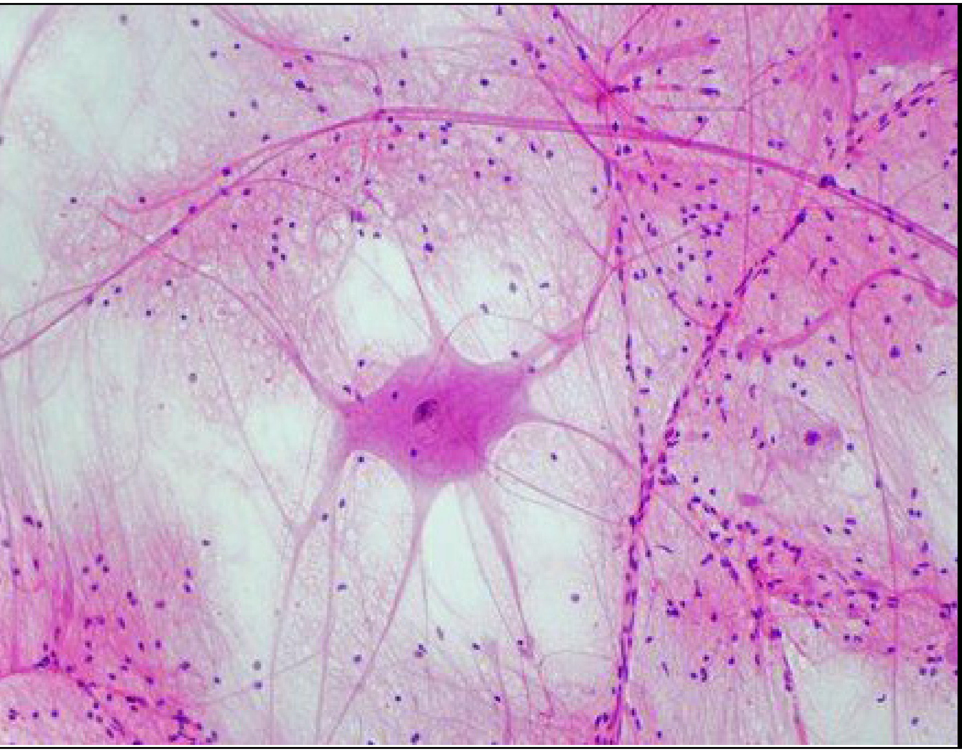
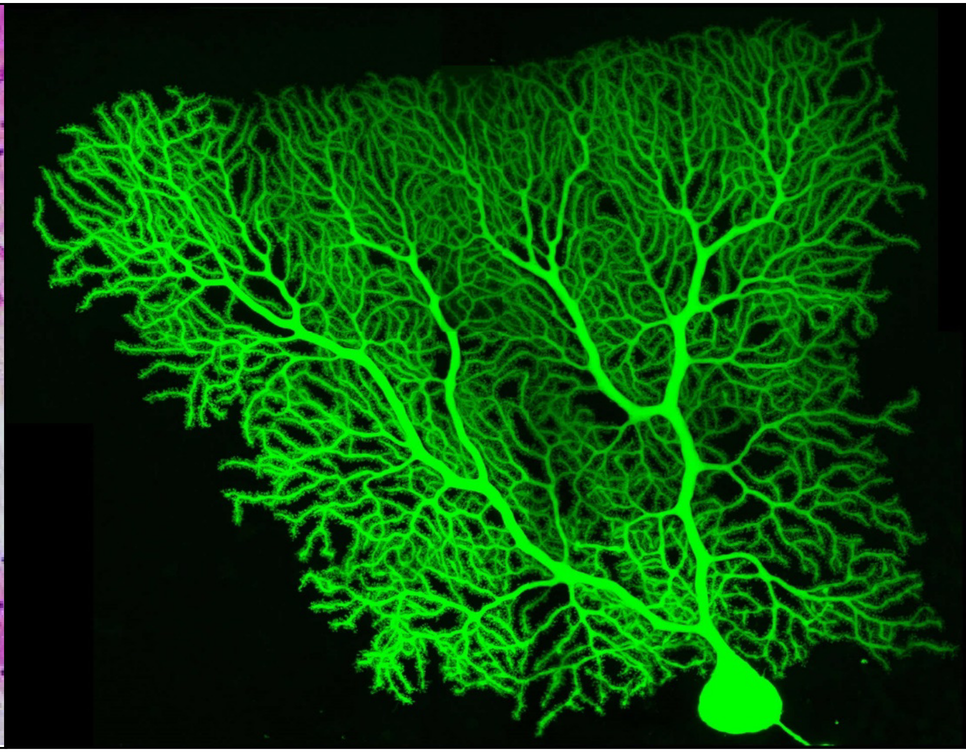
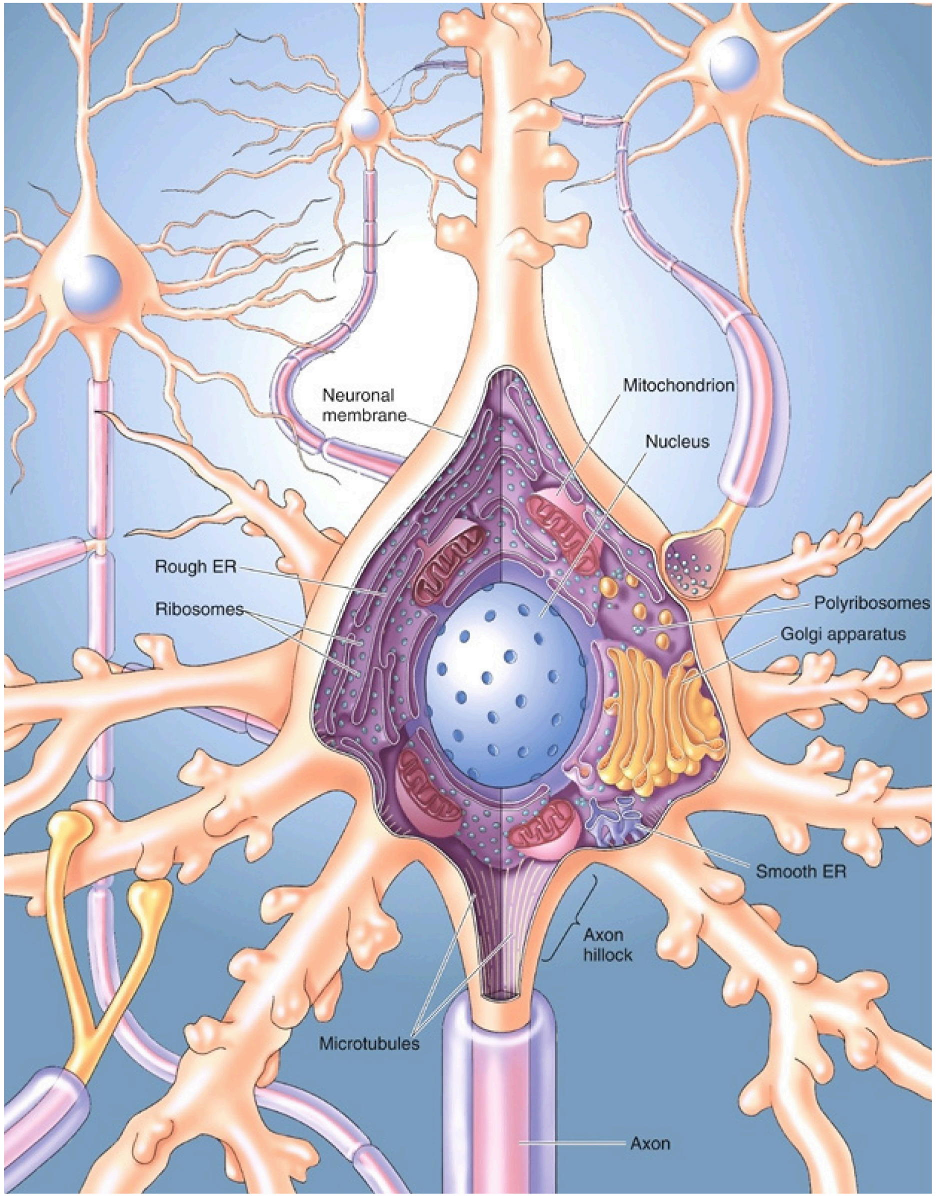
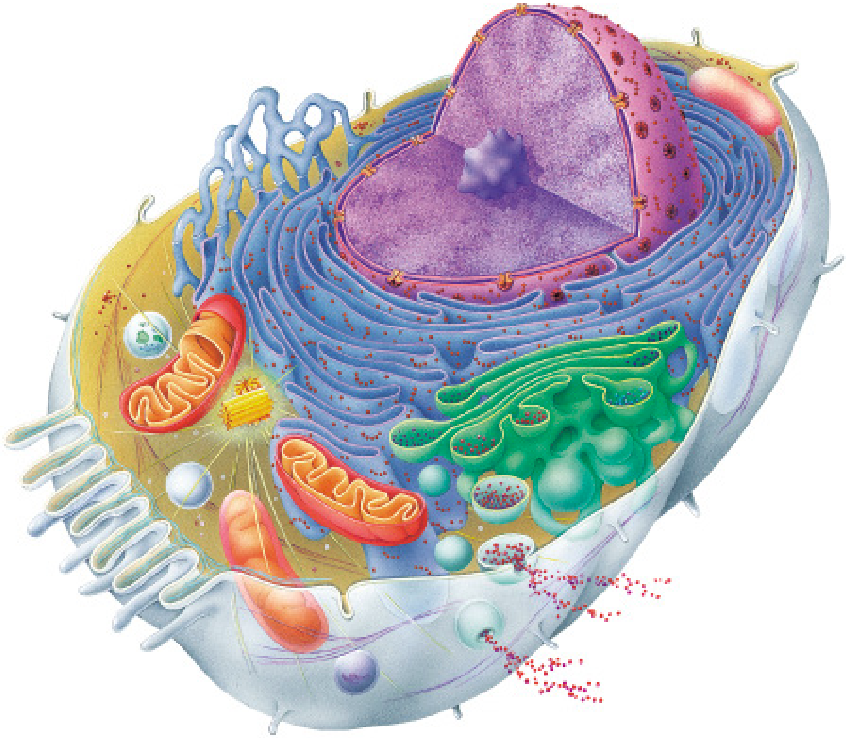
Chapter 7: Cells of the Nervous System



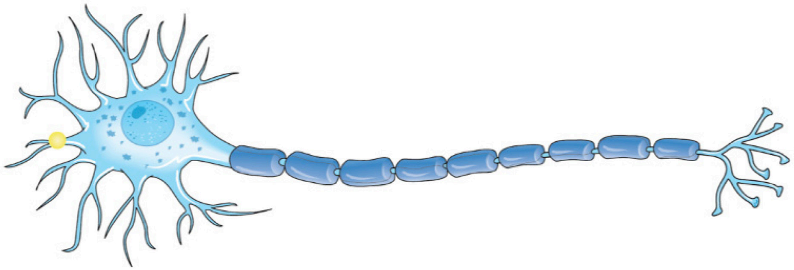


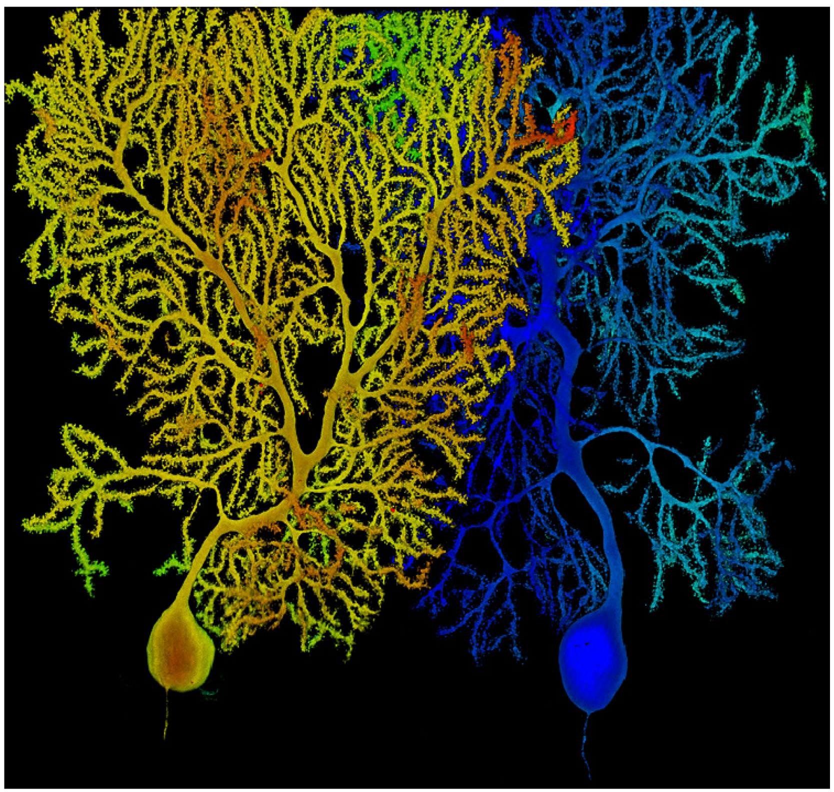
Cell Biology of Neurons



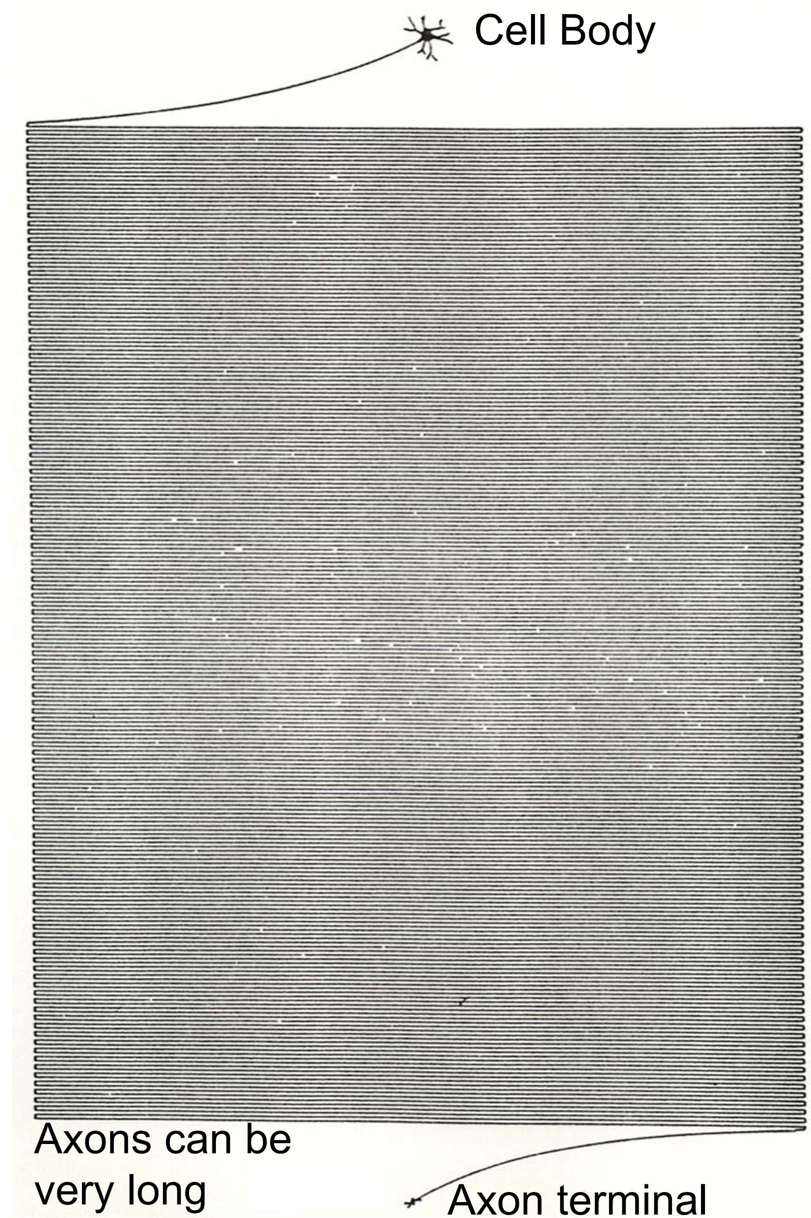


Complex Neuron Shapes



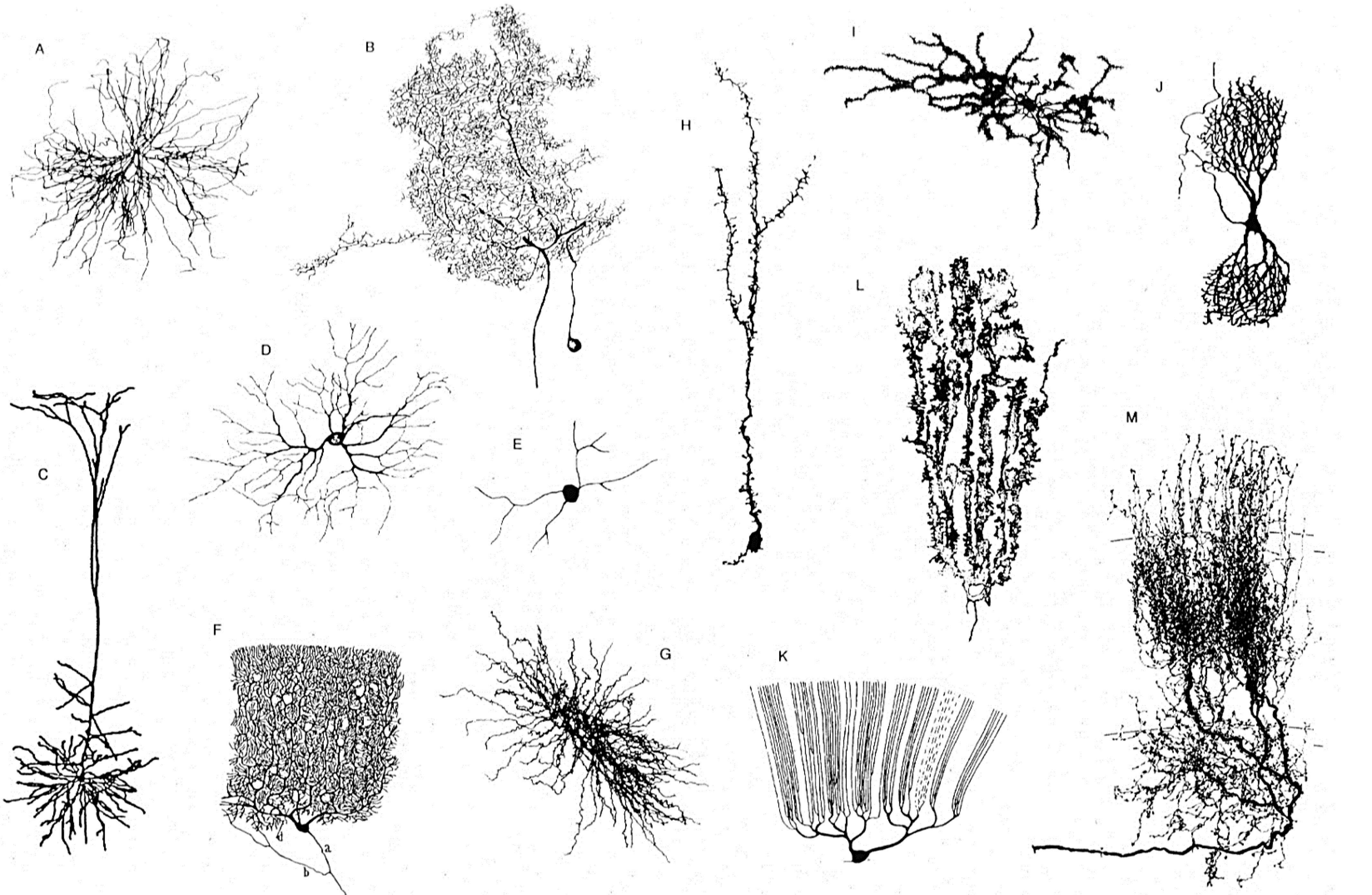


Dendritic arbors
can be extensive

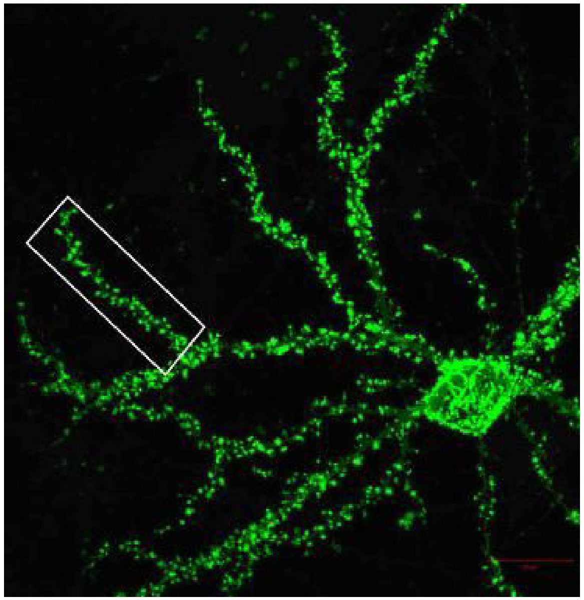


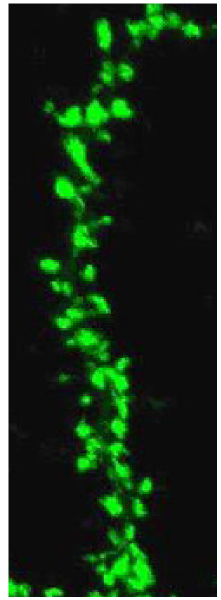
Axons can be
very long

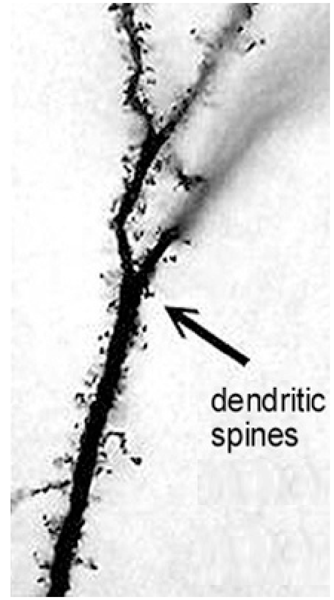
Variety of Dendritic Arbors

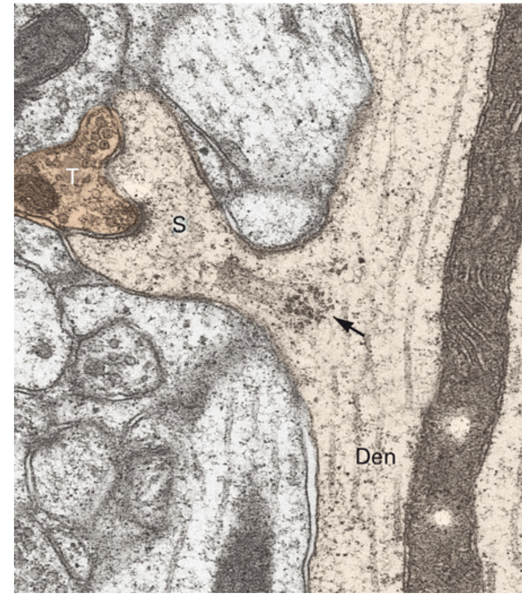


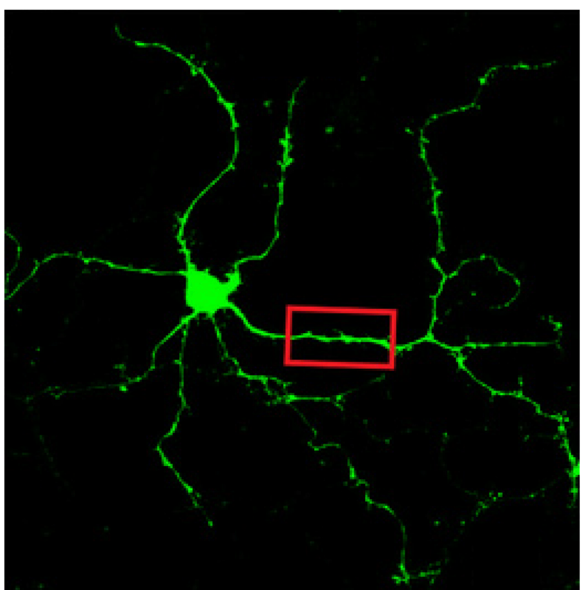
Spiny and Smooth Dendrites

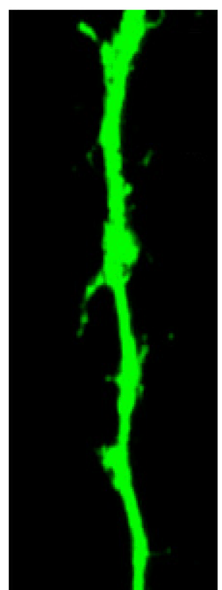


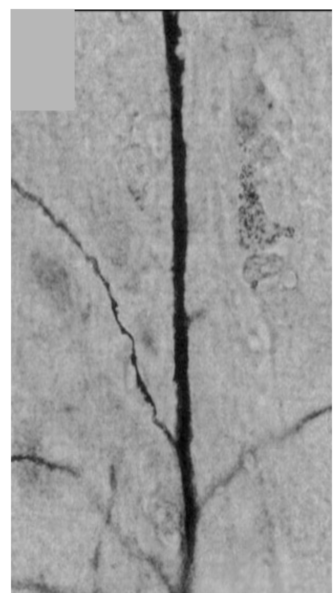






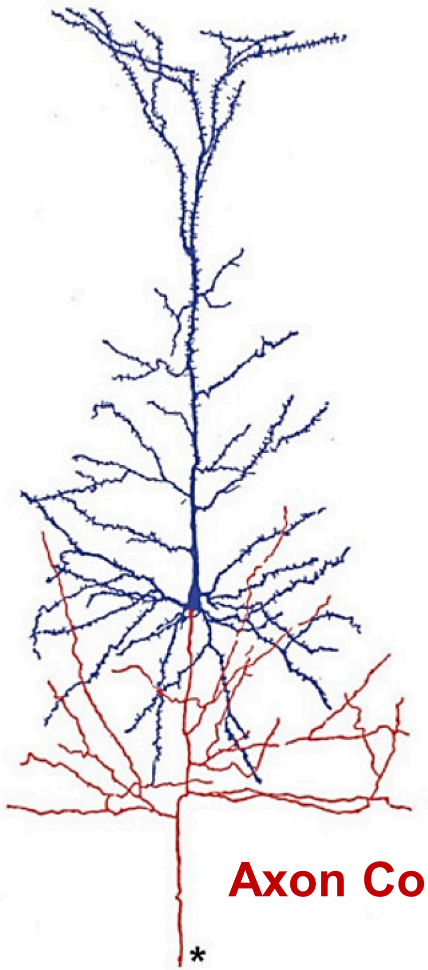


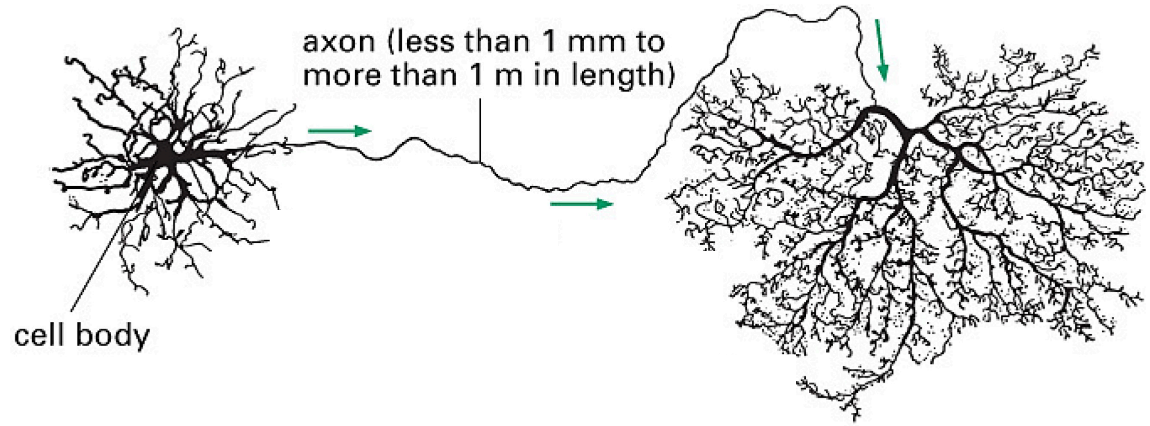




Axon Branching

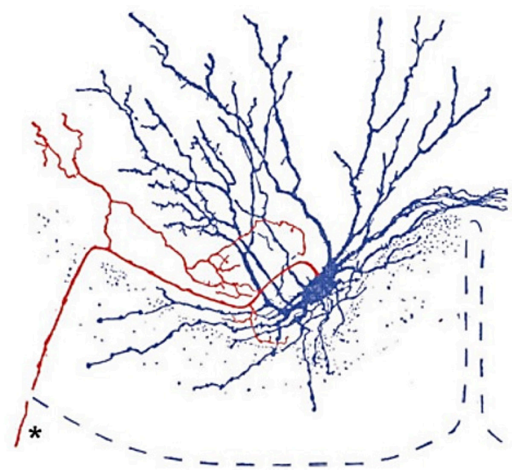
Cortex layer 5 pyramidal neuron





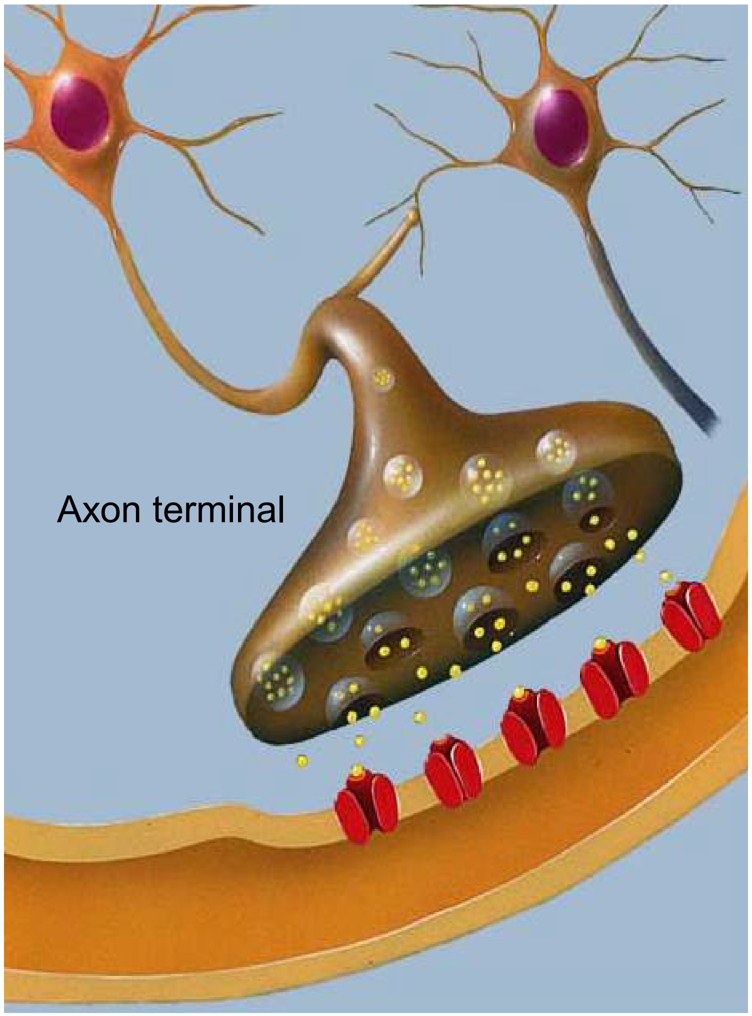
Axon terminal arborization

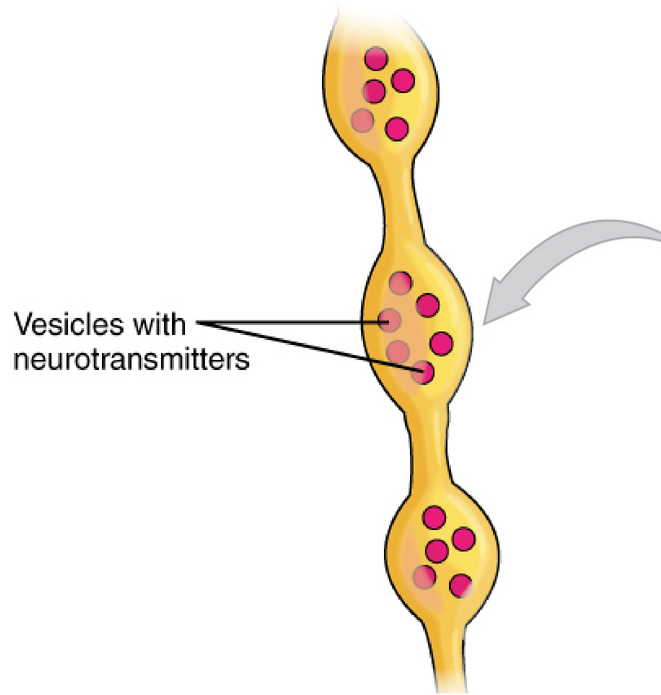
Ventral spinal cord motor neuron



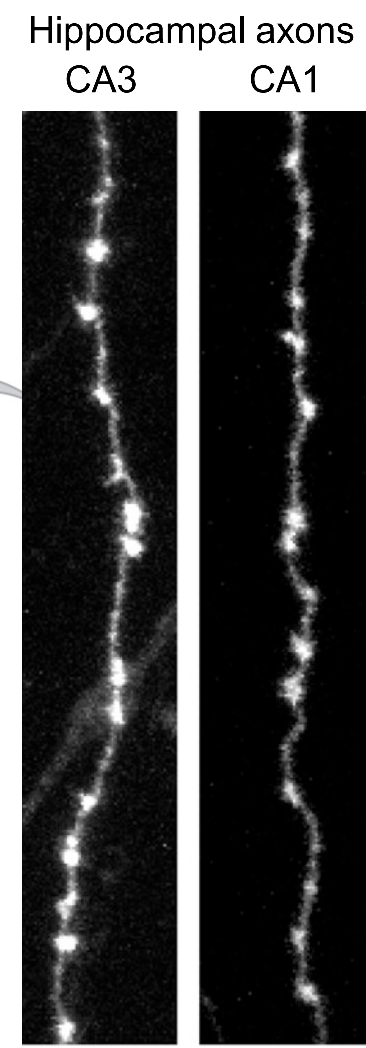
Axon Collaterals

Axon Terminals vs. Varicosities

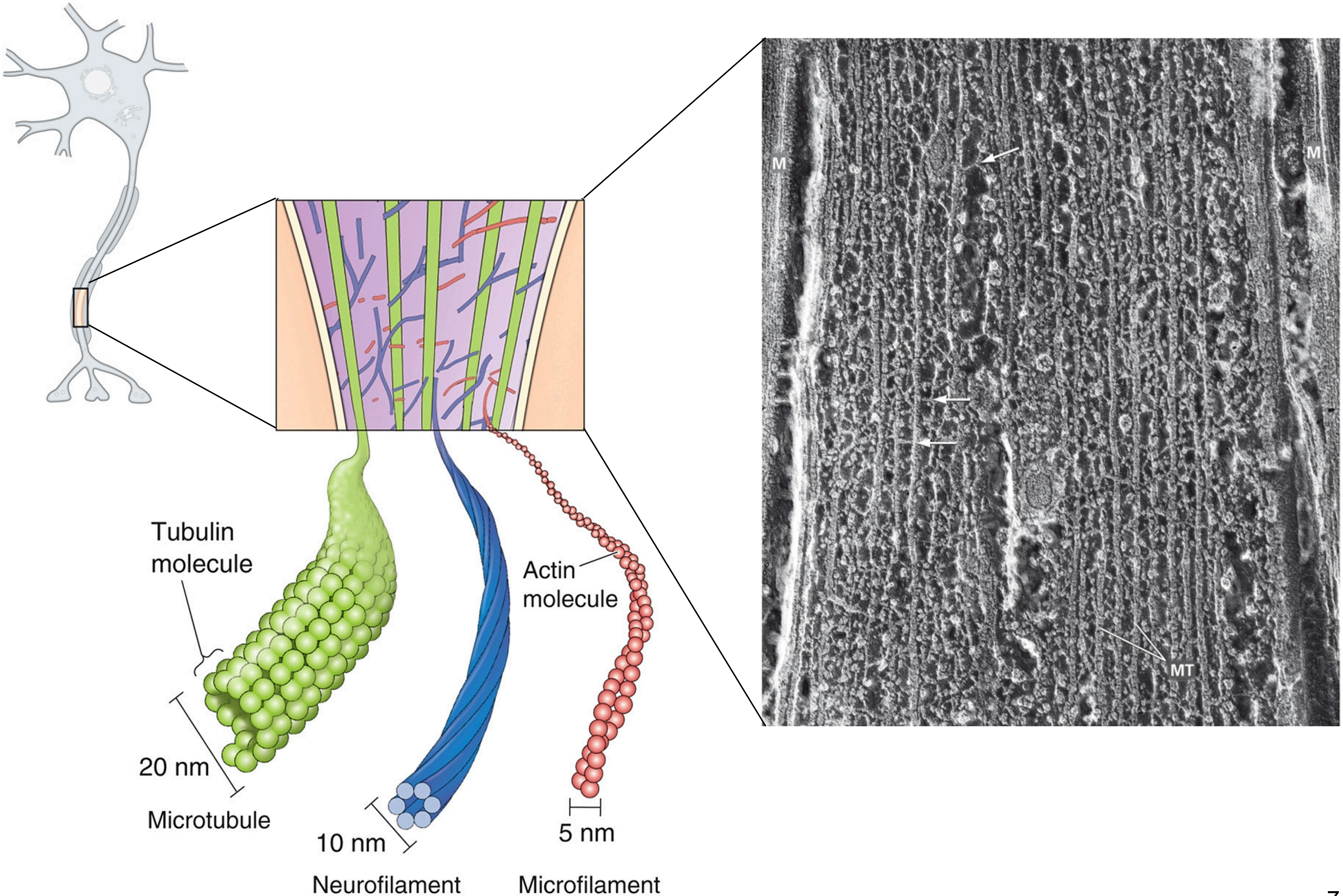




Axons with varicosities
make synapses *en passant*

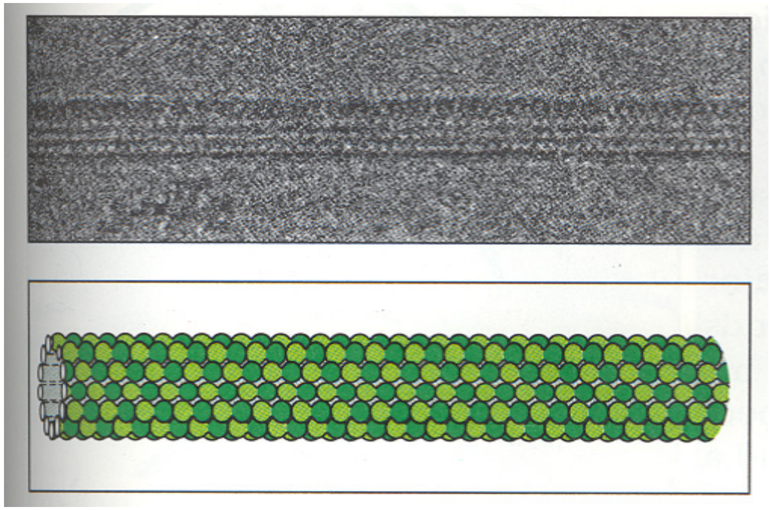


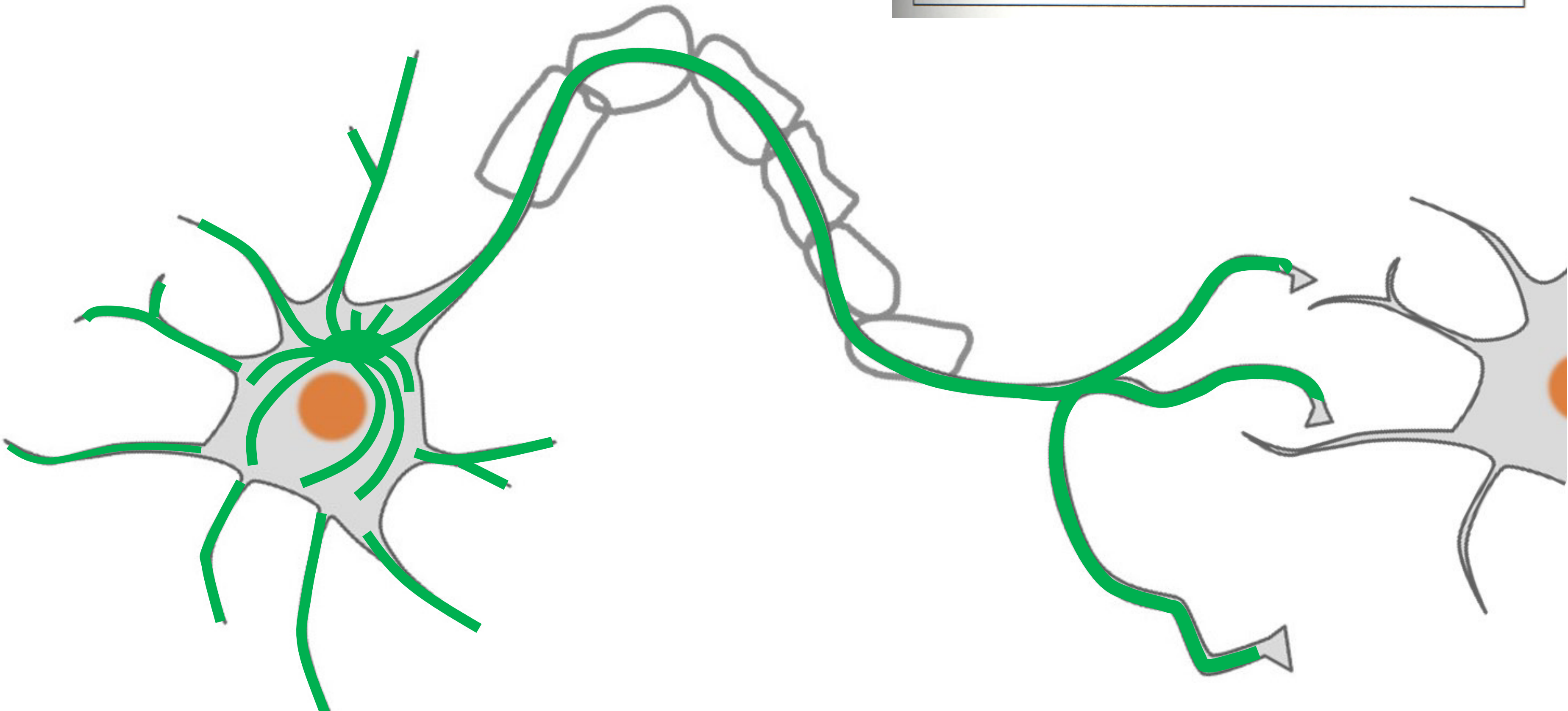
Inside Neurites (Axons and Dendrites)



Microtubules in Neurons

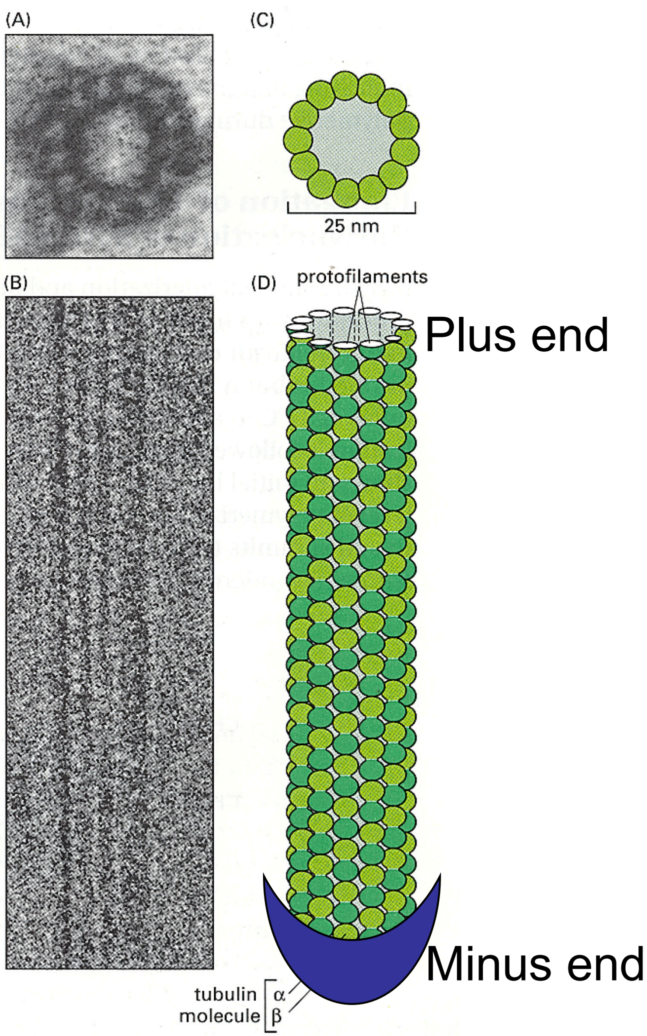
- Run longitudinally in neurite shafts
- Radiate throughout the cell body
- (In relatively stable areas)

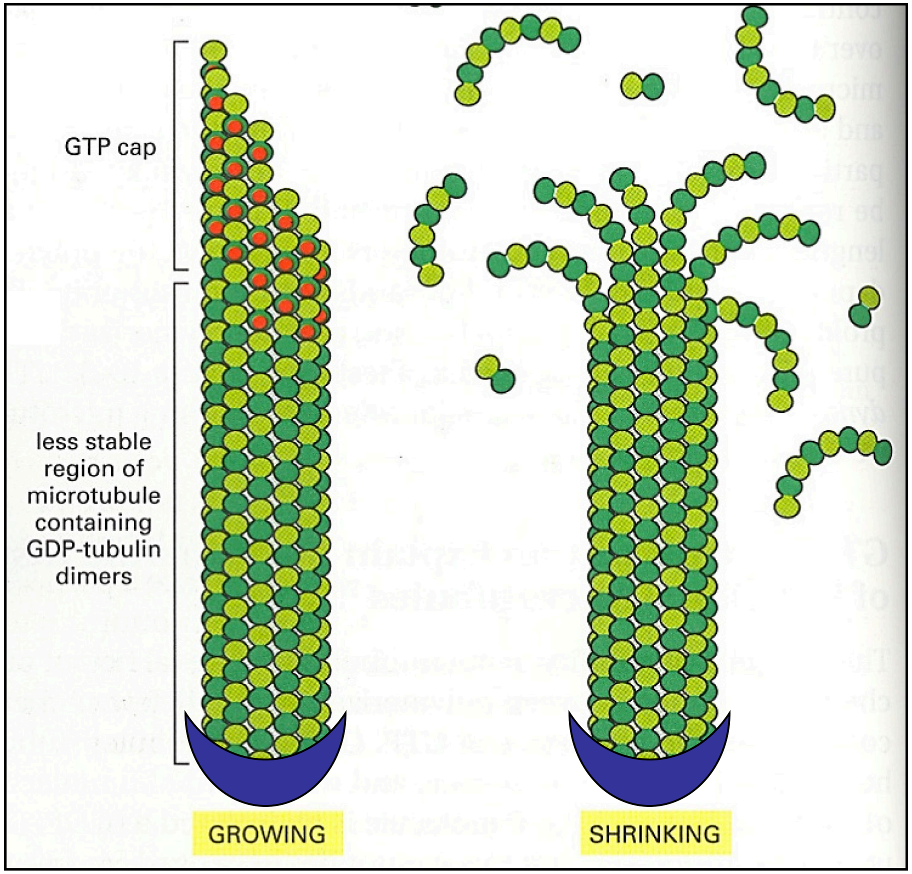




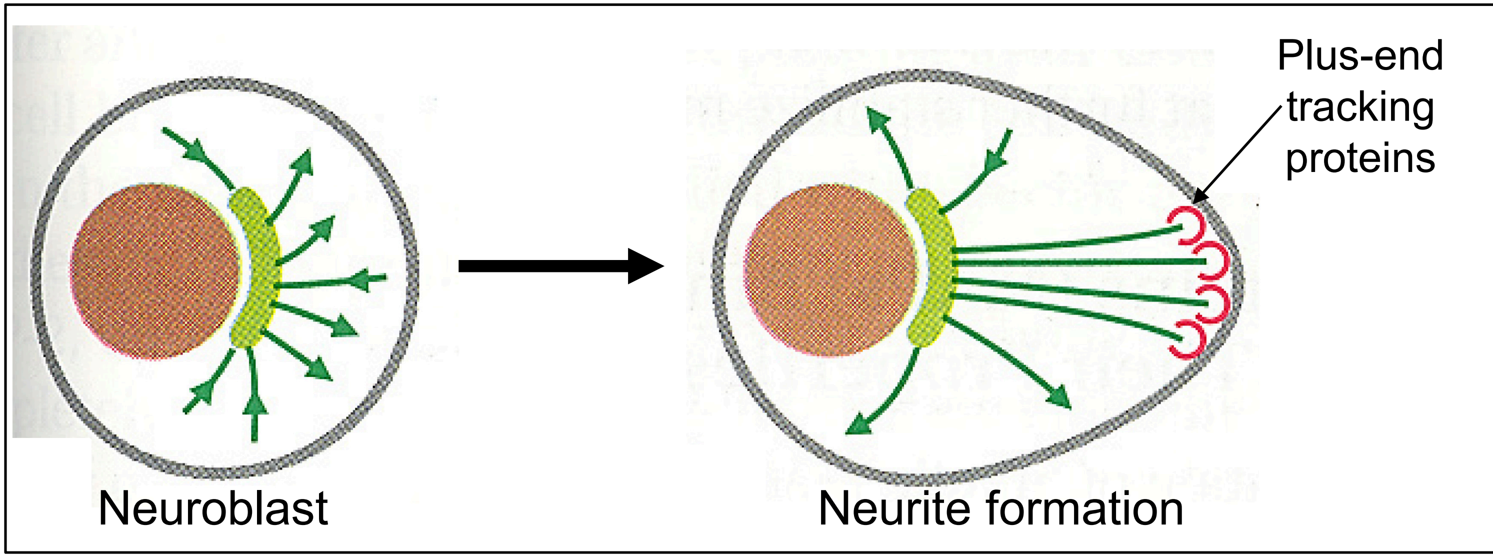
Microtubules

- Polymer of alpha and beta tubulin dimers
- Thick, hollow tube of 13 protofilaments
- Minus (–) end is usually capped with protein
- Plus (+) end undergoes slow lengthening or rapid shortening (dynamic instability)



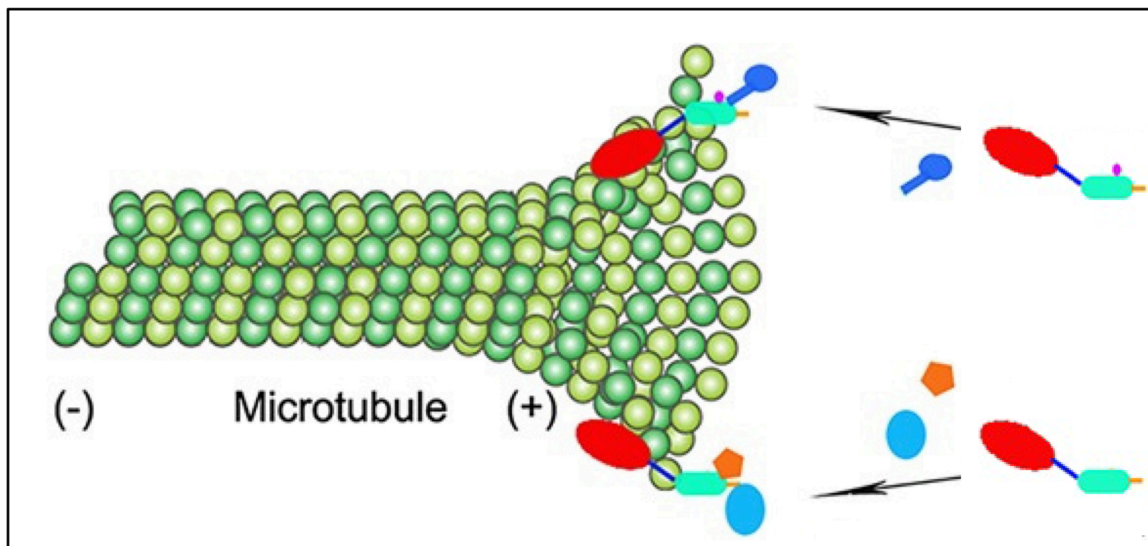


Microtubules in Neurite Formation



Plus-end tracking proteins (+TIPs)

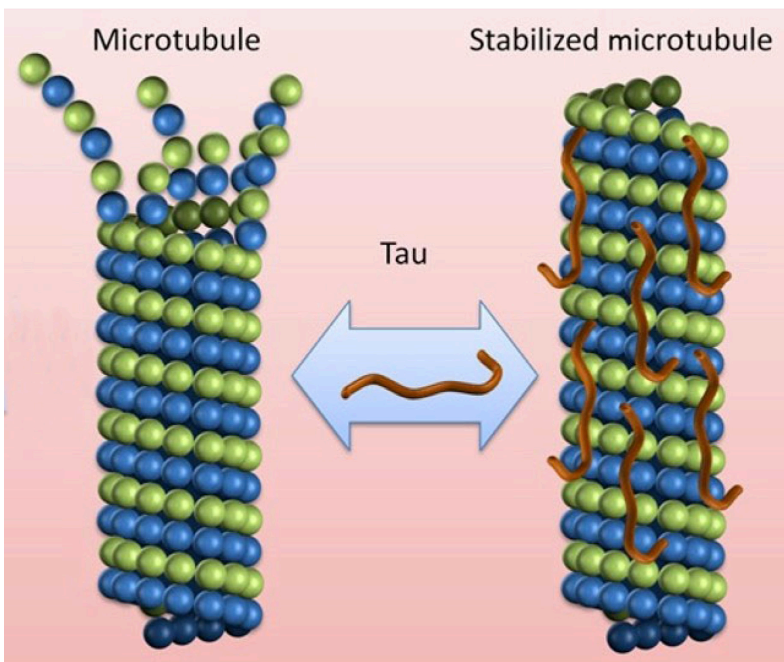
- Allow lengthening of microtubules and prevent disassembly
- Lead to neurite formation



Microtubules in Neurite Stabilization

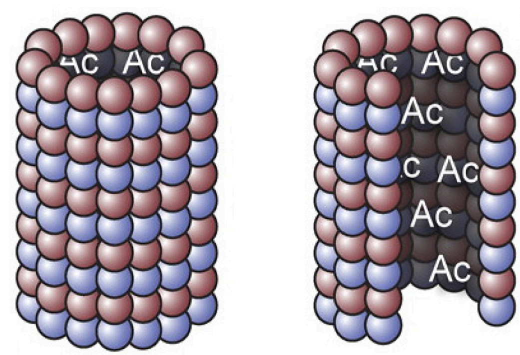
Microtubule associated proteins (*MAPs*)

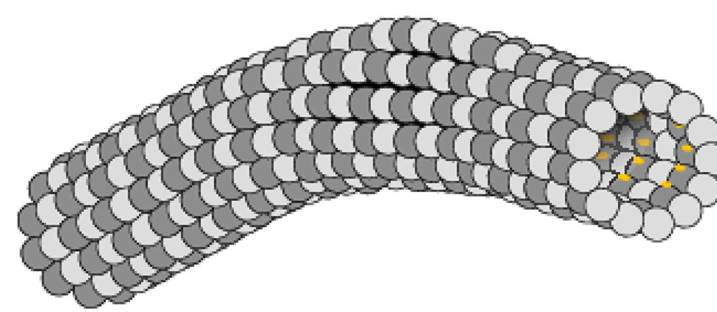
- Promote assembly and stability of microtubules
- Spatially organize microtubules in parallel networks
- *MAP-2* in dendrites, *Tau* in axons



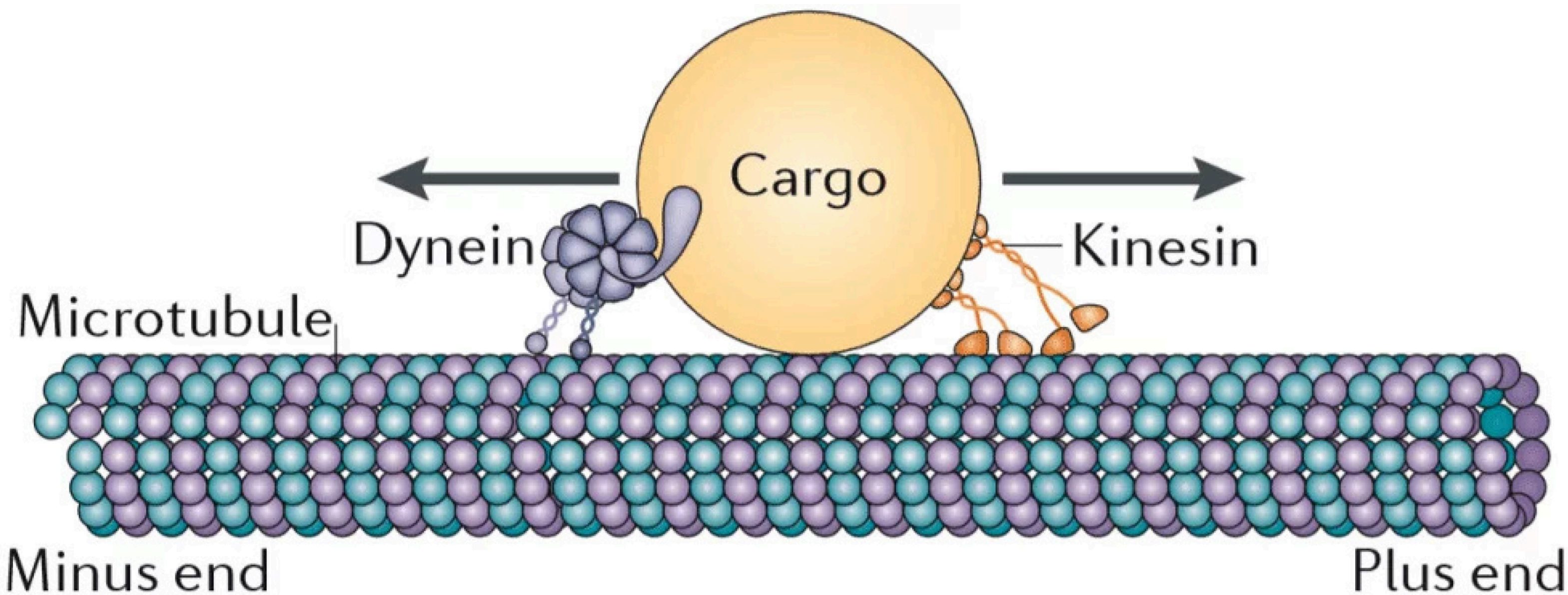
Tubulin acetylation

- Strengthens lateral interactions between neighboring protofilaments
- Allows microtubules to be less brittle and more flexible





Microtubules in Transport Systems



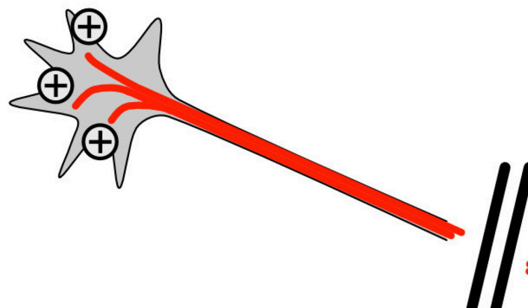
<u>Retrograde axoplasmic transport</u>

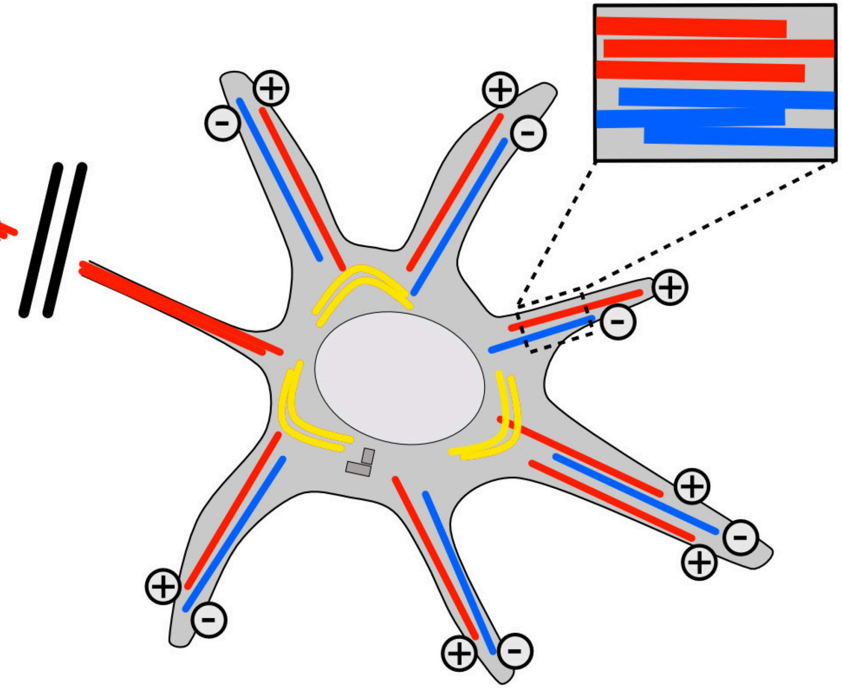
- Organelles and vesicles move toward the soma
- Toxins, herpes virus, rabies virus, polio virus access soma
- Mediated by dynein movement on microtubules

<u>Anterograde axoplasmic transport</u>

- Organelles and vesicles move away from the soma
- Important in keeping the axon healthy
- Mediated by kinesin movement on microtubules

Microtubule Polarity in Neurons



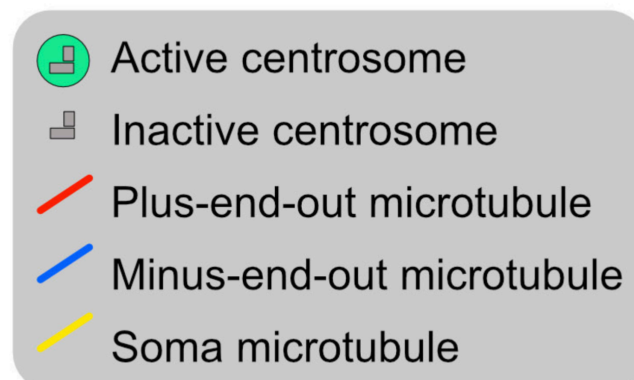


Axonal compartment

- All microtubule plus-ends point distally
- Protein-making machinery is generally absent (very few ribosomes and little rough ER)
- Rich in smooth ER and synaptic vesicles

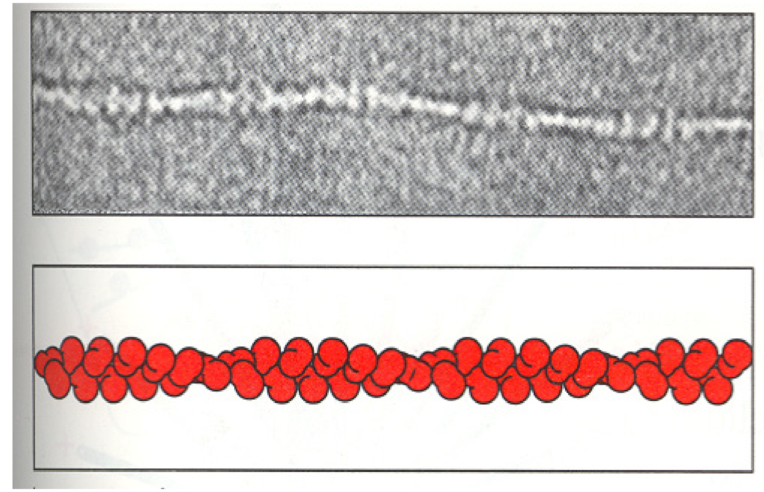
Somatodendritic compartment

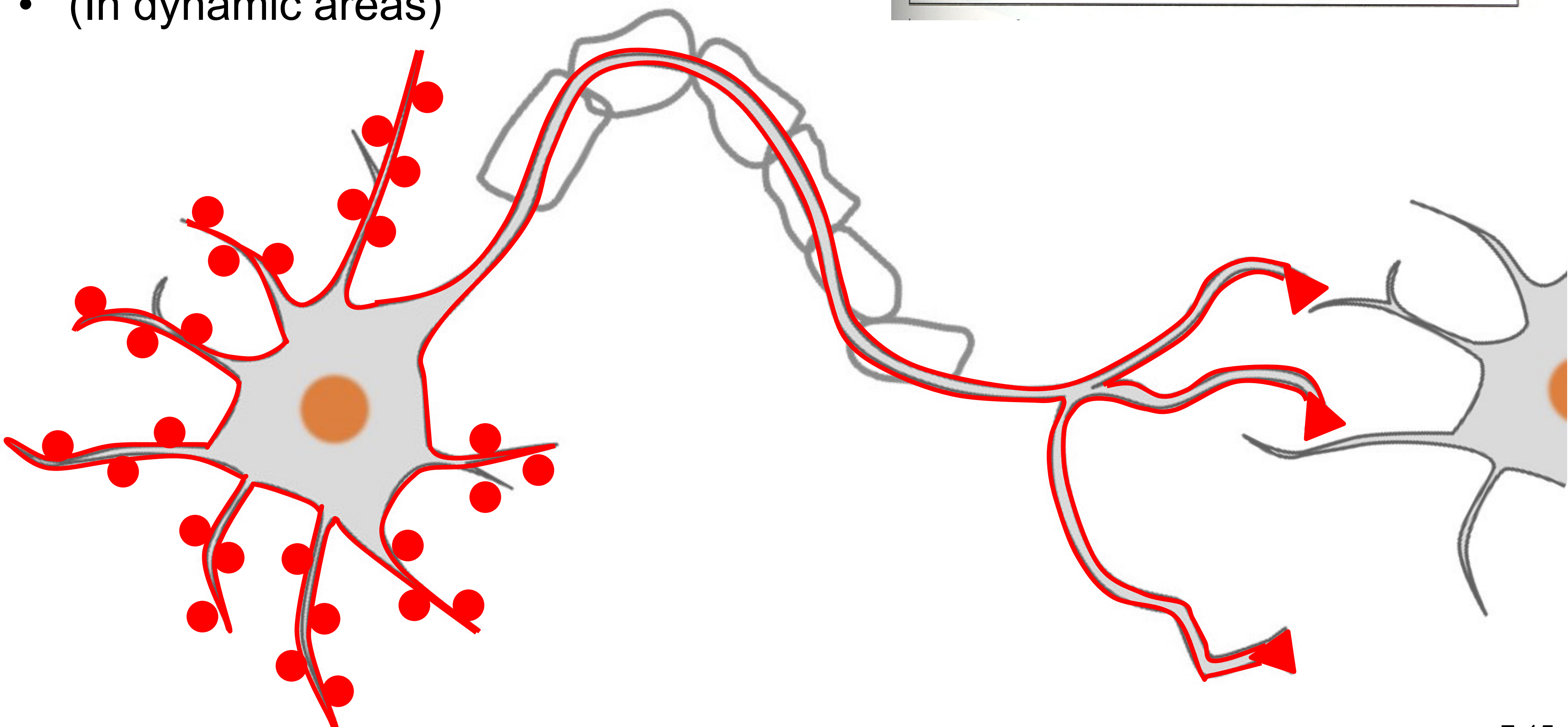
- Mixed microtubule polarity throughout
- Dendrites have same organelles as the cell soma. Protein-making machinery is present throughout, but decreases with distance from the soma.



Microfilaments in Neurons

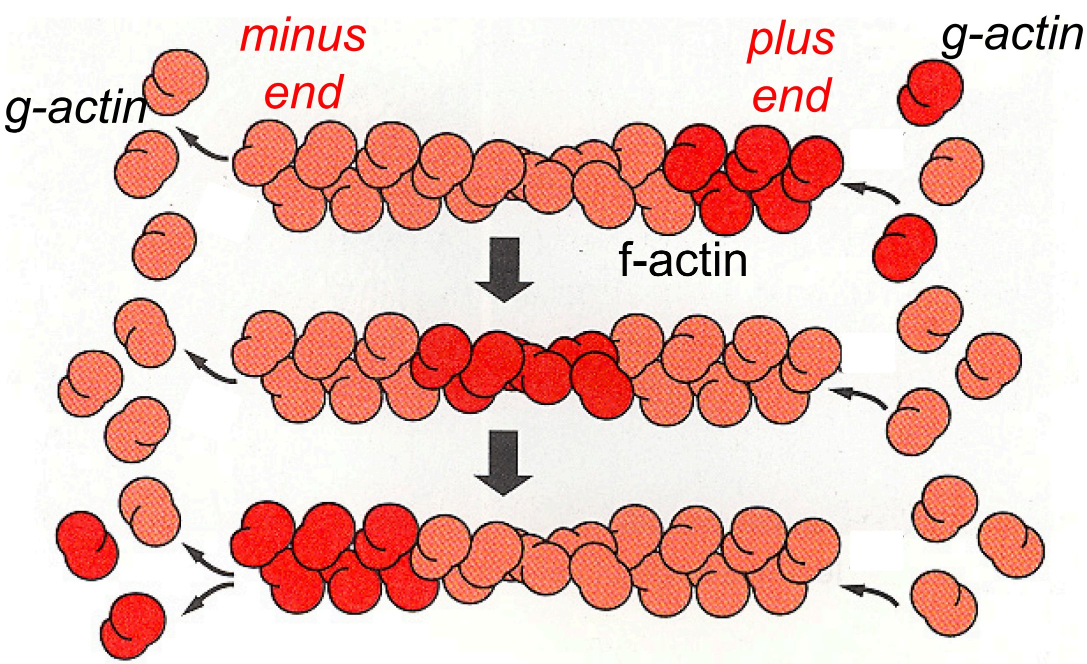
- Immediately beneath membranes throughout the neuron
- Enriched in dendritic spines, axon terminals, and the tips of growing neurites
- (In dynamic areas)



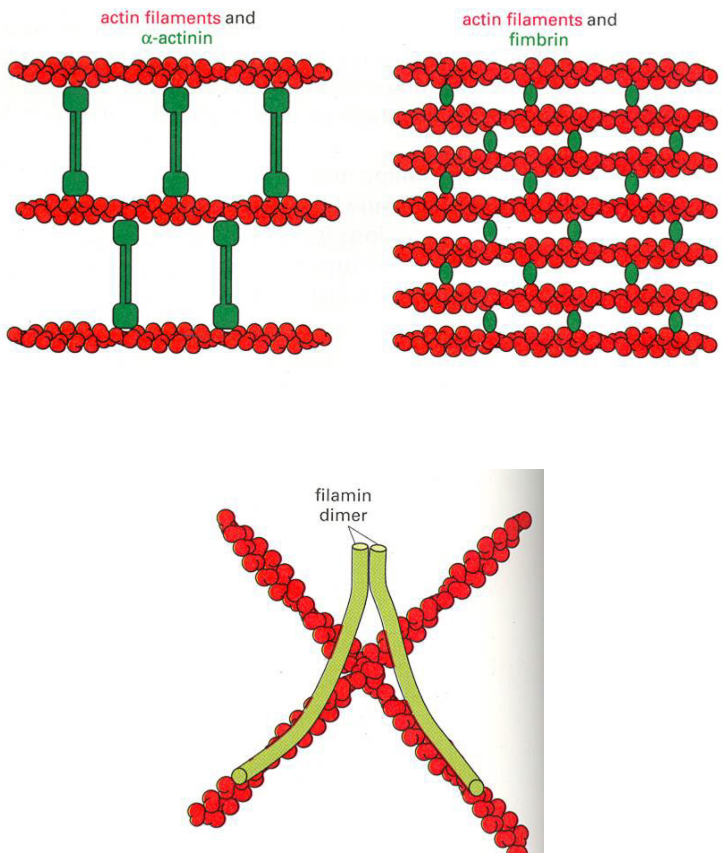


Microfilaments

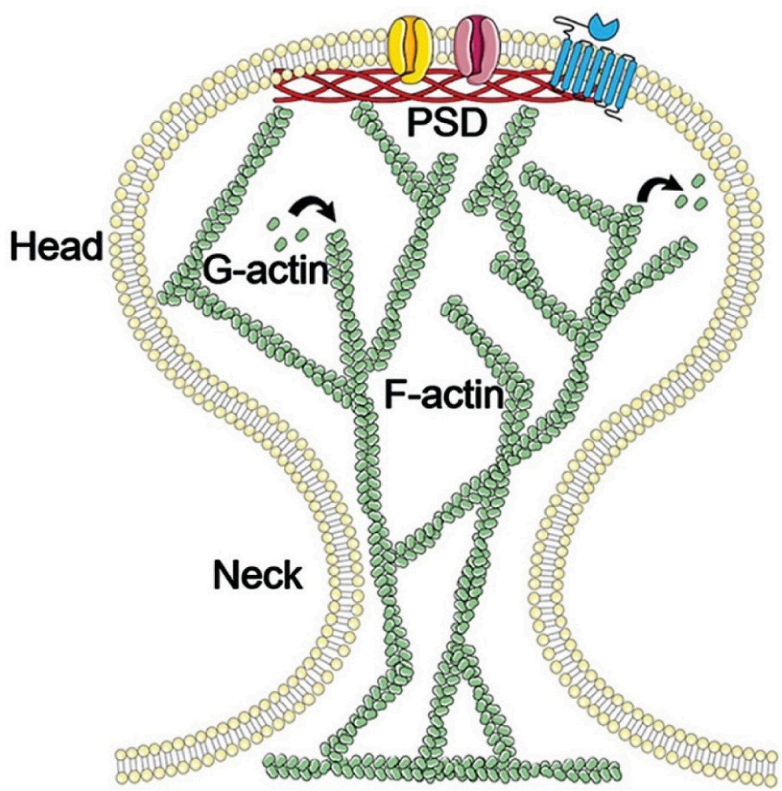
- g-actin monomers polymerize to form thin helices called f-actin
- Monomers add to plus (+) end and leave from minus (-) end
- Constant *treadmilling* leads to high actin dynamics

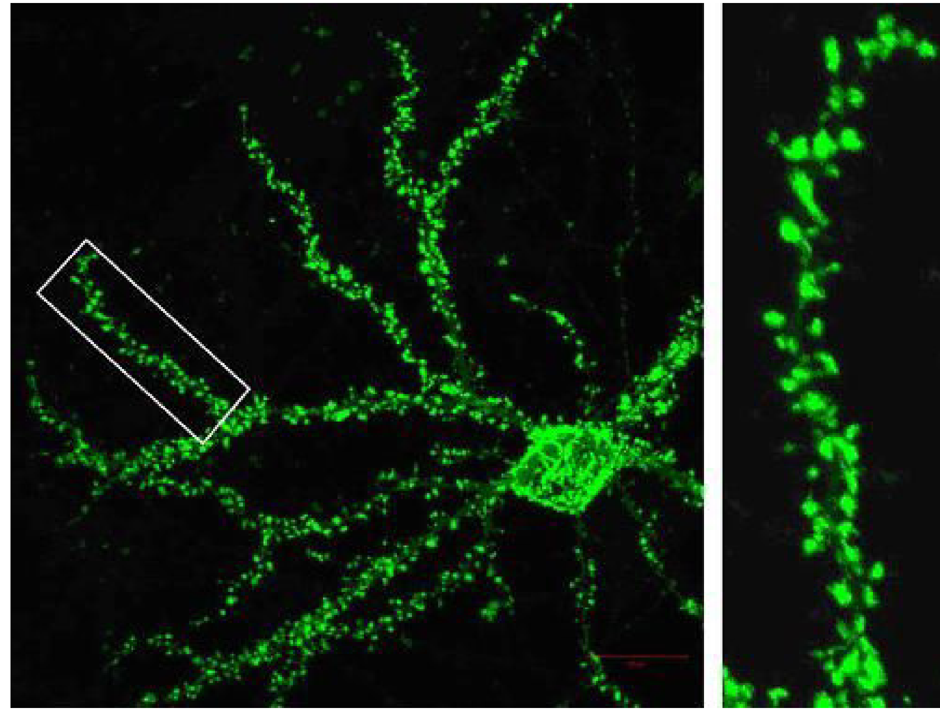


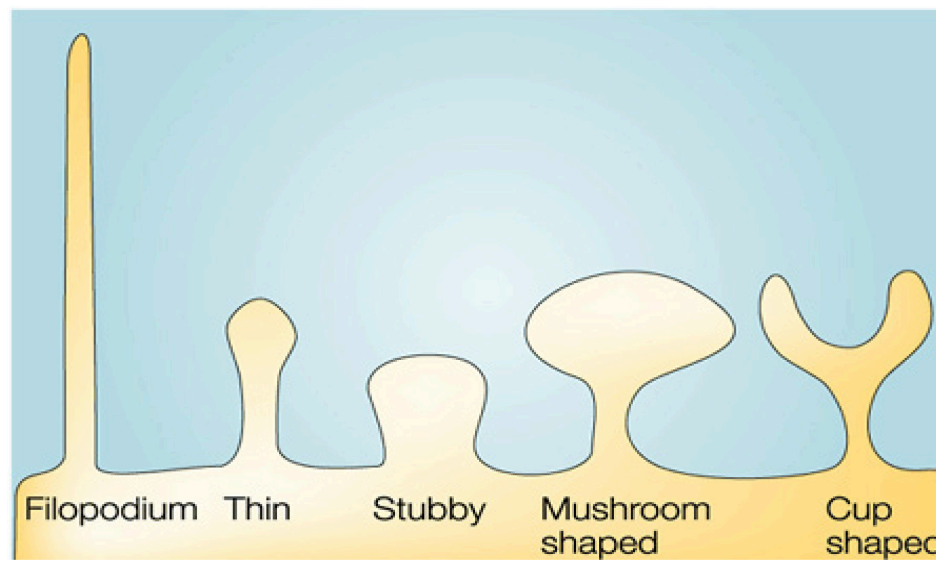
- Actin cross-linking proteins bind microfilaments into bundles and meshes



Microfilaments in Dendritic Spines

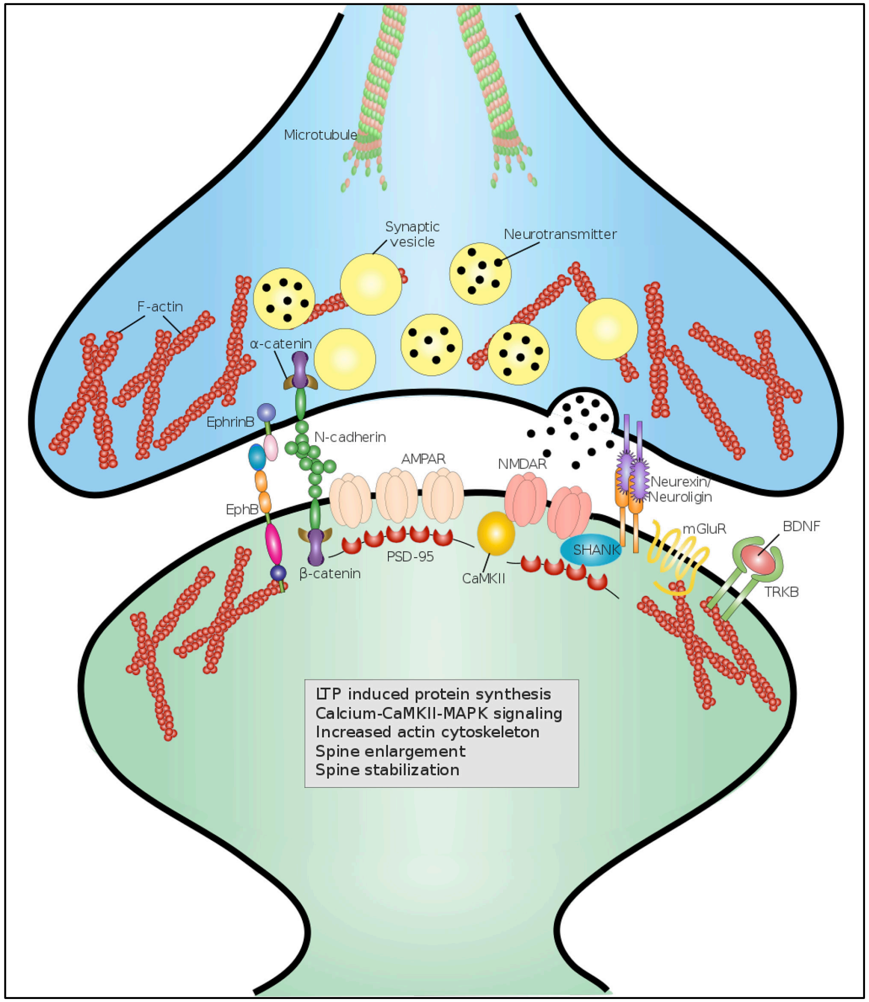




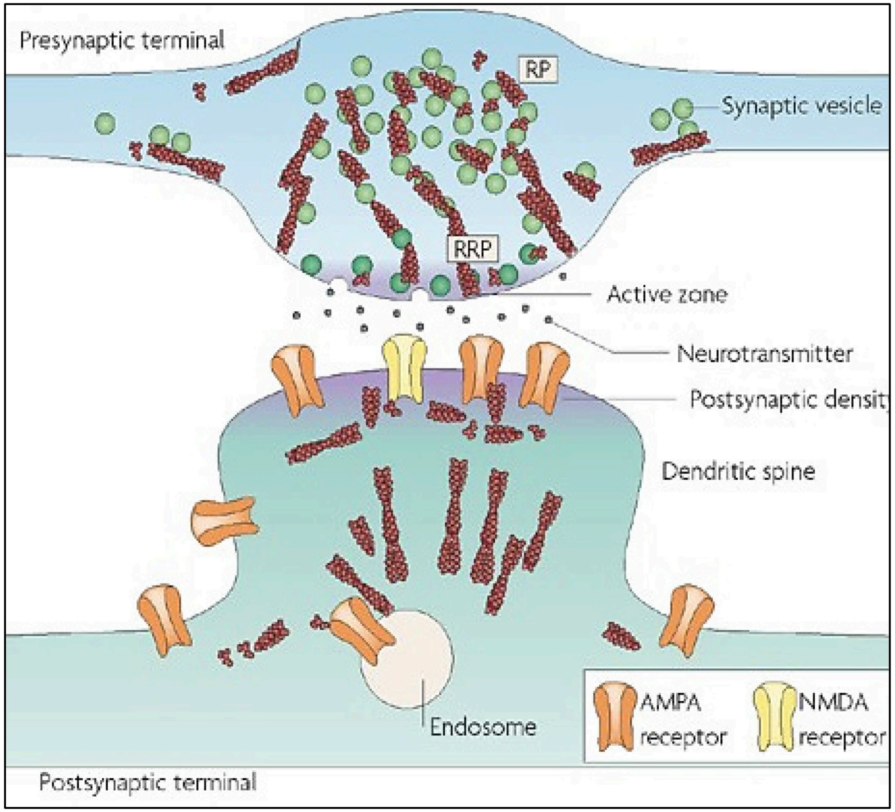


Microfilaments in Presynaptic Terminals

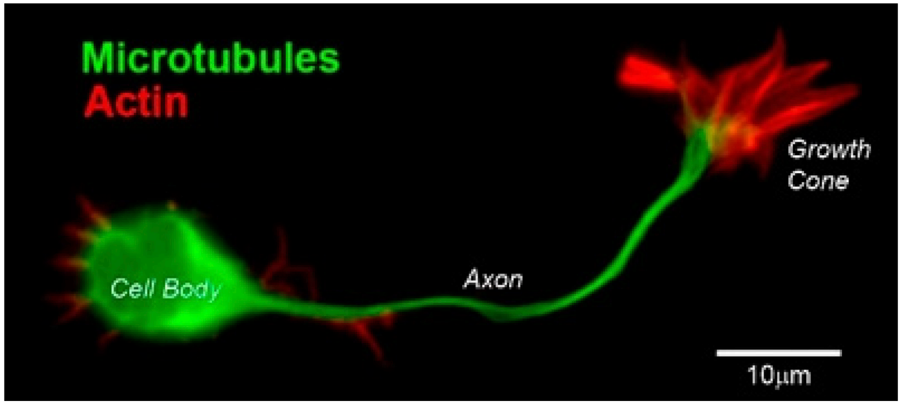
Presynaptic axon terminal

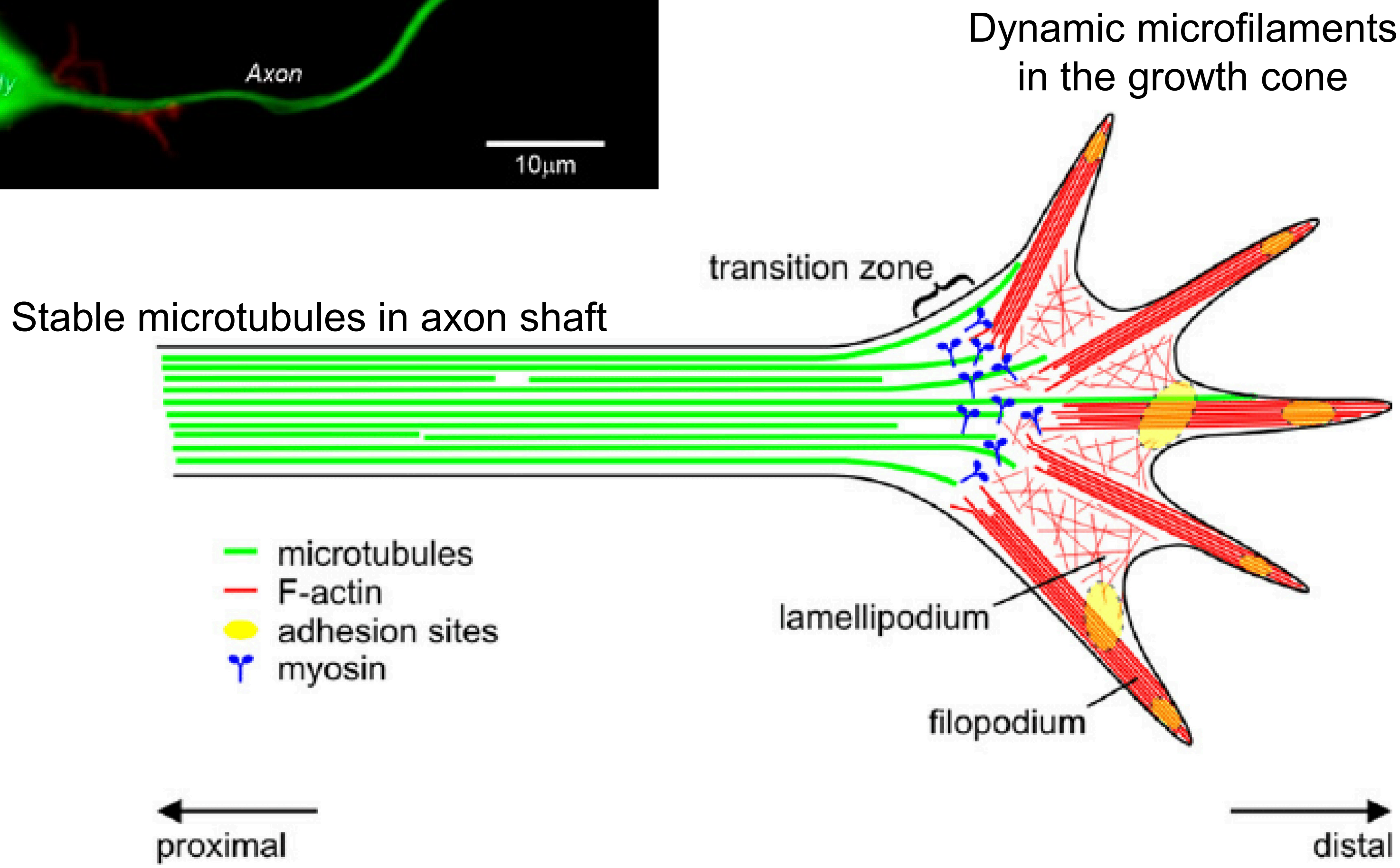


En passant varicosity



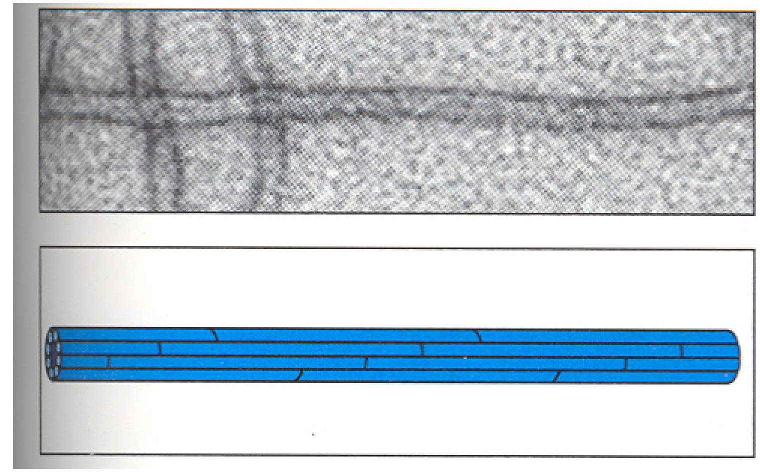
Microfilaments in Growth Cones

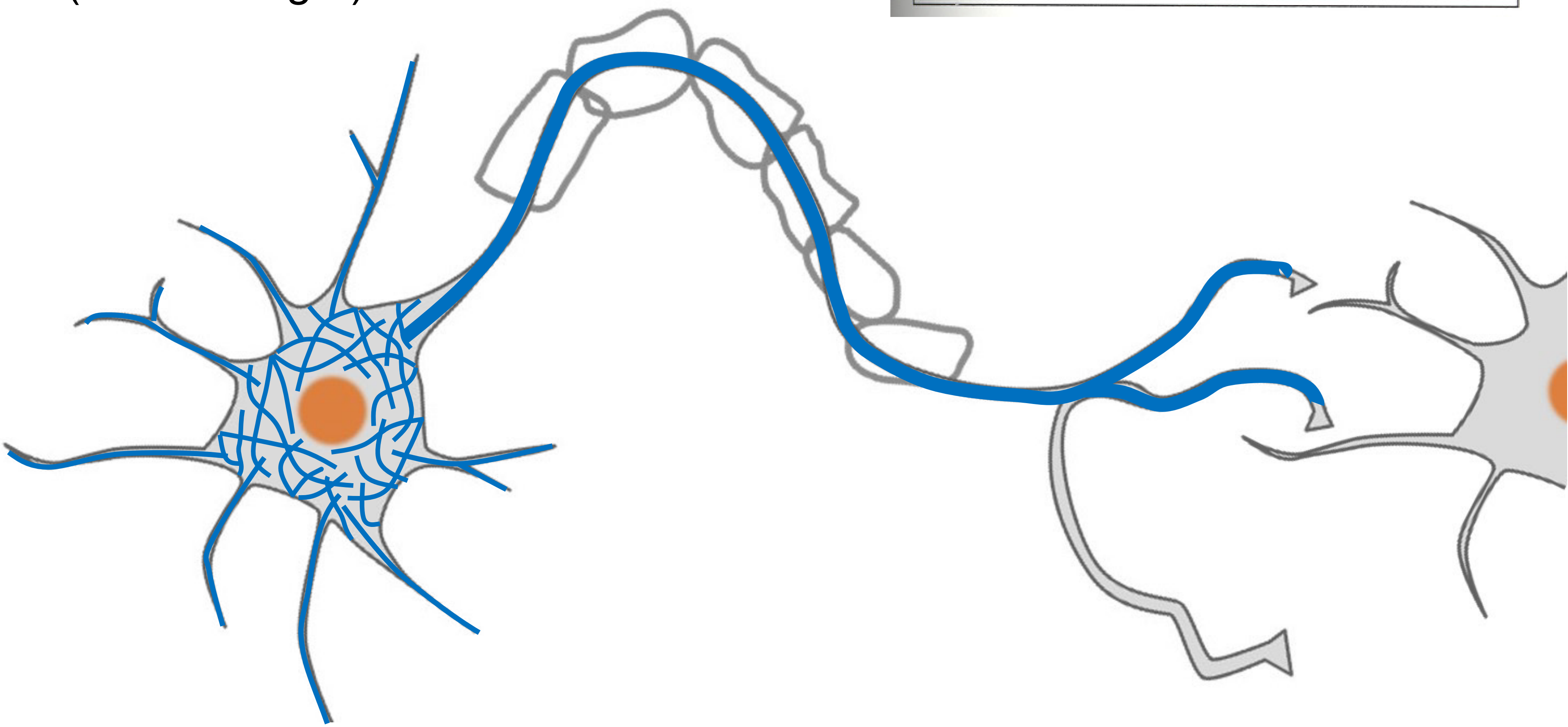




Intermediate Filaments in Neurons

- Throughout the cell body and in mature, healthy neurites
- Especially important in axons
- (Give strength)

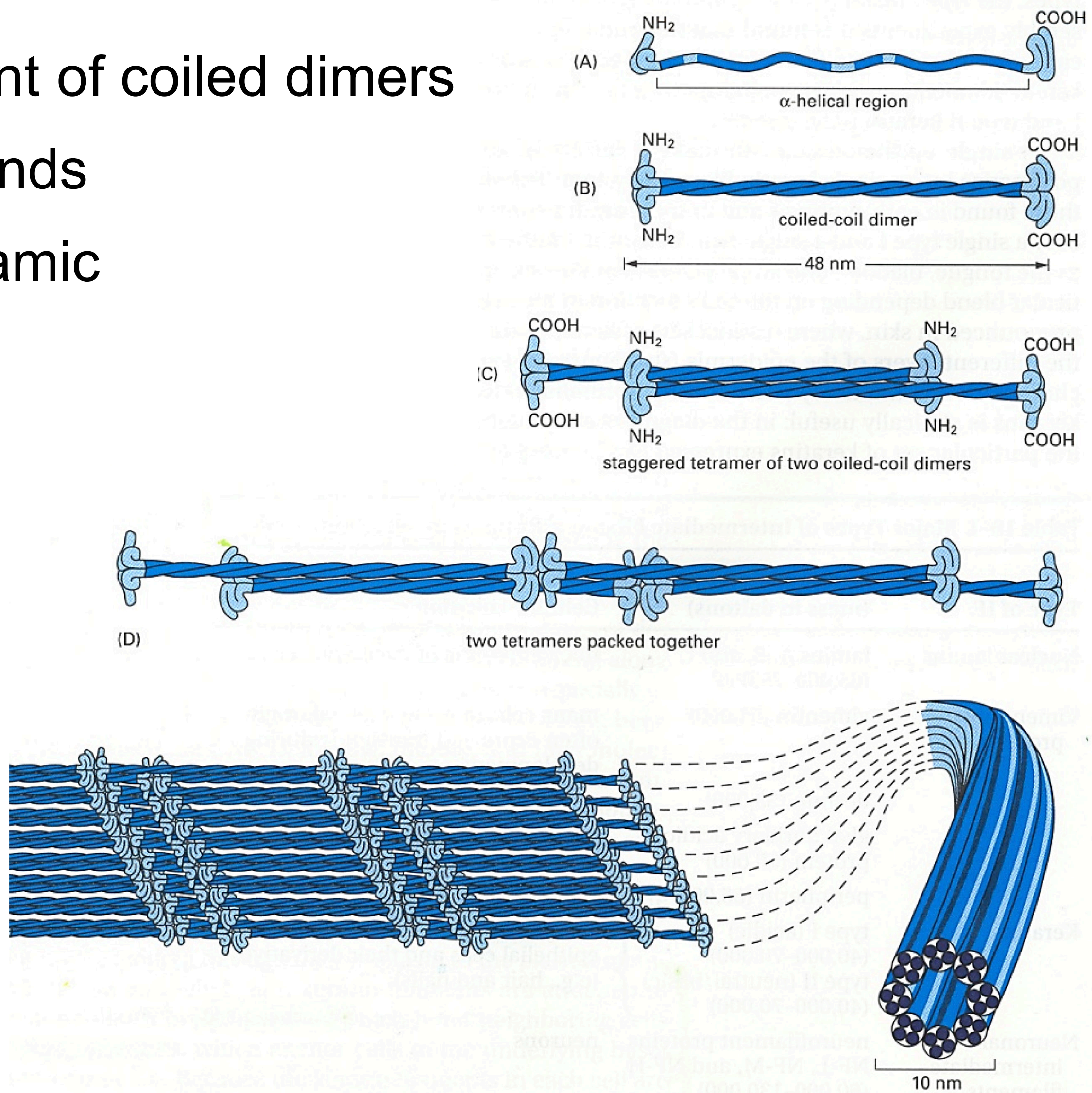




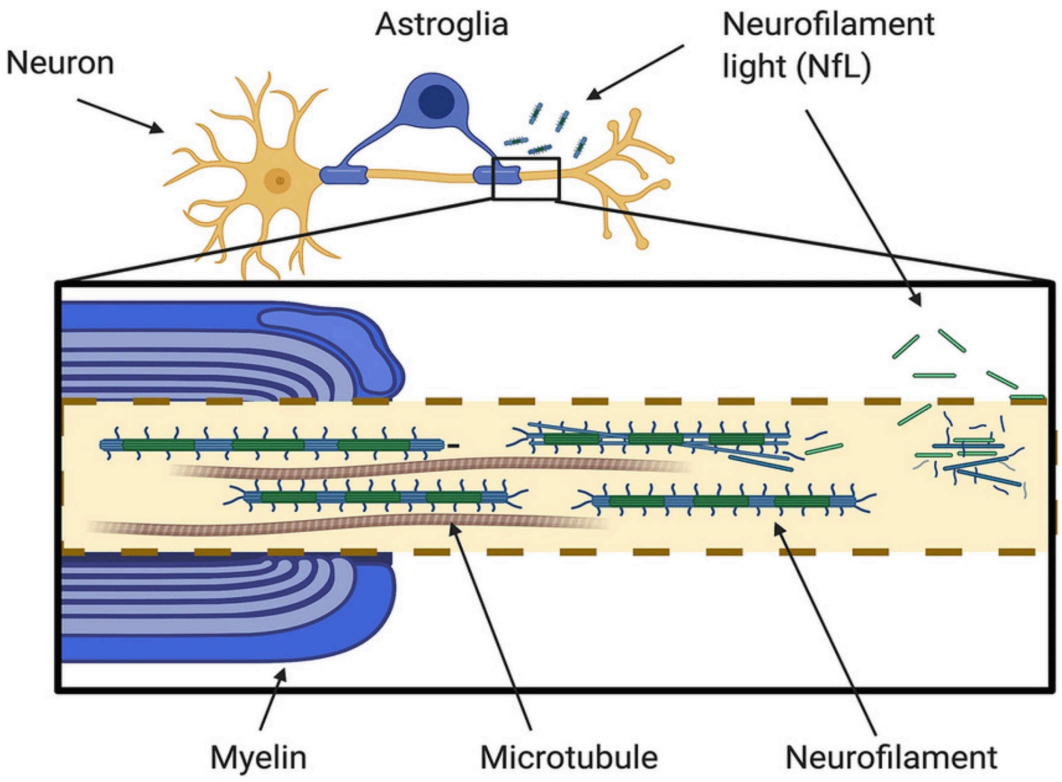
Intermediate Filaments

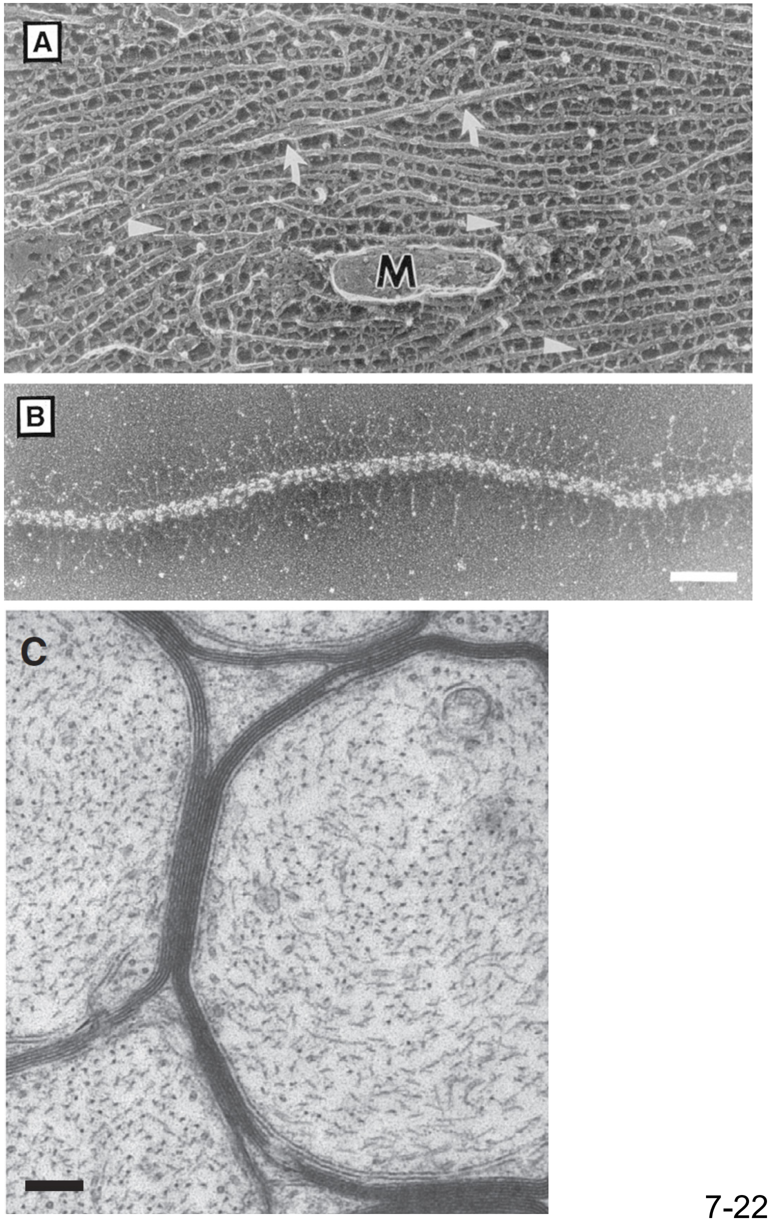
- Complex arrangement of coiled dimers
- No plus and minus ends
- Very stable, not dynamic

- In mature neurons: *neurofilaments (NF)*
- In glial cells: *glial fibrillary acidic protein (GFAP)*



Intermediate Filaments in Axons





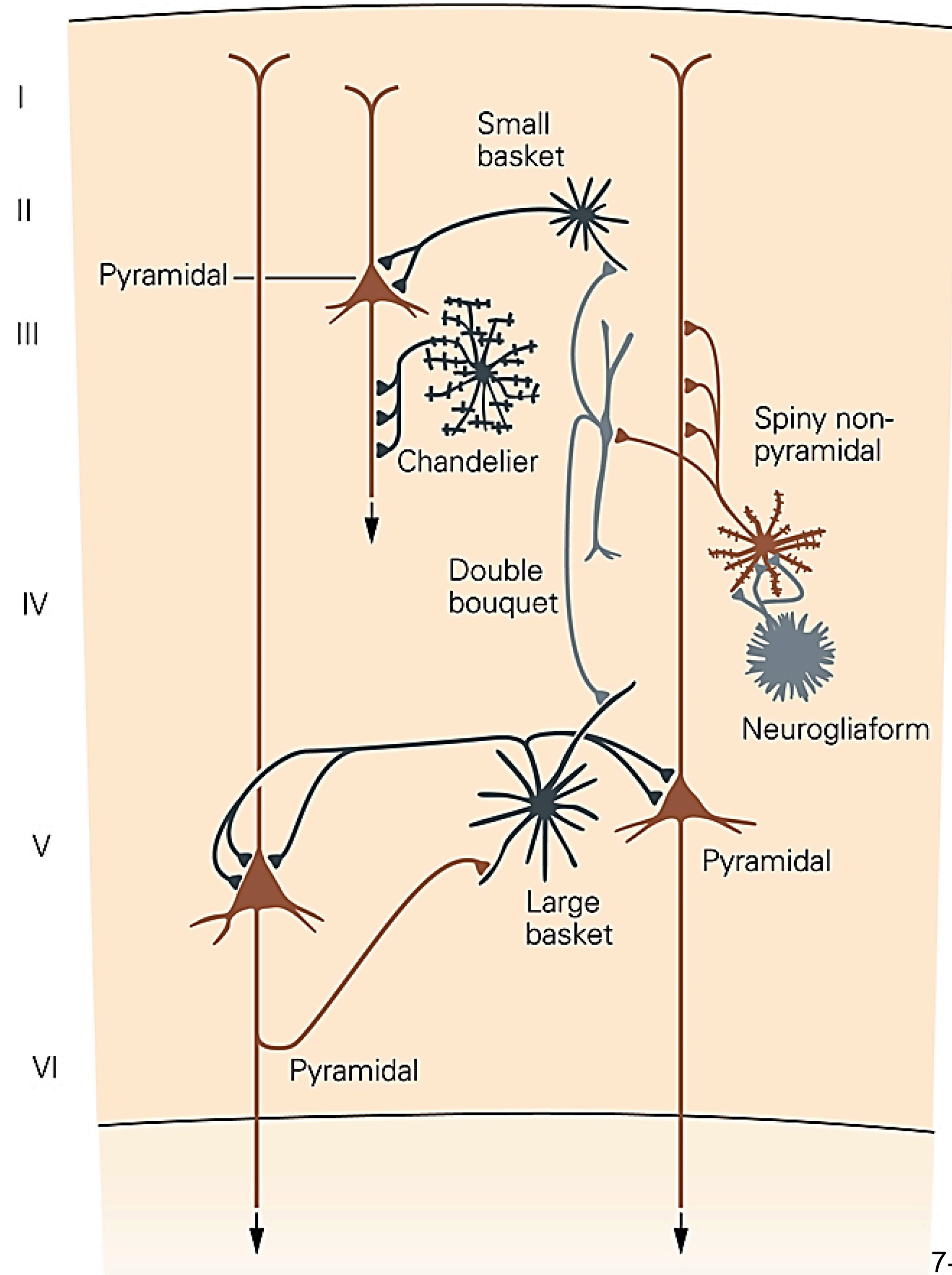
Neurons of the Cerebral Cortex

Projection neurons

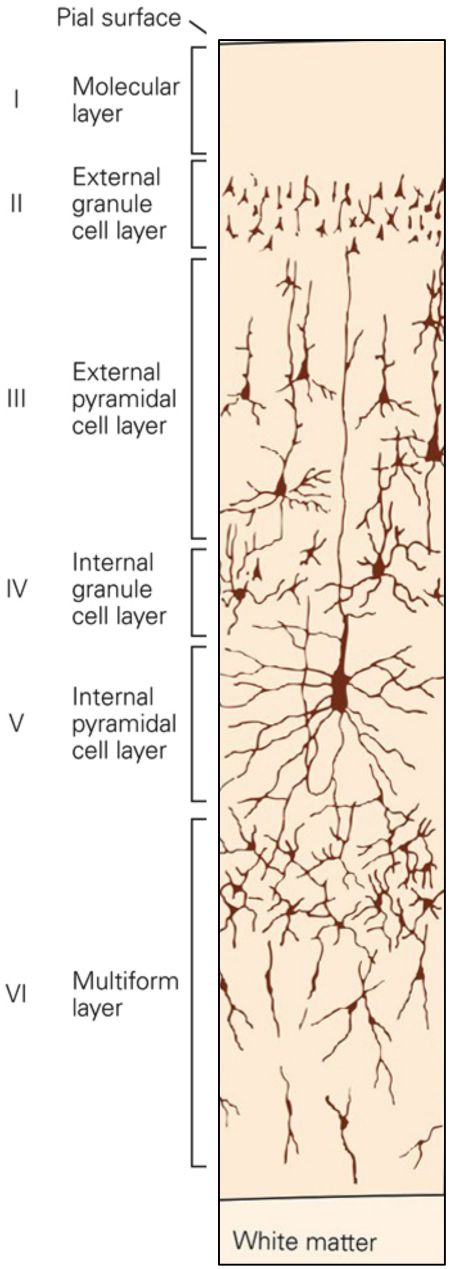
- Pyramidal cells (glutamatergic)

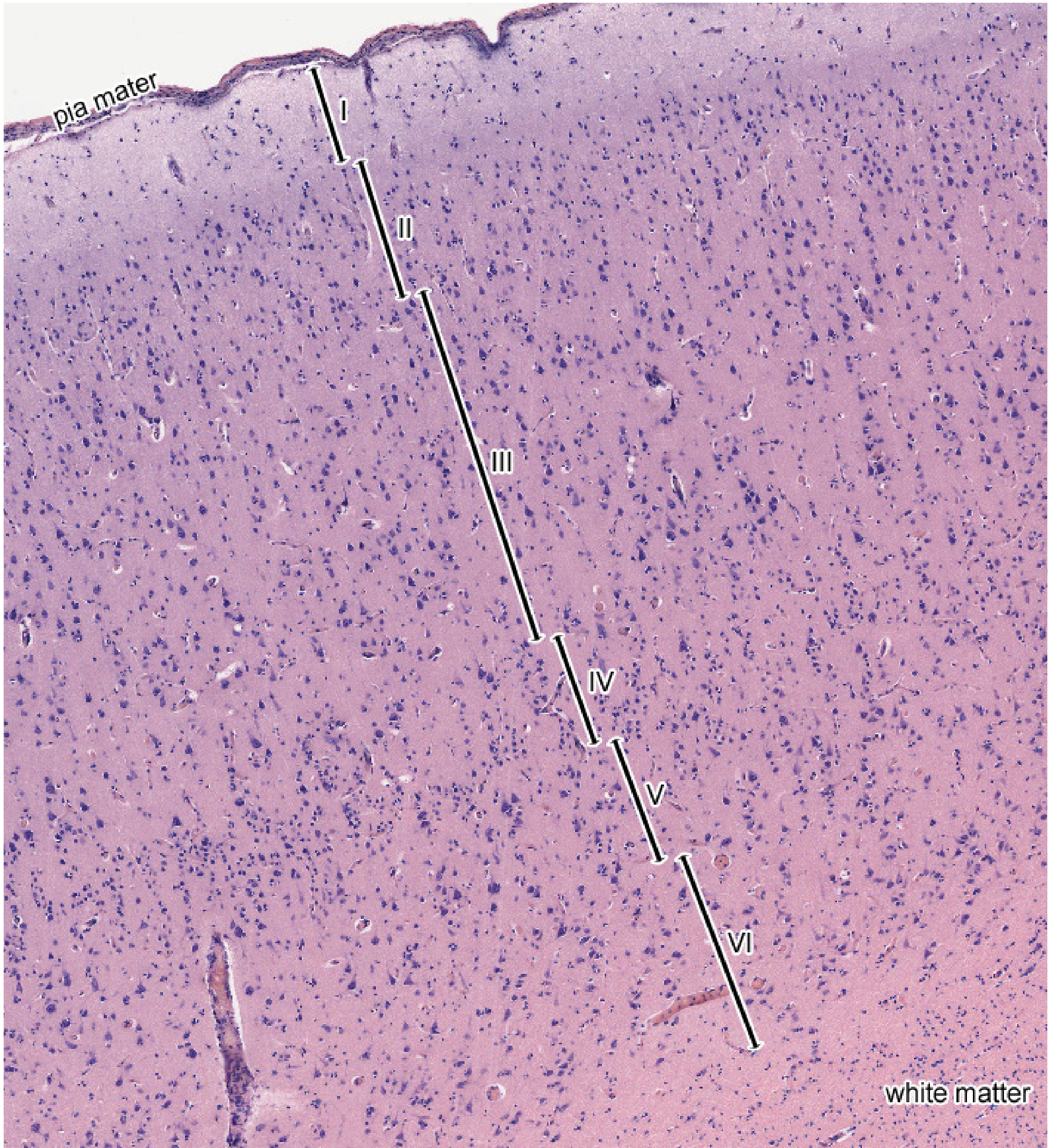
Local interneurons

- Basket, chandelier, double bouquet cells, many others (GABAergic)



Neurons of the Cerebral Cortex



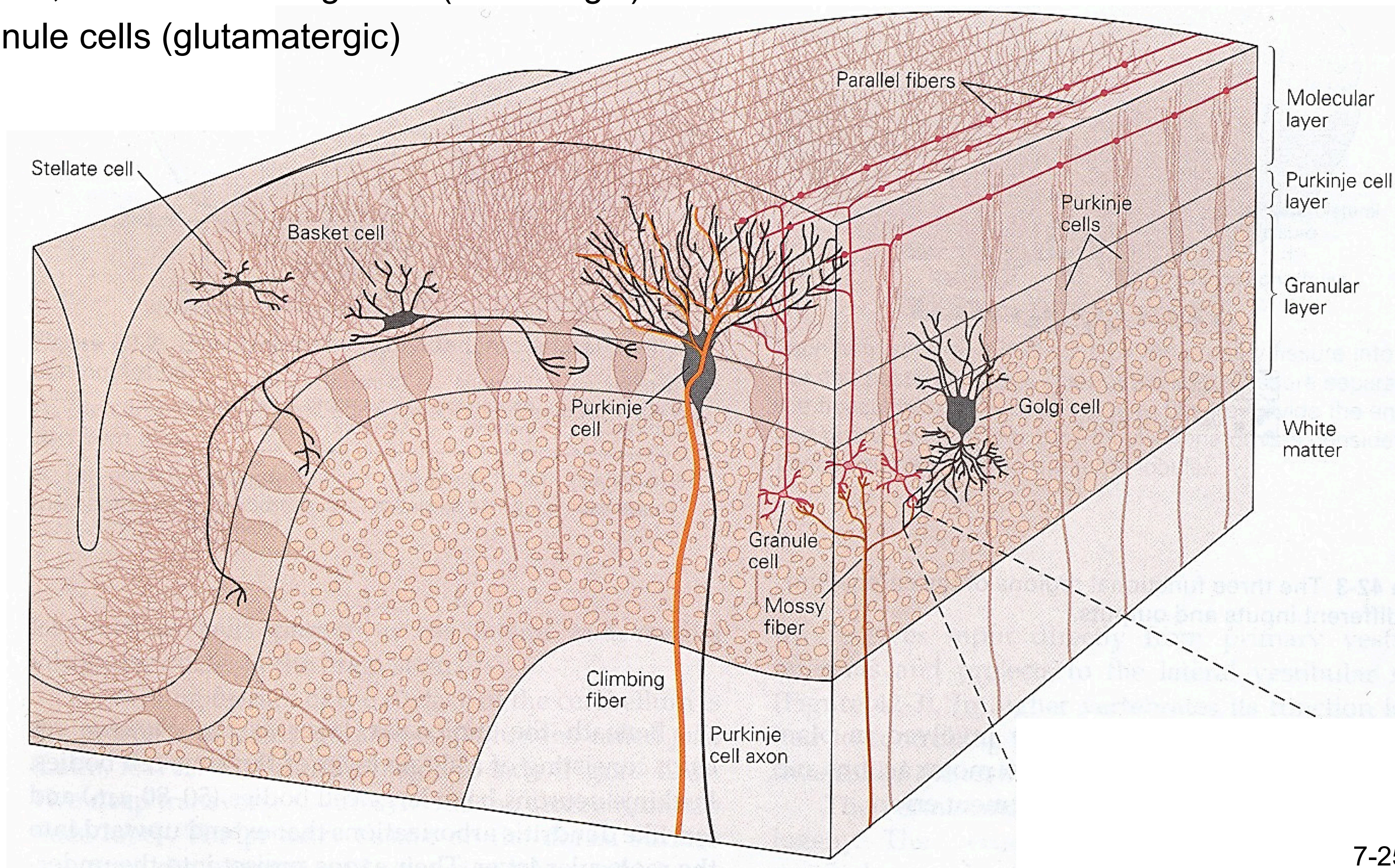


Neurons of the Cerebellar Cortex

Projection neurons: Purkinje cells (GABAergic)

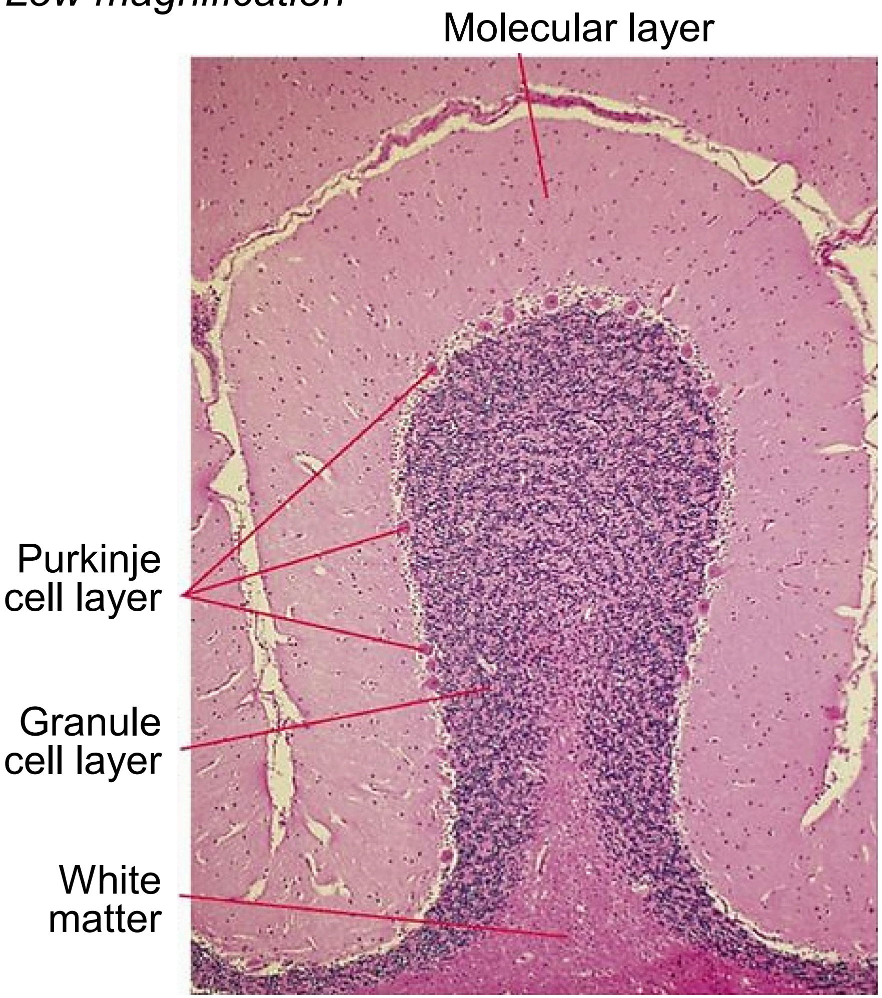
Local interneurons

- Basket, stellate and Golgi cells (GABAergic)
- Granule cells (glutamatergic)



Neurons of the Cerebellar Cortex

Low magnification



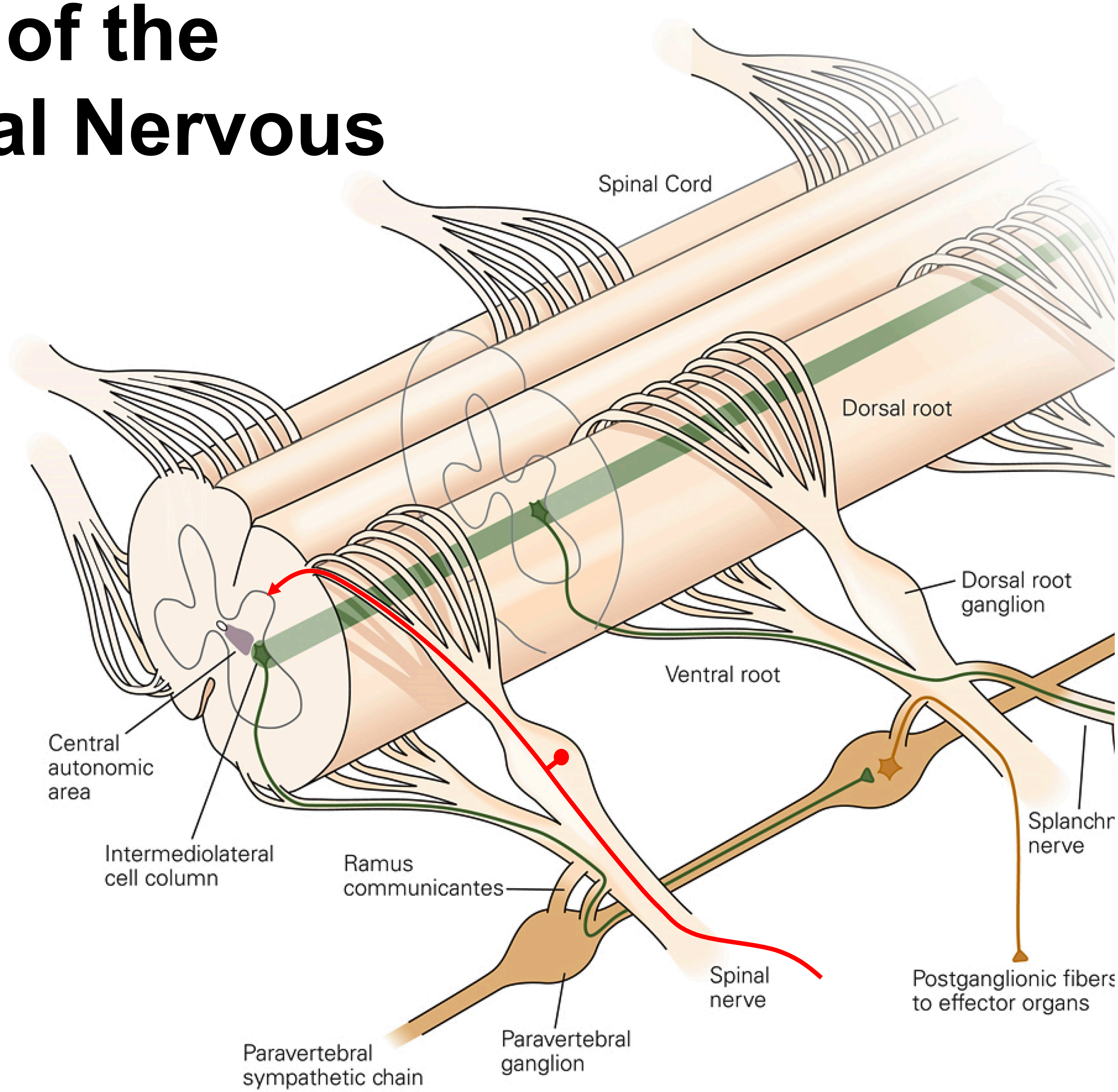
High magnification

Purkinje cell dendritic trees are green, neuronal nuclei are red

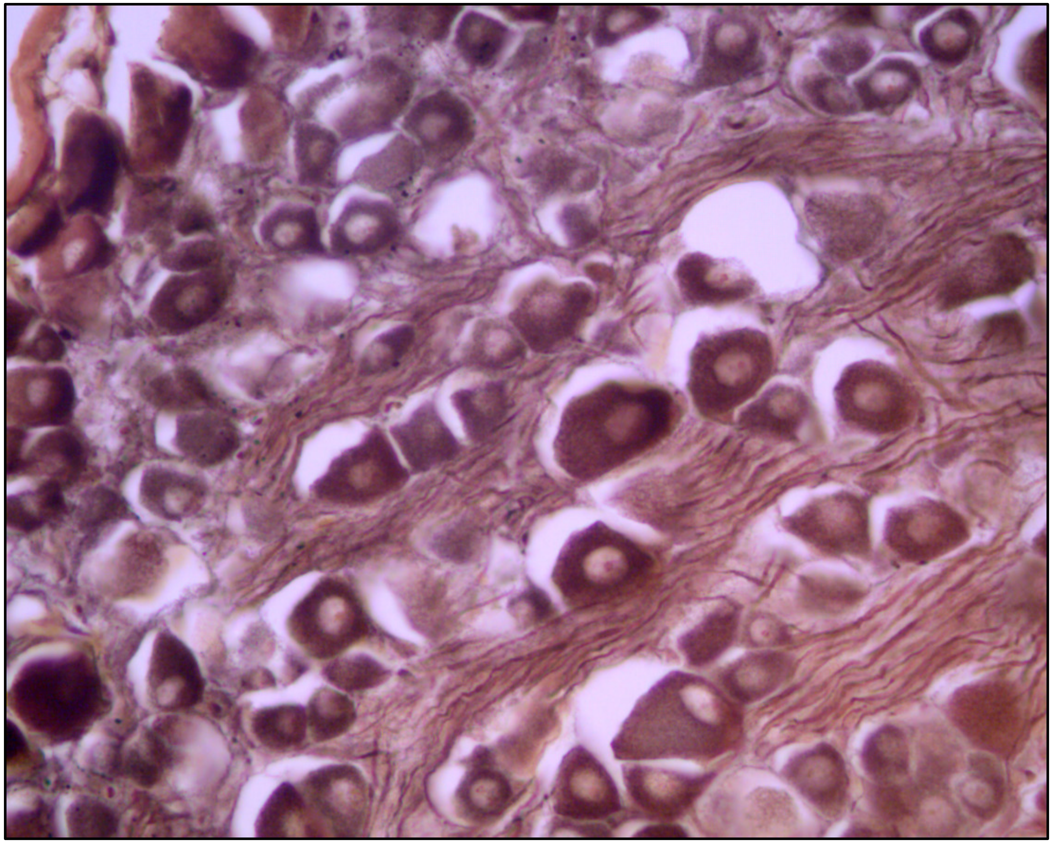
Neurons of the Peripheral Nervous System

Primary sensory neurons in the dorsal root ganglia

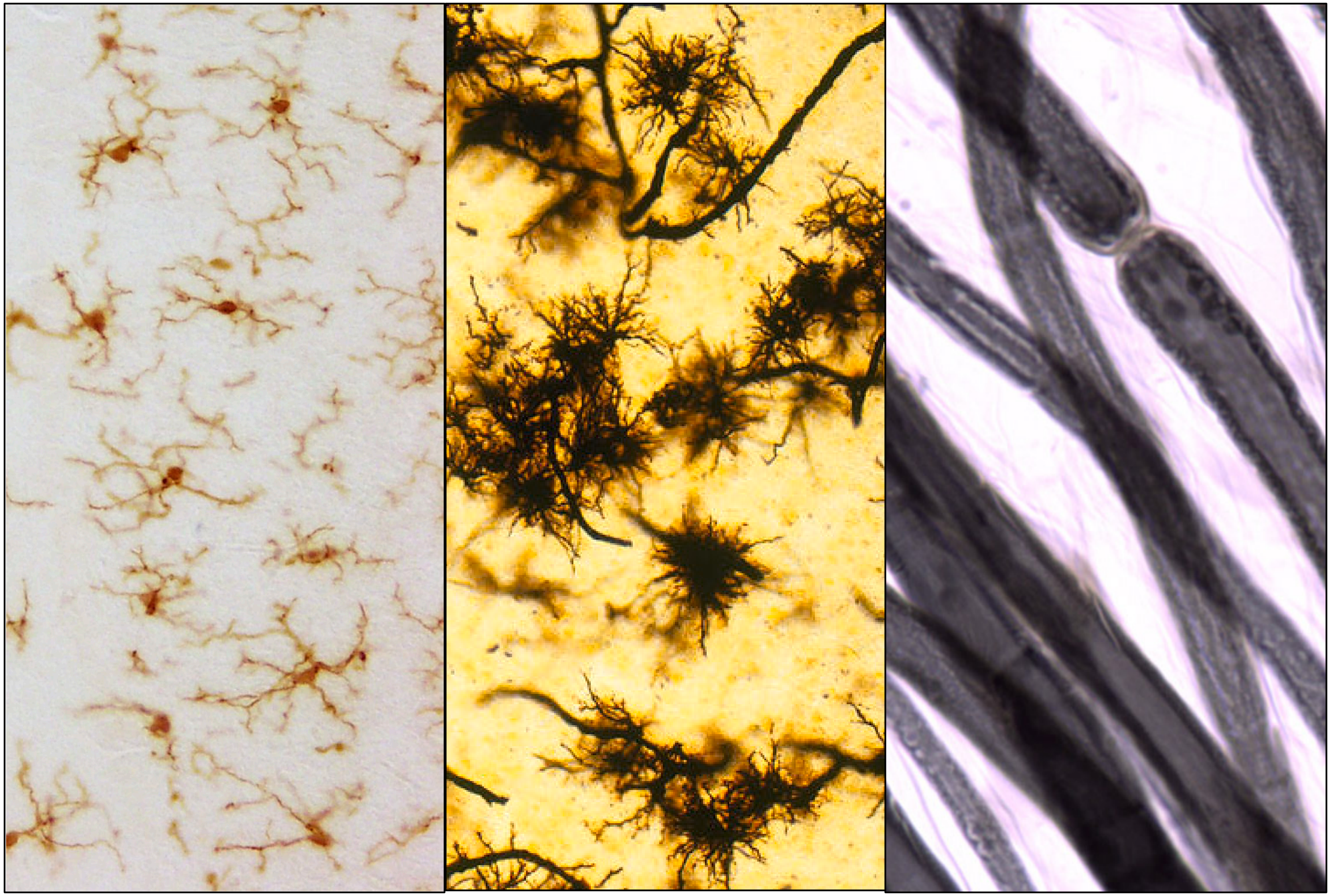
Autonomic nervous system ganglionic neurons



Neurons of the Peripheral Nervous System

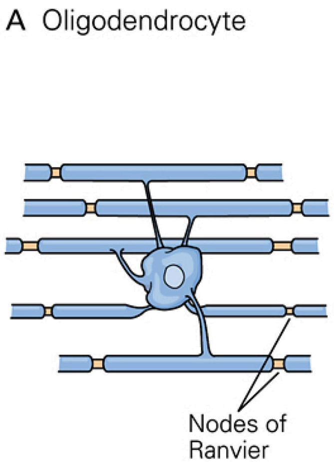


Glial Cells

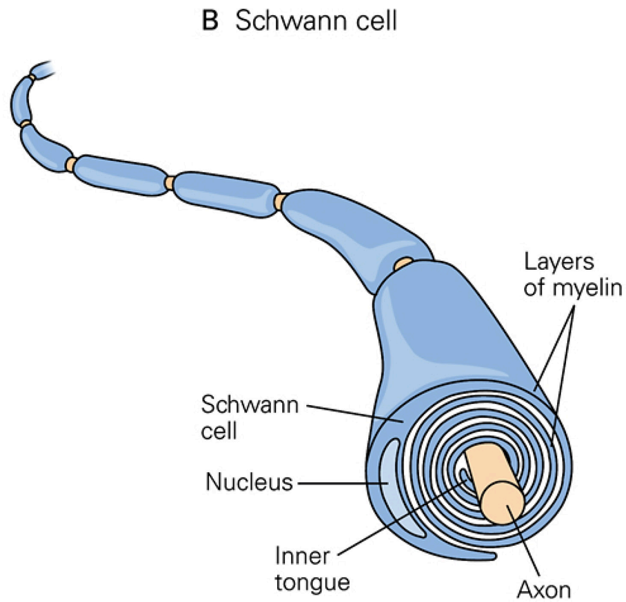


Glial Cell Types

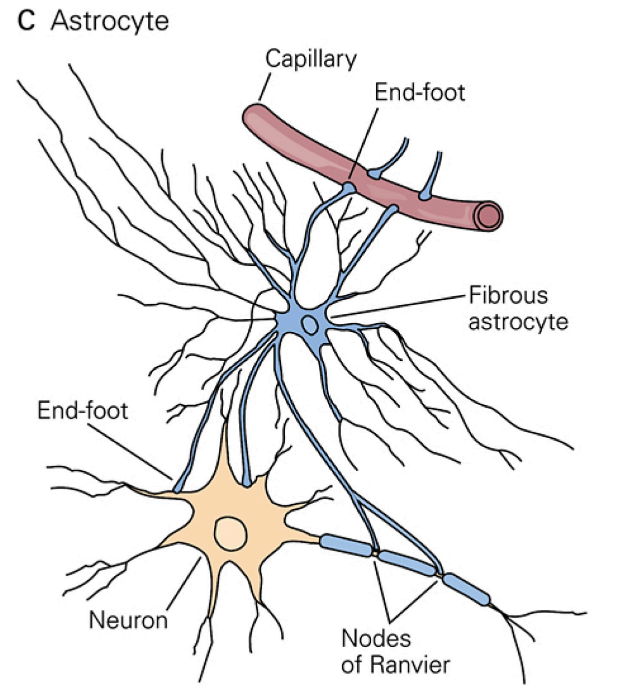
Macroglia



Myelin in the CNS

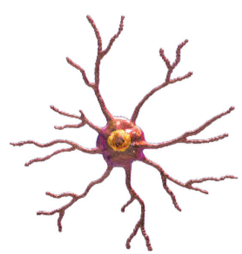


Myelin in the PNS



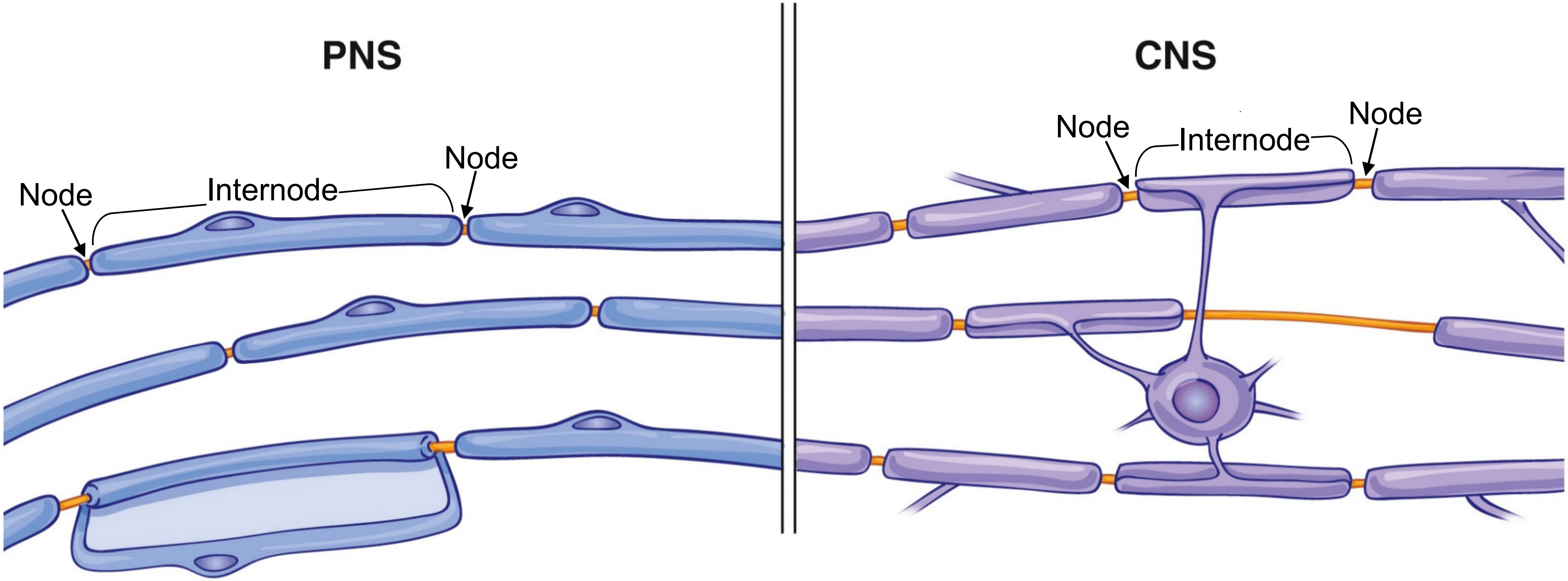
Multiple functions in the CNS

Microglia



Phagocytic cells in the CNS

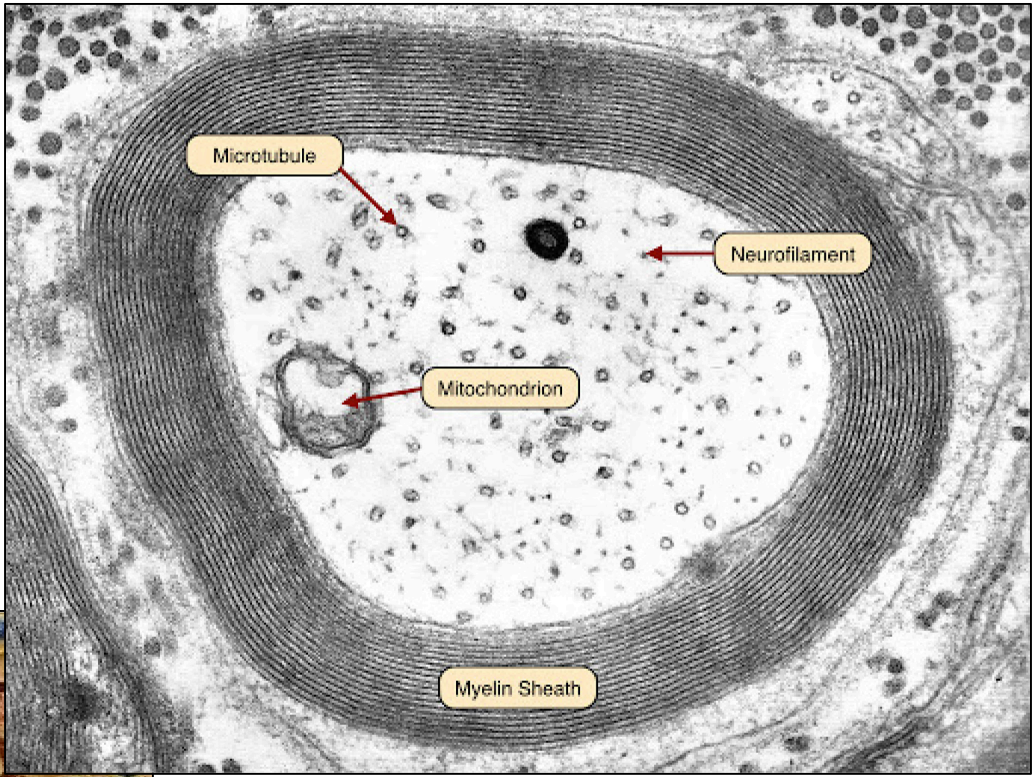
Myelin

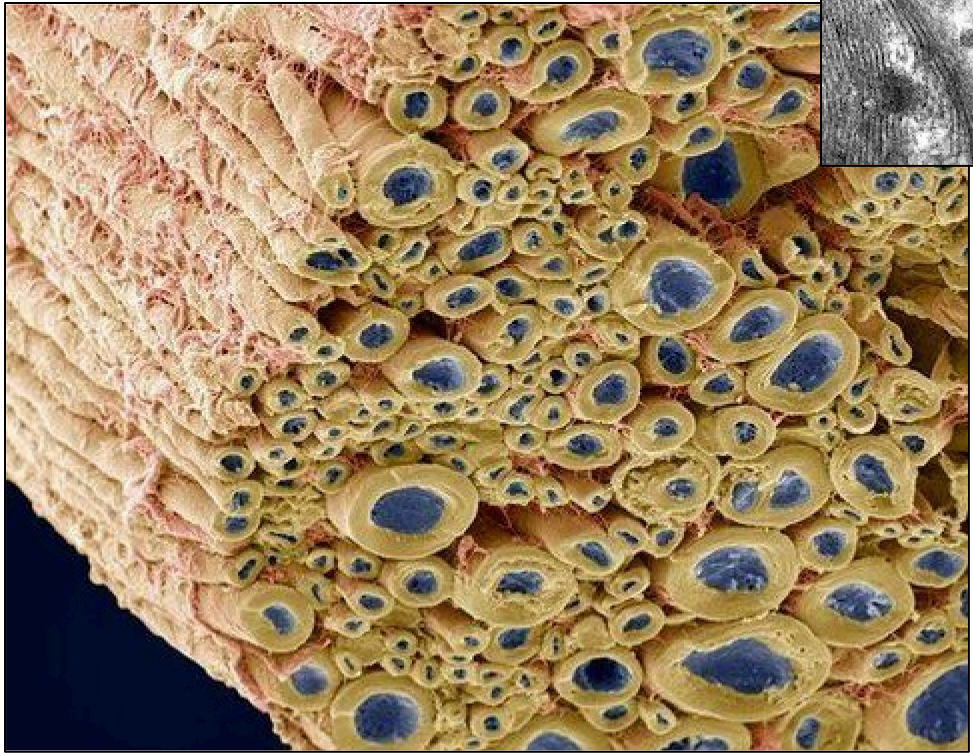


- Myelin is made by Schwann cells (PNS) and oligodendrocytes (CNS)
- Nodes of Ranvier are 1-2 μm long
- Distance between nodes (the internodal distance) is 300-1500 μm

Myelin

Composed of concentric bilayers of lipids interspersed by protein layers (70% lipid, 30% protein)

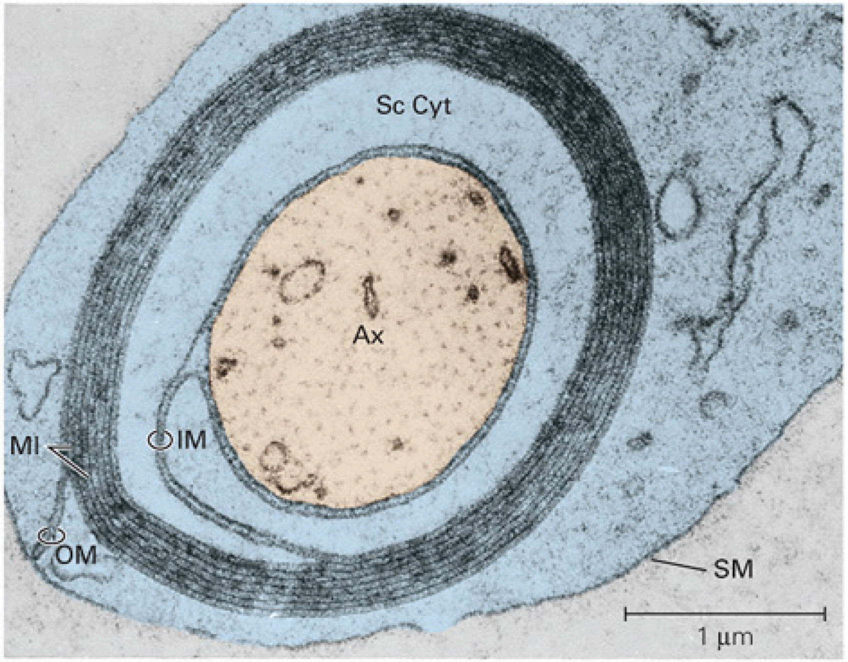




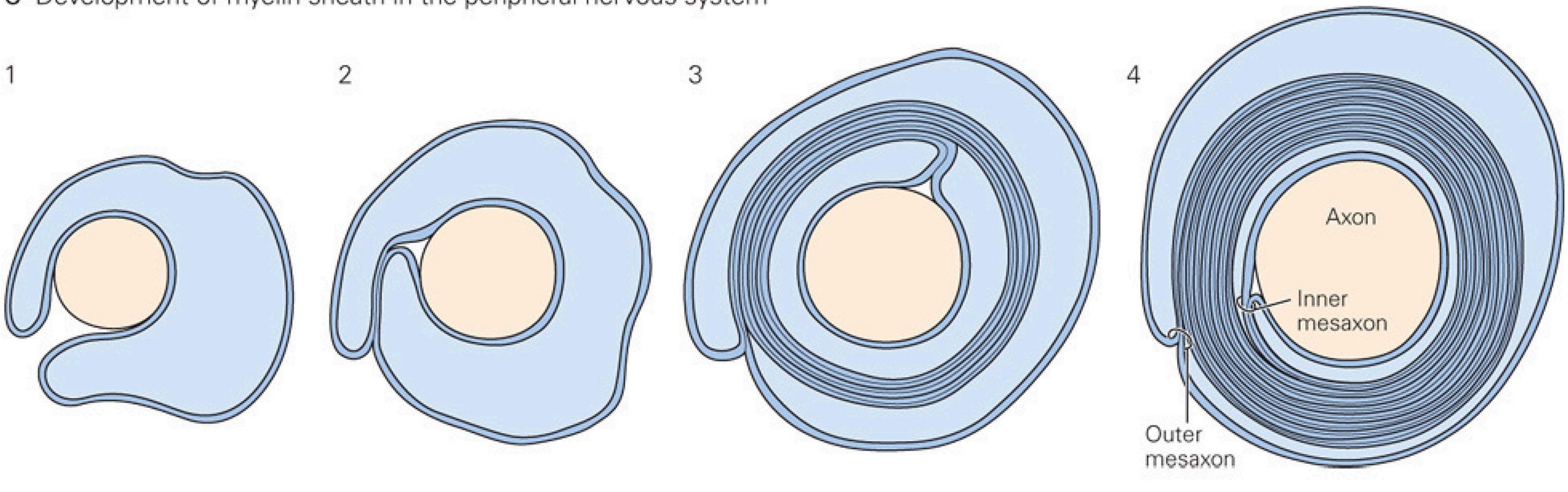
Large-diameter axons tend to have thicker myelin and have nodes spaced further apart than small-diameter axons

Schwann Cell Myelin Formation

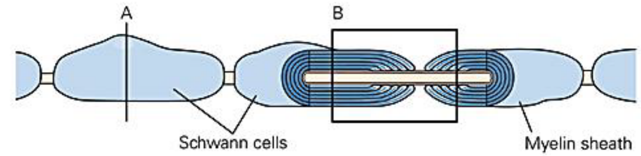
B Myelination in the peripheral nervous system



C Development of myelin sheath in the peripheral nervous system



PNS Myelin Structure

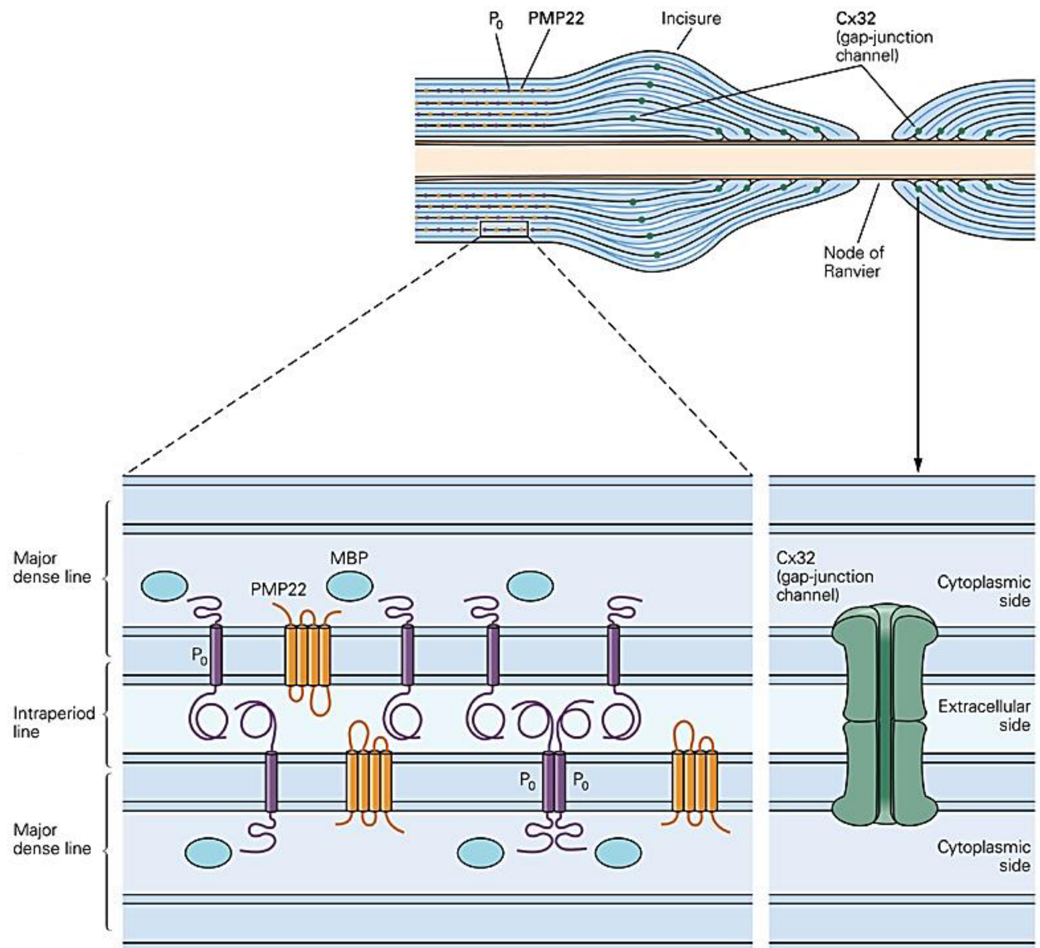


Prevalent PNS myelin proteins

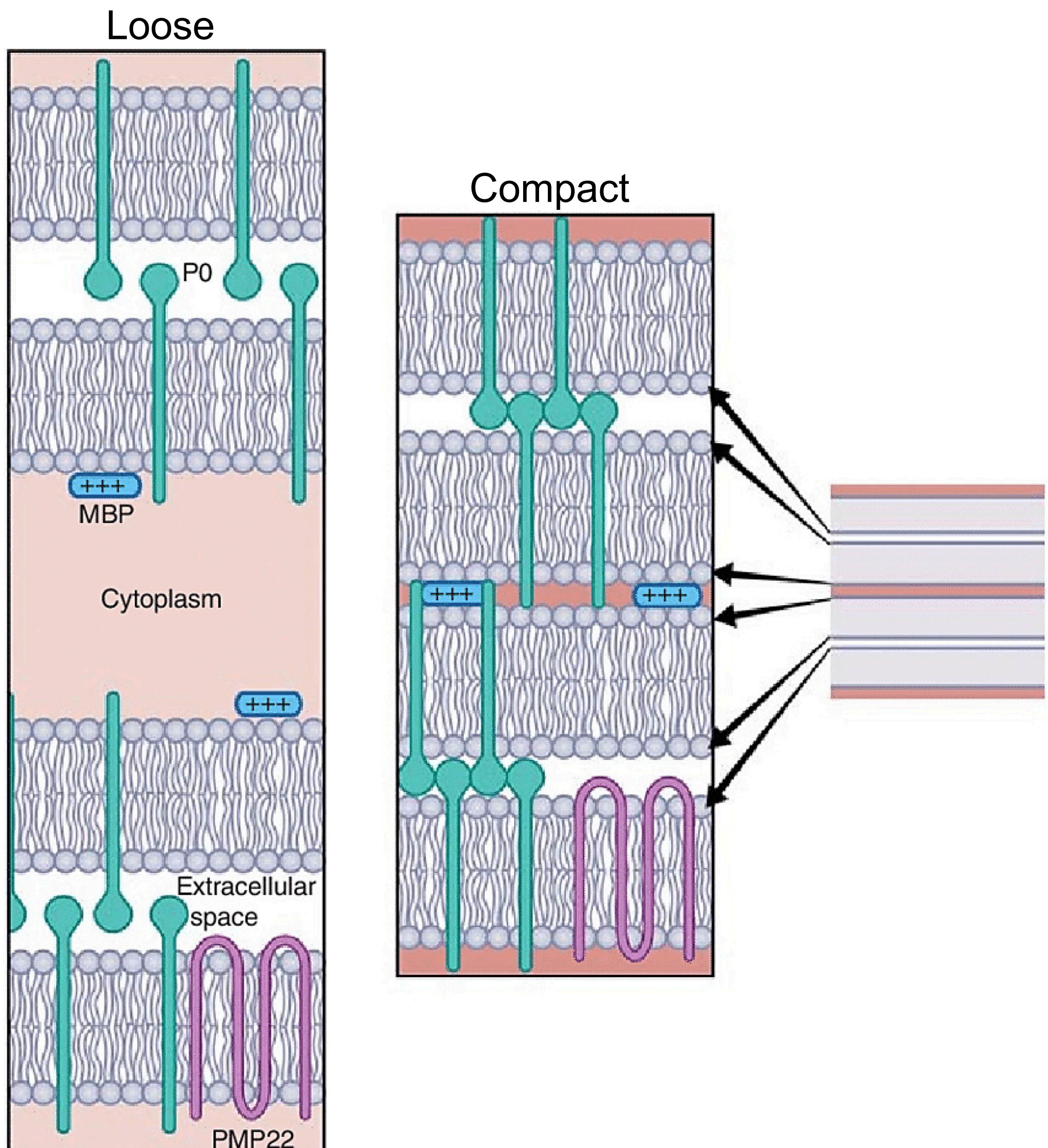
MBP (myelin basic protein): Located in the cytoplasm, responsible for adhesion of the cytosolic surfaces of compact myelin

P0 (myelin protein zero): Transmembrane protein, homophilic adhesion protein that links extracellular layers of compact myelin

Cx32 (connexin): Gap junctions allow myelin layers to communicate

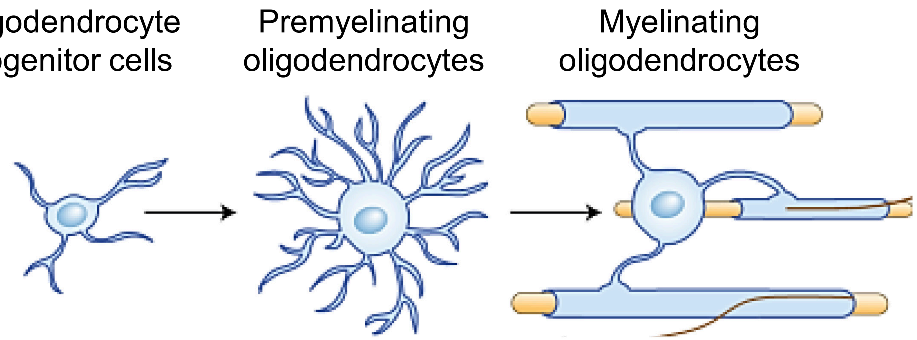


PNS Myelin Structure

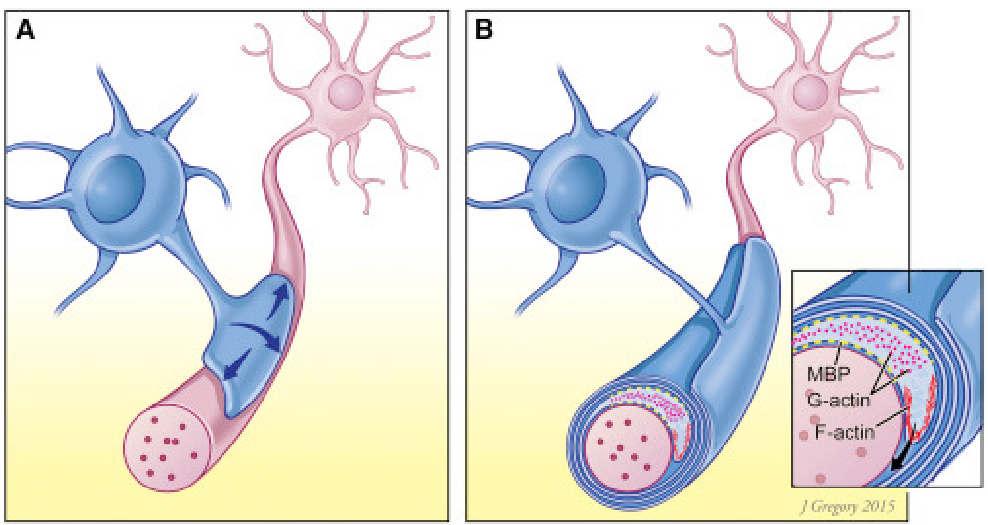


Oligodendrocyte Myelin Formation

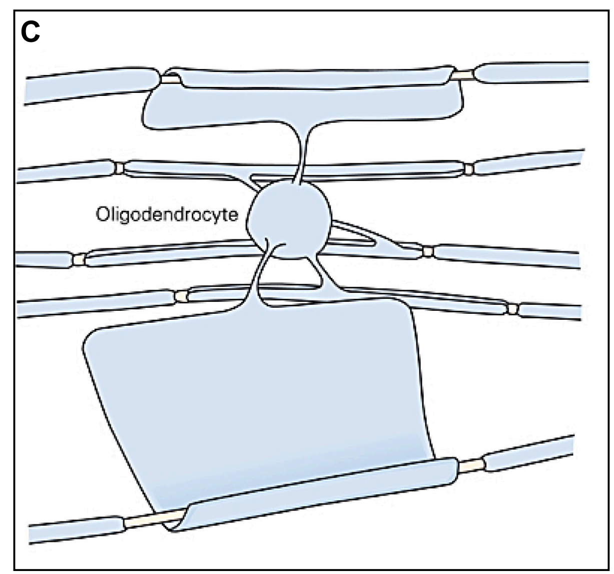
Production of Oligodendrocytes



Ensheathment and Myelination of Axons

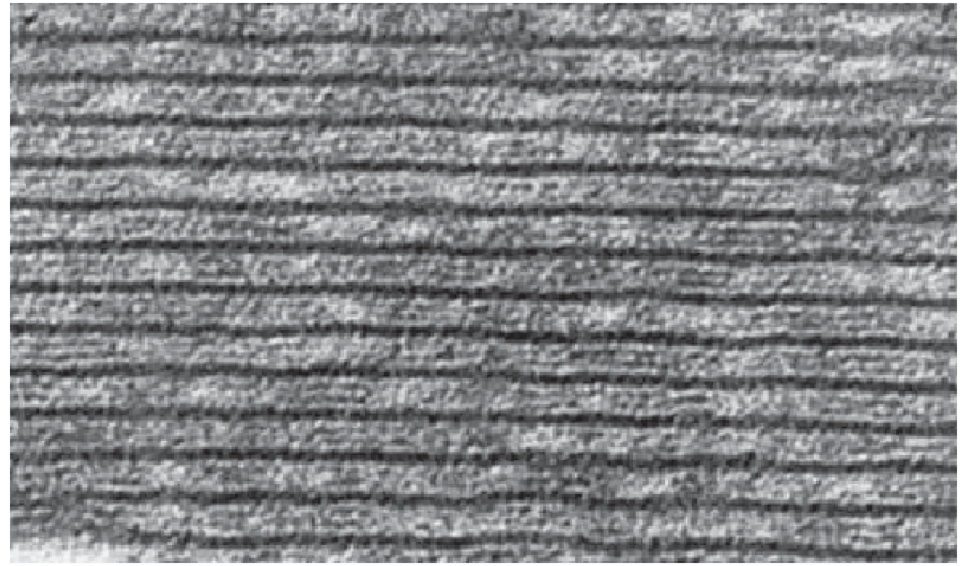


Ensheathment　　　　Myelination



Myelination of multiple axons

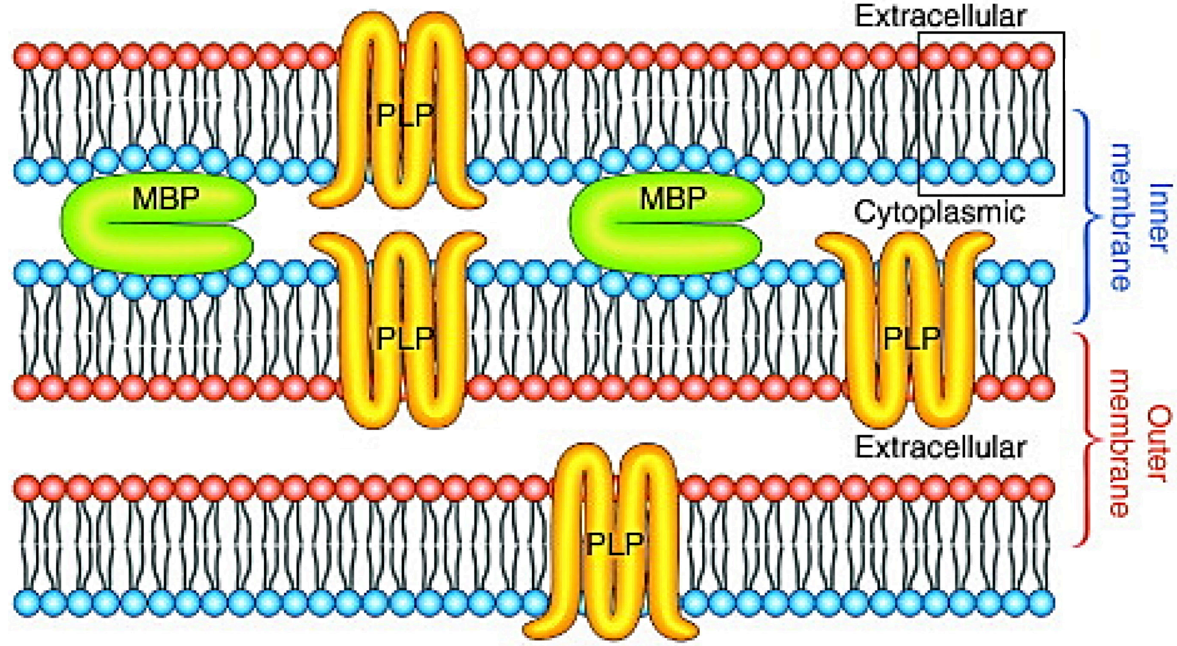
CNS Myelin Structure



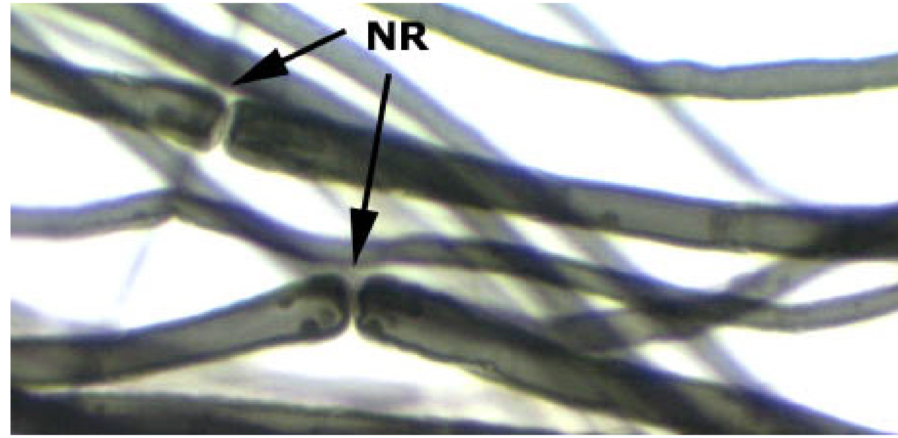
Prevalent CNS myelin proteins

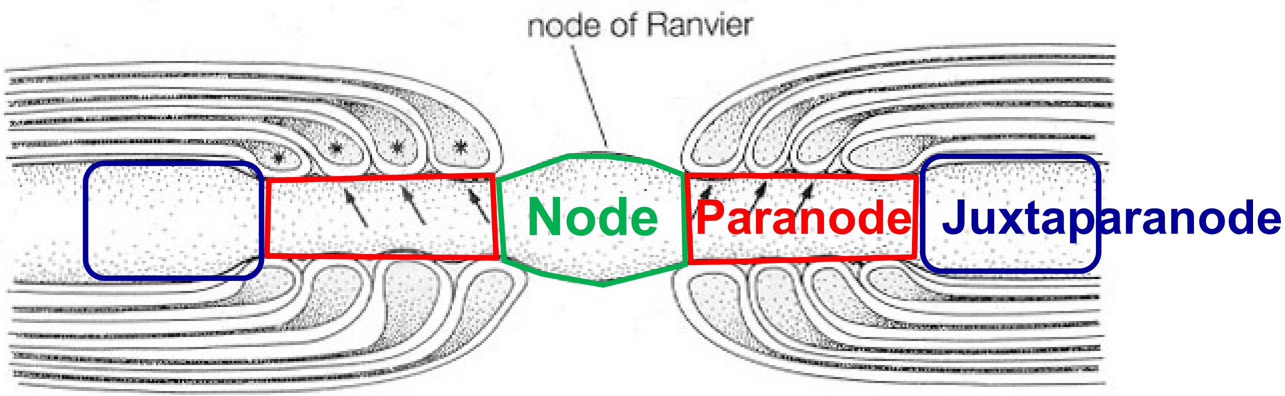
MBP (myelin basic protein): Located in the cytoplasm, responsible for adhesion of the cytosolic surfaces of multilayered compact myelin

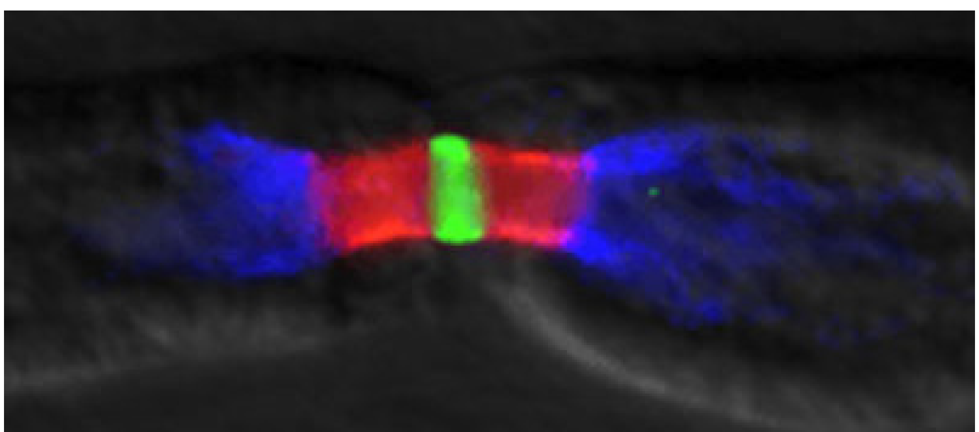
PLP (proteolipid protein): Transmembrane protein, act as struts to properly space the extracellular membranes in compact myelin



Node of Ranvier Organization







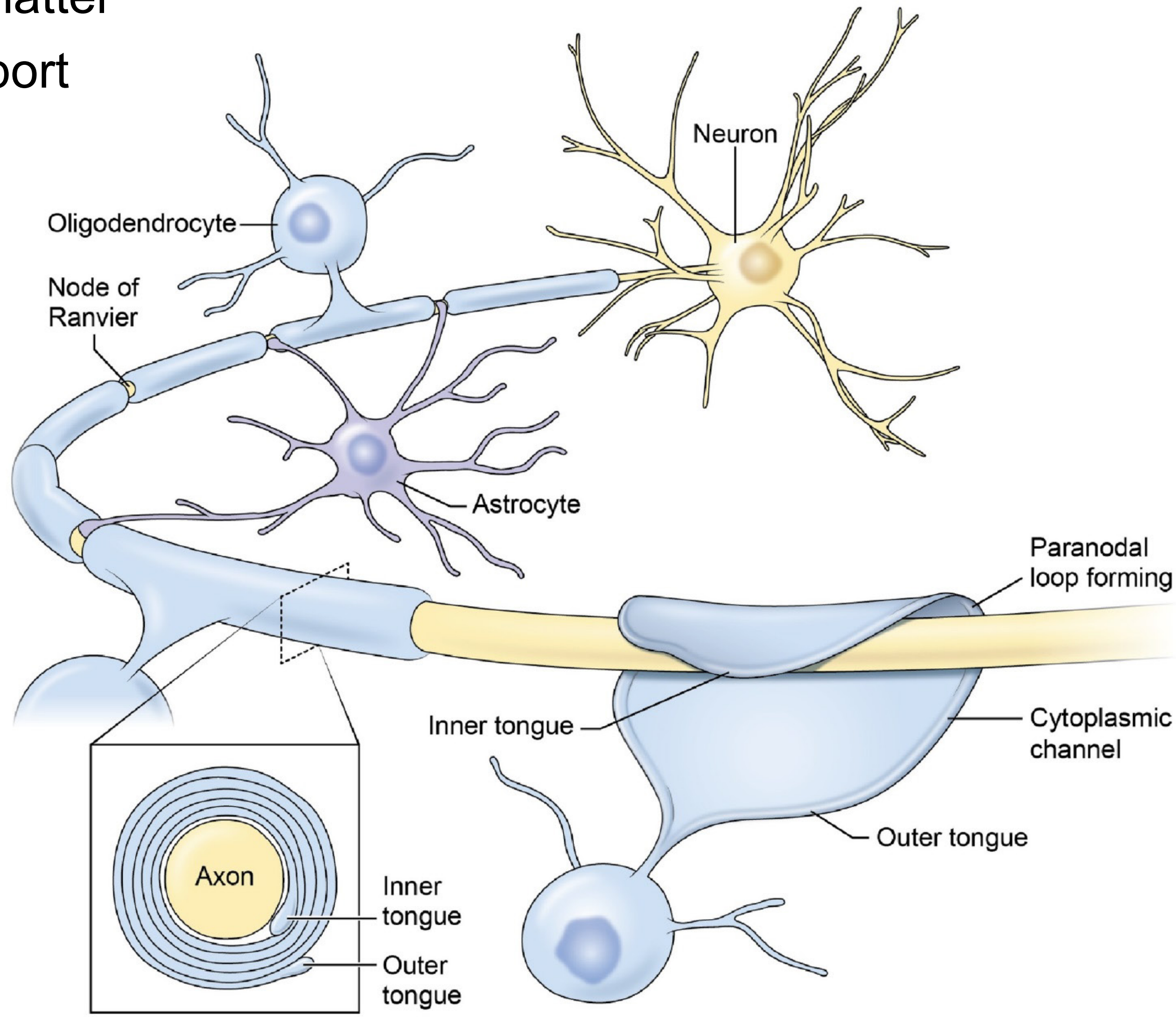
Node:
Voltage-gated Na+ channels

Paranode:
Caspr2 (adhesion protein)

Juxtaparanode:
Voltage-gated K+ channels

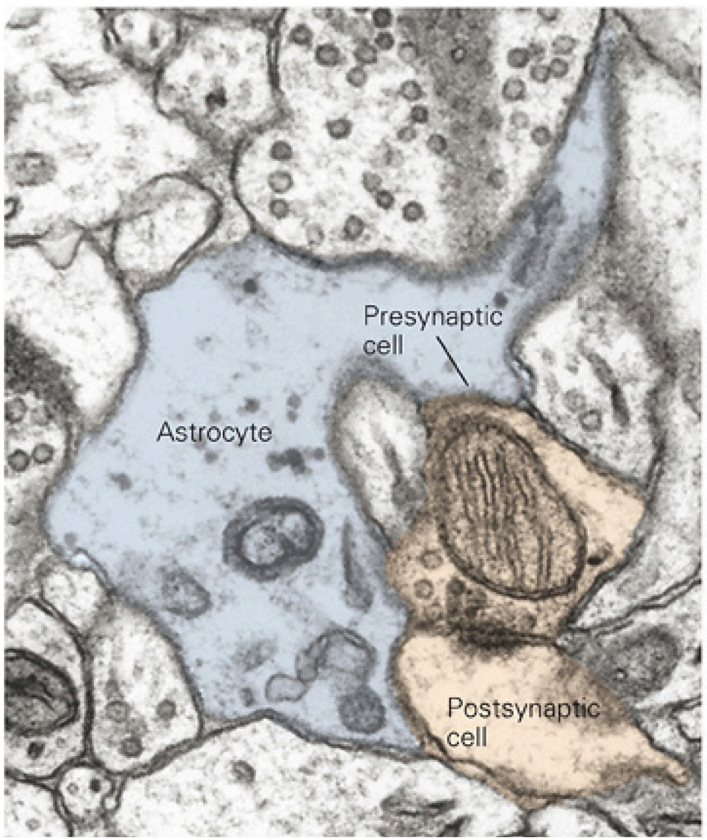
Fibrous (Perinodal) Astrocytes

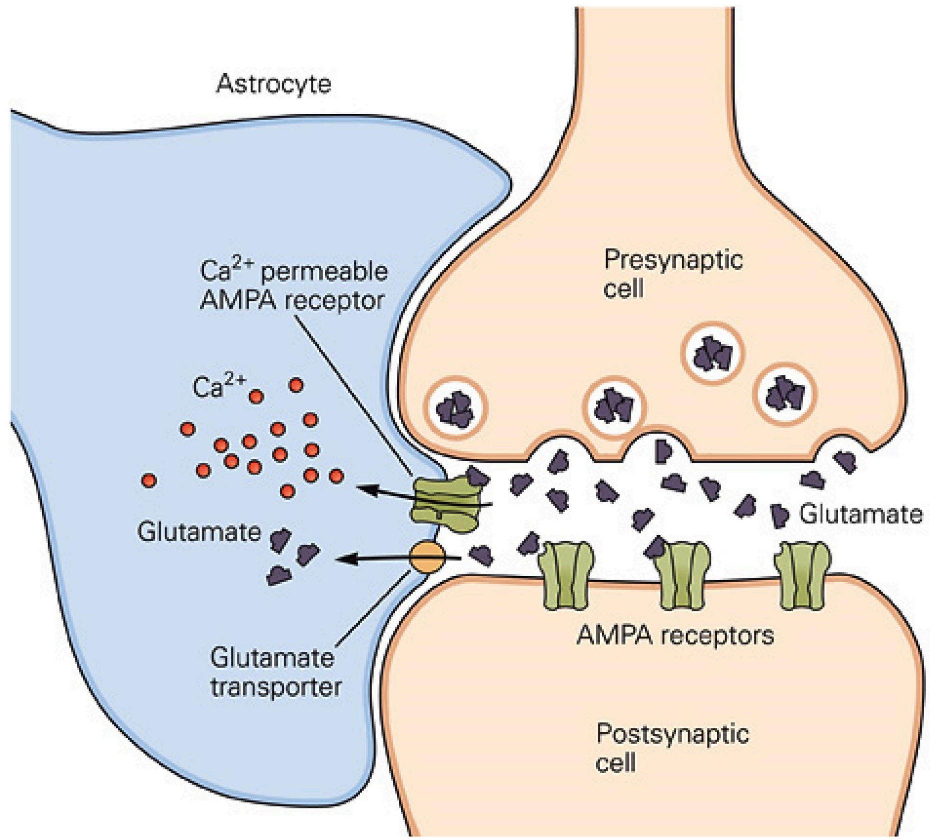
- Reside in white matter
- Contact and support nodes of Ranvier



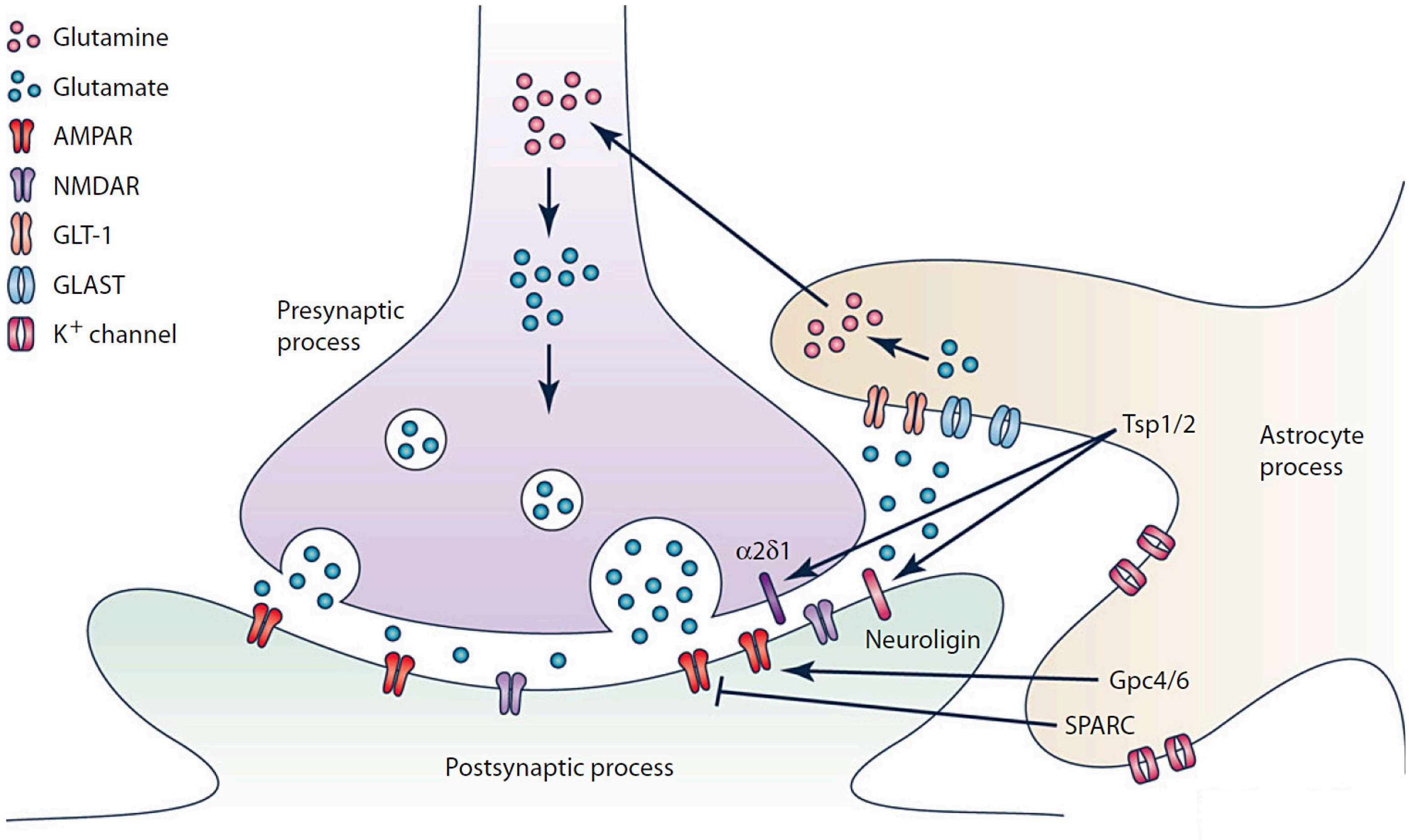
Protoplasmic Astrocytes

- Reside in gray matter
- Surround and envelop synapses
- Modulate synaptic transmission



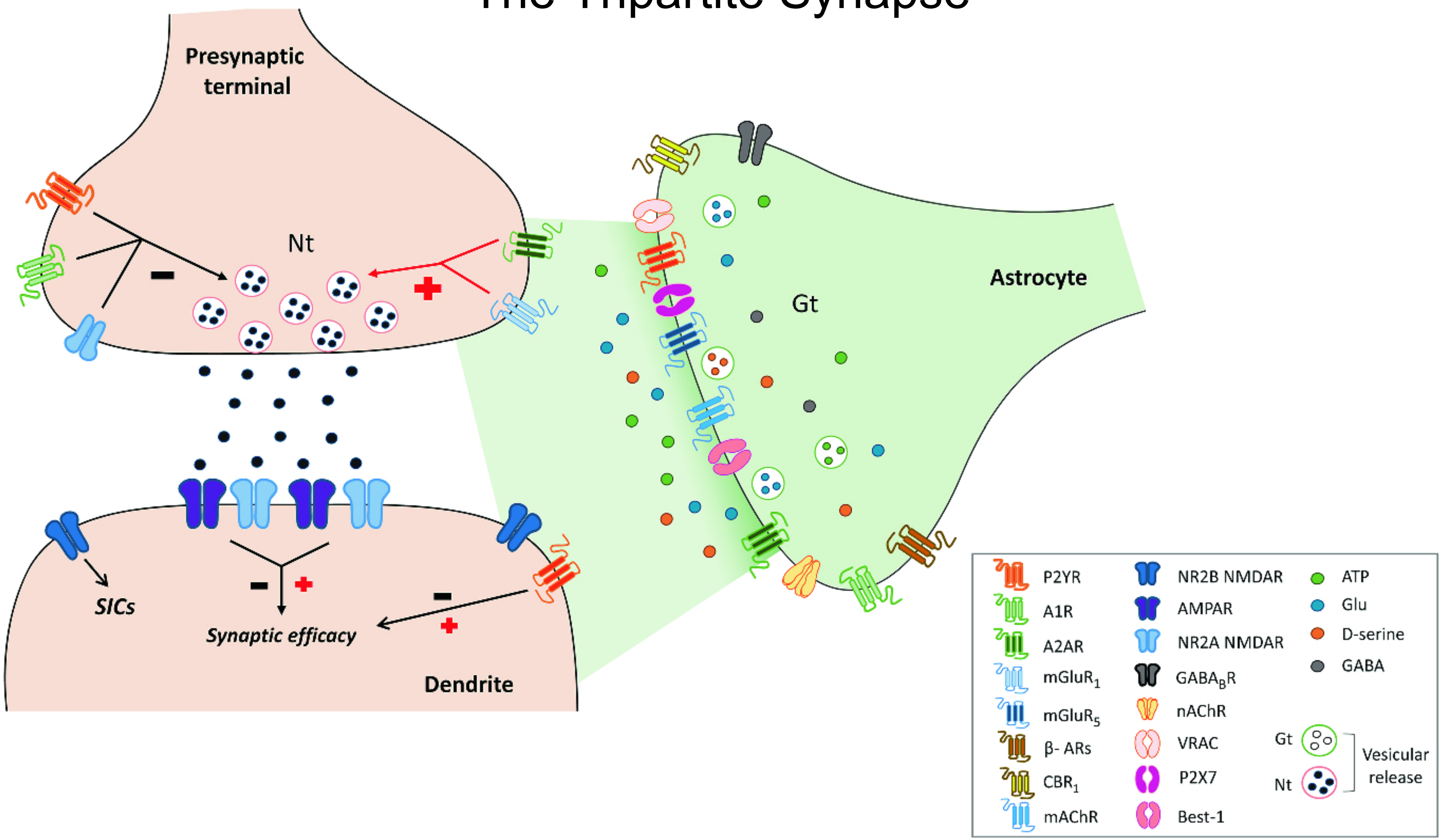


Protoplasmic Astrocytes Promote Synapse Formation

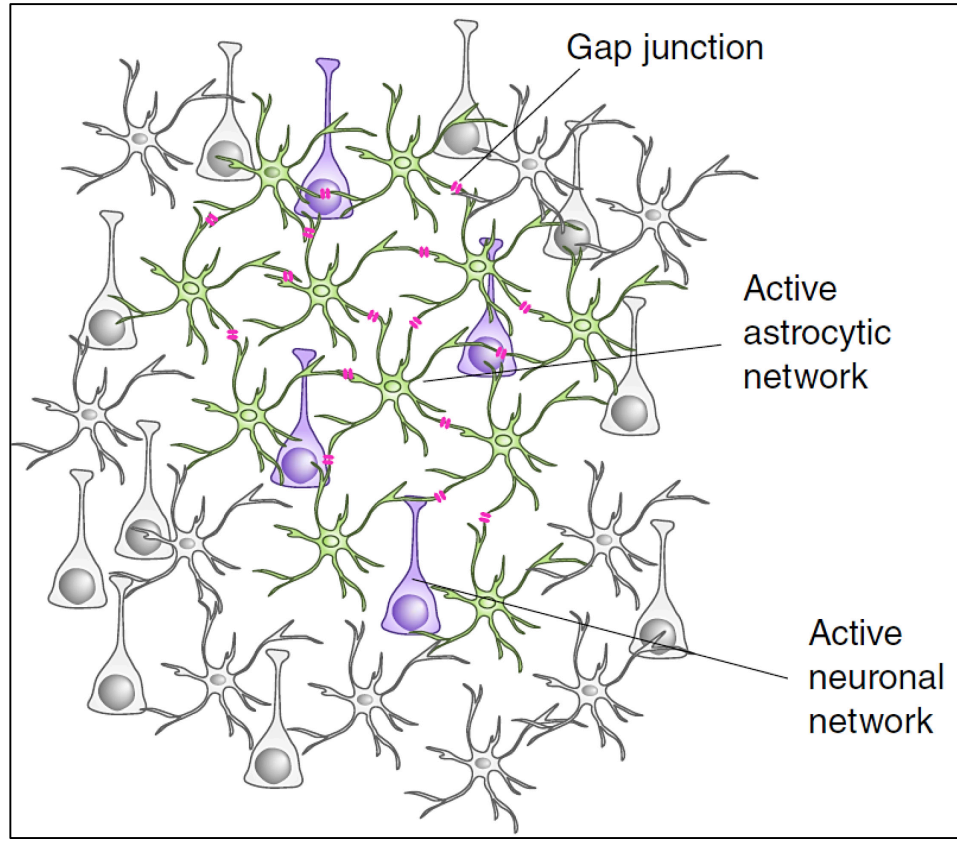


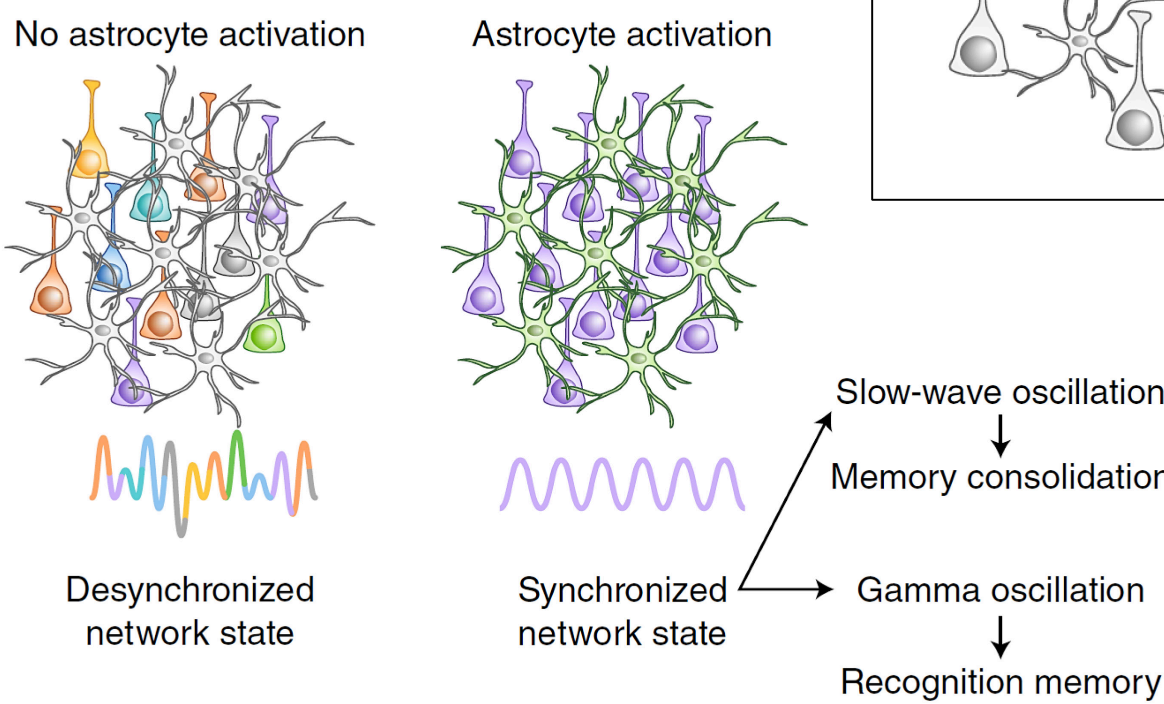
Protoplasmic Astrocytes Modulate Synaptic Activity

The Tripartite Synapse

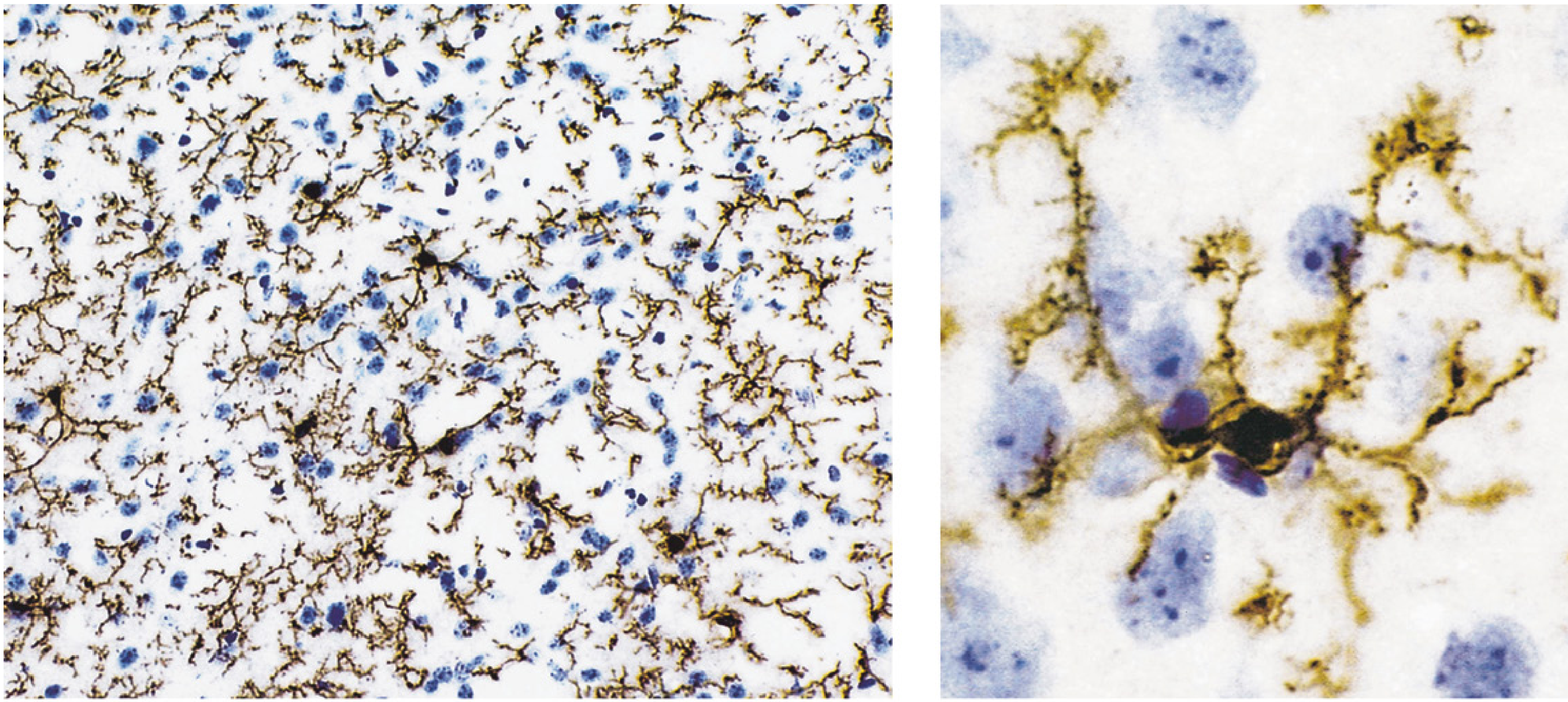


Astrocyte Syncytia Synchronize Neural Activity



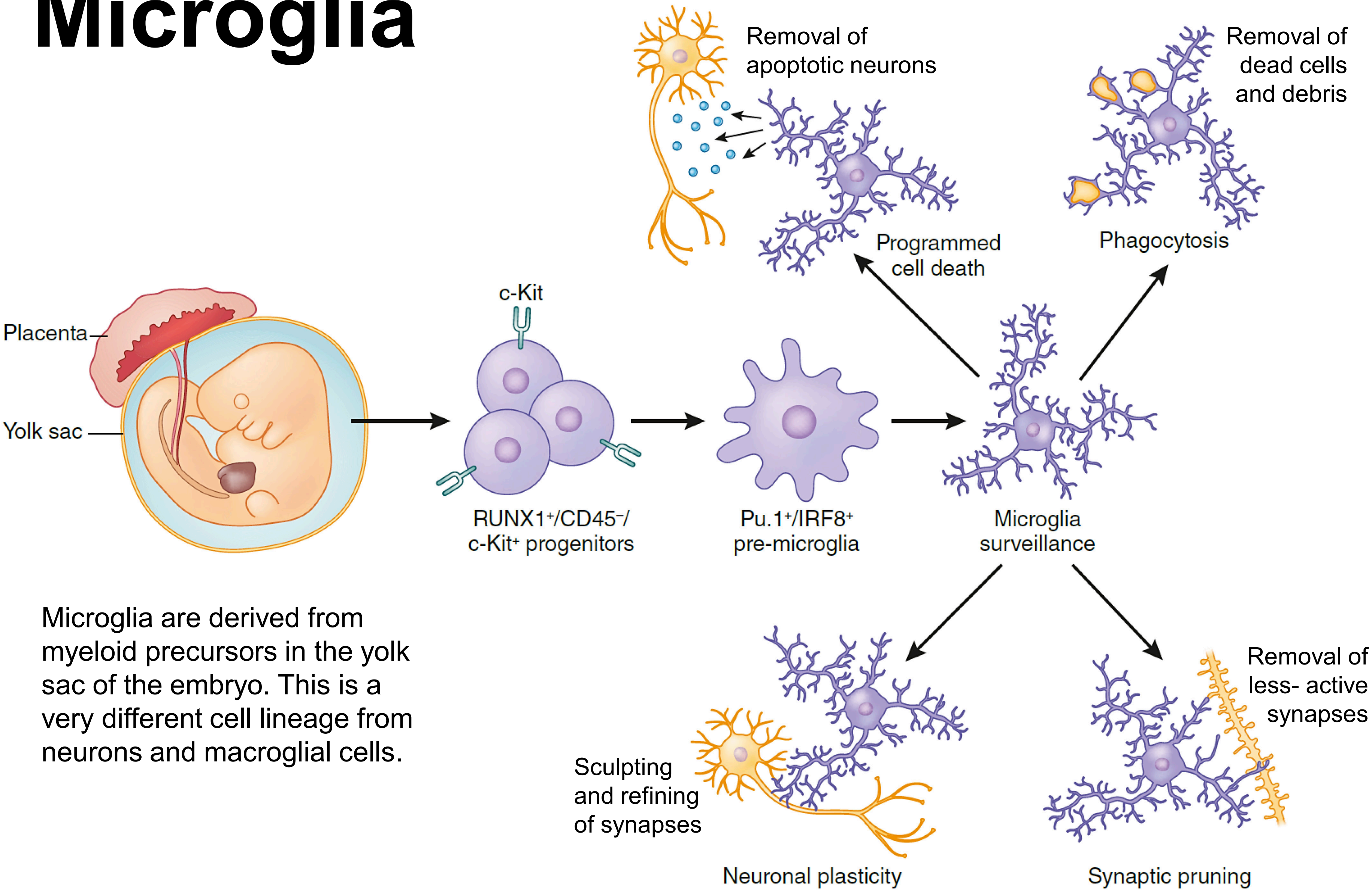


Microglial Cells



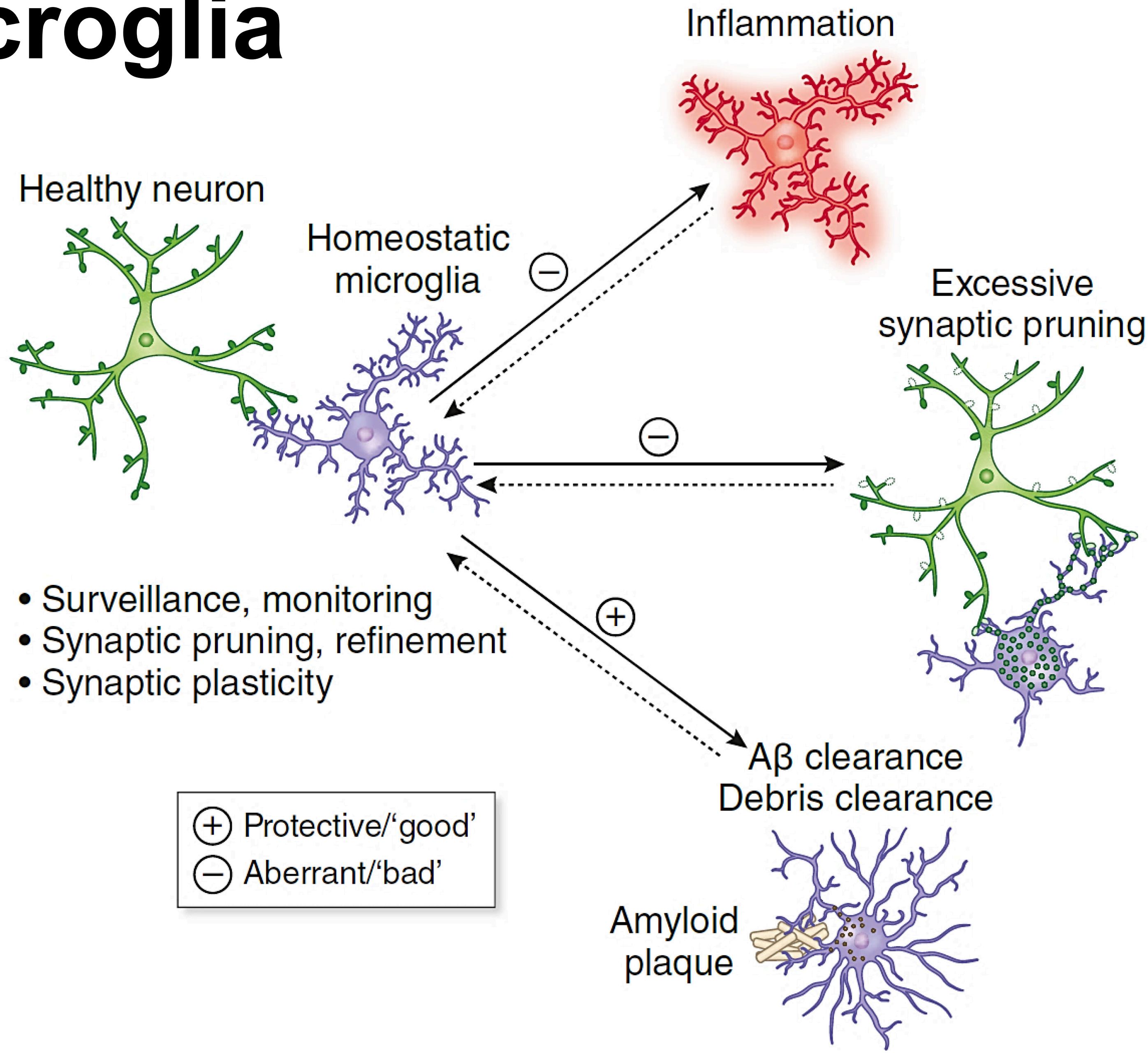
Phagocytic cells of the CNS that eliminate microbes, dead cells, redundant synapses, protein aggregates, and other particulate and soluble antigens that may endanger the CNS

Microglia

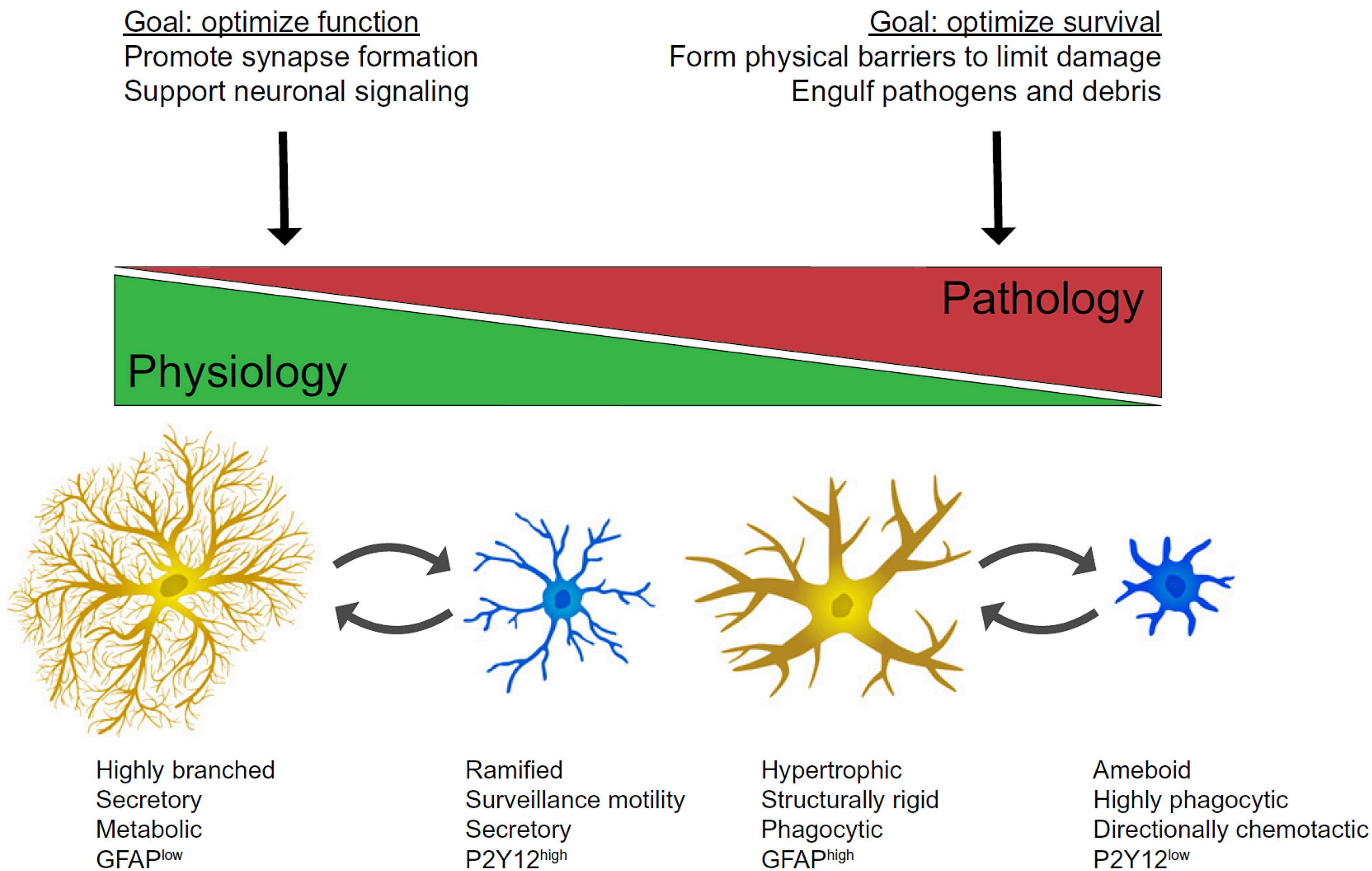


Microglia are derived from myeloid precursors in the yolk sac of the embryo. This is a very different cell lineage from neurons and macroglial cells.

Microglia


Inflammation
Healthy neuron
Homeostatic microglia
Excessive synaptic pruning
• Surveillance, monitoring
• Synaptic pruning, refinement
• Synaptic plasticity
Aβ clearance
Debris clearance
Amyloid plaque
⊕ Protective/‘good’
⊖ Aberrant/‘bad’

Activation of Astrocytes and Microglia Following Injury



Glia to Neuron Ratio

Reports of Glia-Neuron Ratios (GNRs) and Non-Neuron-Neuron Ratios (nNNRs) in Human Cerebral Cortex, Gray Matter (GM) Only, Unless Indicated

GNR	nNNR	Comments	Author	Year
~2		adult: 1.04-2.3, newborn: 0.14-0.2	Muhlmann	1936
1.2-2.1		Adult Superior Frontal Gyrus, all layers	Arutyunova	1938
1.24-1.98		Human Cortex	Friede	1953
1.24-1.98		Human Cortex, layers II-VI	Friede	1954
1.78		Human cortex, layers II-VI	Hawkins & Olszewski	1957
2.9-3.5	4.4-5.2	Striate cortex, GM+WM	Nurnberger & Gordon	1957
0.74-6.6		tabulated by Blinkov and Glezer, 1968 (p. 416)	Schlote	1959
10		No primary data or reference provided	Hyden & Pigon	1960
2		"Human Cortex"	Cragg	1968
2.3		Frontal cortex	Hess & Thalheimer	1971
0.49-0.57		Frontal/parietal cortex (control)	Diamond et al.	1985
0.86-1.09		Frontal/parietal cortex (Albert Einstein)	Diamond et al.	1985
1-1.5		Visual cortex	Leuba & Garey	1989
1.56-2.02		Males and Females, 18-98 years old	Pakkenberg et al.	2003
1.37		Neocortex without archicortex, 60-98 years old	Pelvig et al.	2003
1.65		Frontal cortex, layers II/III	Sherwood et al.	2006
1.32-1.49		Females-Males, 18-93 years old	Pelvig et al.	2008
1.48-1.05[1]	3.72	in GM only	Azevedo et al.	2009
2.48		in GM+WM	Azevedo et al.	2009
1.64-1.15[1]	4.31	in GM only	Andrade-Moraes et al.	2013
3.01		in GM+WM	Andrade-Moraes et al.	2013
	1.2-3.6	for GM, not including WM	Ribeiro et al.	2013

GM, gray matter; GNR, glia-neuron ratio; nN, non-neuronal cells; N, neurons; nNNr, non-neuronal-neuron ratio; WM, white matter.
[1]Based on a 2:1 ratio of glia to endothelial cells (References: 27-30%: Nurnberger, 1958; Blinkov and Glezer, 1968; Brasileiro-Filho et al., 1989; Lyck et al., 2009; Garcia-Amado and Prensa, 2012).

The glia to neuron ratio is about 1.5 to 1 in the Human Cerebral Cortex.
If white matter is included, the glia to neuron ratio is about 3 to 1.

Percentage of Glial Cell Types

Types of Glial Cells Contributing to the Total Number of Glia in the Human Brain

Oligodendrocytes	Astrocytes	Microglia	Comments	Authors	Year
29%	61.5%	9.5%	Visual Cortex	Kryspin-Exner	1952
40%	54%		Caudatum	Kryspin-Exner	1952
57%			Pallidum	Kryspin-Exner	1952
52-74%	30-40%	6-8%	Thalamus	Kryspin-Exner	1952
77.5%			Nucleus ruber	Kryspin-Exner	1952
62%			Substantia nigra, pc	Kryspin-Exner	1952
29-77.5%	30-61.5%	6-9.5%	various regions Review of Kryspin-Exner's work	Glees	1955
51%	40%	9%	Motor Cortex, layer V	Brownson	1956
45%	45%	10%	GM	Pope	1958
<67%	>23%	10%	WM	Pope	1958
52%	39%	9%	Motor Cortex	Windle (Brownson)	1958
45%	45%	10%	GM	Windle (Pope)	1958
67%			WM	Windle (Pope)	1958
36.6%	46.5%	16.8%	Frontal Cortex GM	Pope	1959
69%	24%	6.9%	Frontal Cortex WM	Pope	1959
50.9%[1]	40.8%[1]	16.7%[2]	Frontal Cortex	Schlote	1959
45%	45%	10%	Cortex	Blinkov & Glezer	1968
24.5-69.2%[1]	25.6-63.2%[1]	9-28.1%[2]	Data: Schlote, 1959	Hess & Thalheimer	1971
75%	19%		Neocortex GM	Pelvig et al.	2003
5%	80%	10-15%	CNS	Verkhratsky & Butt	2007
74.6-75.6%	17.3-20.2%	5.2-6.5%	Males, females Neocortex (GM)	Pelvig et al.	2008
		15-18%	Males, Neocortex	Lyck et al.	2009
75%	20%	5%	Neocortex (GM)	Verkhratsky & Butt	2013

GM, gray matter; WM, white matter; studies reporting primary data are shaded in gray.