NEUROHISTOLOGY
(NEURONS & GLIAL CELLS)

Professor Abraham A. A. Osinubi
Fellow of the American College of Endocrinology
Department Of Anatomy
College Of Medicine of The University Of Lagos
Lagos, Nigeria
MB,BS (Ibadan)
M.Sc. Anatomy (Lagos)
MBA (Zaria)
Ph.D. Anatomy (Lagos)
FACE (USA)
FASN (NIGERIA)
FSECAN (NIGERIA)
FAcadMedS (NIGERIA)

- "A prosperous life is never by accident but by design, though the lazy one calls it destiny while the uninformed and misinformed may term it providence."

Author: Abraham A. A. Osinubi, 2008, 2012

“Your way to success is largely determined by what and who you associate with.”

Abraham A. A. Osinubi*, *2004

- "Always bear in mind that you can never be sidetracked by people who were in the first place never on track."

Abraham A. A. Osinubi, 2012

- “Anyone you contact will never leave you the same; you will either increase or decrease; a change is imperative.”

***Abraham A.A. Osinubi*, 2010**

- “Show some gratitude for every atom of kindness. Depreciation is not too far from he that does not show appreciation. He who appreciates always appreciates”

***Abraham A. A. Osinubi*, 2014**

Learning Objectives

At the end of class interaction, the learner should be able to:

1. Describe parts of a neuron including the unique features of soma & axon.
2. Distinguish between dendrites and axons.
3. Give the different forms of classification of neurons.
4. Account for the roles of myelin sheath & neurofilaments in nerve cell.
5. Enumerate various glial tissues & global roles in CNS.
6. Describe the structures of glial cells in CNS and their specific functions.
7. Describe glial cells in the PNS & their functions
8. Describe the anatomical basis of some related clinical conditions.

Lecture Outline

1. Pretest
2. Introduction
3. Neurons
4. Soma and dendrites
5. Axons
6. Axonal transport
7. Microfilaments
8. CNS Neuroglia
   - Astrocytes
   - Microglia
   - Ependymal cells
   - Oligodendrocytes
9. PNS Neuroglia
   - Shwann cells
   - Satellite cells
10. Applied & Clinical Anatomy
11. Post-test

Pretest

The initial segment of the axon is:

1. Where the nerve impulse is generated.
2. The first 400 µm after the axon leaves the axon hillock
3. The specialized part of the soma
4. Characterized by a higher density of voltage-gated sodium channels than in the remainder of the axon
5. Consists of a specialized complex of proteins and is unmyelinated

Nervous Tissue

- Neurons
- Supporting cells
- Special neuronal characteristics
  - Convey APs (excitable)
  - Longevity
  - High metabolic rate

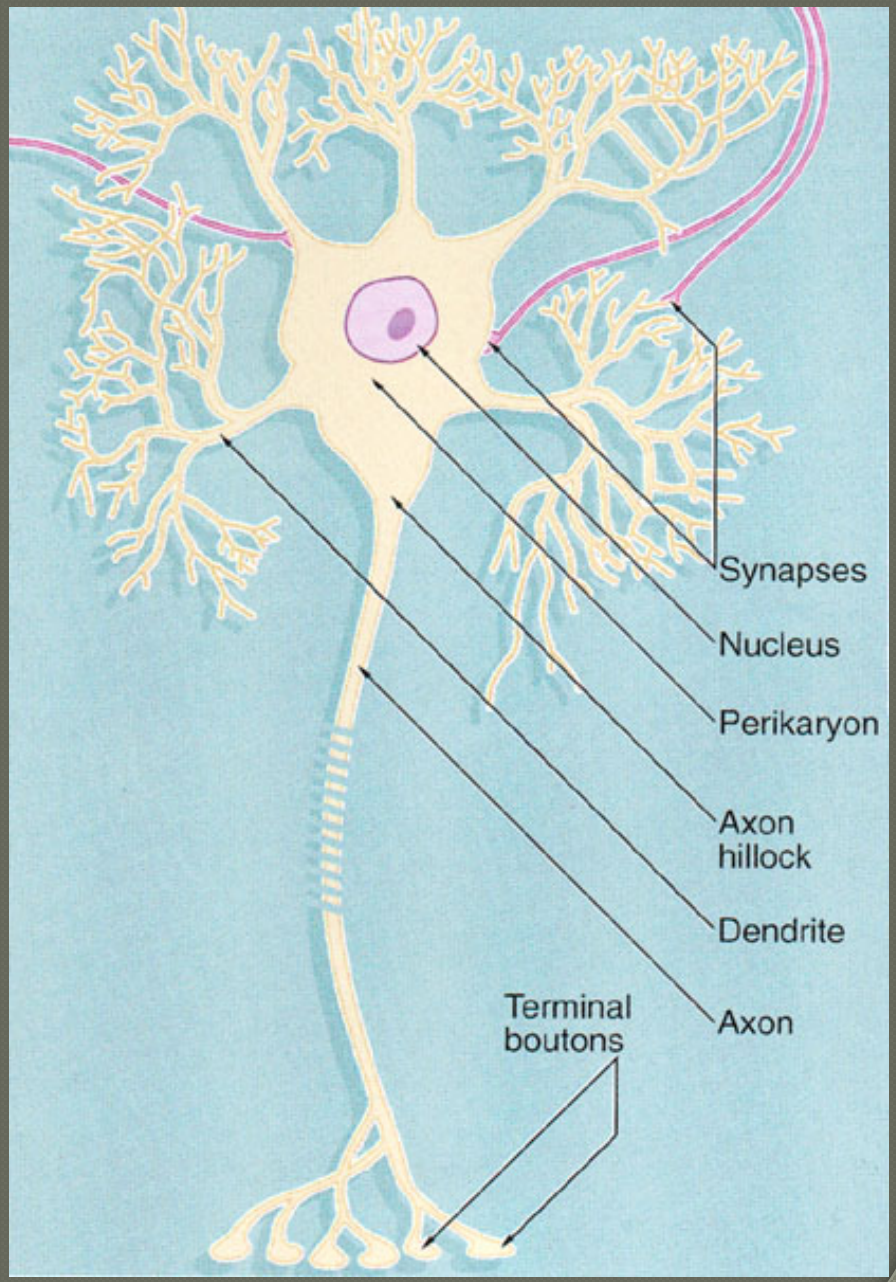
Introduction

Neuron

- Possesses
  - Cell body
  - Neurites
    - Dendrites
    - Axon
- Nerve fibres

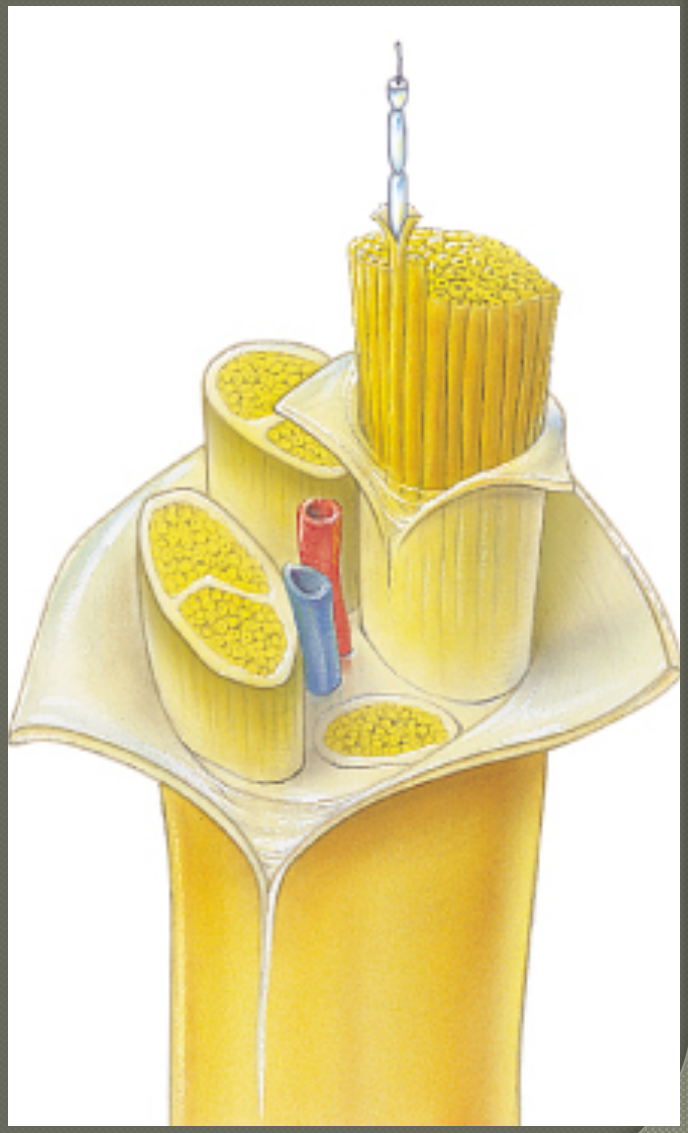
Neuroglia

- Smaller in size



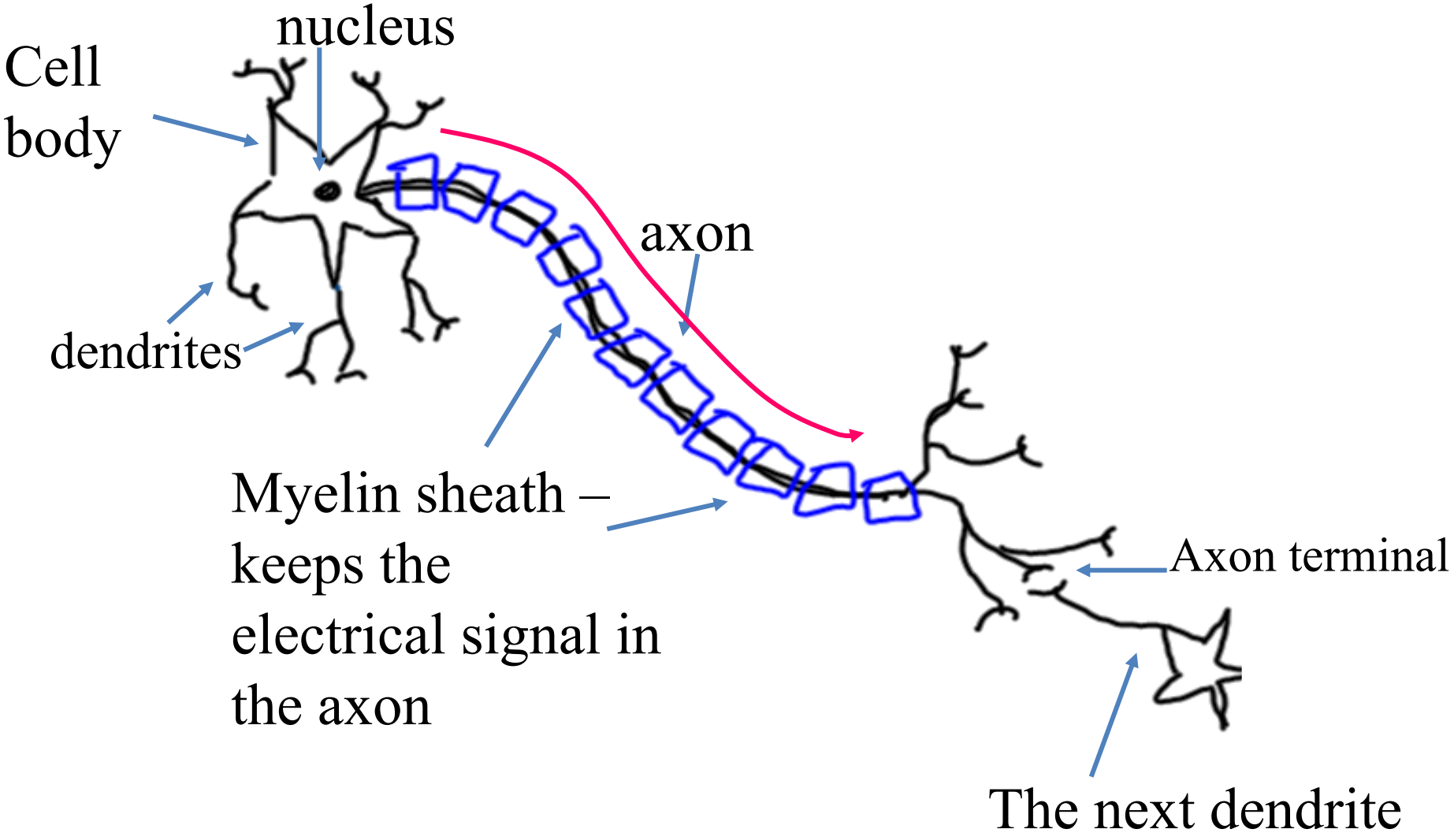
Nerve

- Bundle of axons in PNS
- **Endoneurium**
  - Loose CT around each axon
- **Perineurium**
  - CT around a bundle of axons
- **Epineurium**
  - CT around a nerve



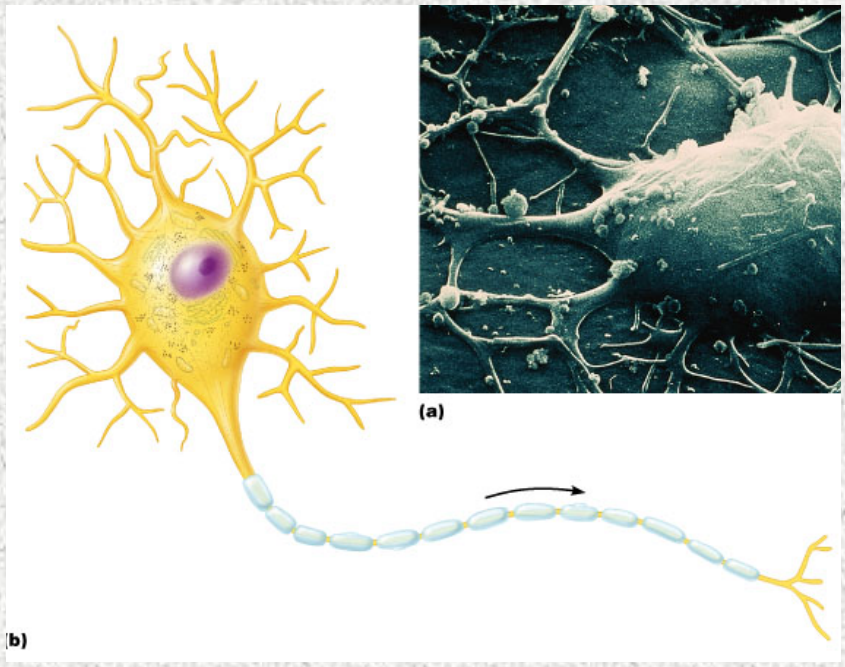
Neurons

- Message = nerve impulse
- The impulse travels in one direction
  - It travels at the same speed within 1 neuron
  - It travels with the same intensity w/in 1 neuron

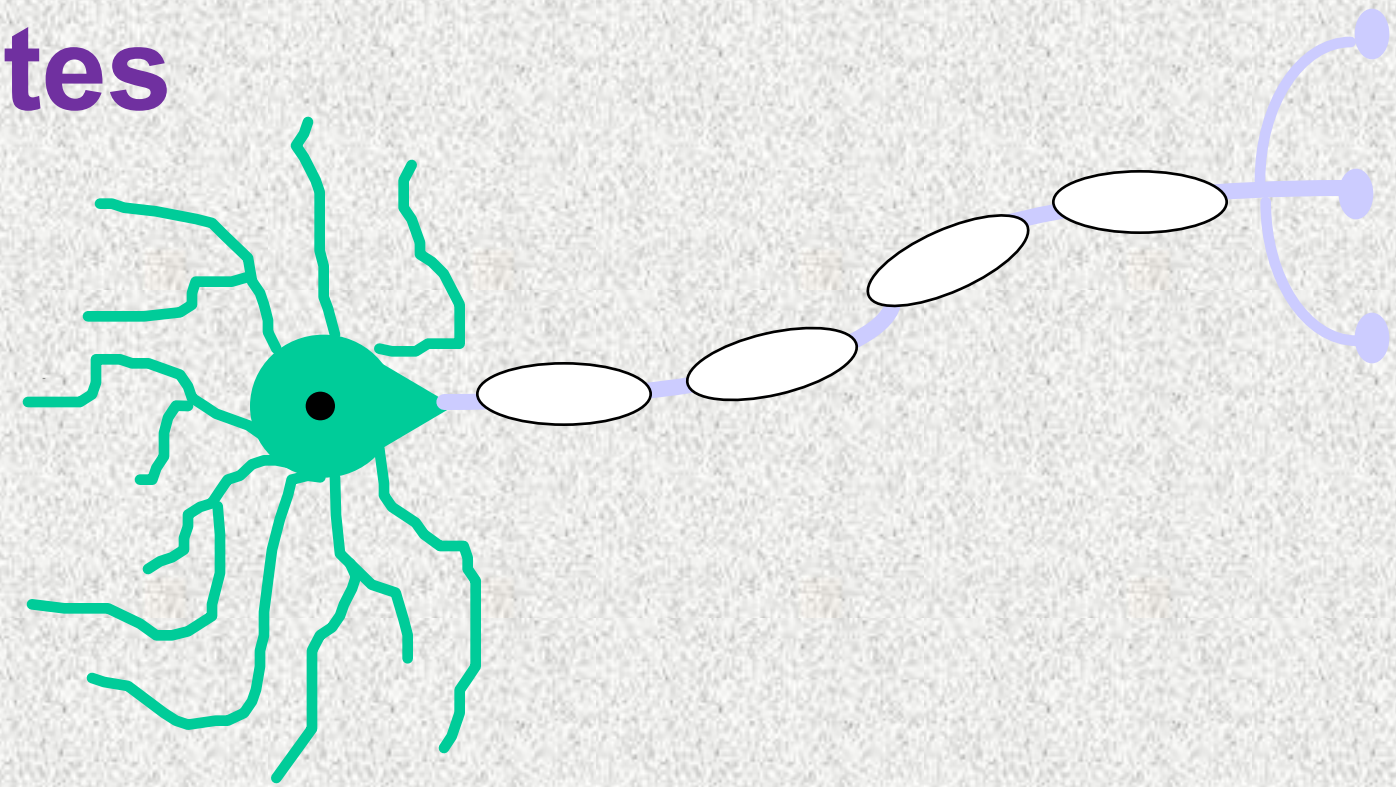

nucleus
Cell body
axon
dendrites
Myelin sheath – keeps the electrical signal in the axon
Axon terminal
The next dendrite

Neuronal Cell Body

- Soma/Perikaryon
- Variable size
  - ~5-140 μm diameter
- Spherical nucleus
  - Nucleolus
- Chromatophilic (Nissl) bodies
  - rER & free ribosomes
  - Not in axon or a. hillock
- Mitochondria
- Golgi App only in cell body
- Neurofibrils
  - Intermediate filaments (neurofilaments)



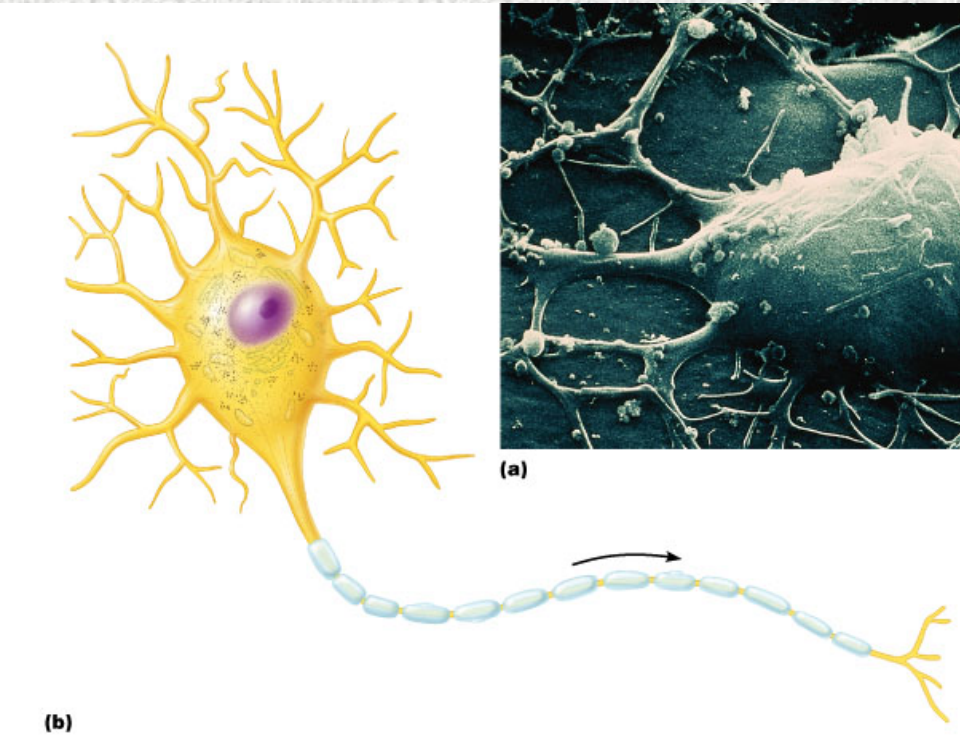
Dendrites



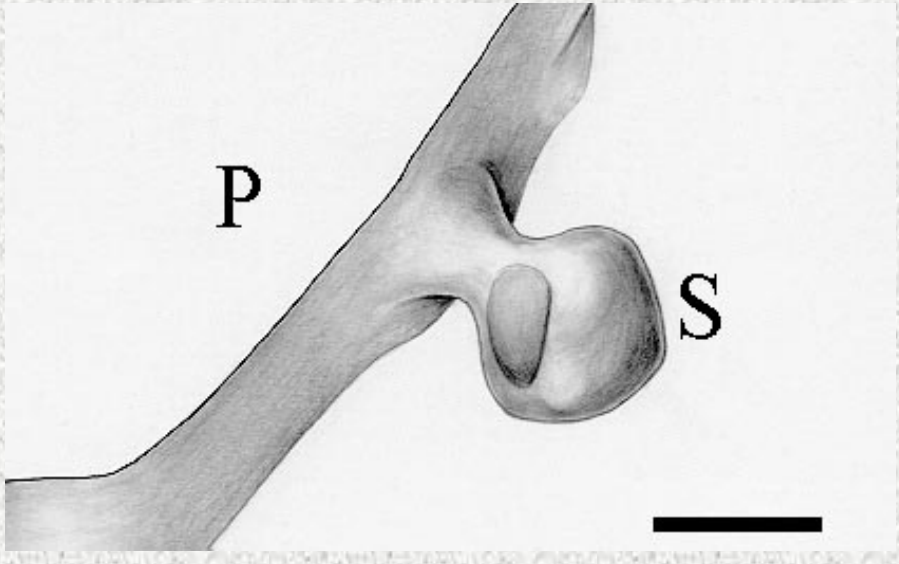
- **Receives & Processes information**

Dendrites

- Usually numerous
- Branched
- Contain rER
- Contain receptors to neurotransmitters
- Send signals to soma



Dendritic Spines



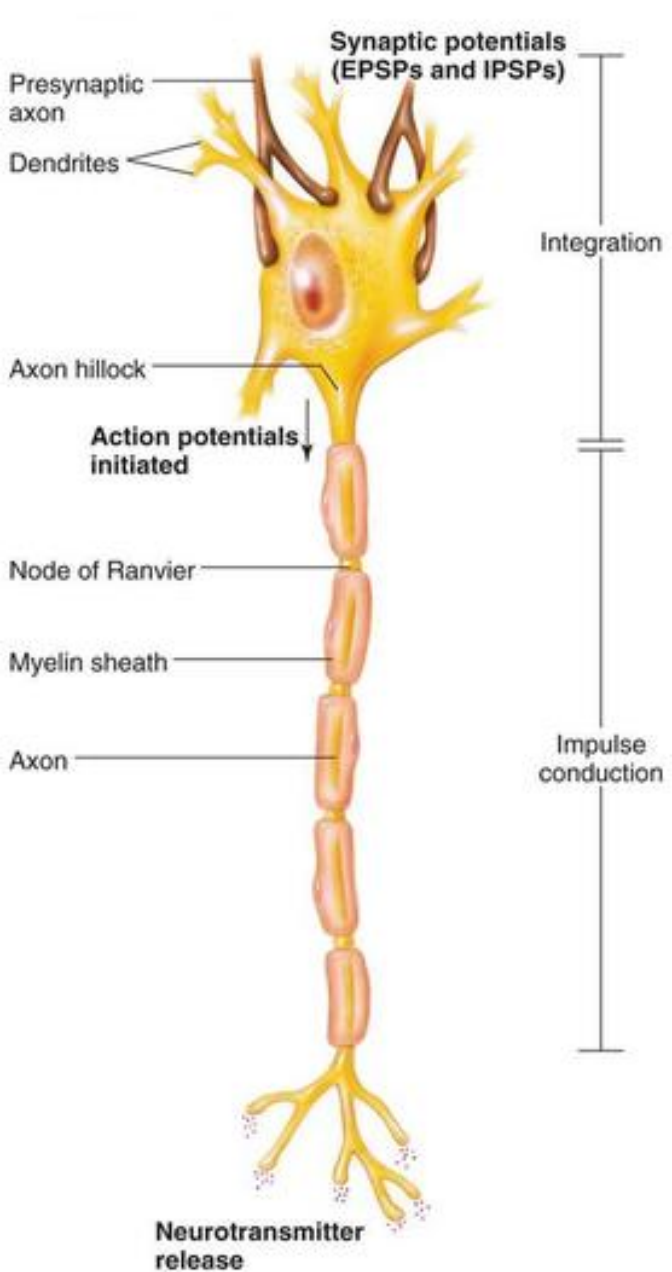
http://synapses.bu.edu/atlas/contents.htm

The dendritic tree is the primary receiving site for synaptic information. The dendritic surface of many neurons has **dendritic spines** which further increase the synaptic surface area.

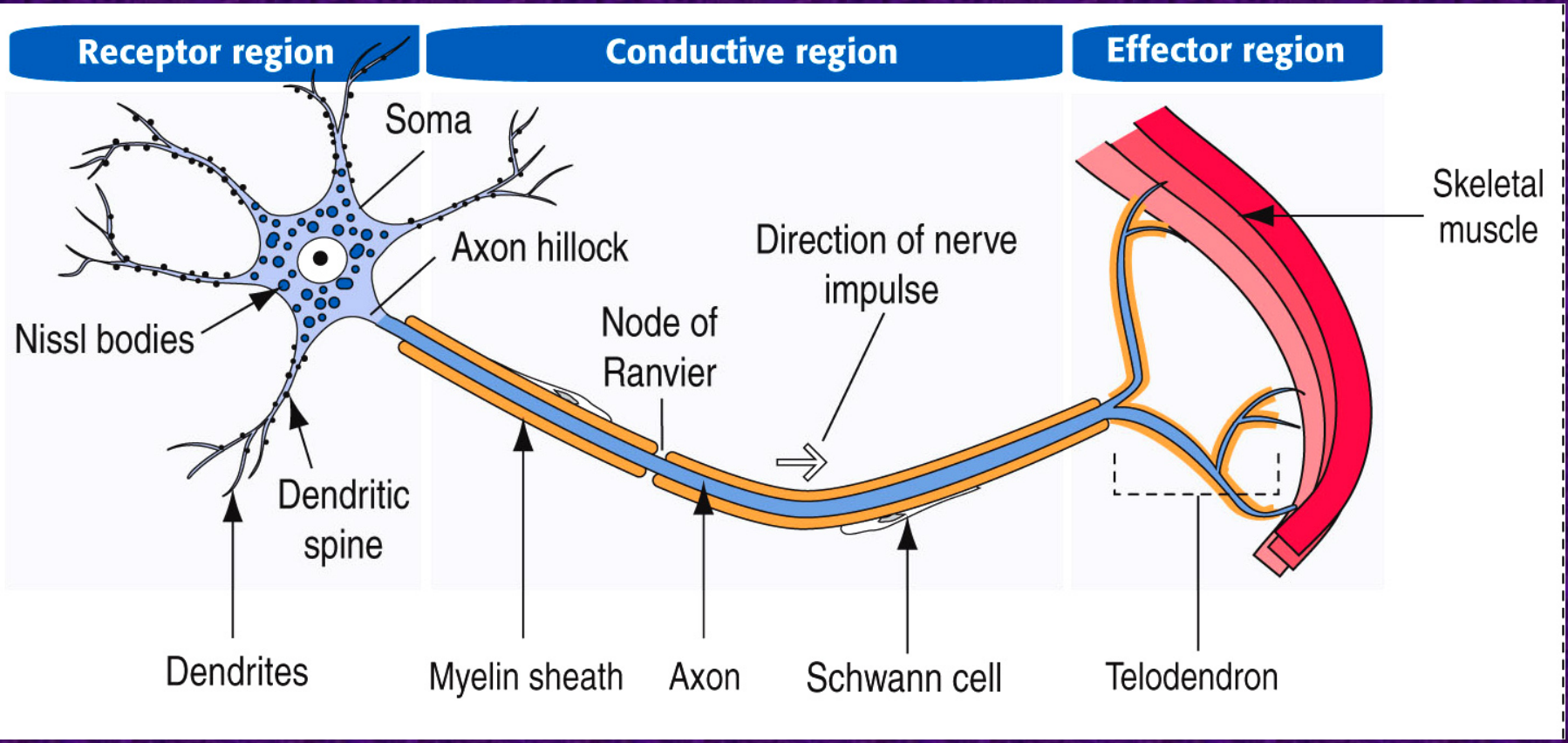
Abundant neurotubules and neurofilaments and components of the rough endoplasmic reticulum (Nissl bodies) may extend into the base of the dendrite.

Axon Hillock

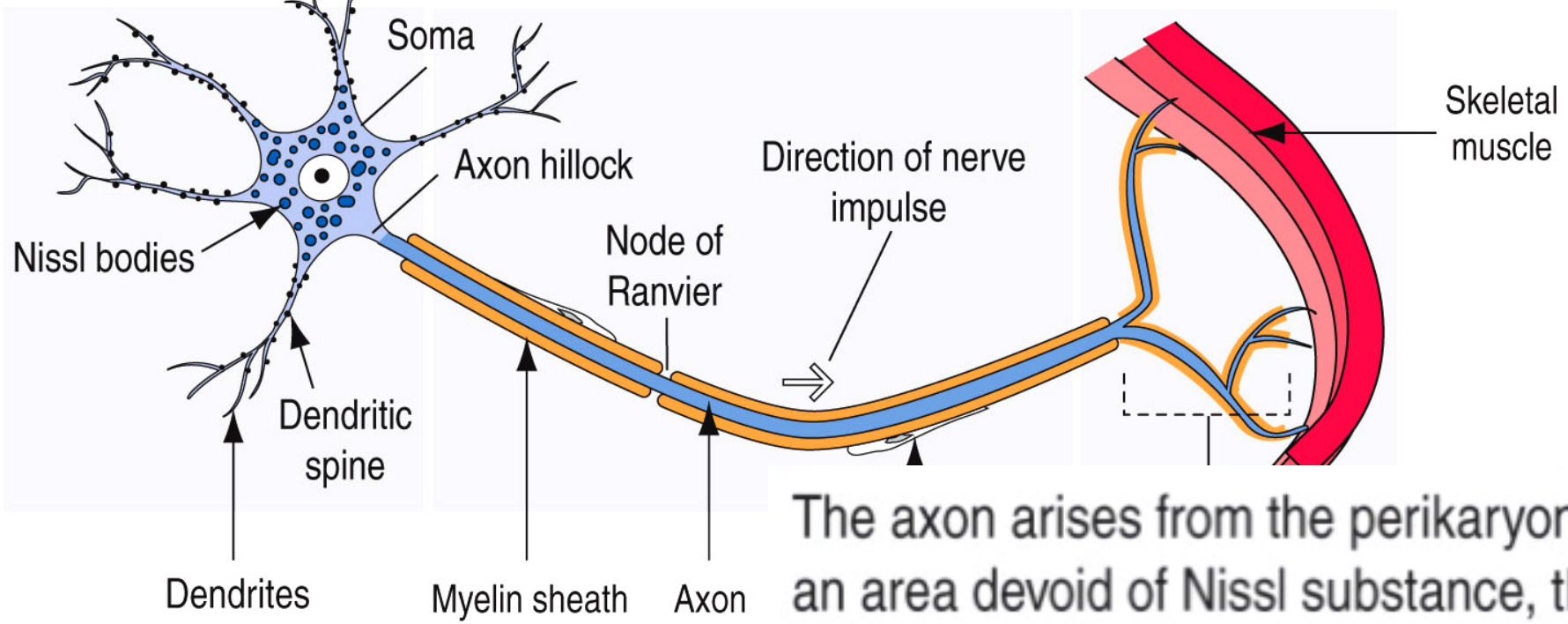
- Specialized part of the soma that connects to axon
- Last site where membrane potentials propagated from synaptic inputs are summated before being transmitted to axon
- Barrier for lateral diffusion of transmembrane proteins & lipids embedded in plasma membrane



Axons (I)

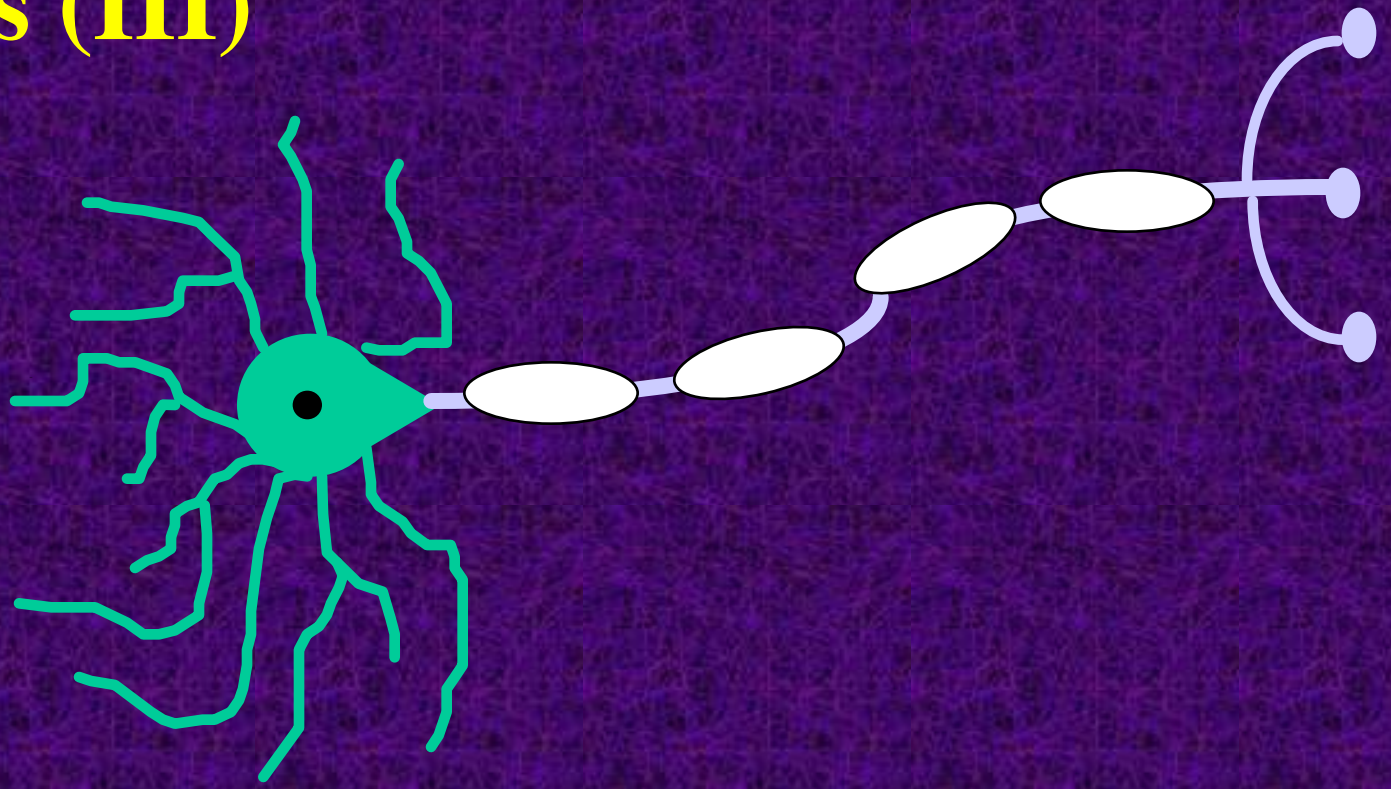


- 1 per soma
- Initial segment from axon hillock
  - ❖ Most excitable
  - ❖ Initiation of AP
- No Nissl bodies



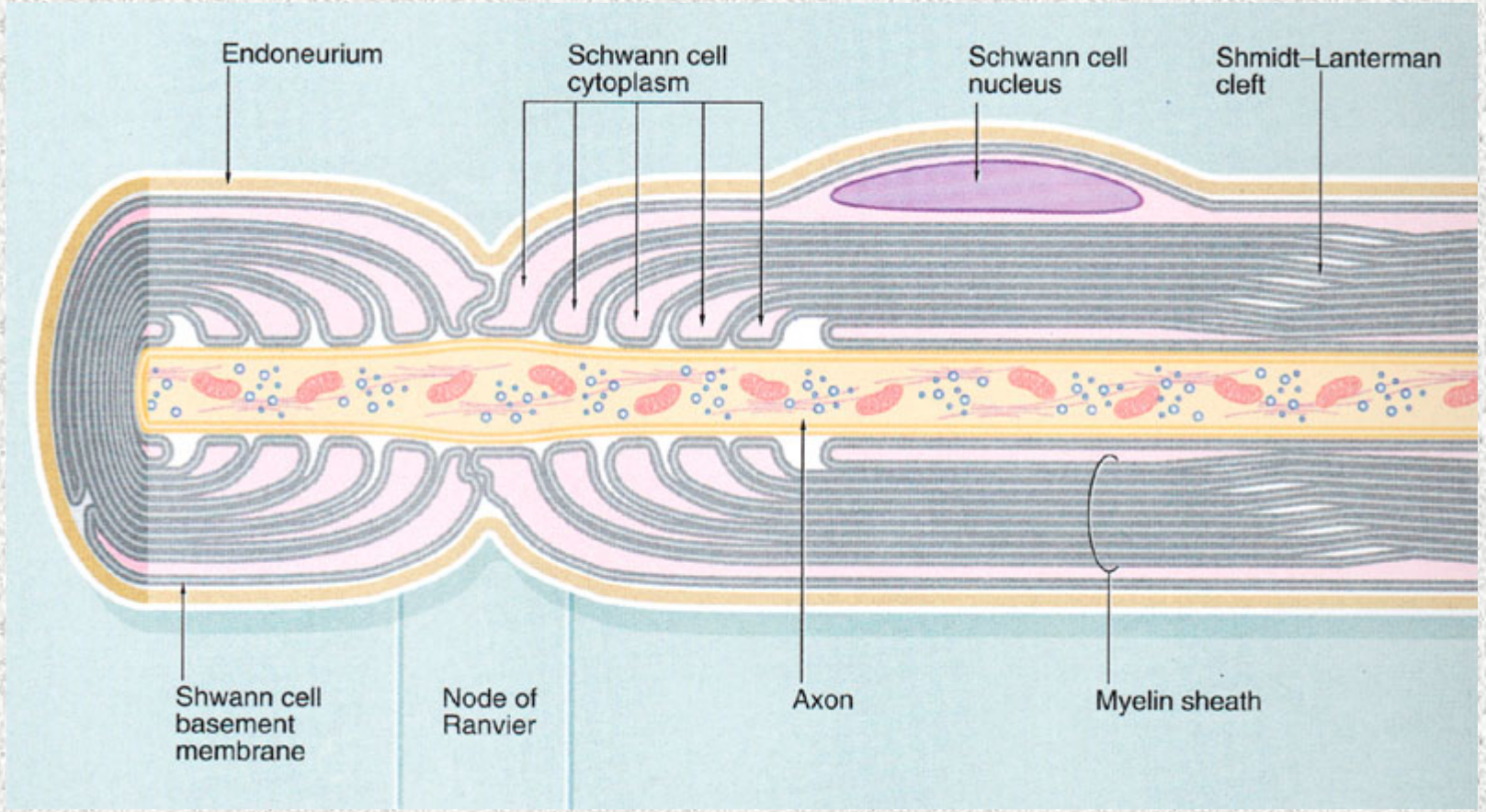
The axon arises from the perikaryon in an area devoid of Nissl substance, the axon hillock. The initial segment of the axon is the site of action potential generation, the trigger zone. Unlike the gradually tapering dendrite, the diameter of the axon remains constant throughout its length. In myelinated axons, a myelin sheath extends from the initial segment to the telodendron. Many axons have collateral branches.

Axons (III)

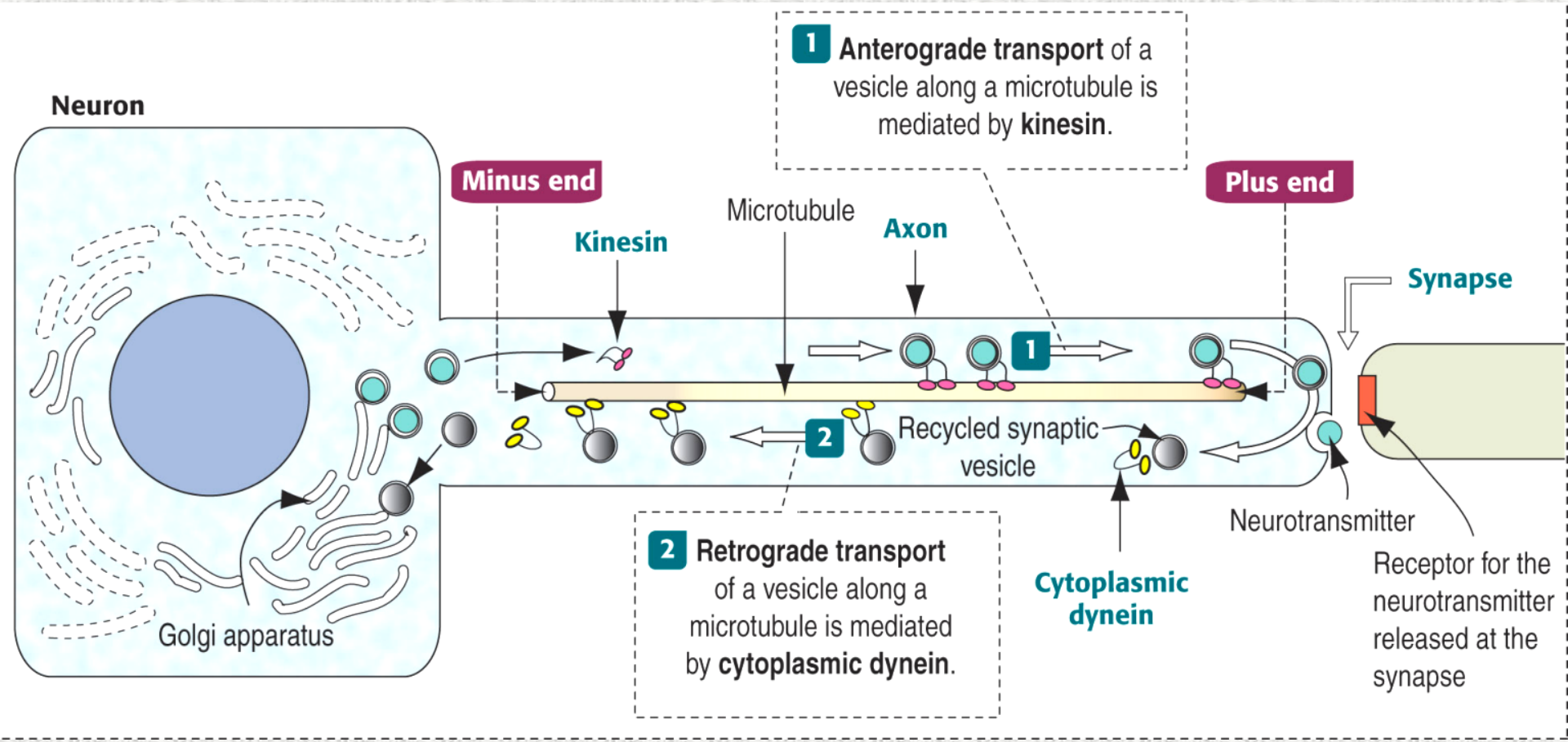


- Axon carries information away from soma
  - Electrical signal within
  - Axon terminal releases chemical message ~

Nodes of Ranvier (I)



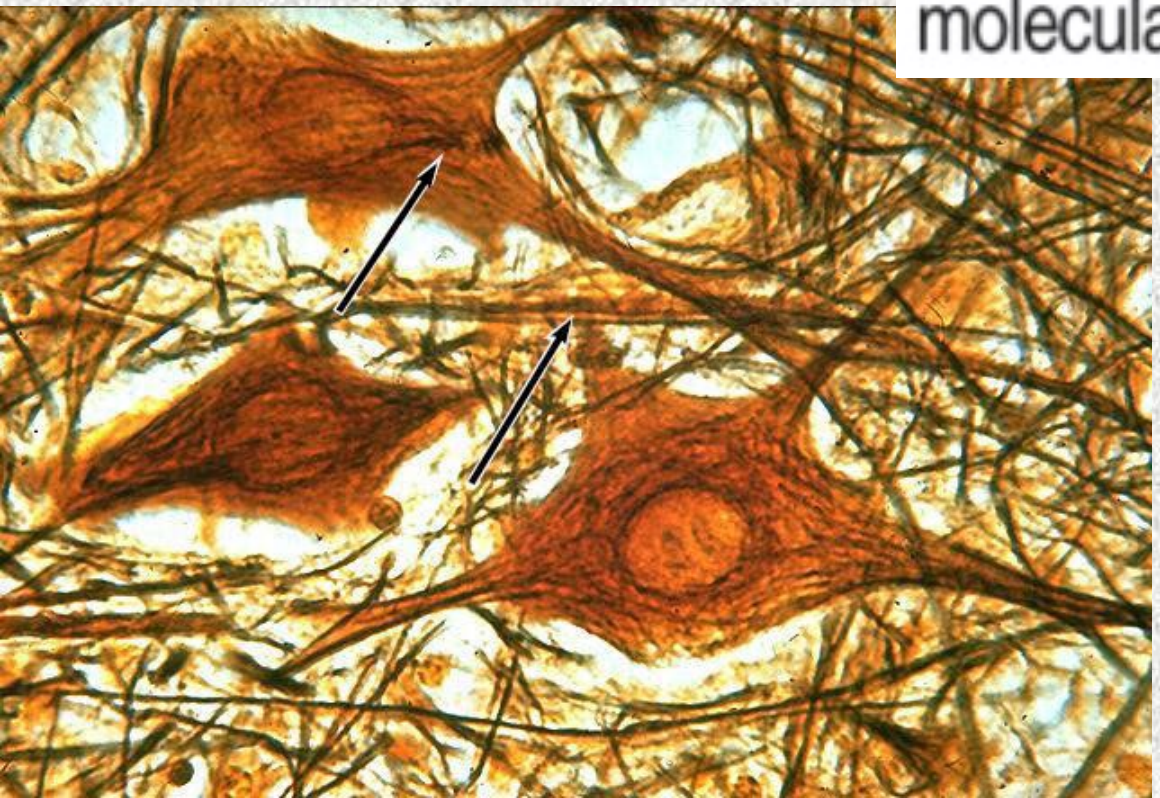
Axonal Transport



Cytoskeletal Elements

- Microtubules (- to +)
- Intermediate Filaments (Neurofilaments)
- Microfilaments

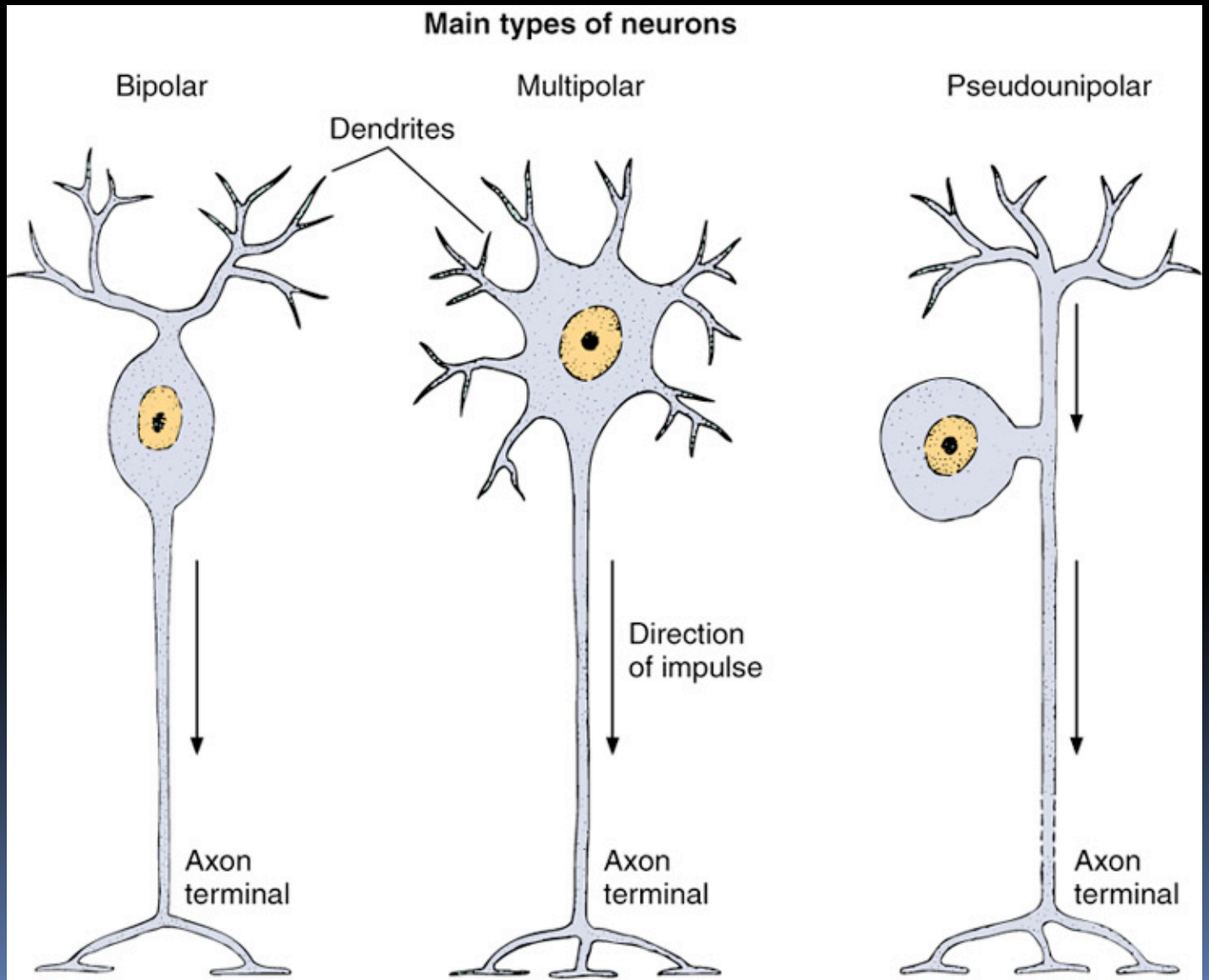
Three types of neurofilaments (NF) are found in axon and dendrites: NF-L, NF-M, and NF-H (for low, middle, and high-molecular mass, respectively).



Classification of Neurons

- **Morphology**
  - Shape of neurons/ Number of neurites
  - Axon diameter
  - Dendrite structure
    - Pyramidal
    - Stellate
  - Dendritic spines
    - Spiny or Aspinous ~
- **Functions**

Neuron Classification by Shape of neurons/Number of Neurites



Multipolar

- >2 processes
- Most neurons of brain & spinal cord
- >99% of neurons

(a) Multipolar neuron

Bipolar Neurons

- 2 processes
- Rare

(b) Bipolar neuron

Pseudounipolar Neurons

- 1 process
- Quickly forms 2 processes
- Sensory neurons – located mainly in dorsal root ganglia

Classification based on Cell Body & Dendrites

- **Pyramidal cells**
  - Pyramid-shaped
- **Stellate cells**
  - Star-shaped
- Cells can also be classified by whether the dendrites have spines or not
  - Those that do are called **Spiny Neurons**
  - Those that don't are called **Aspinous Neurons**
  - Pyramidal cells are spiny, while stellate cells can be spiny or aspinous

Neuron Classification by Axon Length

- **Golgi type I Neurons**
  - Long axon
    - Pyramidal cells
    - Purkinje cells
    - Motor cells of spinal cord
- **Golgi type II Neurons**
  - Have short axon
    - Greatly outnumber type I
    - Numerous in cerebral & cerebellar cortex
    - Often inhibitory in function

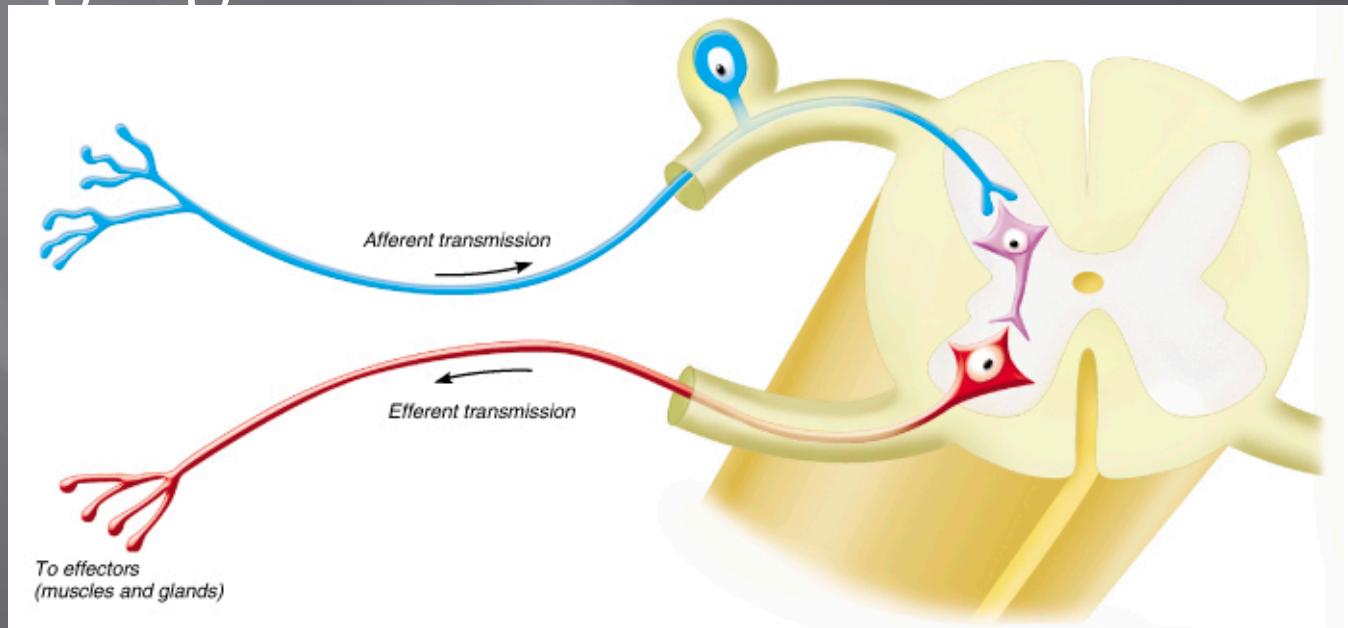
By Axon Diameter

- Sensory afferents
  - Size: largest → smallest
  - Aα, Aβ, Aδ, C
- C: small, unmyelinated
  - pain & temperature
- Aα:
  - Proprioceptors in muscle

Neuron Classifications By Function

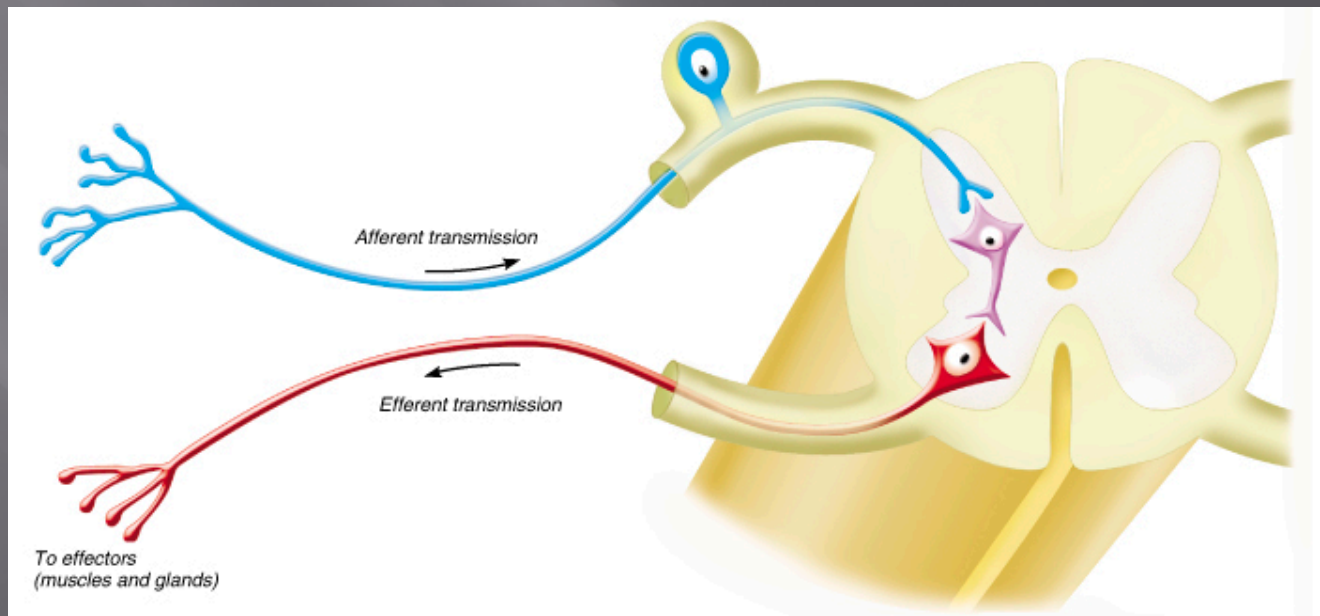
Sensory / afferent neurons

- Sensory receptors in PNS
- Send AP to CNS
- Pseudounipolar soma
  - Located in ganglia in PNS



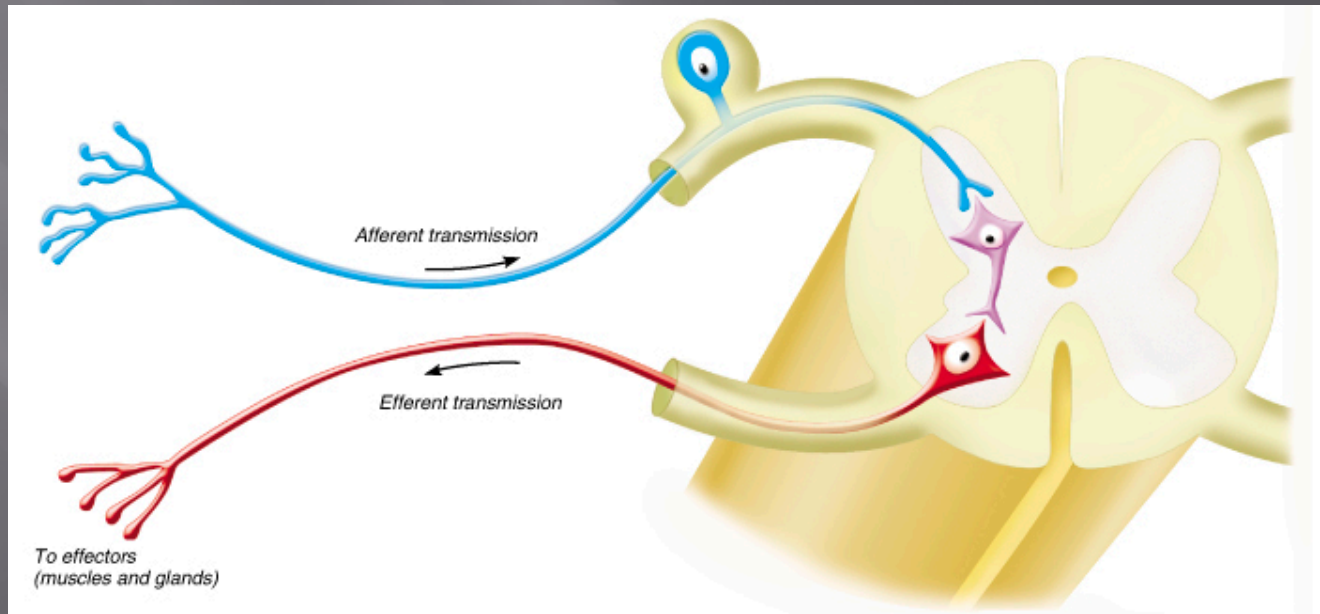
Motor / efferent neurons

- Multipolar
- Soma in CNS
  - Except ANS
- Send AP to muscle or gland



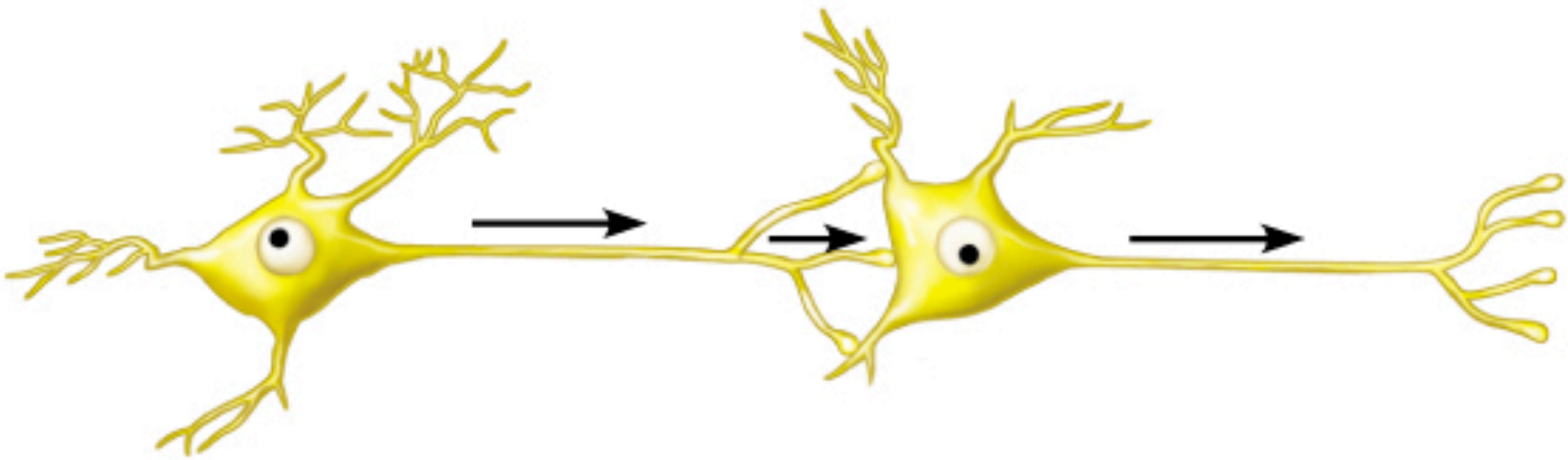
Interneurons / association neurons

- Located in CNS
- >99% of all neurons
- ~ all multipolar
- Integration of information



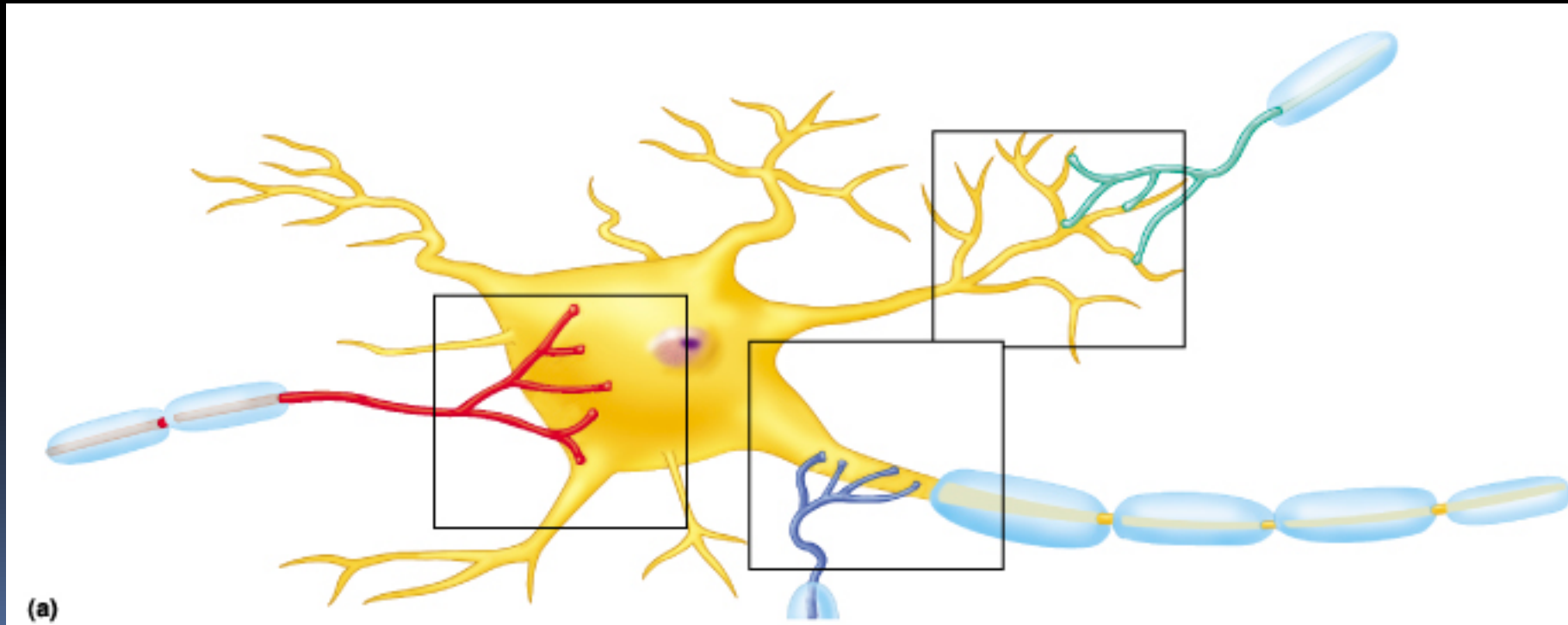
Synapses

- Presynaptic neuron
- Postsynaptic neuron

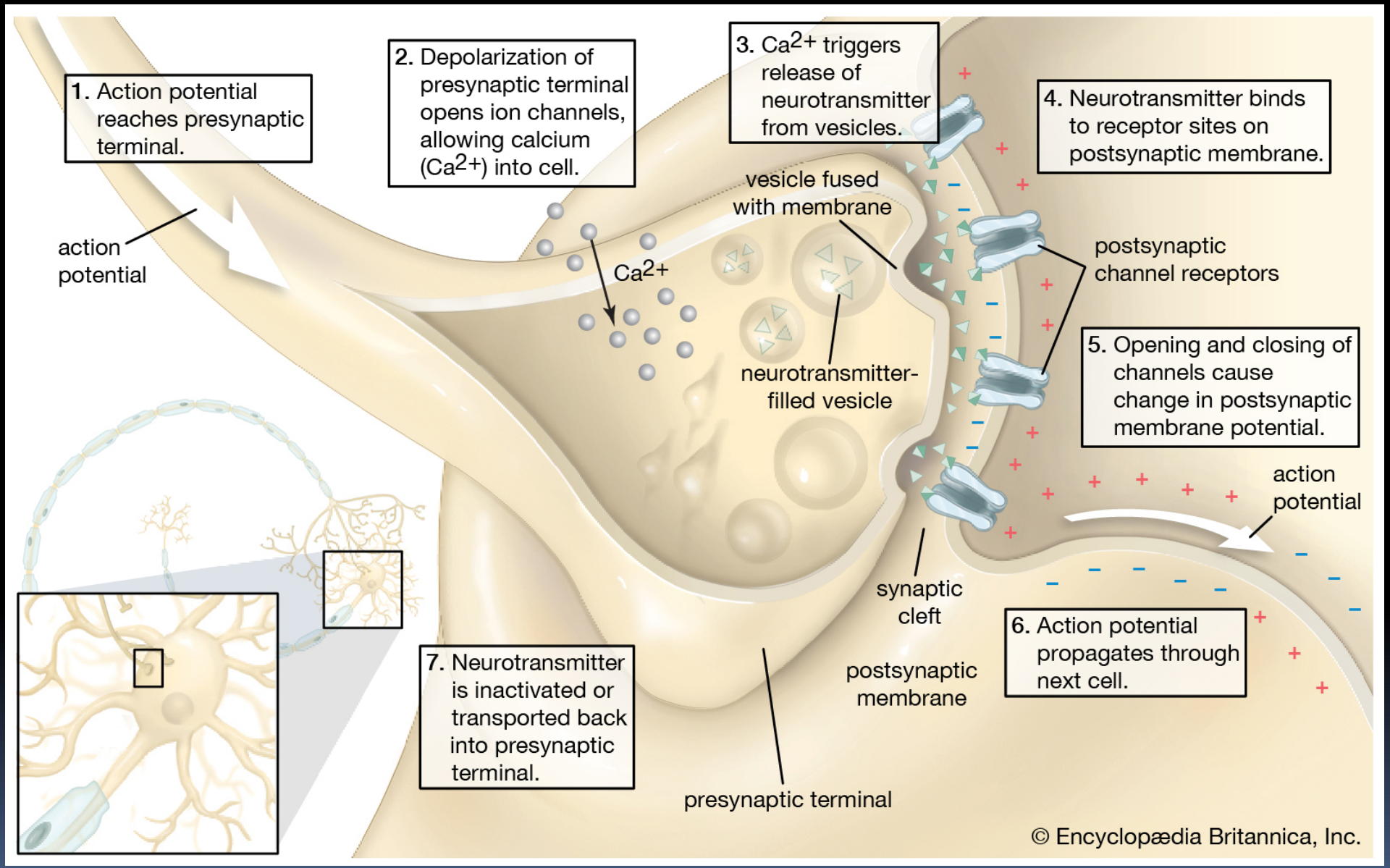


Synapses

- Axodendritic synapses
- Axosomatic synapses
- Axoaxonic synapses



(a)


1. Action potential reaches presynaptic terminal.
2. Depolarization of presynaptic terminal opens ion channels, allowing calcium (Ca^{2+}) into cell.
3. Ca^{2+} triggers release of neurotransmitter from vesicles.
4. Neurotransmitter binds to receptor sites on postsynaptic membrane.
5. Opening and closing of channels cause change in postsynaptic membrane potential.
6. Action potential propagates through next cell.
7. Neurotransmitter is inactivated or transported back into presynaptic terminal.
action potential
Ca^{2+}
vesicle fused with membrane
neurotransmitter-filled vesicle
postsynaptic channel receptors
action potential
synaptic cleft
postsynaptic membrane
presynaptic terminal
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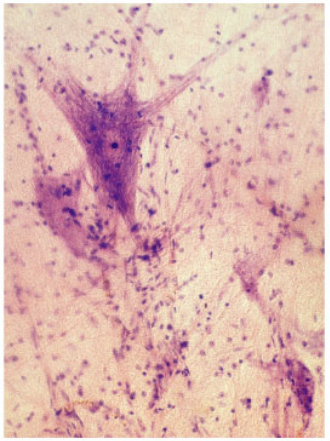
Electrical Synapse

- Link bw 2 abutting neurons formed at a narrow gap bw pre- & postsynaptic neurons - gap junction
- Synaptic cleft ~3.5 nm; shorter than 20-40 nm distance that separates cells at chemical synapse
- In many animals, electrical synapse-based systems co-exist with chemical synapses.
- Compared to chemical synapses, electrical synapses conduct nerve impulses faster
- Unlike chemical synapses they do not have gain (the signal in the postsynaptic neuron is the same or smaller than that of the originating neuron)
  - Often found in neural systems that require fastest possible response, such as defensive reflexes

Supporting cells in CNS

- Neuroglia / glial cells
- Ratio glia:neurons
- Smaller than neurons
- Can divide



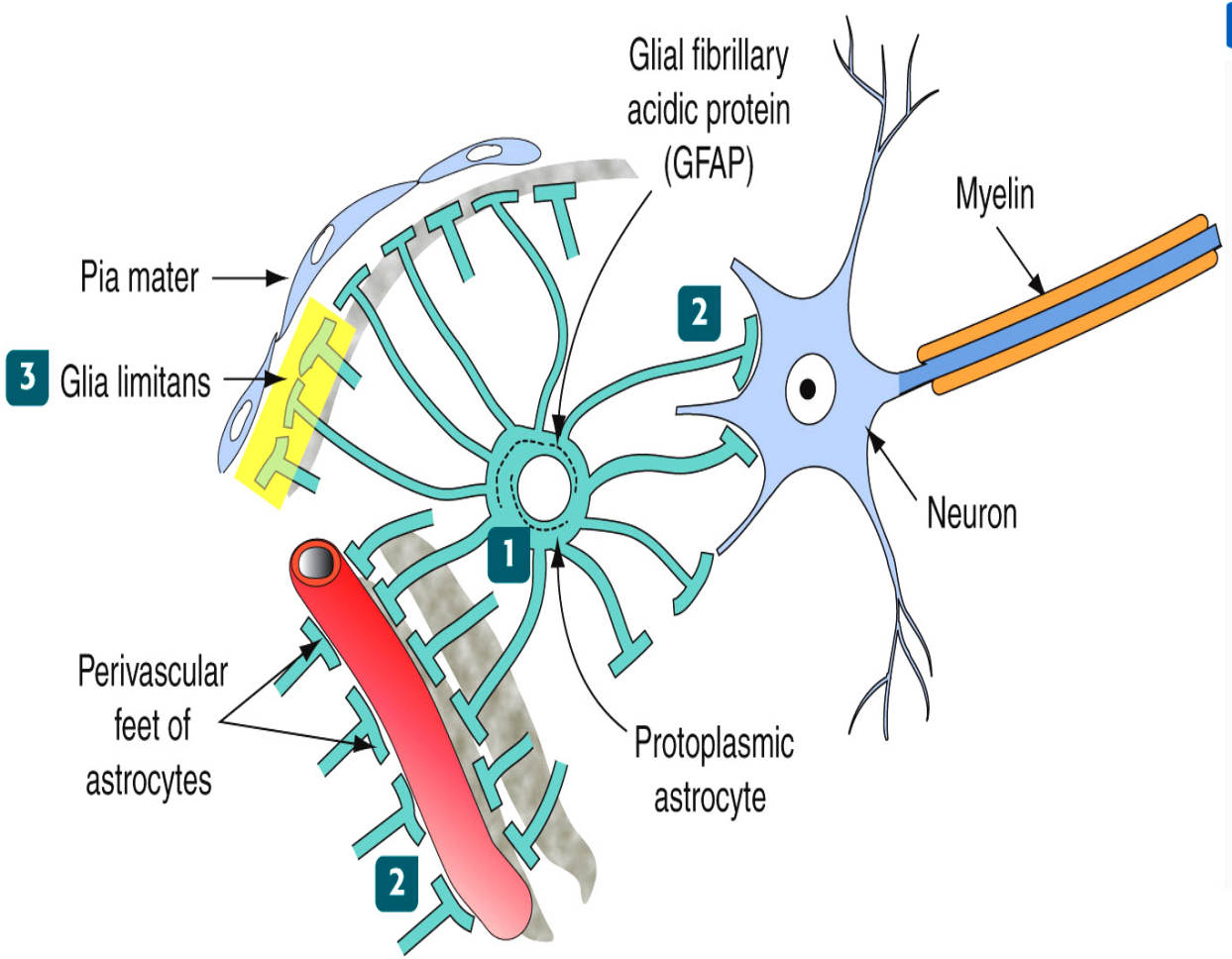
CNS Neuroglia

- Astrocytes
  - Control [ion]
- Microglia
  - Phagocytic
- Ependymal cells
  - Line ventricles
- Oligodendrocytes
  - Form myelin

Astrocytes

- Star-shaped
- Bind neurons to capillaries & pia mater

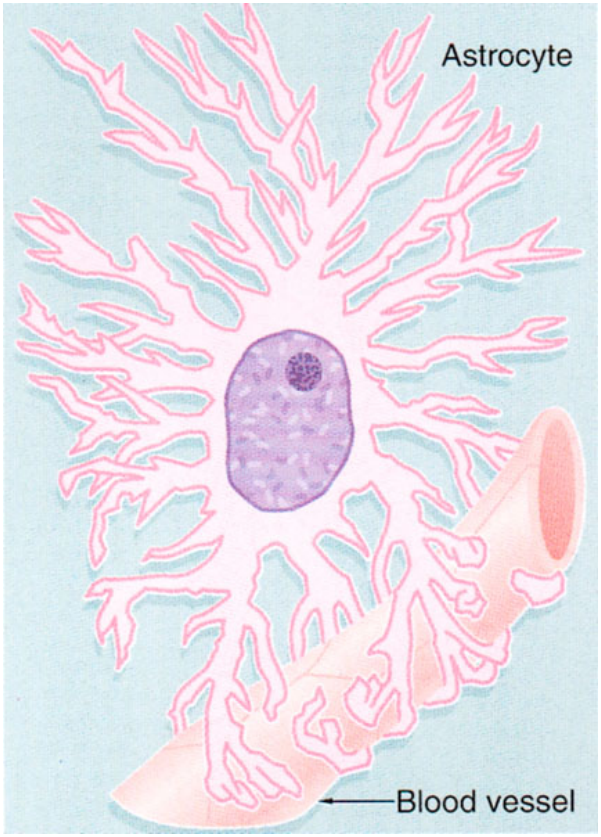
- Most abundant glial cells



Astrocytes (2)

Functions

1) Supportive
2) Insulating, particularly with regard to synapses
3) Electrolyte balance, particularly regarding K+ ions
4) pH balance of extracellular milieu
5) Sequestration of neurotransmitters
6) Communicate with capillary endothelial cells
7) Interactions with immune system

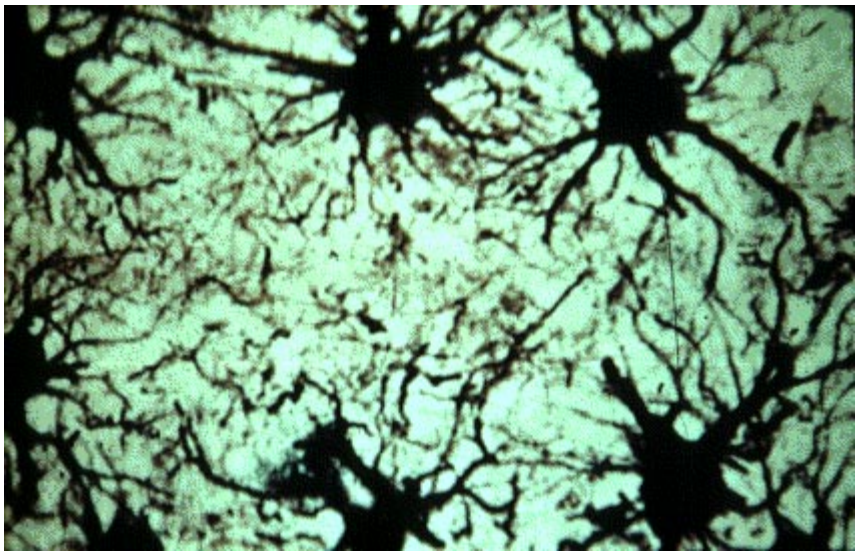


Astrocytes (4)

Fibrous astrocytes

-prominent in white matter

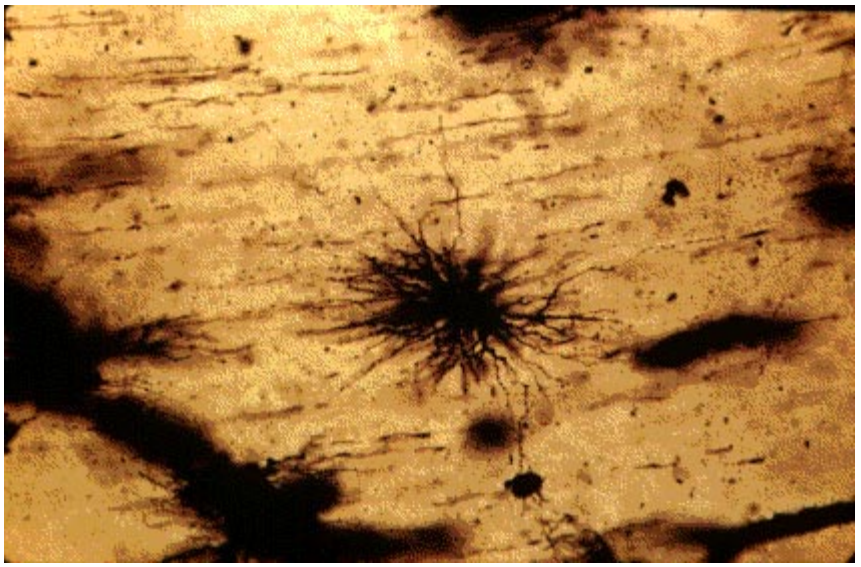
-fine, long, straight processes



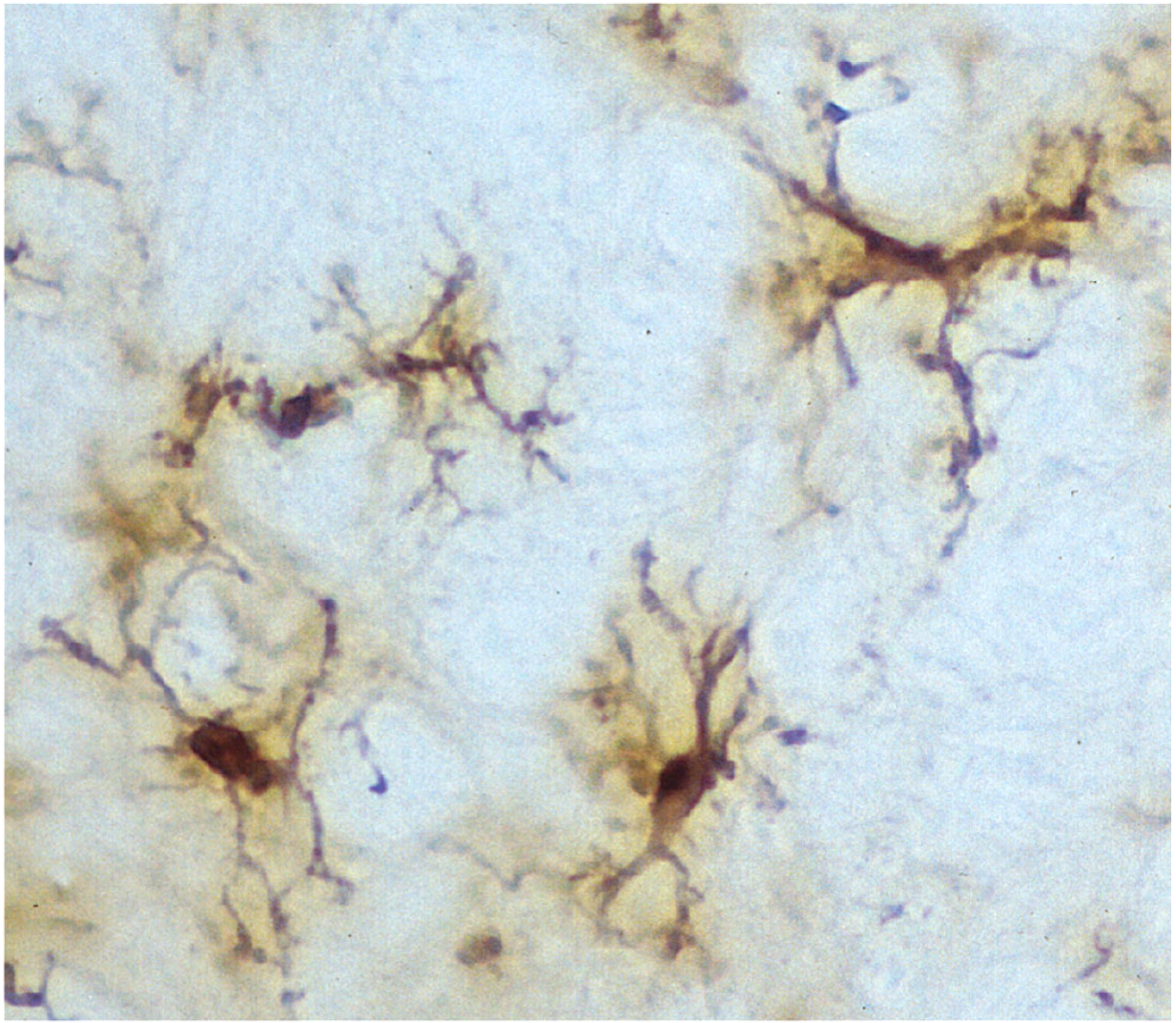
Protoplasmic astrocytes

-prominent in gray matter

-wavy, thin, fluffy processes



Microglia



Immunocytochemical preparation courtesy of Wan-hua Amy Yu

Small elongated cells with short irregular processes
Dense elongated nuclei

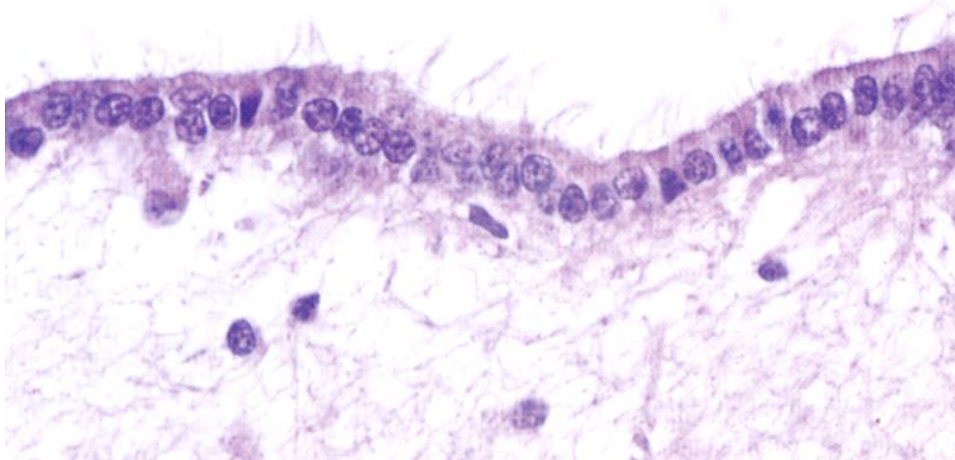
Microglia (II)

- Derived from precursor cells in bone marrow
- Phagocytic cells
  - Involved with inflammation & repair in the adult CNS
  - Produce & release neutral proteases & oxidative radicals
- When activated, microglia retract their processes & assume the morphologic characteristics of macrophages, becoming phagocytic & acting as APCs

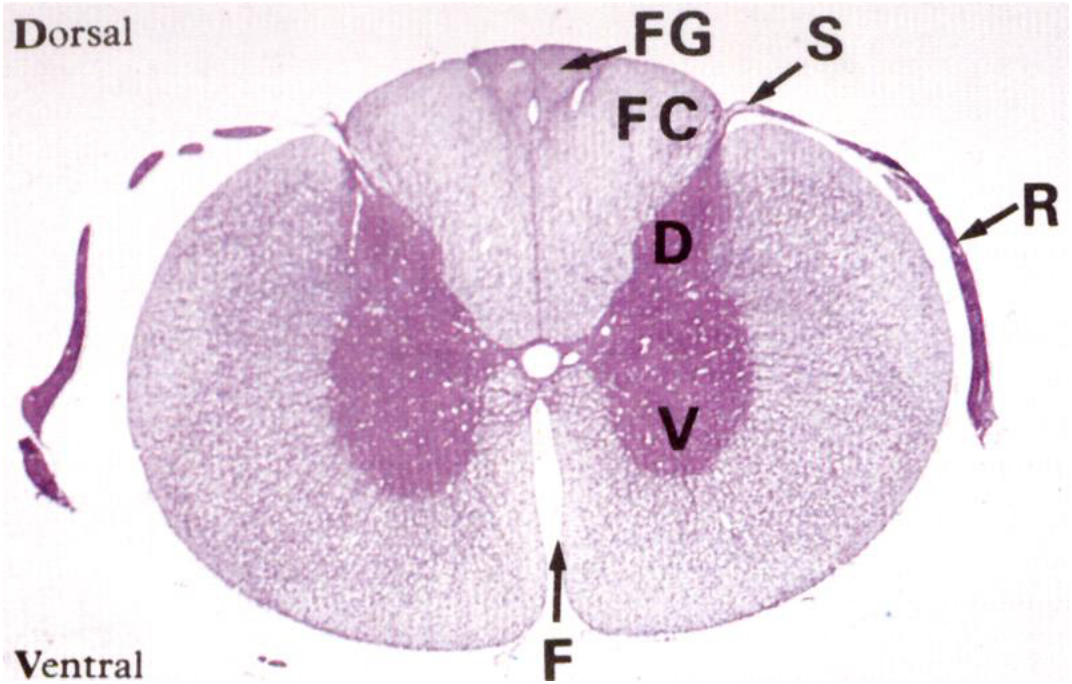
Ependyma

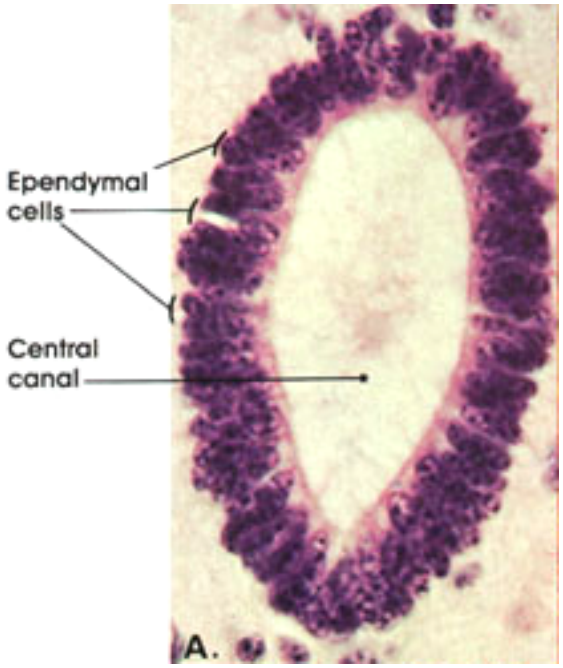
- Low columnar epithelial cells lining the ventricles of the brain & central canal of the spinal cord
- In some locations, ependymal cells are ciliated, which facilitates the movement of cerebrospinal fluid

- Their apical surfaces are also covered with microvilli, which absorb CSF



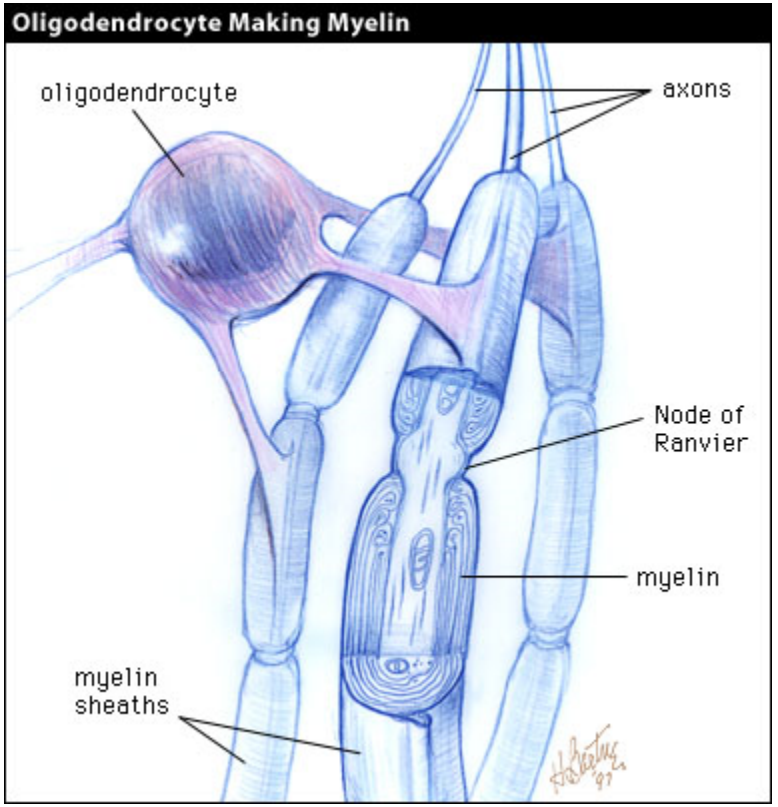
Ependyma





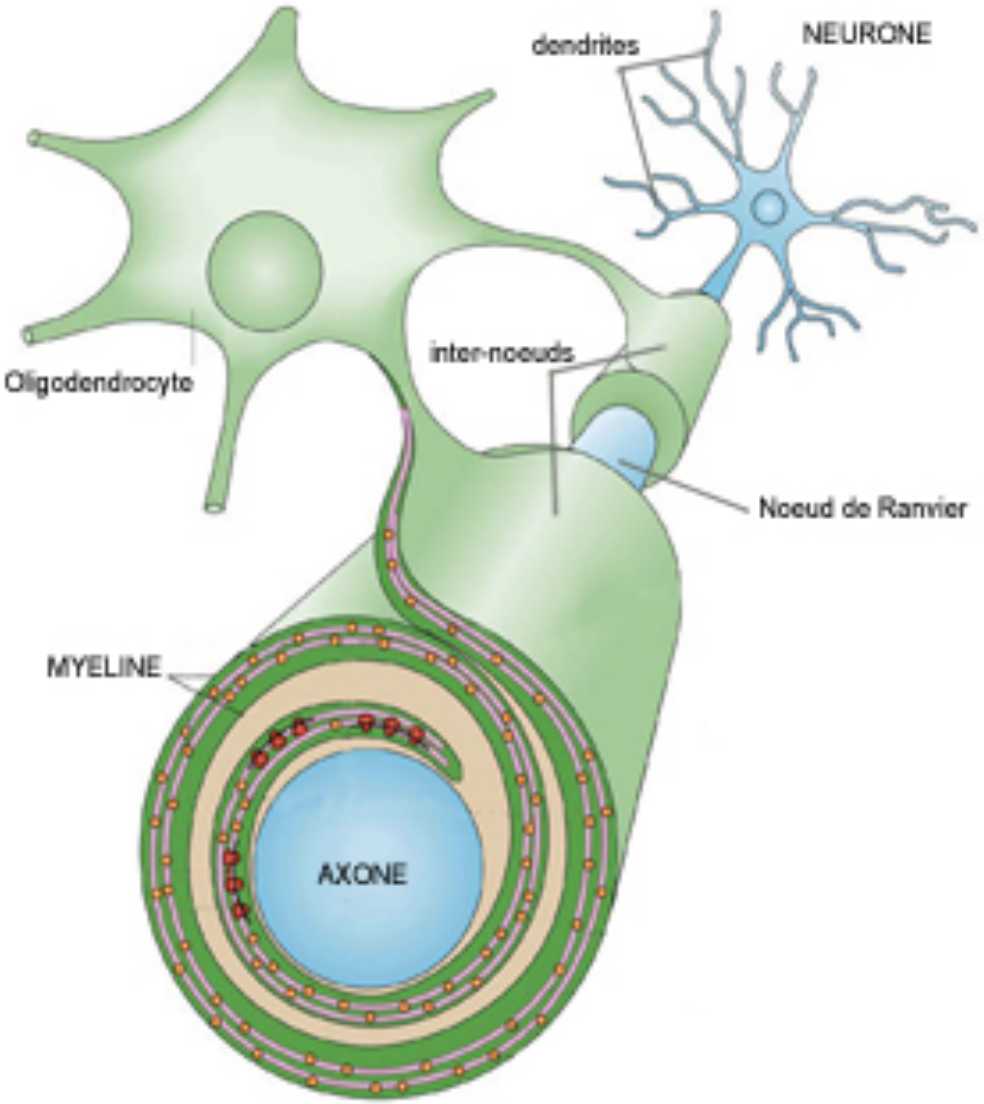
Oligodendrocytes

- Principal function= provide support to axons & to produce the myelin sheath, which insulates axons
- Myelin is 80% lipid & 20% protein & allows for efficient conduction of action potentials down the axon



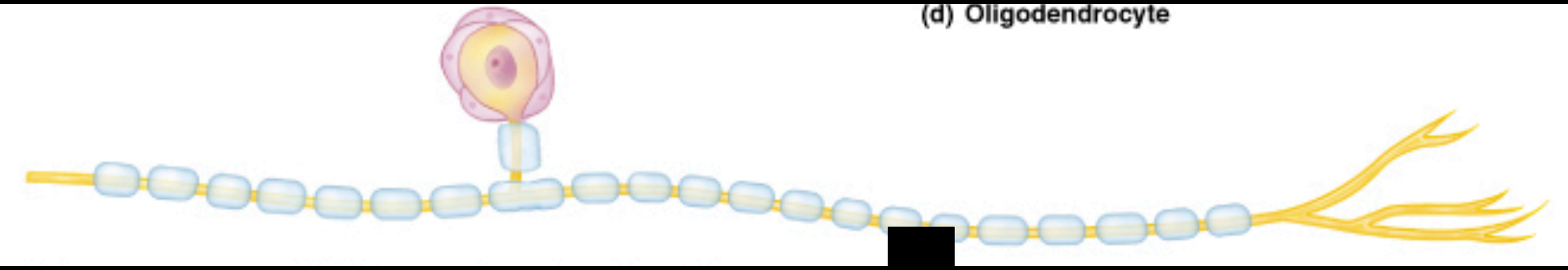
Oligodendrocytes (II)

- Unlike Schwann cells, form segments of myelin sheaths of numerous neurons at once
- Processes of a given OD wrap themselves around portions of surrounding axons
  - As each process wraps itself around, it forms layers of myelin
  - Each process thus becomes a segment of the axon's myelin sheath



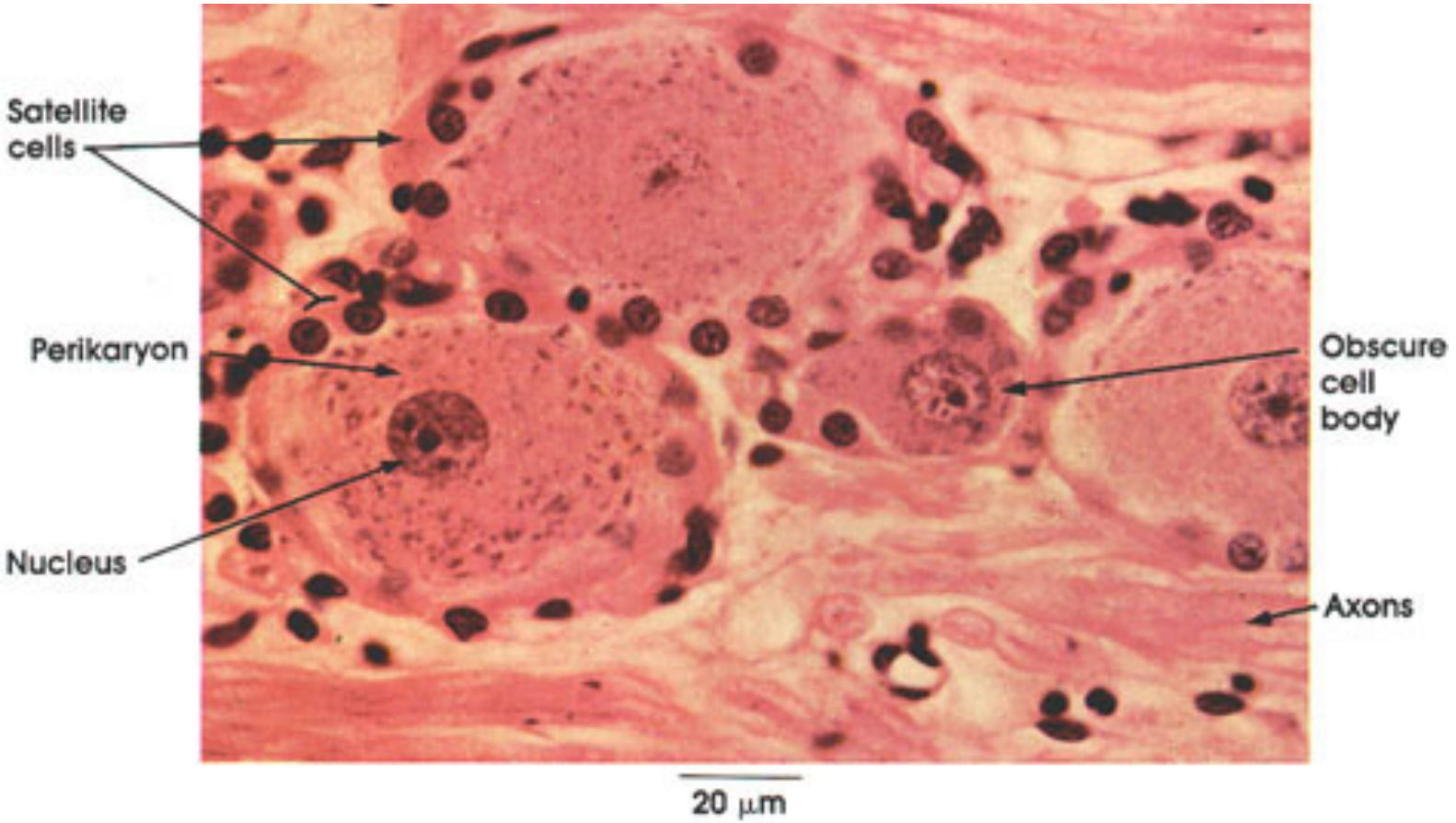
SUPPORTING CELLS IN THE PNS

- **Satellite cells**
  - Located around nerve cell bodies in ganglia
- **Schwann cells** / neurolemmocytes
  - Form myelin around axon in PNS



Both derived from the neural crest of the embryo during development

Satellite Cells



- Current theories suggest that SGCs have a significant role in controlling the microenvironment of the sympathetic ganglia.
- Help regulate & stabilize the environment.

Applied & Clinical Anatomy (Clinical Correlates)

Parkinson's disease

-Neurons that produces **dopamine** in the substantia nigra begin to degenerate.

-Results in a decrease in the amount of the available dopamine.

-Loss of dopamine results in a lack of coordination of movements: tremor, stiff muscles and joints (rigidity), and/or difficulty moving.

-Therapies are directed to slow the decline in function that occurs with Parkinson's disease.

Neuromelanin

Mitochondrial dysfunction, α-synuclein aggregation, oxidative stress, neuroinflammation, and impaired protein degradation are involved in the neurodegeneration of **dopaminergic neurons containing neuromelanin in Parkinson's disease.**

Parkinson's Disease & Glutathione

- In people with PD, **glutathione** levels are lower in the brain, specifically in the substantia nigra.
- Level of reduction in **glutathione** has been associated with **PD** severity (less **glutathione**, more advanced PD).

Lysosomal Storage Diseases

NEURONAL LIPIDOSIS	Storage in neuronal body and processes	Neurological regression, seizures, blindness	Gangliosidoses, mucopolysa-ccharidoses, neuronal ceroid lipofuscinoses

The prototype of the neuronal lipidosis phenotype is **Tay-Sachs disease**

Tay-Sachs Disease

- Autosomal recessive disease
- Mutations in both alleles of a gene (HEX A) on chromosome 15
- HEX A codes for the alpha subunit of the enzyme beta-hexosaminidase found in lysosomes
- Juvenile: paralysis, dementia, blindness and early death (3 yrs)
- Chronic adult form: neuron dysfunction and psychosis

Shingles (Herpes Zoster) (I)

- Shingles is a disease caused by same virus that causes chickenpox (*varicella zoster*). After chickenpox, virus remains dormant in DRG neurons for life.

- The virus can become active again and cause shingles (unusual skin sensation, itching or a burning, tingling, or shooting pain).

Shingles (Herpes Zoster) (II)

- The skin reddens/swells, and a rash of fluid-filled blisters develops. The blisters usually crust over within a week and eventually heal.
- Symptoms of shingles appear on only one side of the body, usually on the torso or face.
- Intense, debilitating pain in areas where the blisters occurred may remain (postherpetic neuralgia, clinical depression).

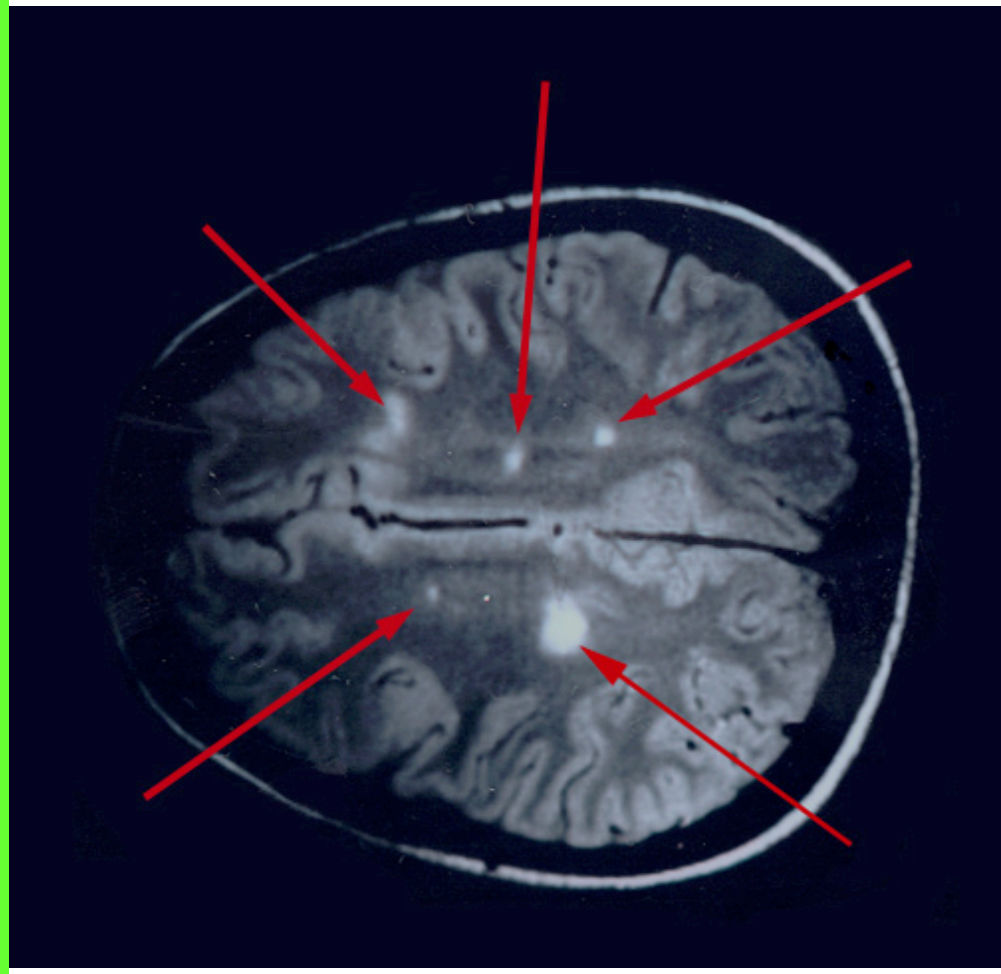
Stem Cells (I)

- Some researchers believe that ependyma is the prime candidate for the location of neural stem cells.

- **Neurogenesis predominantly occurs in the subventricular and subgranular zones of the brain.**

Multiple Sclerosis

- Chronic disease of CNS, predominantly affects young adults
- Autoimmune and/or viral disease, but genetic & environmental factors may contribute
- women > men



MRI Scan: Demyelination in Cerebrum

Multiple Sclerosis (II)

Two characteristic microscopic features are: (1) infiltration of inflammatory cells (T cells and macrophages) inside and around multiple sclerosis plaques; (2) plaques of astrocytic aggregates.

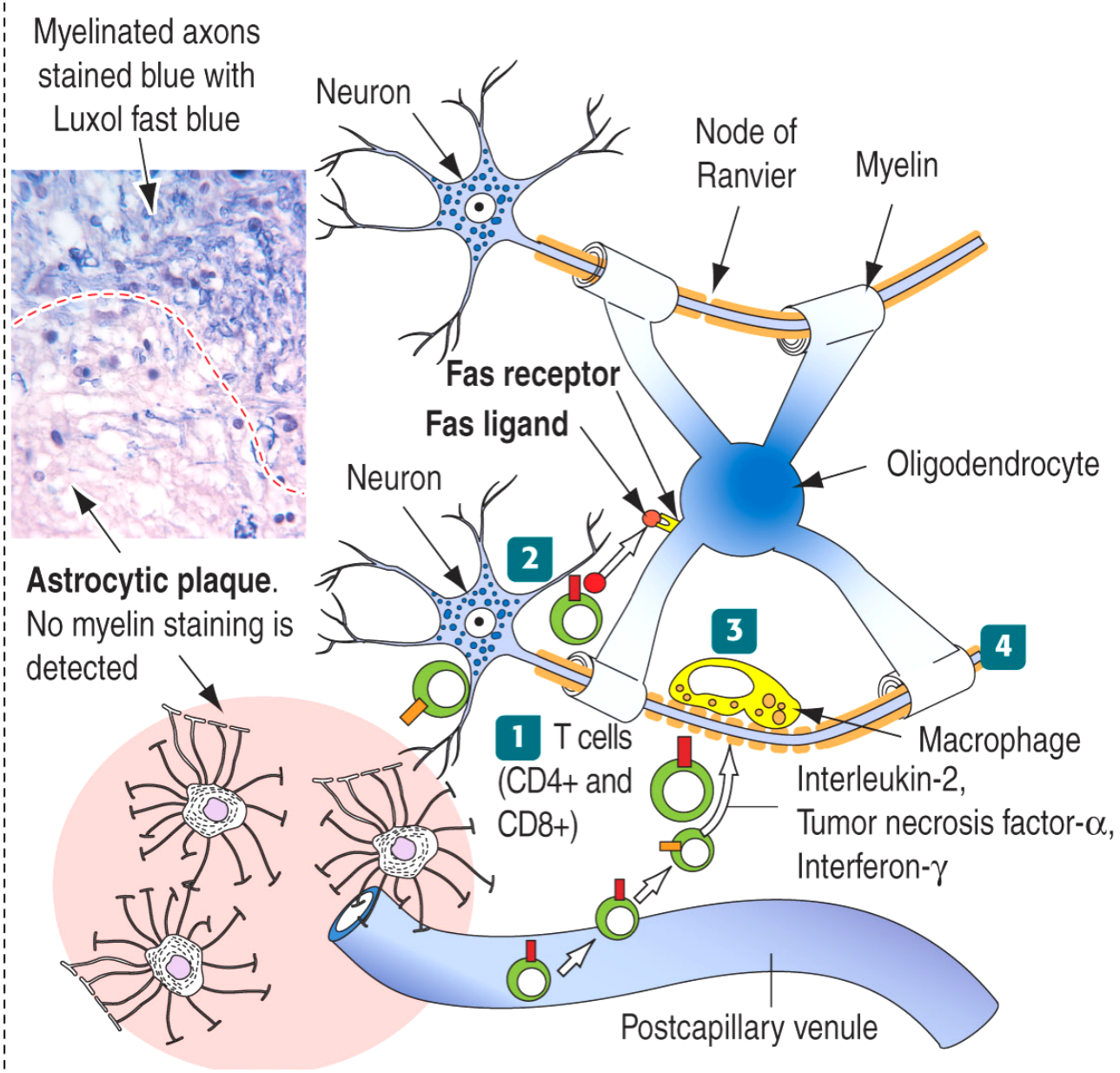
1 **CD8+ and CD4+ T cells**, recruited to multiple sclerosis lesions, **secrete cytokines** (interleukin-2, tumor necrosis factor-α, and interferon-γ).

2 T cells secrete **Fas ligand** which binds to **Fas receptor** on oligodendrocytes to induce their programmed cell death.

3 Macrophages strip myelin off the axons. Macrophages contain myelin in phagocytic vacuoles.

4 Conduction in the demyelinated axon is blocked.

Multiple Sclerosis (III)



Multiple Sclerosis (IV)

- Characterized by areas of demyelination and T-cell predominant perivascular inflammation in the brain white matter
- Symptoms- numbness, paraesthesia, double vision, optic neuritis, ataxia & bladder control problems
  - Subsequent symptoms involve upper motor neurons: spasticity, para- or quardriparesis. Vertigo, incoordination and other cerebellar problems, depression, emotional lability, gait abnormalities, dysarthria, fatigue & pain

Leukodystrophy

- They may be inherited in a **recessive, dominant, or X-linked** manner, depending on the type of leukodystrophy.
- There are some leukodystrophies that do not appear to be inherited, but rather arise spontaneously.
  - They are still caused by a mutation in a particular gene, but it just means that the mutation was not inherited. In this case, the birth of one child with the disease does not necessarily increase the likelihood of a second child having the disease.

Leukodystrophies vs. MS

- Leukodystrophies do share some common features with multiple sclerosis (MS).
- Like the leukodystrophies, MS is caused by the loss of myelin from the axons. However, the cause is different; whereas leukodystrophies are generally caused by **a defect in one of the genes involved with the growth or maintenance of the myelin**, MS is thought to be caused by **an attack on the myelin by the body's own immune system**.

Neuroplasticity (I)

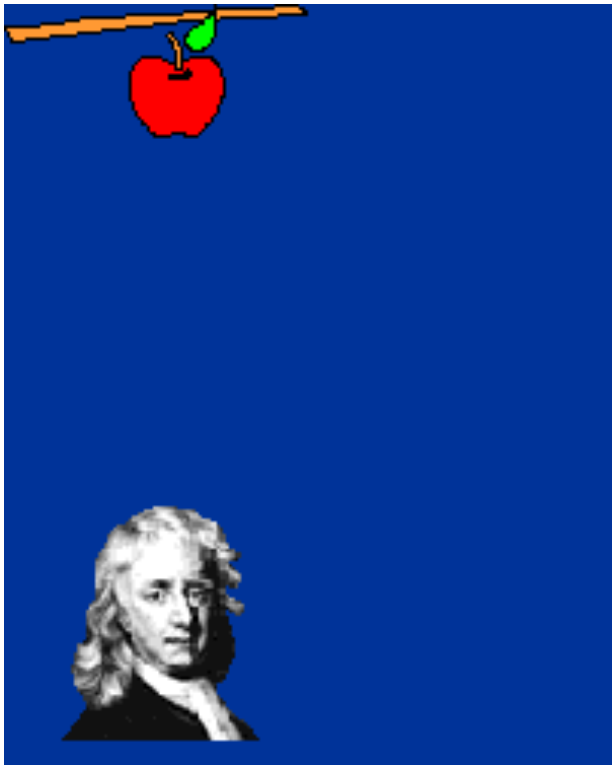
- Brain **plasticity (**synaptic **plasticity** & non-synaptic **plasticity.**

- Changes in neural pathways & synapses due to changes in behaviour, environment, neural processes, thinking, emotions, as well as changes resulting from bodily injury.

Neuroplasticity (II)

- The brain's ability to reorganize itself by forming new neural connections throughout life.
- Neuroplasticity allows the neurons in the brain to :
  - **Compensate for injury disease**
  - **Adjust their activities in response to new situations or to changes in their environment.**

- **In everything…**



QUESTIONS & COMMENTS

WhatsApp: +2348023034954

E-mails:
aosinubi@unilag.edu.ng
abrahamosinubi@gmail.com

Websites:

- www.profosinubi.com
- www.abrammax.com
- www.researchgate.net/profile/Abraham_Osinubi2
- https://unilag.academia.edu/AbrahamOsinubi
- www.linkedin.com