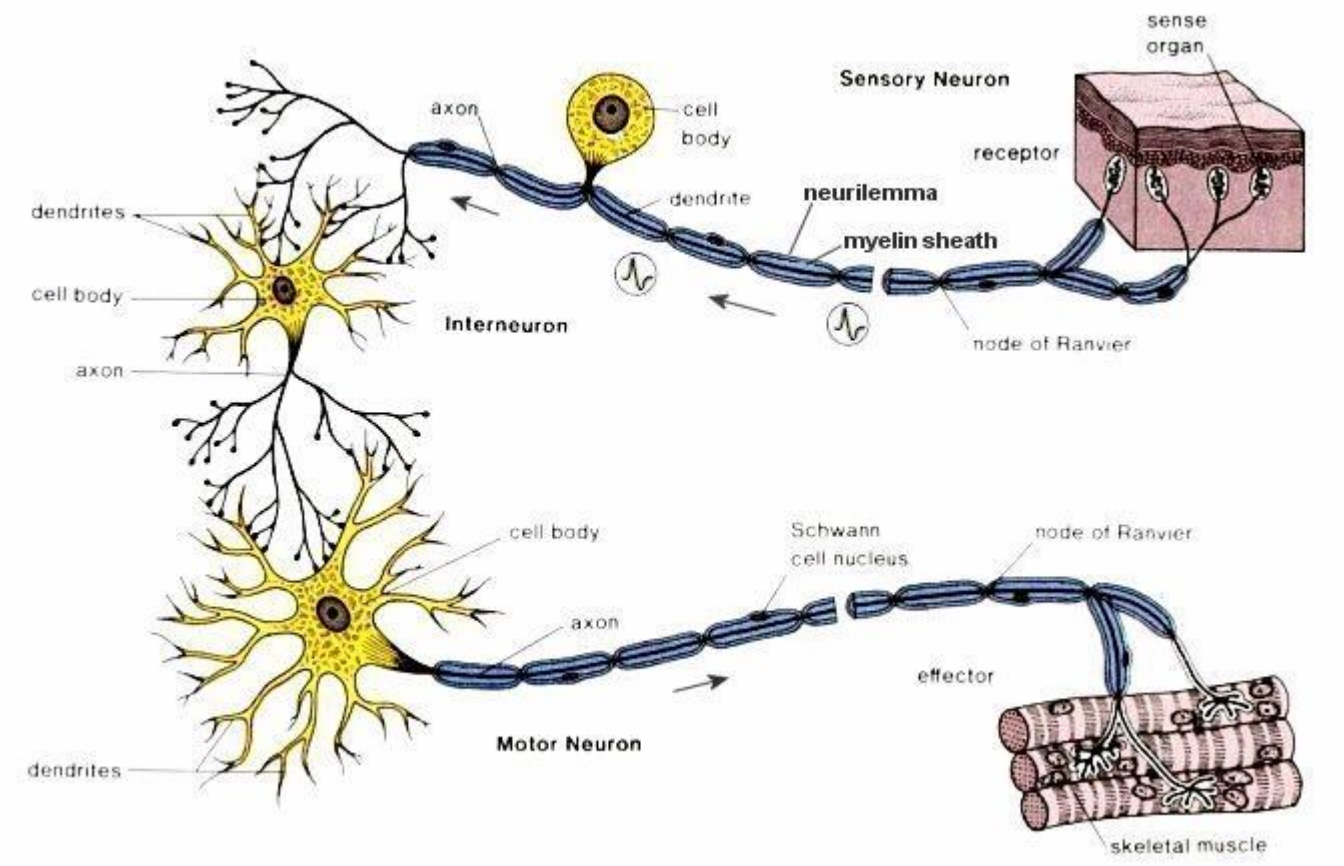
Axosomatic Synapse



Axoaxonic Synapse

Types of Synapses

- ***Axodendritic – synapses between the axon of one neuron and the dendrite of another***
- ***Axosomatic – synapses between the axon of one neuron and the soma of another***
- ***Other types of synapses include:***
  - **Axoaxonic (axon to axon)**
  - **Dendrodendritic (dendrite to dendrite)**
  - **Dendrosomatic (dendrites to soma)**



Types of synapse

l ***Axosomatic*:** to the neuron's body.

2 ***Axodendritic*:** e.g., from climbing fibres to Purkinje cells' dendrites.

3 ***Axodendritic* to *spines*,** e.g., from parallel fibres to Purkinje cells' dendritic spines. (The presence of spines on dendrites is used to subclassify neurons in many brain regions.)

4 ***Glomerular*:** a rounded structure serving several dendrites, e.g., from mossy fibres to cerebellar granule neurons.

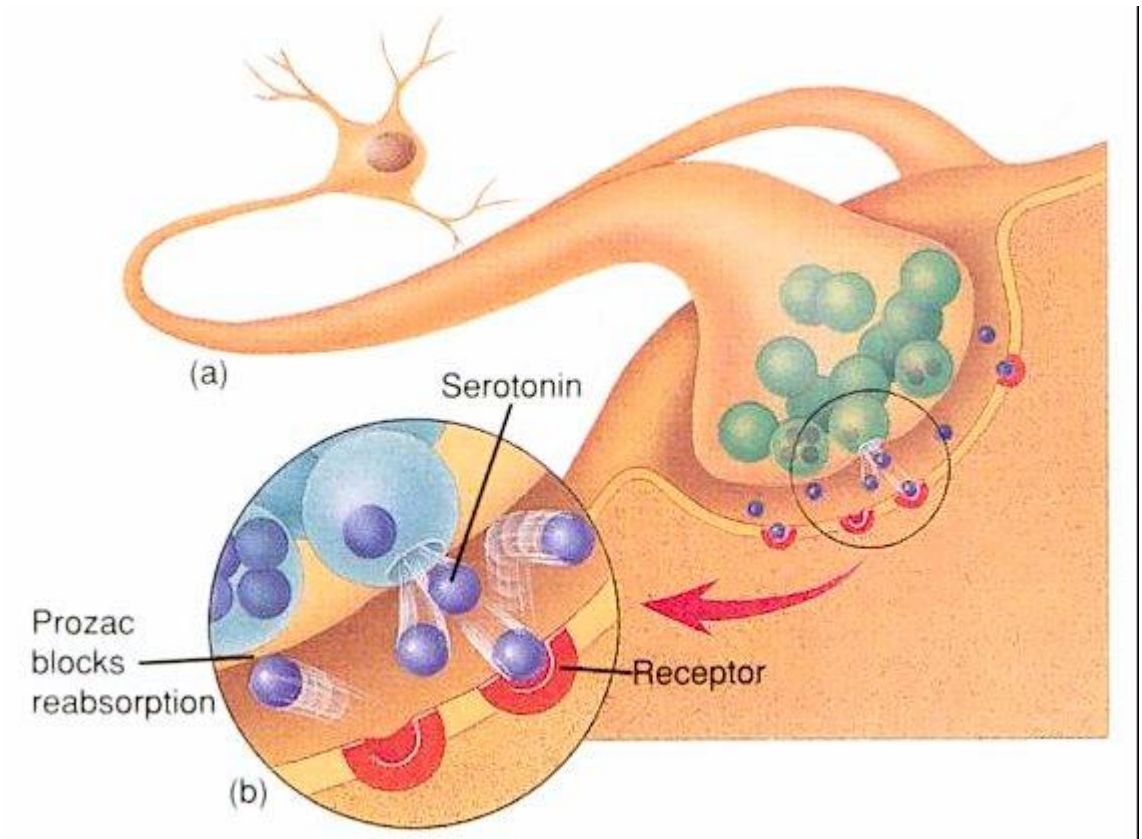
5 ***En passant***: made 'in passing' on the way to other synapses.

6 ***Axo-axonic*:** synapse onto another synapse or the axon's initial segment (for presynaptic inhibition).

7 **Reciprocal *dendro-dendritic***: e.g., in retina and olfactory bulb.

2 Synapses also differ in the number, size and density of their vesicles, in the transmitter and neuromodulator substances that these hold, in the organelles present, and in the cleft material and membrane densities.

3 Chemical neuroanatomy involves mapping which connections of the CNS employ particular neurotransmitters, e.g., serotonin, acetylcholine, dopamine, etc



Electrical Synapses

- ***Electrical synapses:***
  - **Are less common than chemical synapses**
  - **Correspond to gap junctions found in other cell types**
  - **Are important in the CNS in:**
    - **Arousal from sleep**
    - **Mental attention**
    - **Emotions and memory**
    - **Ion and water homeostasis**

Chemical Synapses

- ***Specialized for the release and reception of neurotransmitters***
- ***Typically composed of two parts:***
  - **Axonal terminal of the presynaptic neuron, which contains synaptic vesicles**
  - **Receptor region on the dendrite(s) or soma of the postsynaptic neuron**

Synaptic Cleft

- ***Fluid-filled space separating the presynaptic and postsynaptic neurons***
- ***Prevents nerve impulses from directly passing from one neuron to the next***
- ***Transmission across the synaptic cleft:***
  - **Is a chemical event (as opposed to an electrical one)**
  - **Ensures unidirectional communication between neurons**

-Synaptic Cleft: Information Transfer

- ***Nerve impulses reach the axonal terminal of the presynaptic neuron and open Ca^{2+} channels***
- ***Neurotransmitter is released into the synaptic cleft via exocytosis in response to synaptotagmin***
- ***Neurotransmitter crosses the synaptic cleft and binds to receptors on the postsynaptic neuron***
- ***Postsynaptic membrane permeability changes, causing an excitatory or inhibitory effect***

-Termination of Neurotransmitter Effects

- ***Neurotransmitter bound to a postsynaptic neuron:***
  - **Produces a continuous postsynaptic effect**
  - **Blocks reception of additional "messages"**
  - **Must be removed from its receptor**
- ***Removal of neurotransmitters occurs when they:***
  - **Are degraded by enzymes**
  - **Are reabsorbed by astrocytes or the presynaptic terminals**
  - **Diffuse from the synaptic cleft**

Synaptic Delay

- ***Neurotransmitter must be released, diffuse across the synapse, and bind to receptors***
- ***Synaptic delay – time needed to do this (0.3-5.0 ms)***
- ***Synaptic delay is the rate-limiting step of neural transmission***

Postsynaptic Potentials

- ***Neurotransmitter receptors mediate changes in membrane potential according to:***
  - The amount of neurotransmitter released
  - The amount of time the neurotransmitter is bound to receptors
- ***The two types of postsynaptic potentials are:***
  - EPSP – excitatory postsynaptic potentials
  - IPSP – inhibitory postsynaptic potentials

Excitatory Postsynaptic Potentials(EPSP)

- ***EPSPs are graded potentials that can initiate an action potential in an axon***
  - Use only chemically gated channels
  - Na^+ and K^+ flow in opposite directions at the same time
- ***Postsynaptic membranes do not generate action potentials***

Inhibitory Synapses and IPSPs

- ***Neurotransmitter binding to a receptor at inhibitory synapses:***
  - Causes the membrane to become more permeable to potassium and chloride ions
  - Leaves the charge on the inner surface negative
  - Reduces the postsynaptic neuron's ability to produce an action potential

Summation

- A single EPSP cannot induce an action potential
- EPSPs must summate temporally or spatially to induce an action potential
- Temporal summation – presynaptic neurons transmit impulses in rapid-fire order
- Spatial summation – postsynaptic neuron is stimulated by a large number of terminals at the same time
- IPSPs can also summate with EPSPs, canceling each other out

Neurotransmitters

- Acetylcholine (AcH)
- Dopamine (DA)
- Histamine
- Norepinephrine (NE)
- Epinephrine
- Serotonin (5-HT)

Peptides

- Gamma-Aminobutyric Acid (GABA)
- Glutamate
- Aspartate
- Glycine

Neuropeptides (there are more neuropeptides; to find out visit www.faculty.washington.edu/chudler/)

- Insulin
- Beta-endorphin
- Neuropeptide Y
- Calcitonin

Transmitters

Neurotransmitters either excite or inhibit the postsynaptic neurone. The most prominent excitatory transmitter in the CNS is L-glutamate. The most prominent inhibitory transmitter in the CNS is GABA (gamma-amino butyric acid). Other "main" neurotransmitters are e.g. dopamine, serotonin, acetylcholine, noradrenaline and glycine. Each neurone uses only one of the main transmitters, and this transmitter is used at all synaptic boutons that originate from the neurone.
One or more of the "minor" transmitters (there are several dozens of them - such as cholecystokinin, endogenous opioids, somatostatin, substance P) may be used together with a main transmitter.

The molecular machinery which is needed to mediate the events occurring at excitatory synapses differs from that at inhibitory synapses. Differences in the

morphological appearances of the synapses accompany the functional differences.

Receptors

Usually there exists a multitude of receptors which are all sensitive to one particular neurotransmitter. Different receptors have different response properties, i.e. they allow the flux of different ions over the plasma membrane of the neurone or they may address different second messenger systems in the postsynaptic neurones. The precise reaction of the neurone to the various neurotransmitters released onto its plasma membrane at the synapses is determined by the types of receptors expressed by the neurone.

Neurotransmitters

- ***Chemicals used for neuronal communication with the body and the brain***
- ***50 different neurotransmitters have been identified***
- ***Classified chemically and functionally***

Chemical Neurotransmitters

- ***Acetylcholine (ACh)***
- ***Biogenic amines***
- ***Amino acids***
- ***Peptides***
- ***Novel messengers: ATP and dissolved gases NO and CO***

Neurotransmitters: Acetylcholine

- ***First neurotransmitter identified, and best understood***
- ***Released at the neuromuscular junction***
- ***Synthesized and enclosed in synaptic vesicles***
- ***Degraded by the enzyme acetylcholinesterase (AChE)***
- ***Released by:***
  - **All neurons that stimulate skeletal muscle**
  - **Some neurons in the autonomic nervous system**

Neurotransmitters: Biogenic Amines

- ***Include:***
  - **Catecholamines – dopamine, norepinephrine (NE), and epinephrine**
  - **Indolamines – serotonin and histamine**
- ***Broadly distributed in the brain***
- ***Play roles in emotional behaviors and our biological clock***

Synthesis of Catecholamines

- ***Enzymes present in the cell determine length of biosynthetic pathway***
- ***Norepinephrine and dopamine are synthesized in axonal terminals***
- ***Epinephrine is released by the adrenal medulla***

Neurotransmitters: Amino Acids

- ***Include:***
  - **GABA – Gamma (γ)-aminobutyric acid**
  - **Glycine**
  - **Aspartate**
  - **Glutamate**
- ***Found only in the CNS***

Neurotransmitters: Peptides

- ***Include:***
  - **Substance P – mediator of pain signals**
  - **Beta endorphin, dynorphin, and enkephalins**
- ***Act as natural opiates; reduce pain perception***
- ***Bind to the same receptors as opiates and morphine***
- ***Gut-brain peptides – somatostatin, and cholecystokinin***

Neurotransmitters: Novel Messengers

- ***ATP***
  - **Is found in both the CNS and PNS**
  - **Produces excitatory or inhibitory responses depending on receptor type**
  - **Induces Ca^{2+} wave propagation in astrocytes**
  - **Provokes pain sensation**
- ***Nitric oxide (NO)***
  - **Activates the intracellular receptor guanylyl**

cyclase
- Is involved in learning and memory
- *Carbon monoxide (CO) is a main regulator of cGMP in the brain*

Functional Classification of Neurotransmitters

- *Two classifications: excitatory and inhibitory*
  - Excitatory neurotransmitters cause depolarizations (e.g., glutamate)
  - Inhibitory neurotransmitters cause hyperpolarizations (e.g., GABA and glycine)
- *Some neurotransmitters have both excitatory and inhibitory effects*
  - Determined by the receptor type of the postsynaptic neuron
  - Example: acetylcholine
    - Excitatory at neuromuscular junctions with skeletal muscle
    - Inhibitory in cardiac muscle

Neurotransmitter Receptor Mechanisms

- *Direct: neurotransmitters that open ion channels*
  - Promote rapid responses
  - Examples: ACh and amino acids
- *Indirect: neurotransmitters that act through second messengers*
  - Promote long-lasting effects
  - Examples: biogenic amines, peptides, and dissolved gases

Channel Linked Receptors

- *Composed of integral membrane protein*
- *Mediate direct neurotransmitter action*
- *Action is immediate, brief, simple, and highly localized*
- *Ligand binds the receptor, and ions enter the cells*
- *Excitatory receptors depolarize membranes*
- *Inhibitory receptors hyperpolarize membranes*

G Protein Linked Receptors

- *Responses are indirect, slow, complex, prolonged, and often diffuse*
- *These receptors are transmembrane protein complexes*
- *Examples: muscarinic ACh receptors, neuropeptides, and those that bind biogenic amines*

G Protein-Linked Receptors: Mechanism

- *Neurotransmitter binds to G protein-linked receptor*
- *G protein is activated and GTP is hydrolyzed to GDP*
- *The activated G protein complex activates adenylate cyclase*
- *Adenylate cyclase catalyzes the formation of cAMP from ATP*
- *cAMP, a second messenger, brings about various cellular responses*

G Protein-Linked Receptors: Effects

- *G protein-linked receptors activate intracellular second messengers including Ca^{2+}, cGMP, diacylglycerol, as well as cAMP*
- *Second messengers:*
  - Open or close ion channels
  - Activate kinase enzymes
  - Phosphorylate channel proteins
  - Activate genes and induce protein synthesis

Neural Integration: Neuronal Pools

- *Functional groups of neurons that:*
  - Integrate incoming information
  - Forward the processed information to its appropriate destination
- *Simple neuronal pool*
  - Input fiber – presynaptic fiber
  - Discharge zone – neurons most closely associated with the incoming fiber
  - Facilitated zone – neurons farther away from incoming fiber

Types of Circuits in Neuronal Pools

- *Divergent – one incoming fiber stimulates ever increasing number of fibers, often amplifying circuits*

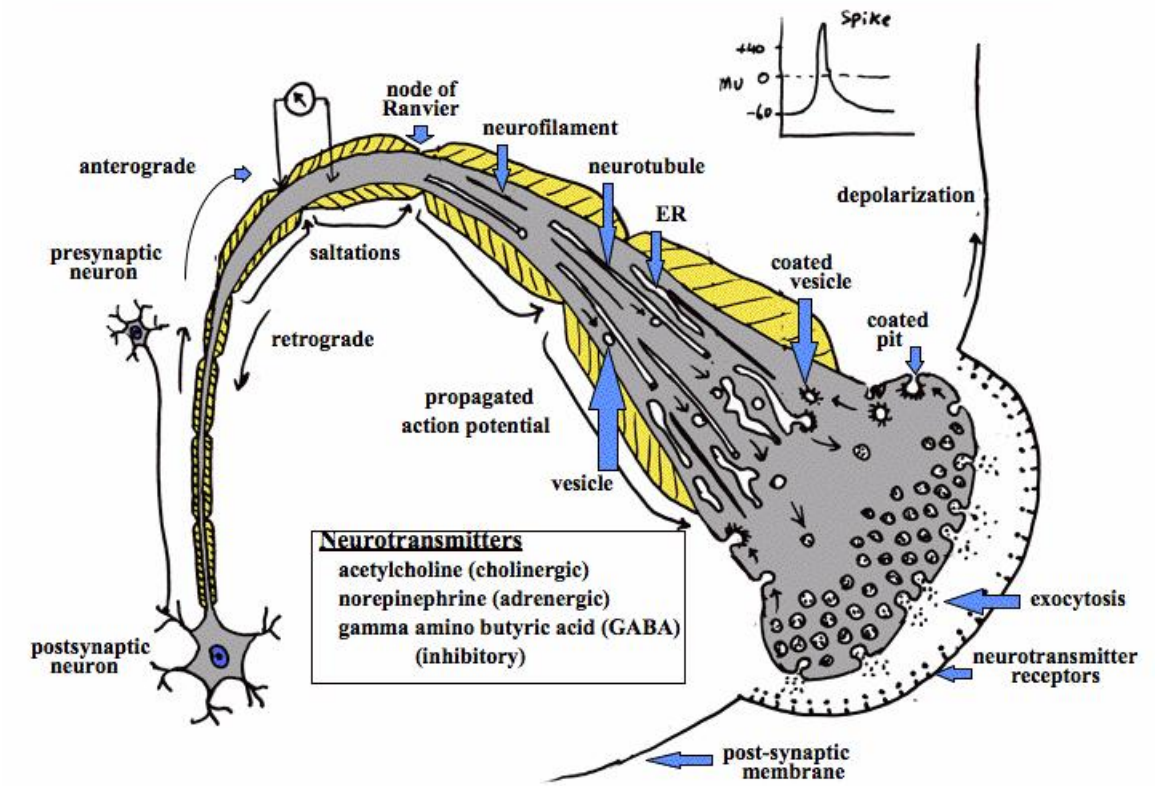
Types of Circuits in Neuronal Pools

- *Convergent – opposite of divergent circuits, resulting in either strong stimulation or inhibition*
- *Reverberating – chain of neurons containing collateral synapses with previous neurons in the chain*
- *Parallel after-discharge – incoming neurons stimulate several neurons in parallel arrays*

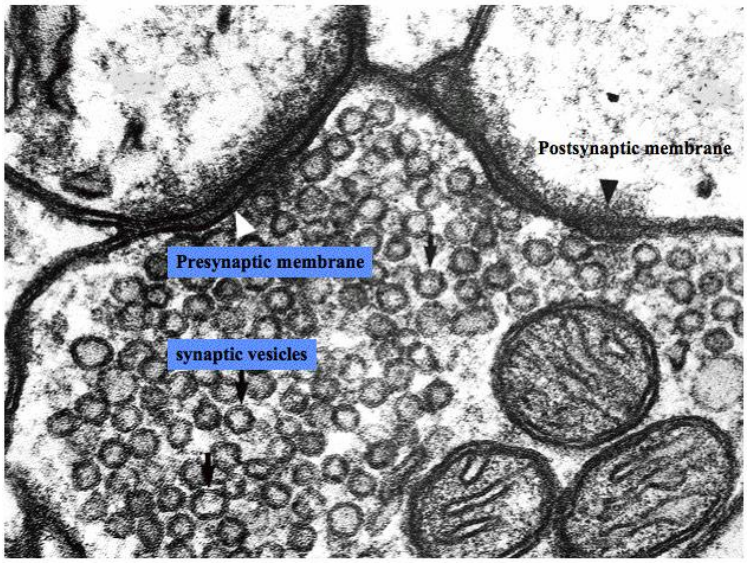
Patterns of Neural Processing

- *Serial Processing*
  - Input travels along one pathway to a specific destination
  - Works in an all-or-none manner
  - Example: spinal reflexes
- *Parallel Processing*
  - Input travels along several pathways
  - Pathways are integrated in different CNS systems
  - One stimulus promotes numerous responses
- *Example: a smell may remind one of the odor and associated experiences*

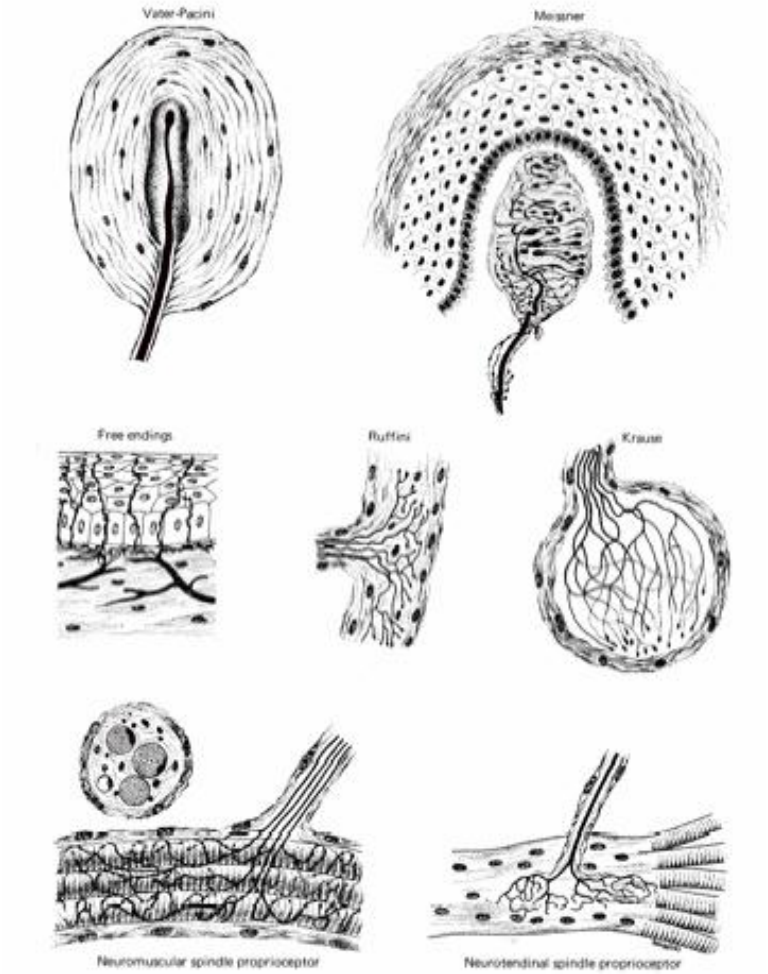
IMPLUSE PROPAGATION AND CHEMICAL SYNAPSES



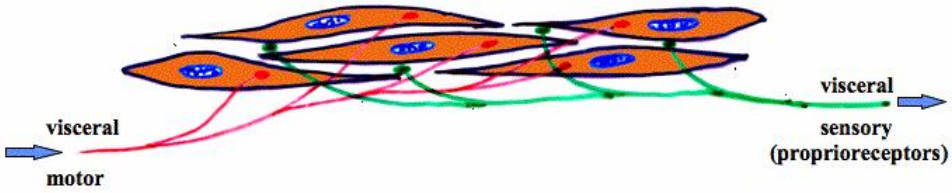
SYNAPTIC VESICLES

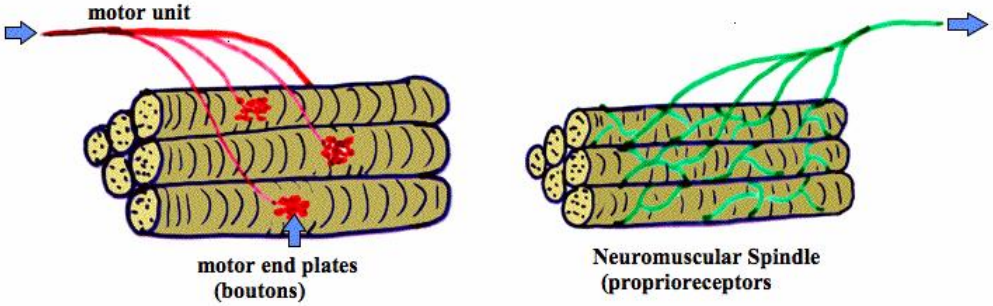


Sensory Nerve Endings



PERIPHERAL NERVE ENDINGS-(MUSCLE)





MOTOR END PLATES

SEM- Motor End Plates