BMD ENG 301
Quantitative Systems Physiology
(Nervous System)

Lecture 4: Glial Cells

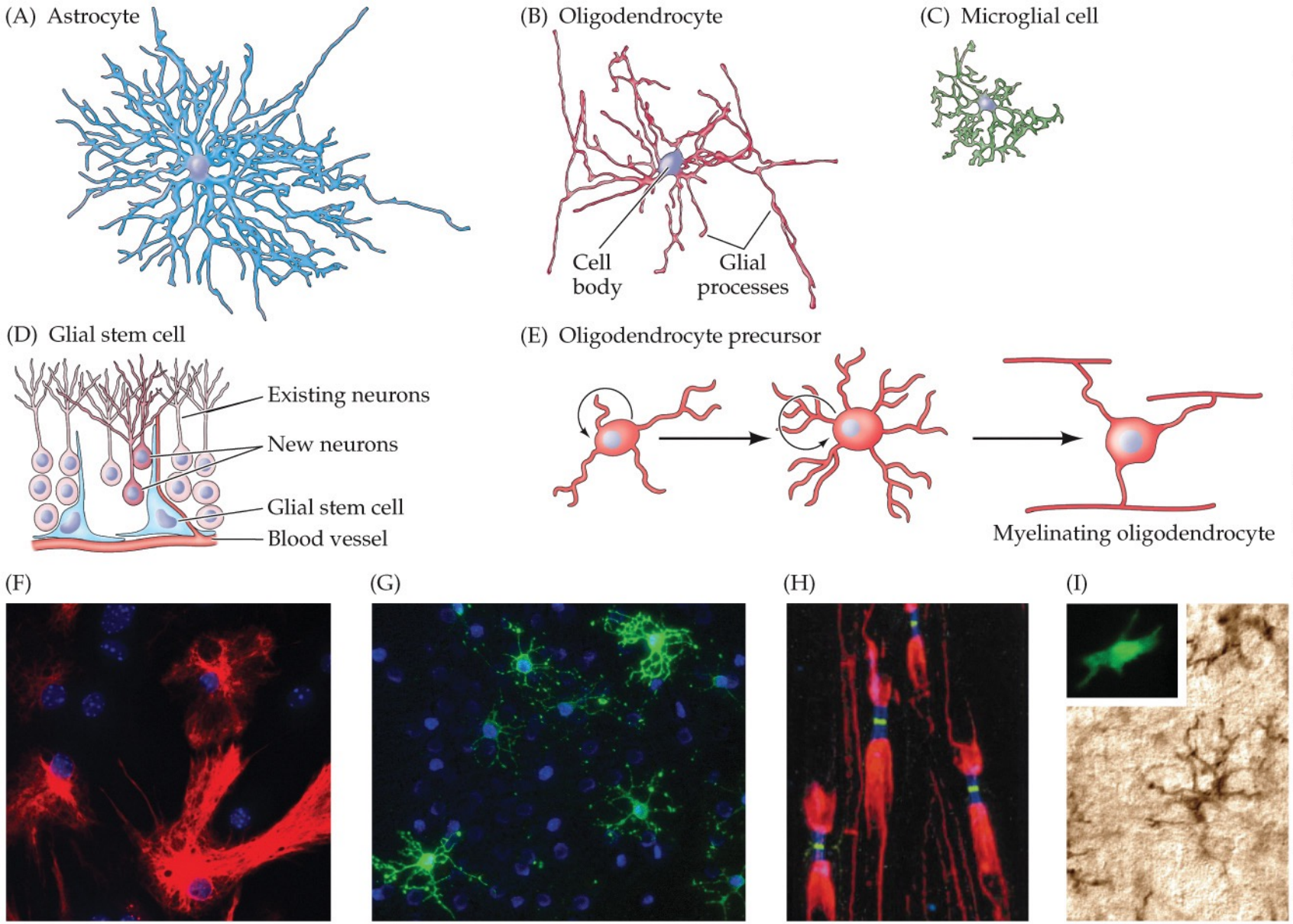
Professor Malcolm A. MacIver

Quote of the day

The best time to plant a tree is 20 years ago

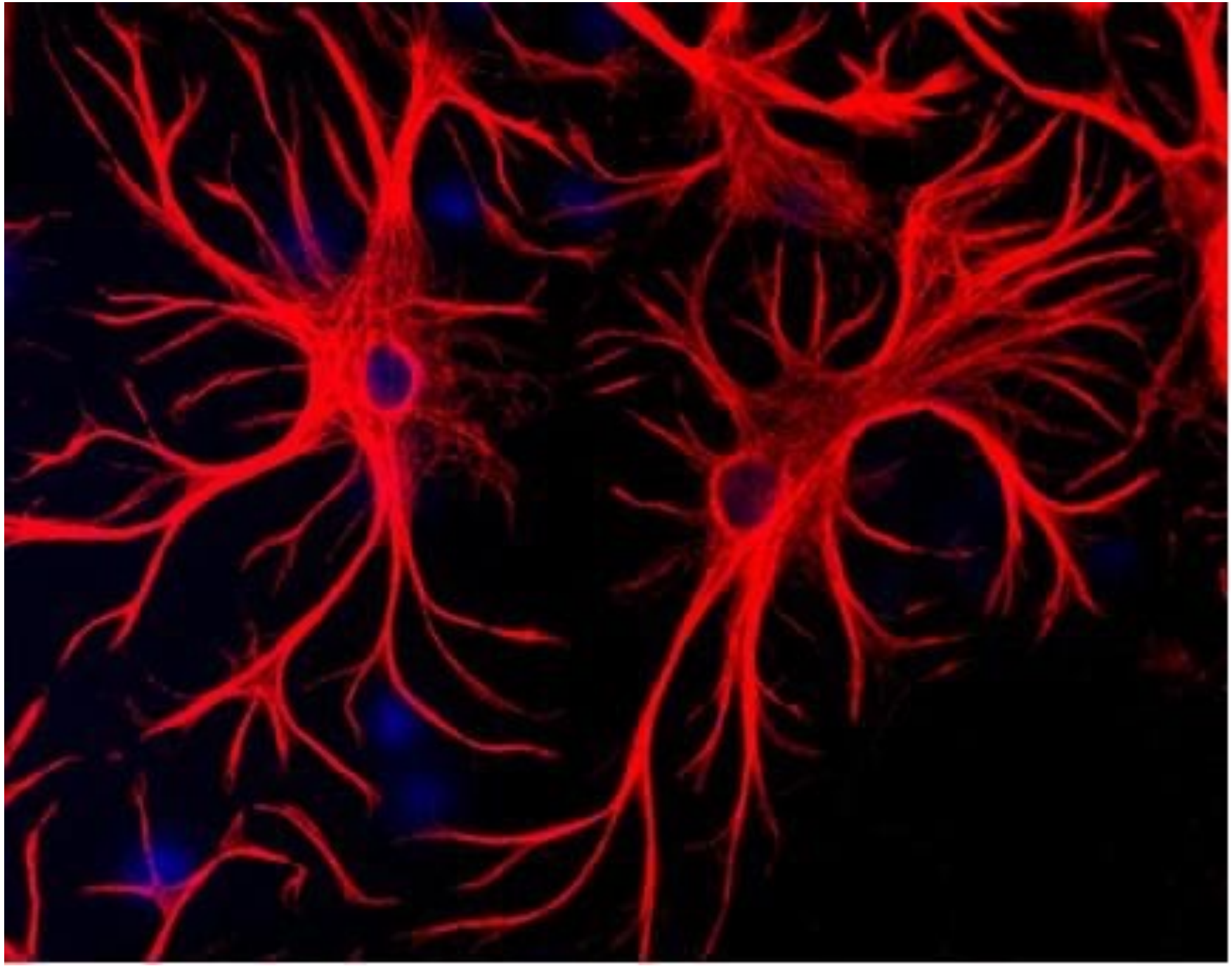
The second best time is right now

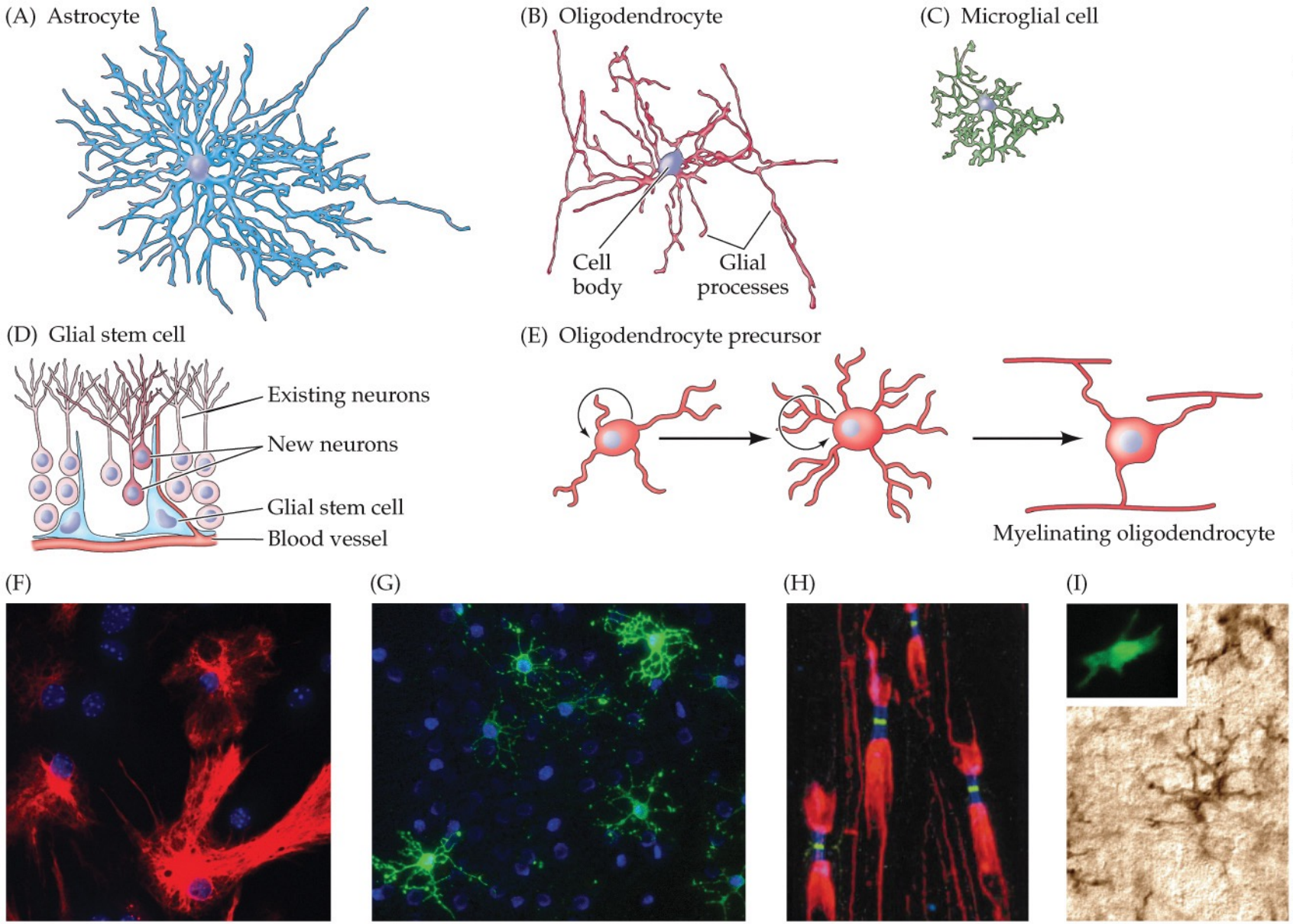
Chinese Proverb



A–C from Jones and Cowan (1983) *The Structural Basis of Neurobiology*. New York: Elsevier: 282–370. D, E from Nishiyama et al. (2009) *Nature Rev. Neurosci.* 10: 9–22. F,G courtesy of A.-S. LaMantia. H: From Bhat et al. (2001) *Neuron* 30(2): 369–383. I courtesy of A. Light. (inset) Courtesy of G. Matsushima.

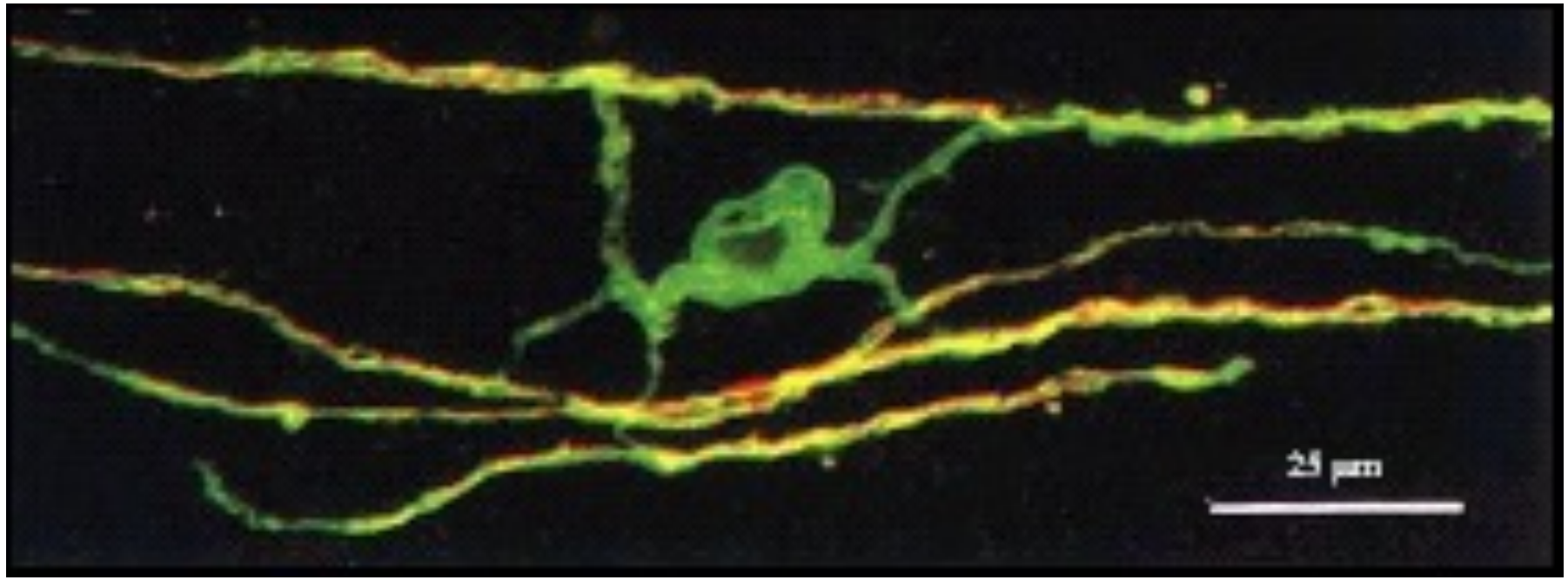
***NEUROSCIENCE 6e*, Figure 1.5**

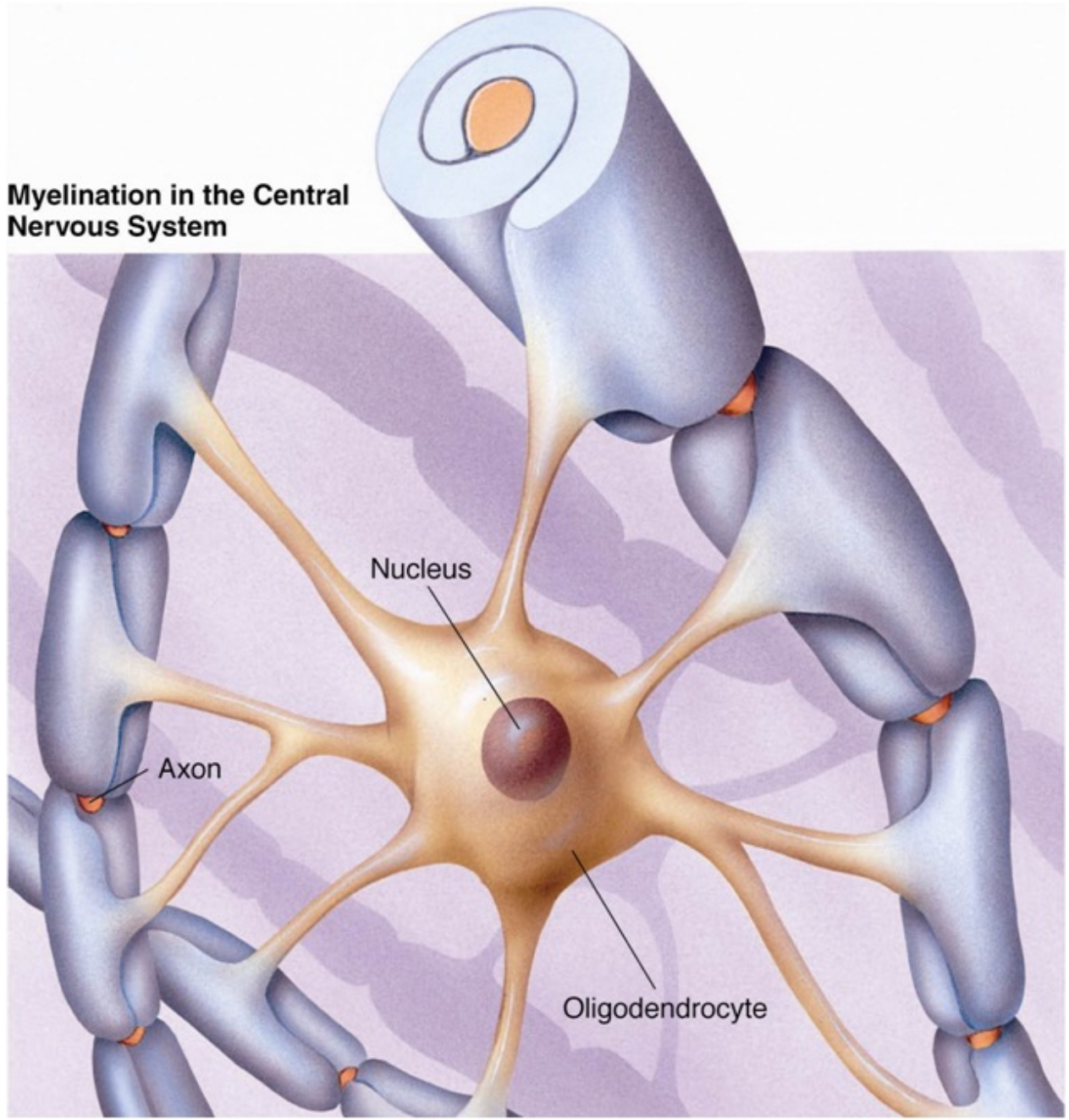


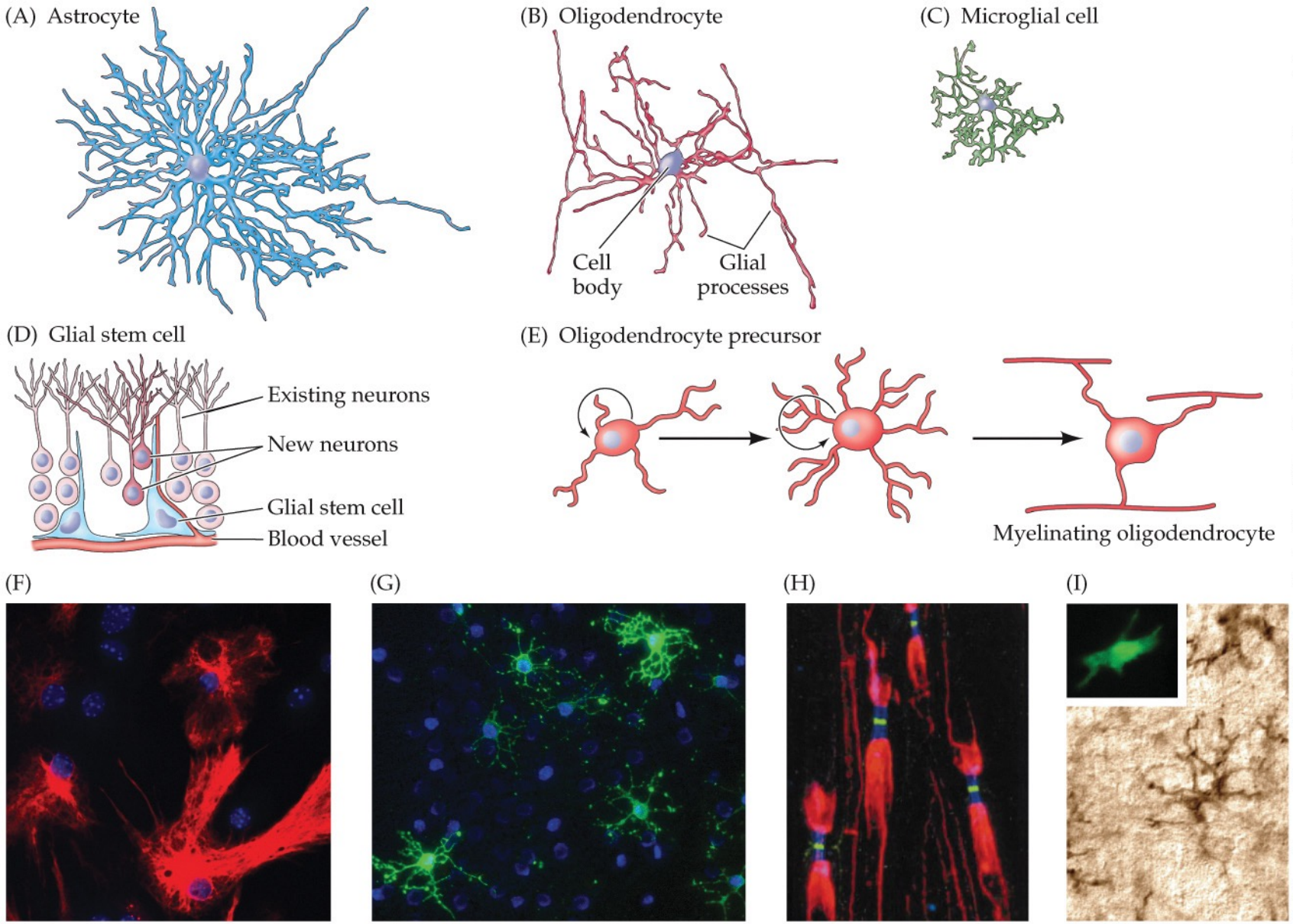


A–C from Jones and Cowan (1983) *The Structural Basis of Neurobiology*. New York: Elsevier: 282–370. D, E from Nishiyama et al. (2009) *Nature Rev. Neurosci.* 10: 9–22. F,G courtesy of A.-S. LaMantia. H: From Bhat et al. (2001) *Neuron* 30(2): 369–383. I courtesy of A. Light. (inset) Courtesy of G. Matsushima.

***NEUROSCIENCE 6e*, Figure 1.5**


25 µm


Myelination in the Central Nervous System
Nucleus
Axon
Oligodendrocyte



A–C from Jones and Cowan (1983) *The Structural Basis of Neurobiology*. New York: Elsevier: 282–370. D, E from Nishiyama et al. (2009) *Nature Rev. Neurosci.* 10: 9–22. F,G courtesy of A.-S. LaMantia. H: From Bhat et al. (2001) *Neuron* 30(2): 369–383. I courtesy of A. Light. (inset) Courtesy of G. Matsushima.

***NEUROSCIENCE 6e*, Figure 1.5**

Microglia

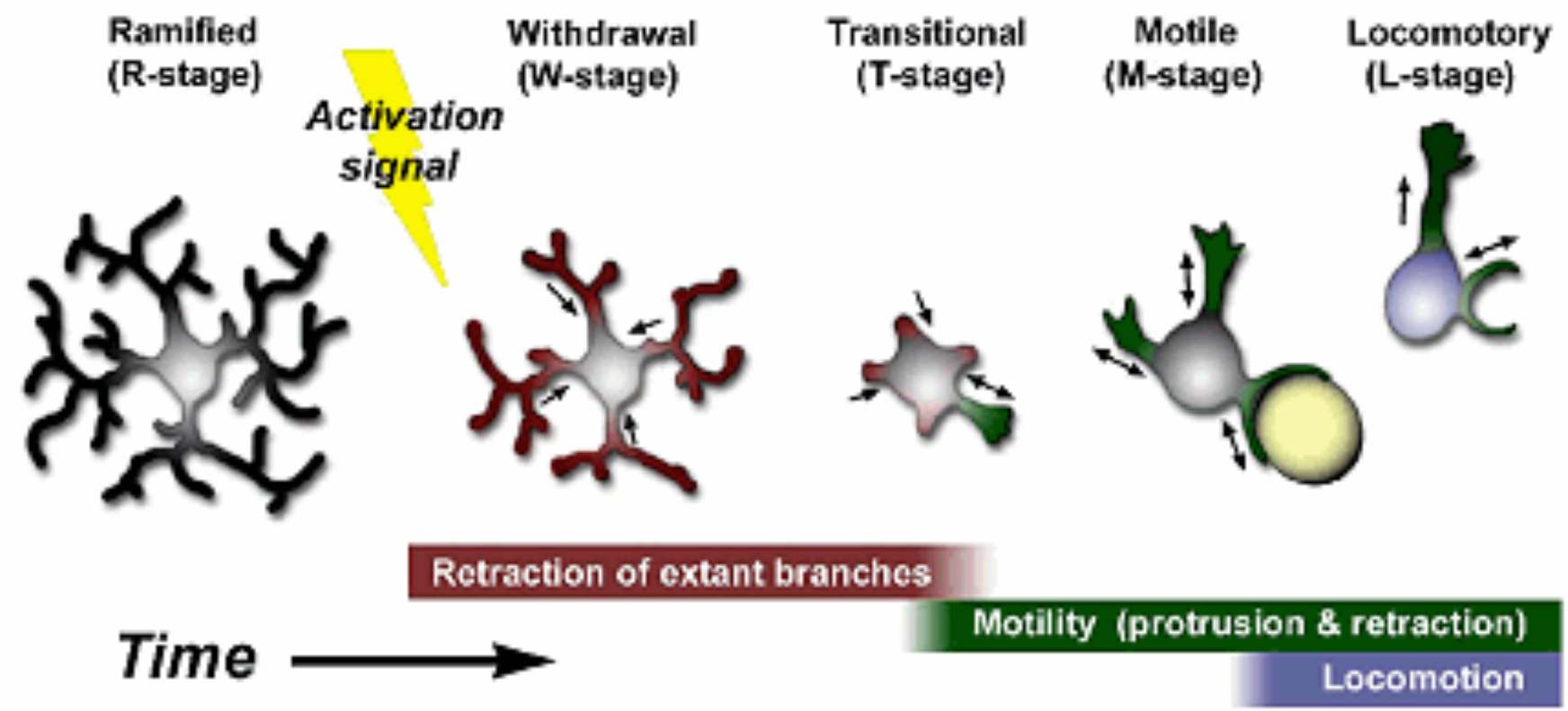
CNS emergency response team

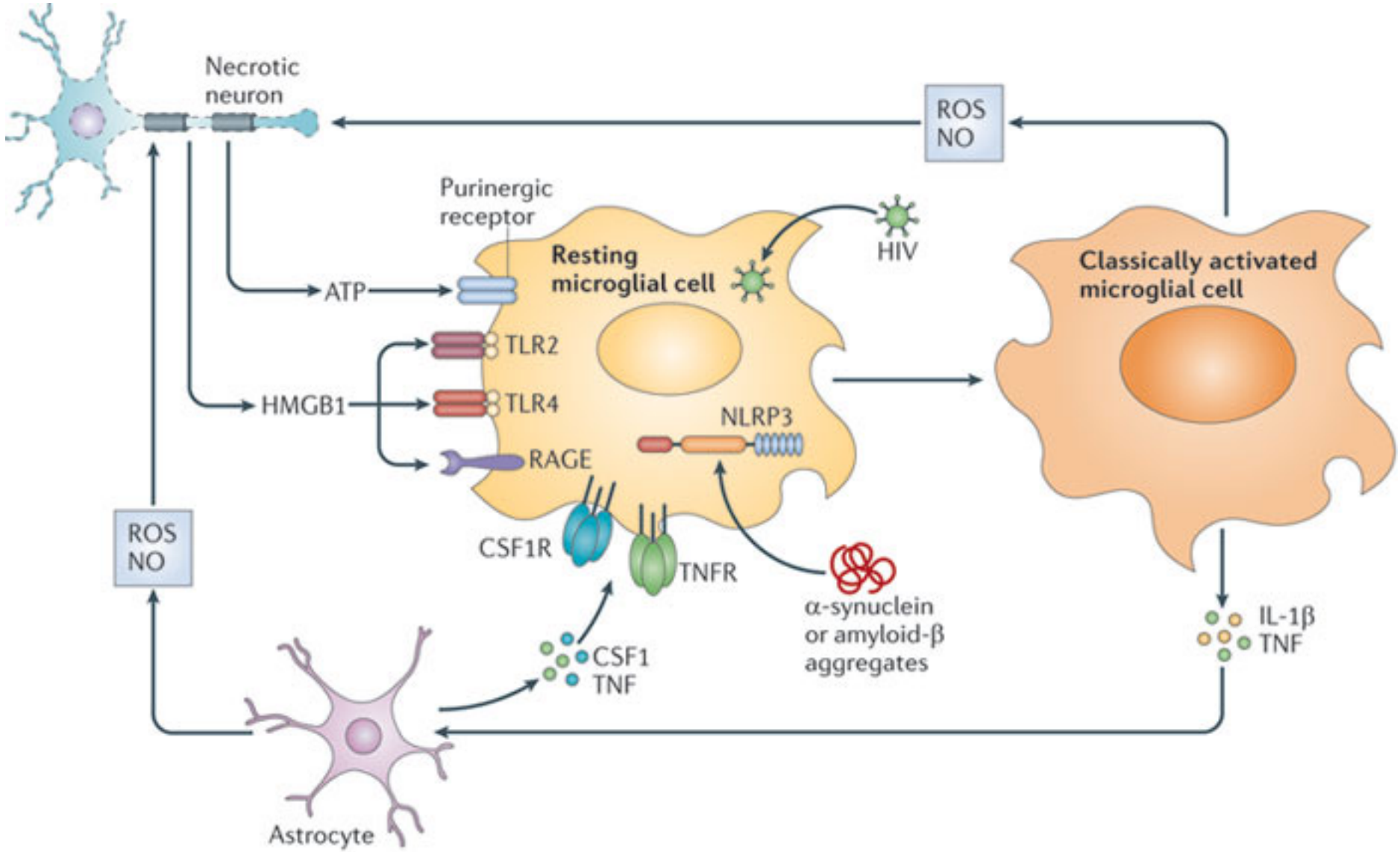
Microglial Cell

Cleaning To Do List

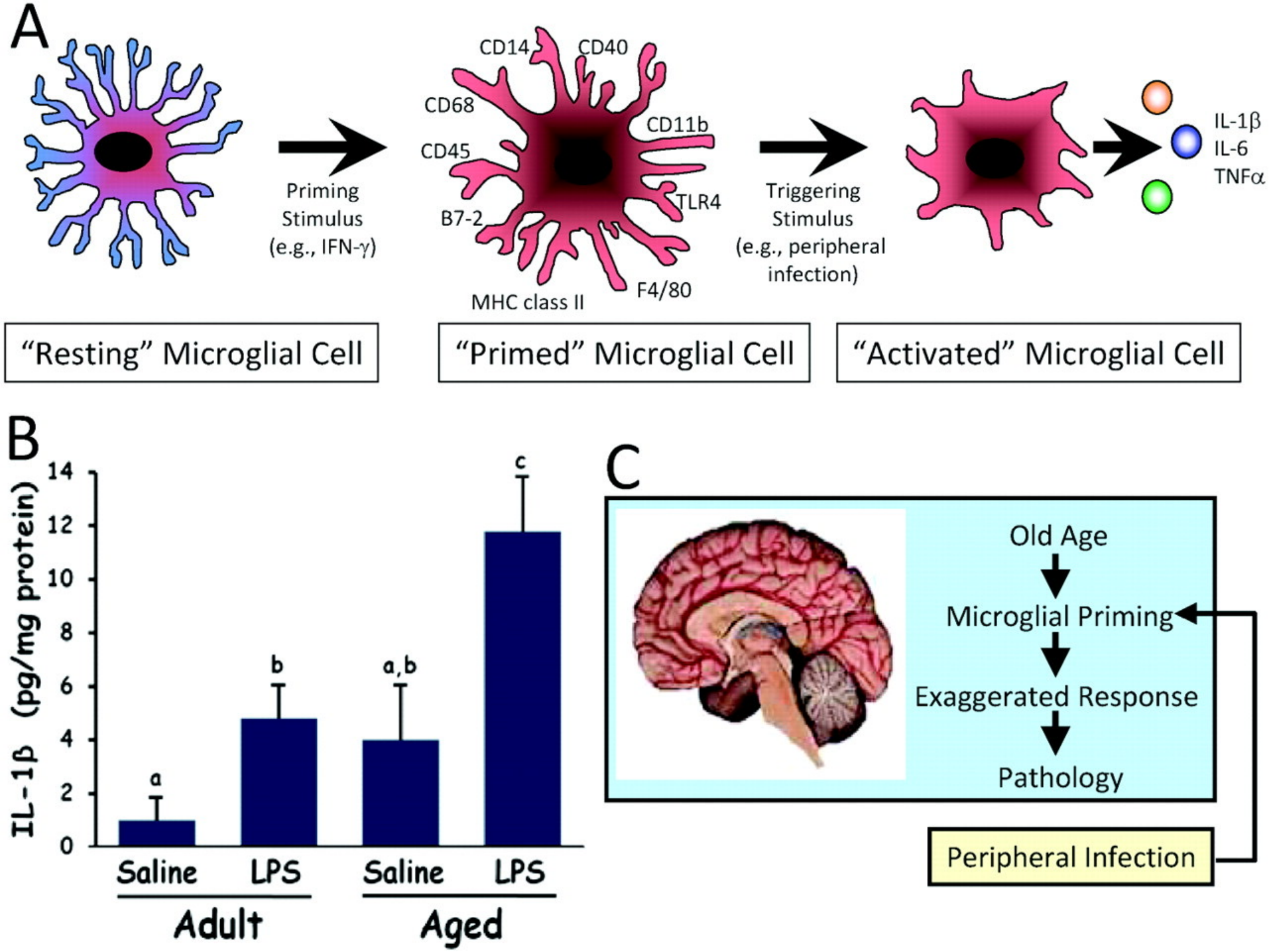
- Remove injured cells
- Fight infections
- Eliminate memories

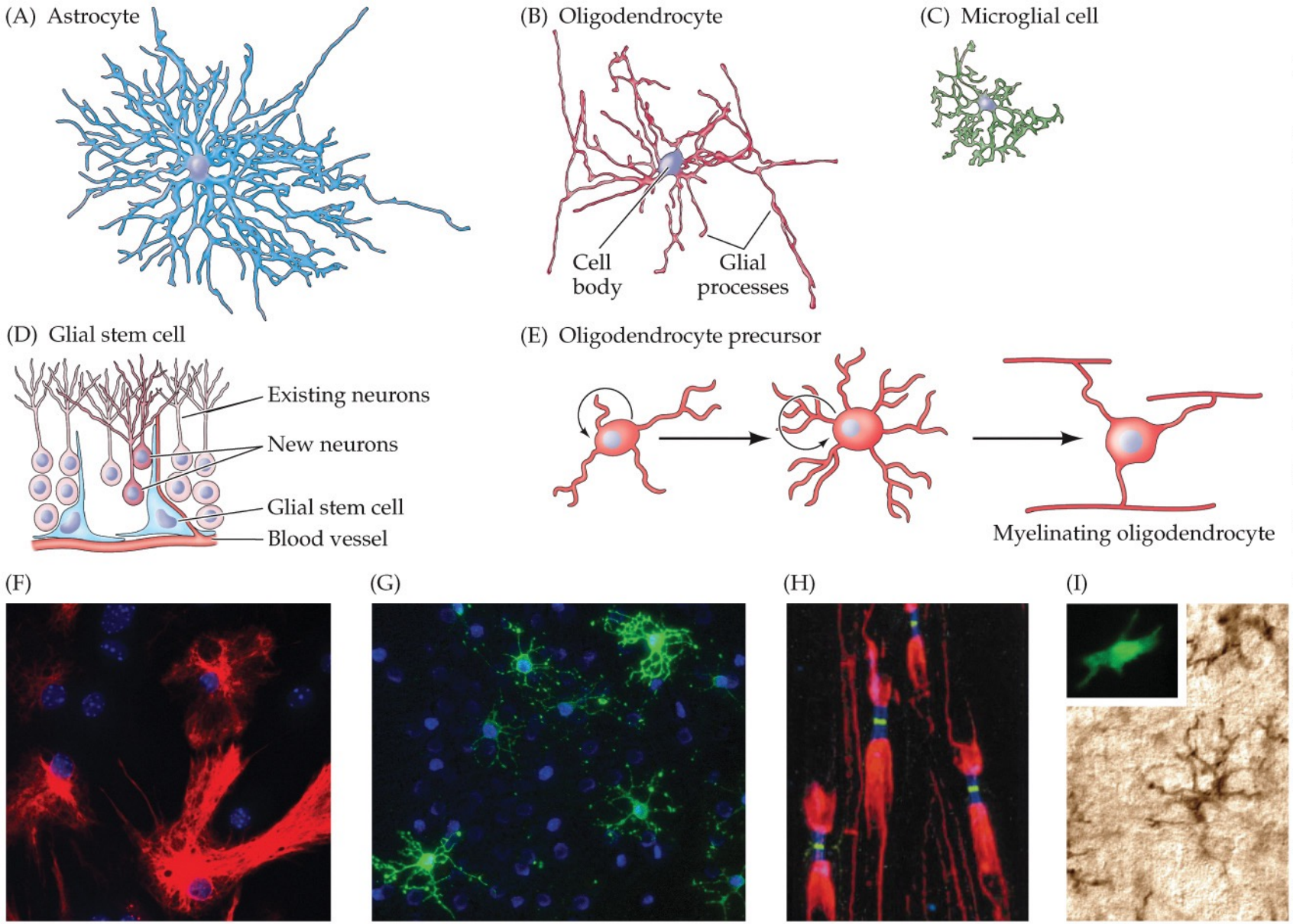
Microglial activation sequence





Nature Reviews | Immunology

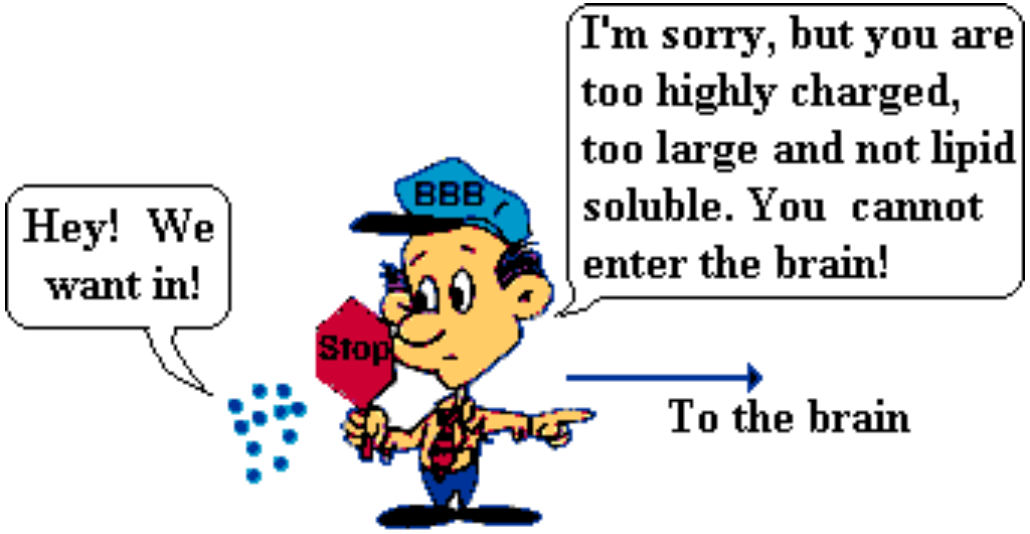

A
CD14
CD40
CD68
CD11b
CD45
TLR4
B7-2
MHC class II
F4/80
Priming Stimulus (e.g., IFN-γ)
Triggering Stimulus (e.g., peripheral infection)
IL-1β
IL-6
TNFα
"Resting" Microglial Cell
"Primed" Microglial Cell
"Activated" Microglial Cell
B
IL-1β (pg/mg protein)
0
2
4
6
8
10
12
14
a
b
a,b
c
Saline
LPS
Saline
LPS
Adult
Aged
C
Old Age
Microglial Priming
Exaggerated Response
Pathology
Peripheral Infection

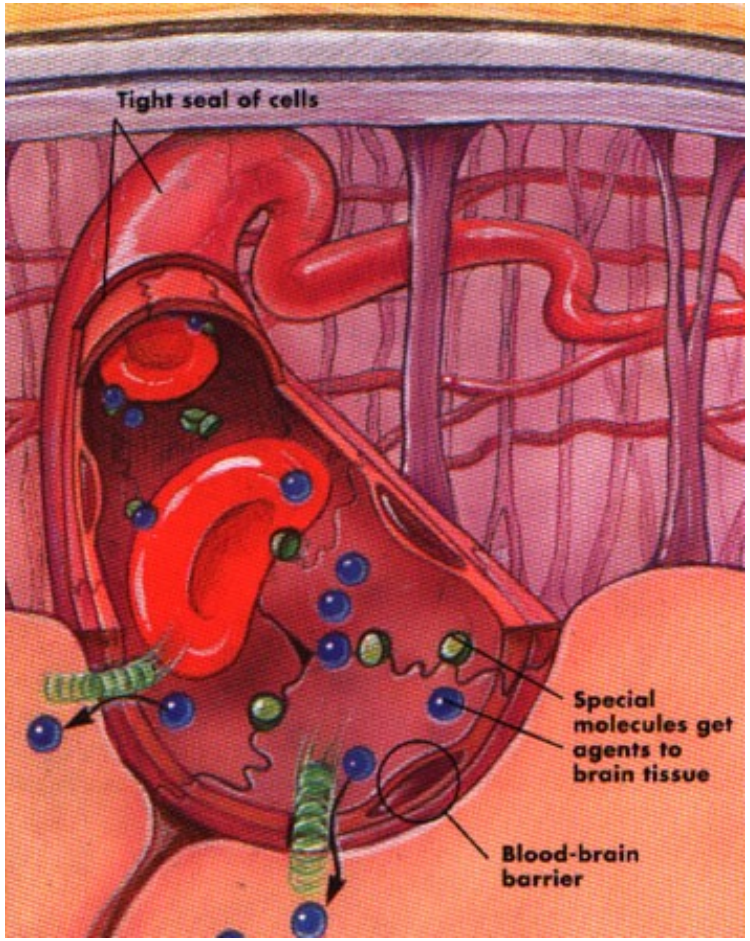


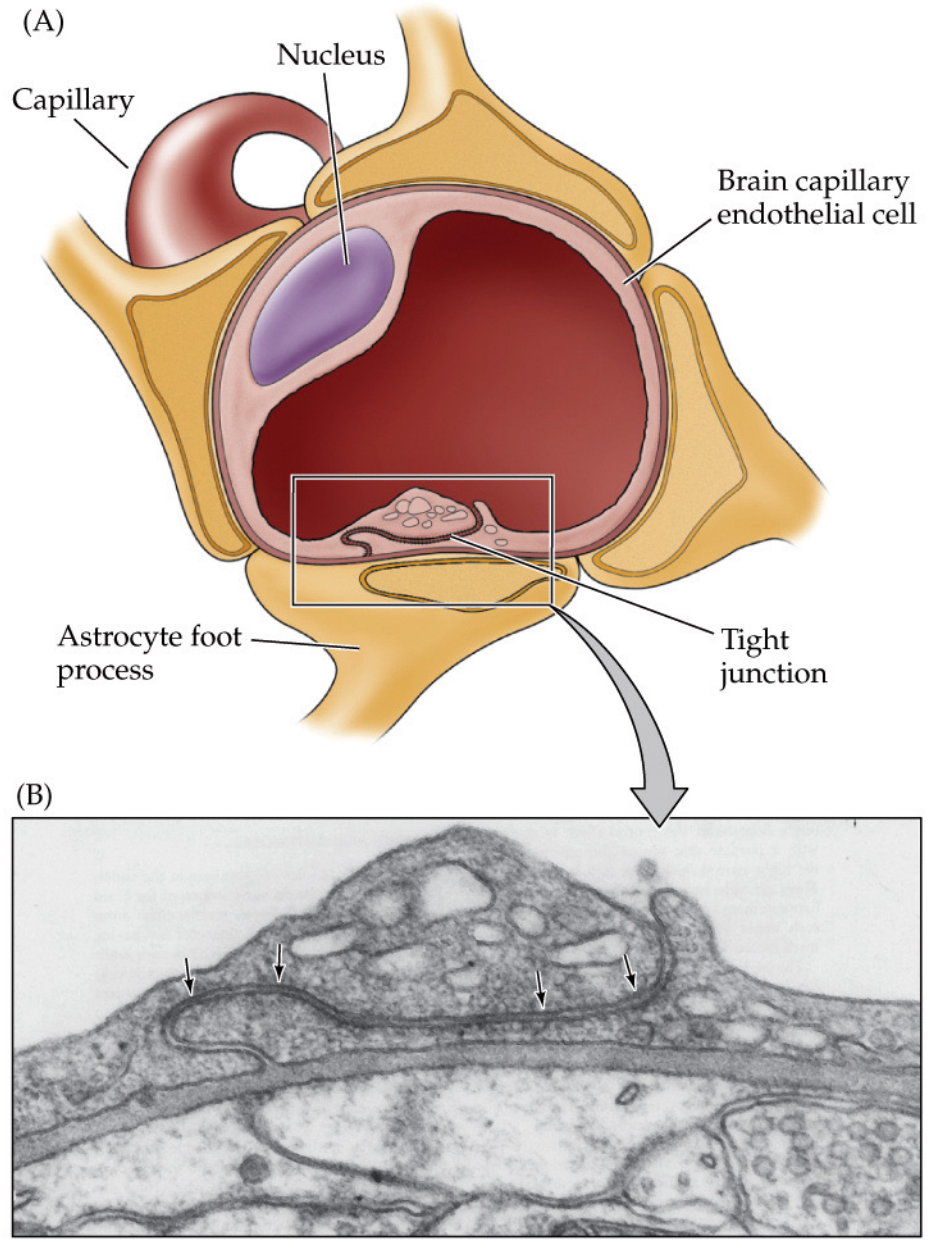
A–C from Jones and Cowan (1983) *The Structural Basis of Neurobiology*. New York: Elsevier: 282–370. D, E from Nishiyama et al. (2009) *Nature Rev. Neurosci.* 10: 9–22. F,G courtesy of A.-S. LaMantia. H: From Bhat et al. (2001) *Neuron* 30(2): 369–383. I courtesy of A. Light. (inset) Courtesy of G. Matsushima.

***NEUROSCIENCE 6e*, Figure 1.5**

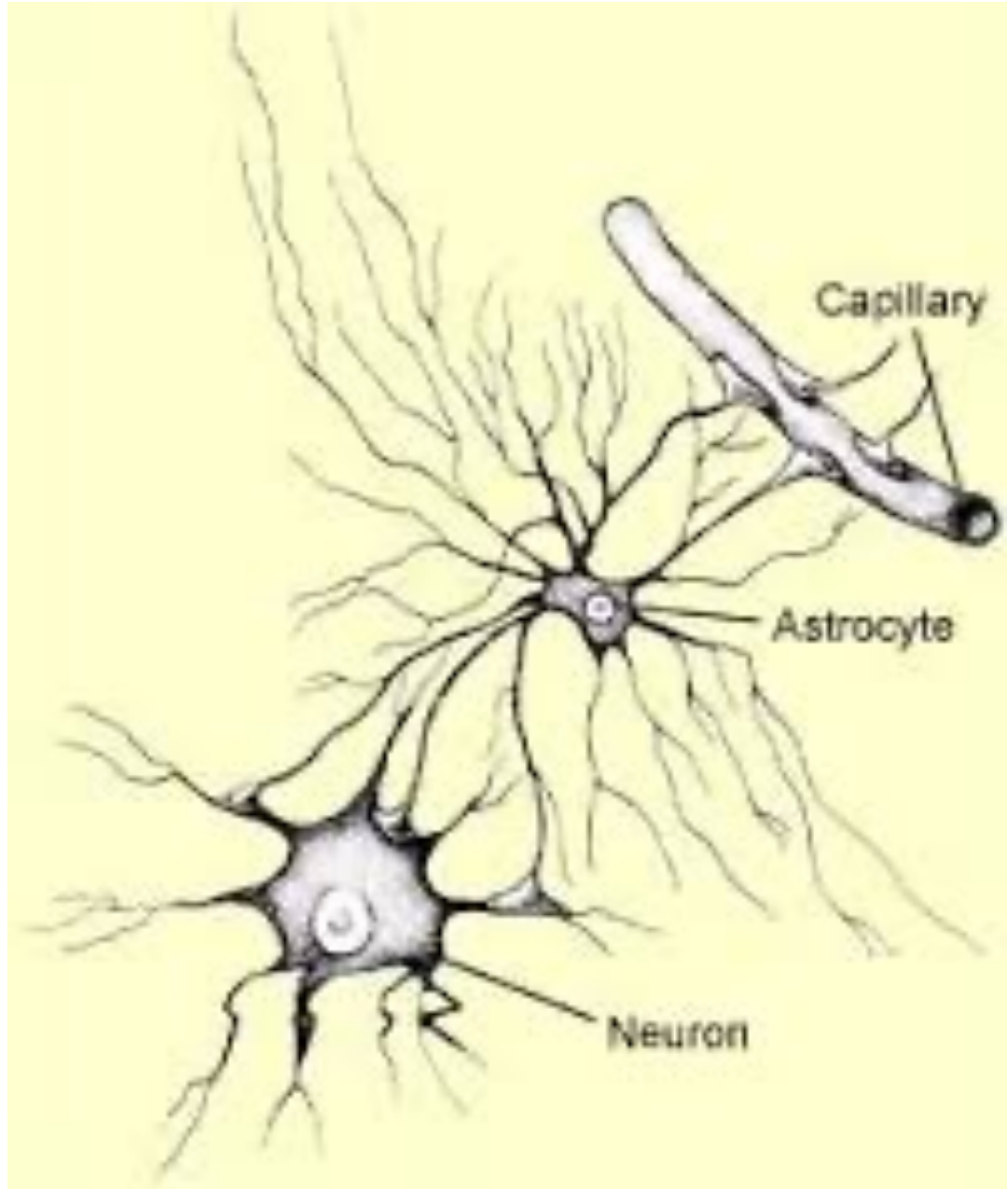
Blood-brain barrier

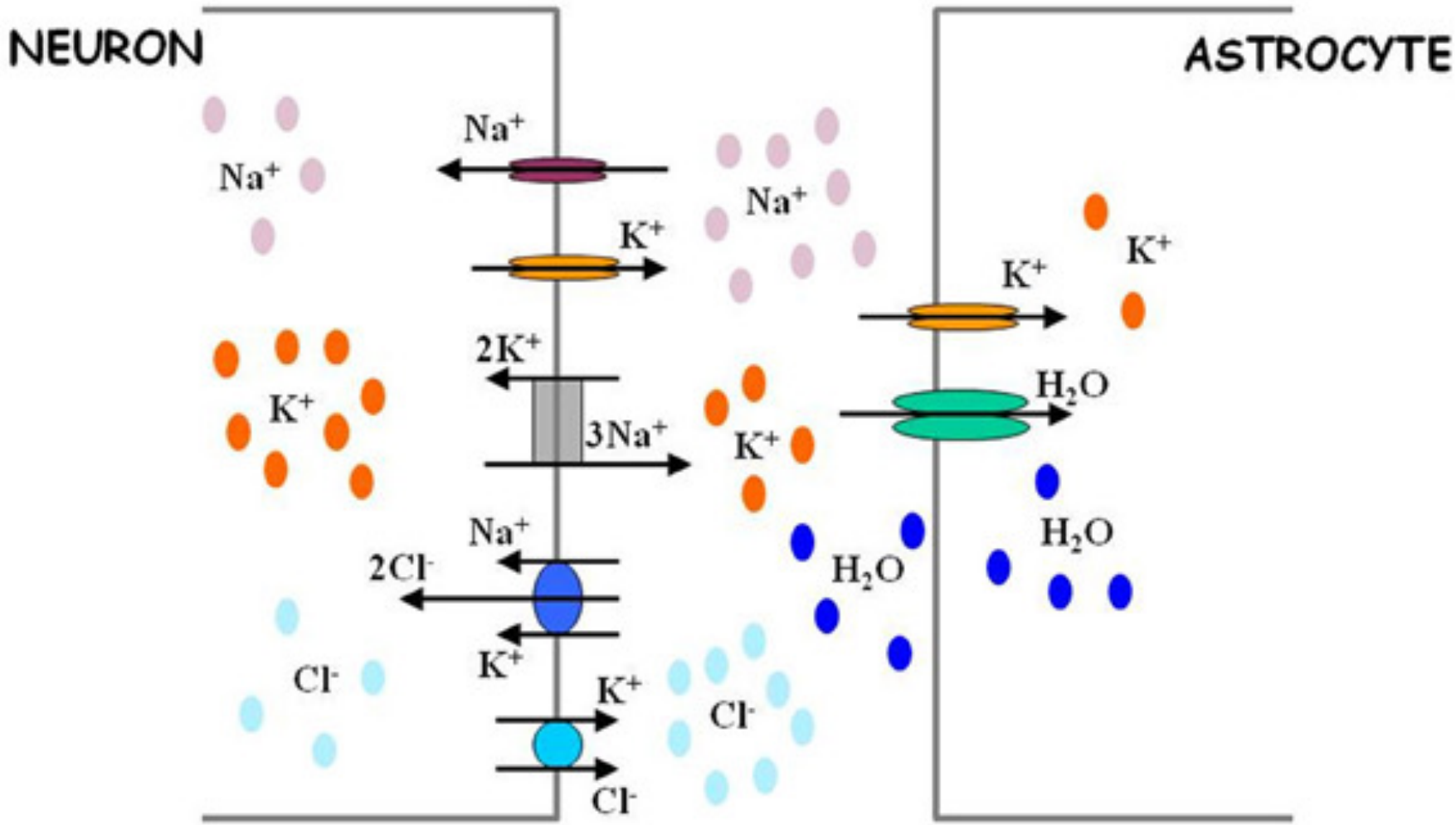


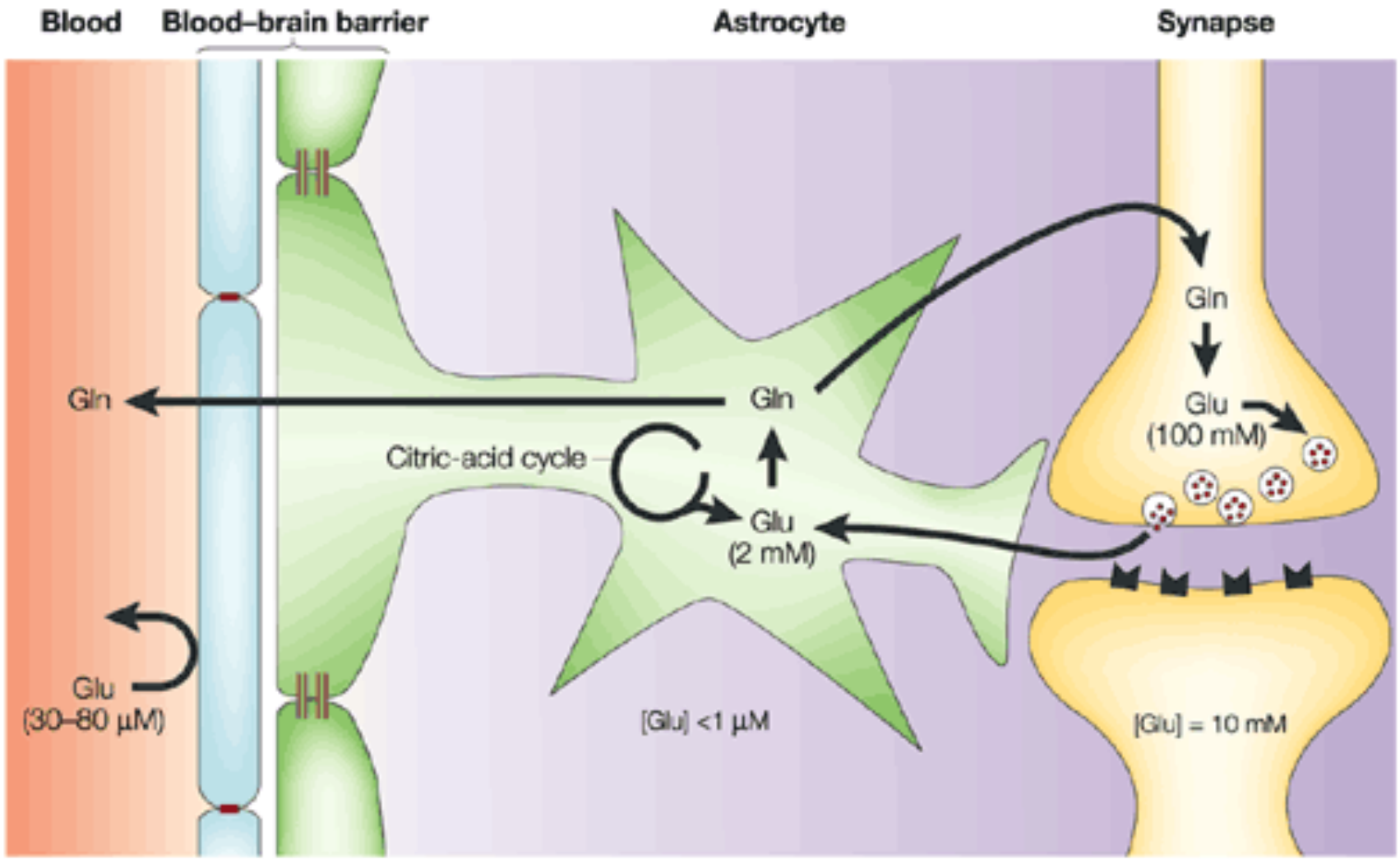




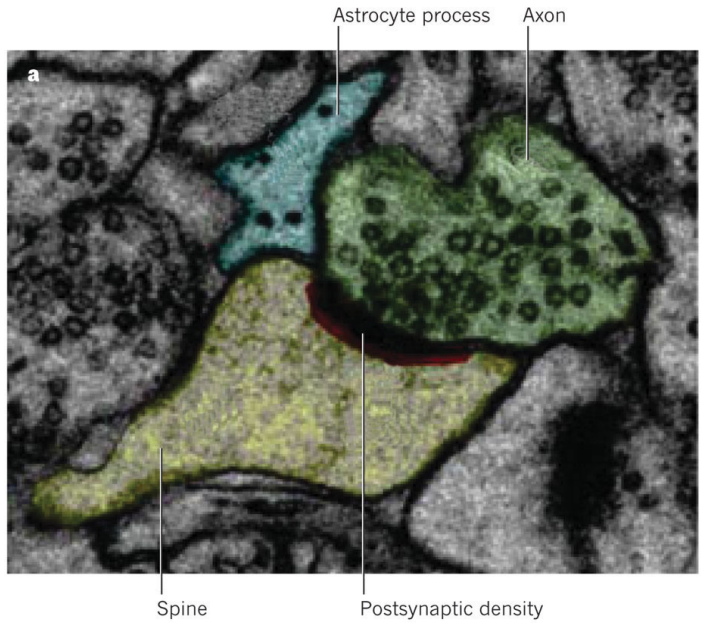
NEUROSCIENCE 6e, Figure A22

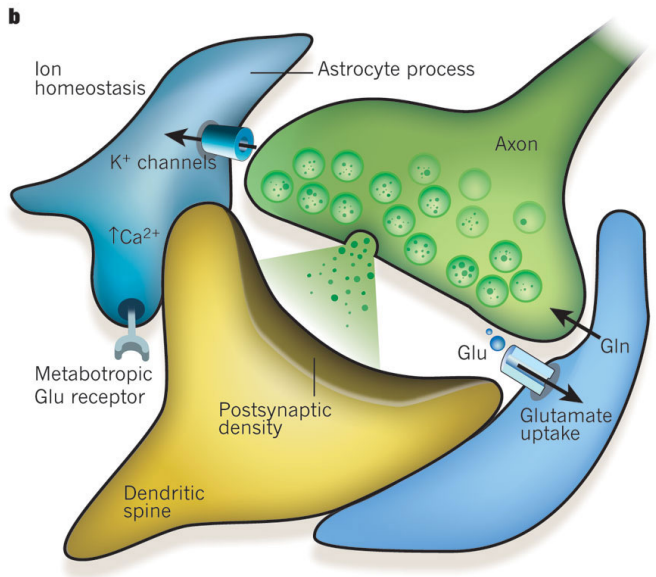

Capillary
Astrocyte
Neuron

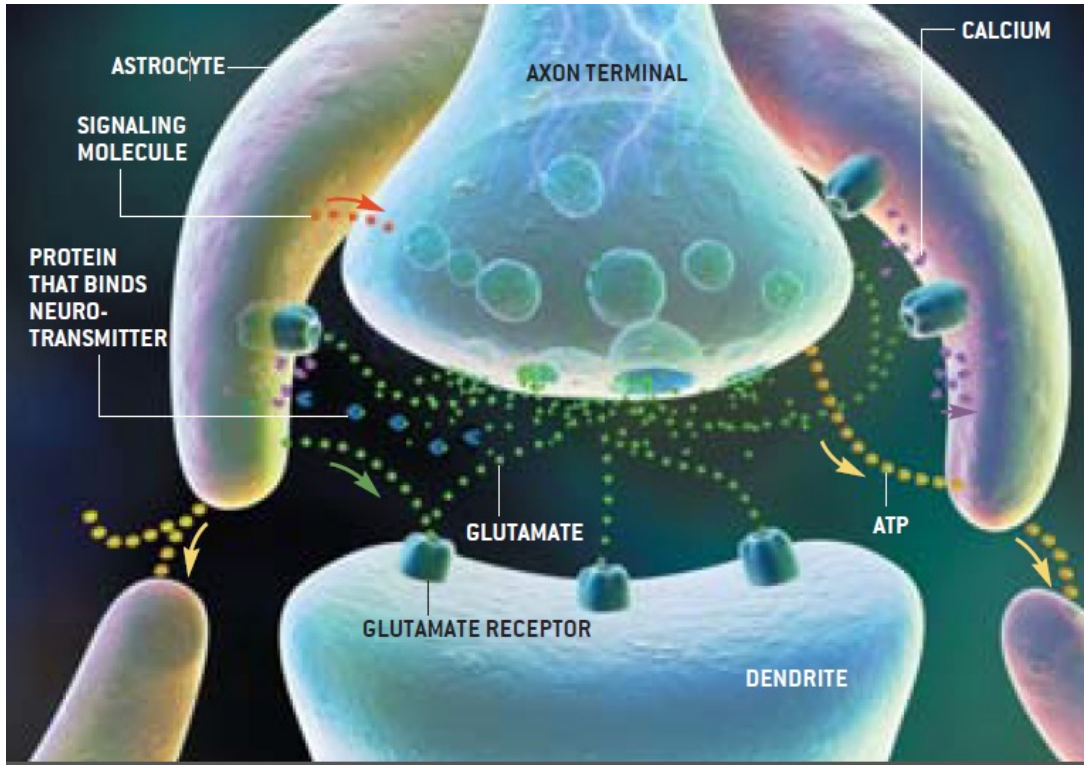

NEURON
ASTROCYTE
Na+
Na+
Na+
K+
K+
K+
2K+
K+
3Na+
K+
H2O
Na+
2Cl-
K+
H2O
H2O
Cl-
K+
Cl-
Cl-



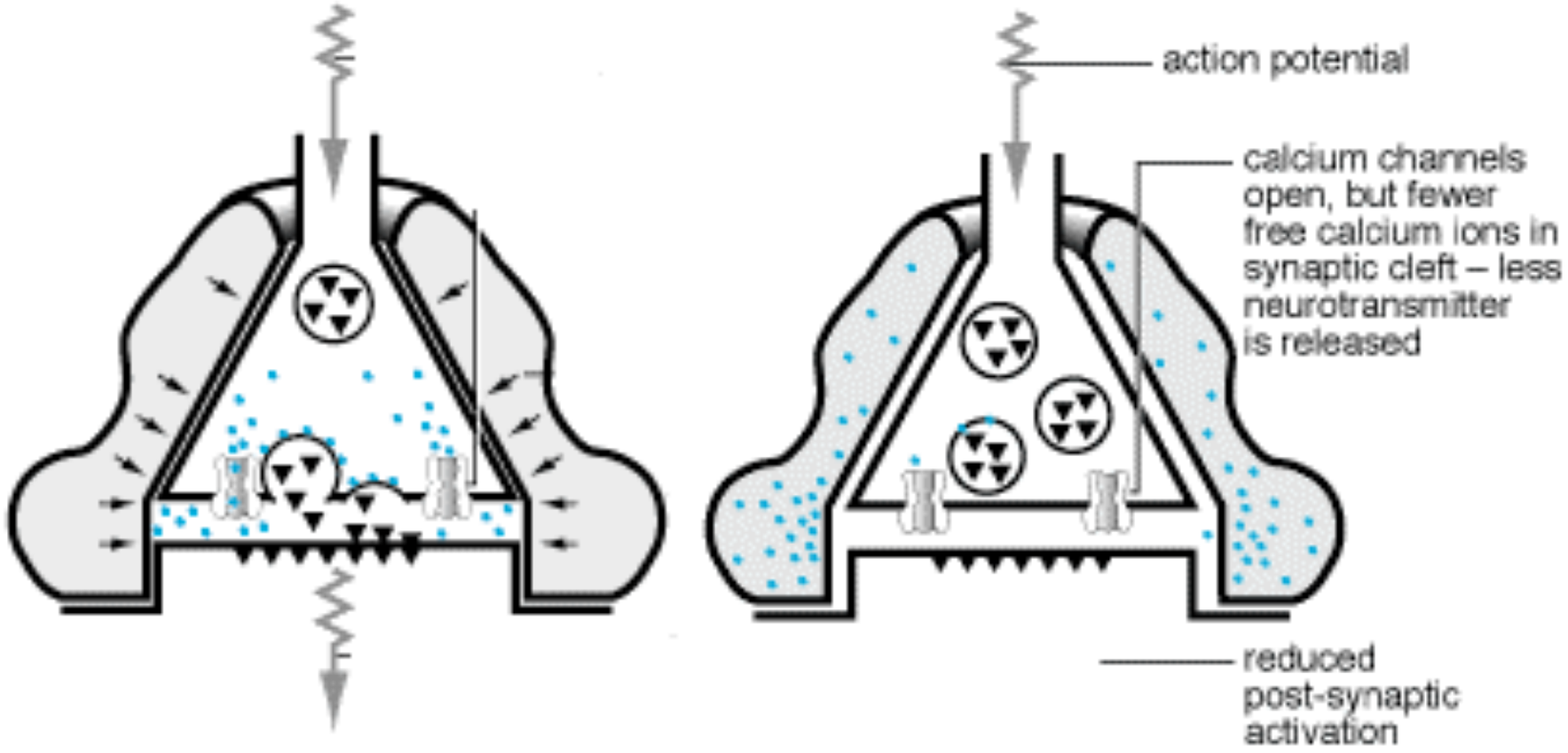
Nature Reviews | Neuroscience

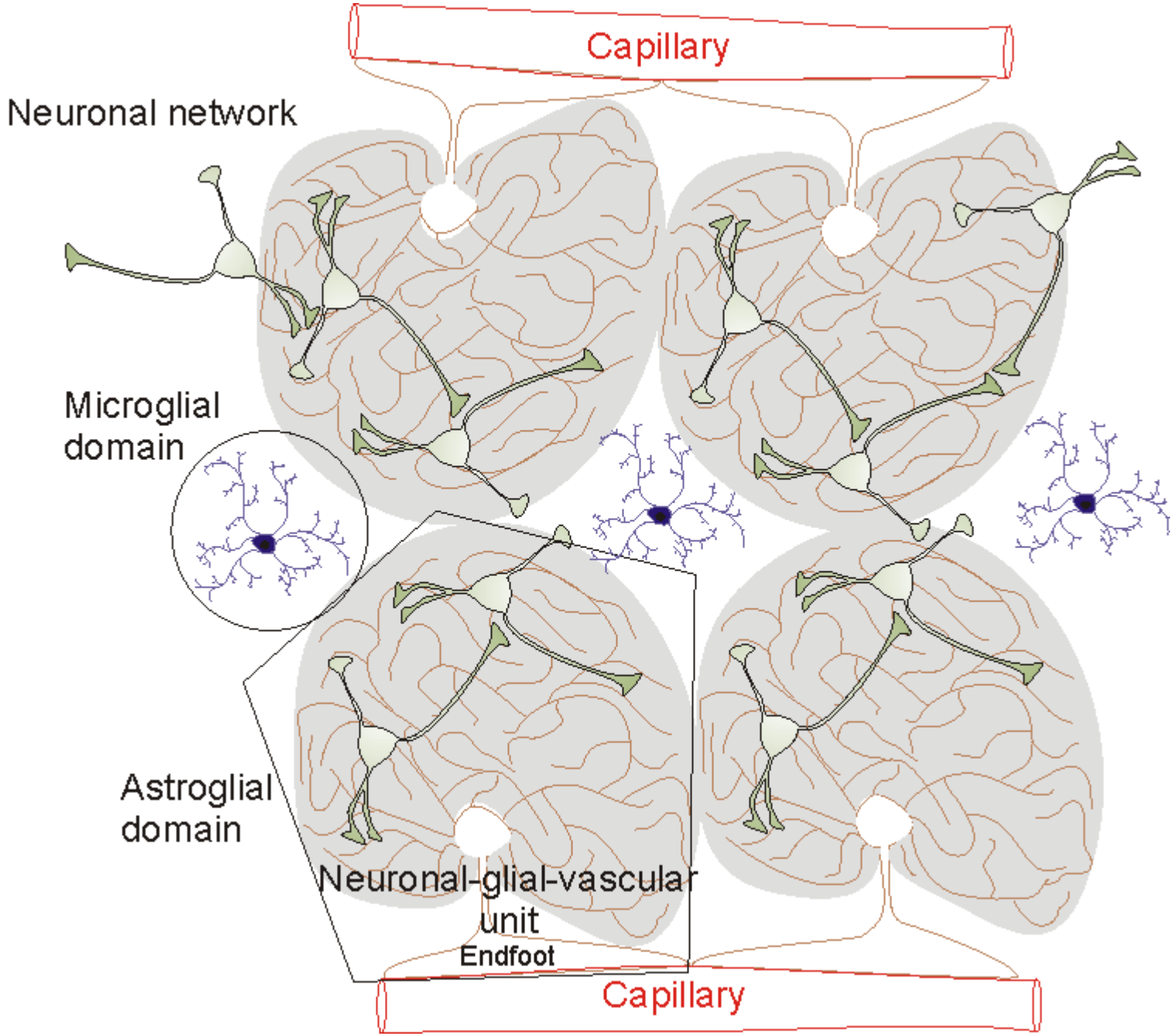

a
Astrocyte process
Axon
Spine
Postsynaptic density

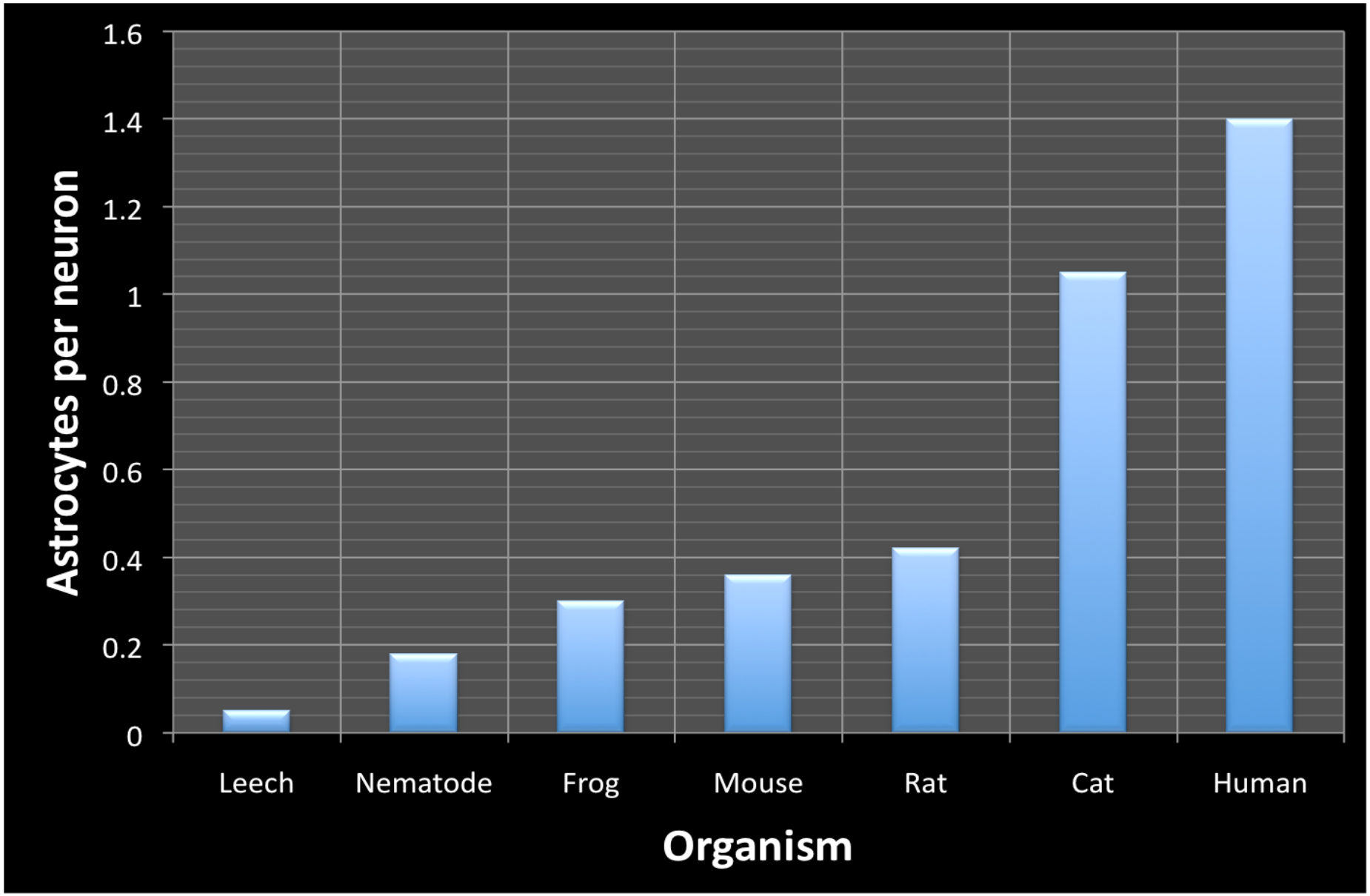

b
Ion homeostasis
Astrocyte process
Axon
K+ channels
↑Ca2+
Metabotropic Glu receptor
Postsynaptic density
Glu
Gln
Glutamate uptake
Dendritic spine


ASTROCYTE
AXON TERMINAL
CALCIUM
SIGNALING MOLECULE
PROTEIN THAT BINDS NEURO-TRANSMITTER
GLUTAMATE
ATP
GLUTAMATE RECEPTOR
DENDRITE

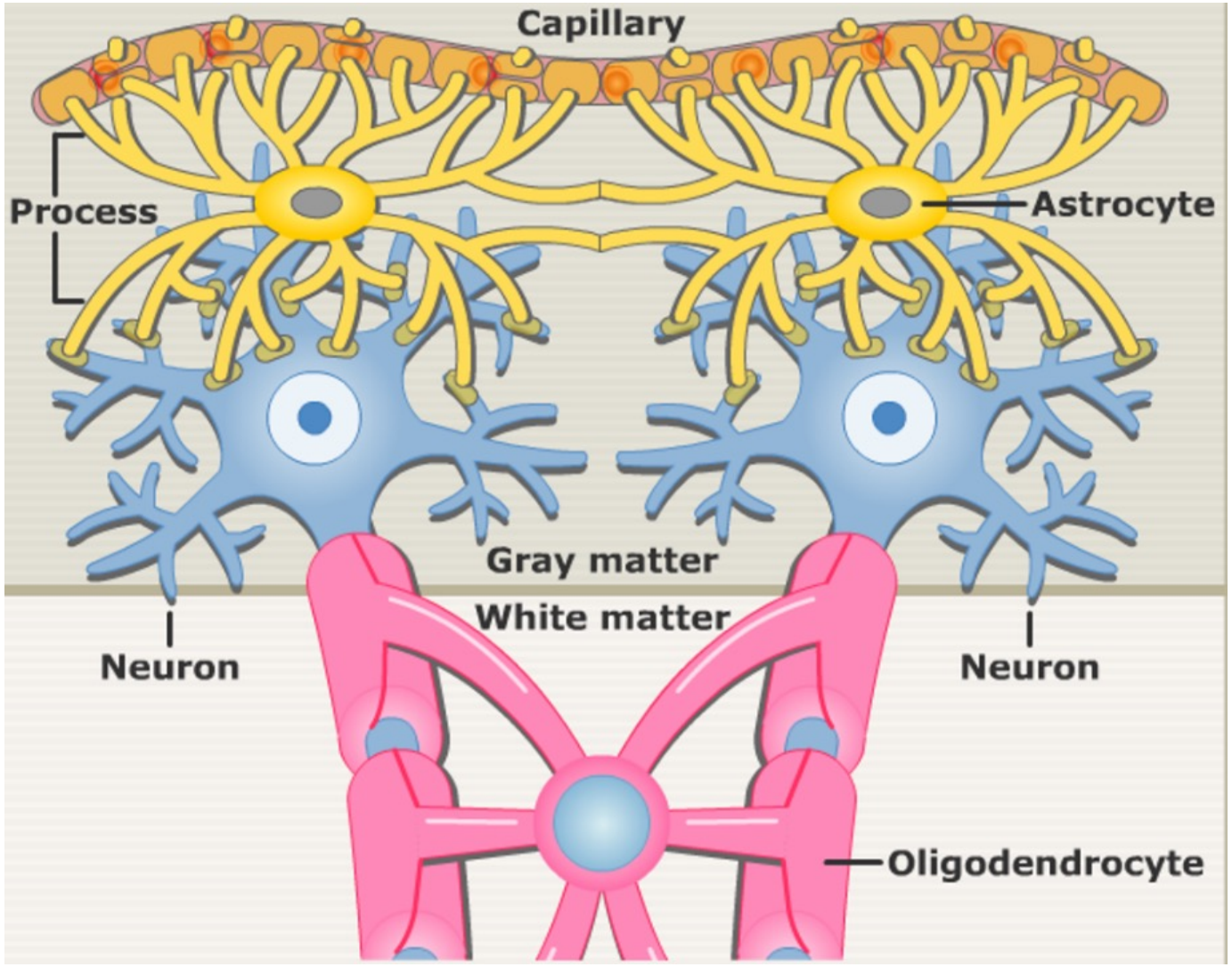
Ca^{2+} and Synaptic Efficacy

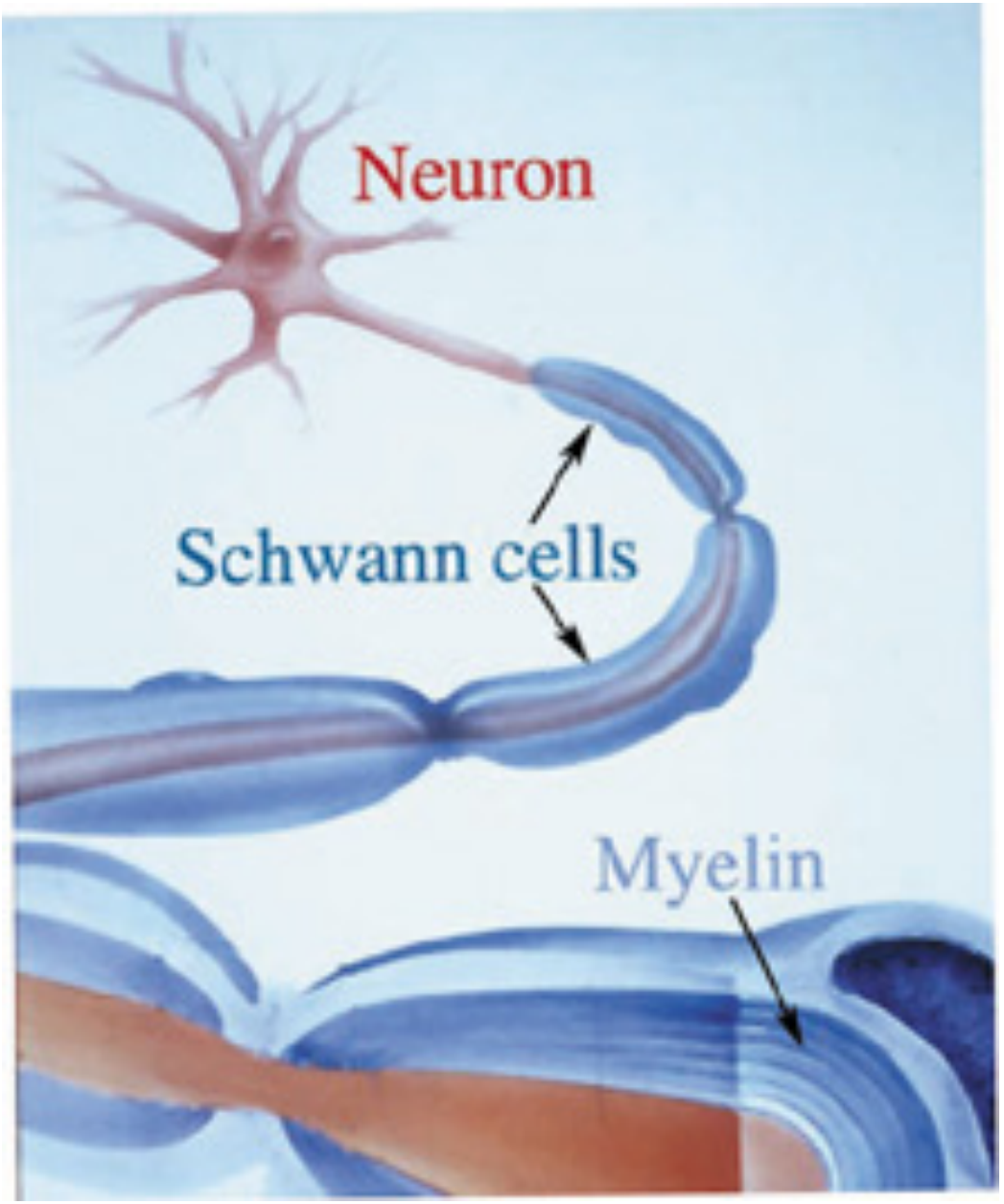



Capillary
Neuronal network
Microglial domain
Astroglial domain
Neuronal-glial-vascular unit
Endfoot
Capillary

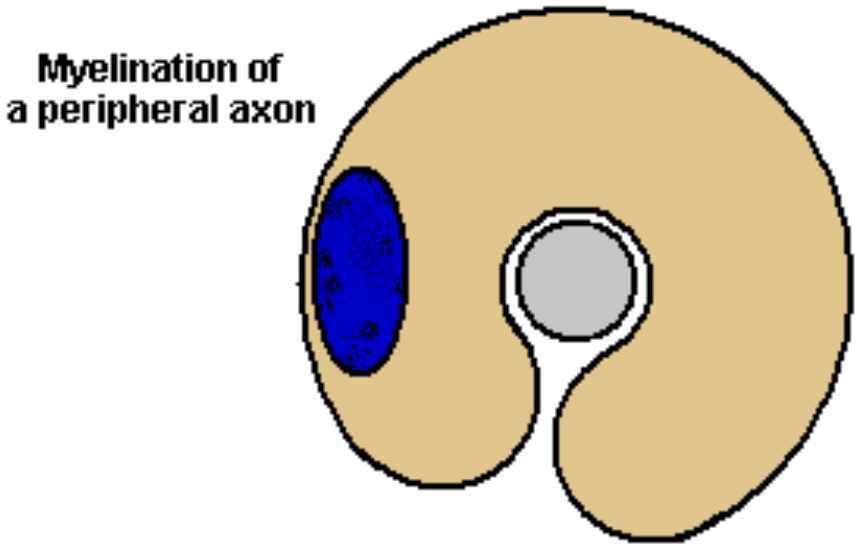

Astrocytes per neuron
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Leech
Nematode
Frog
Mouse
Rat
Cat
Human
Organism

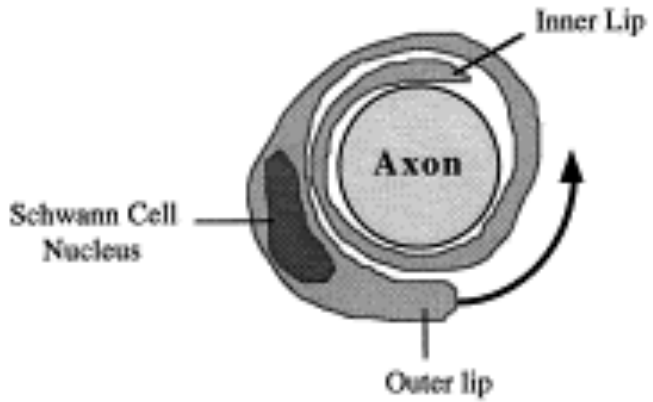
Astrocytes and Oligondendrocytes are in the Service of Neurons



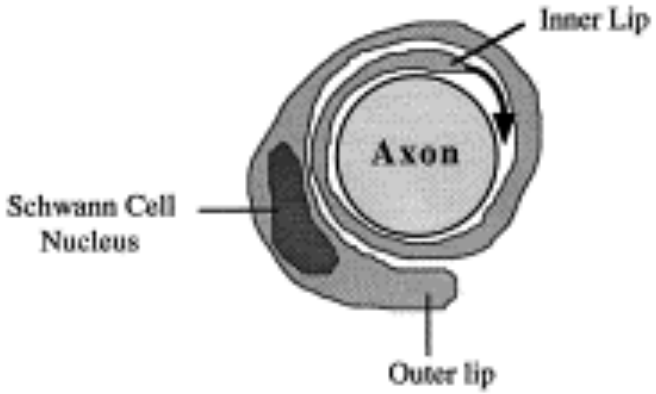

Neuron
Schwann cells
Myelin

Myelinating Schwann cells

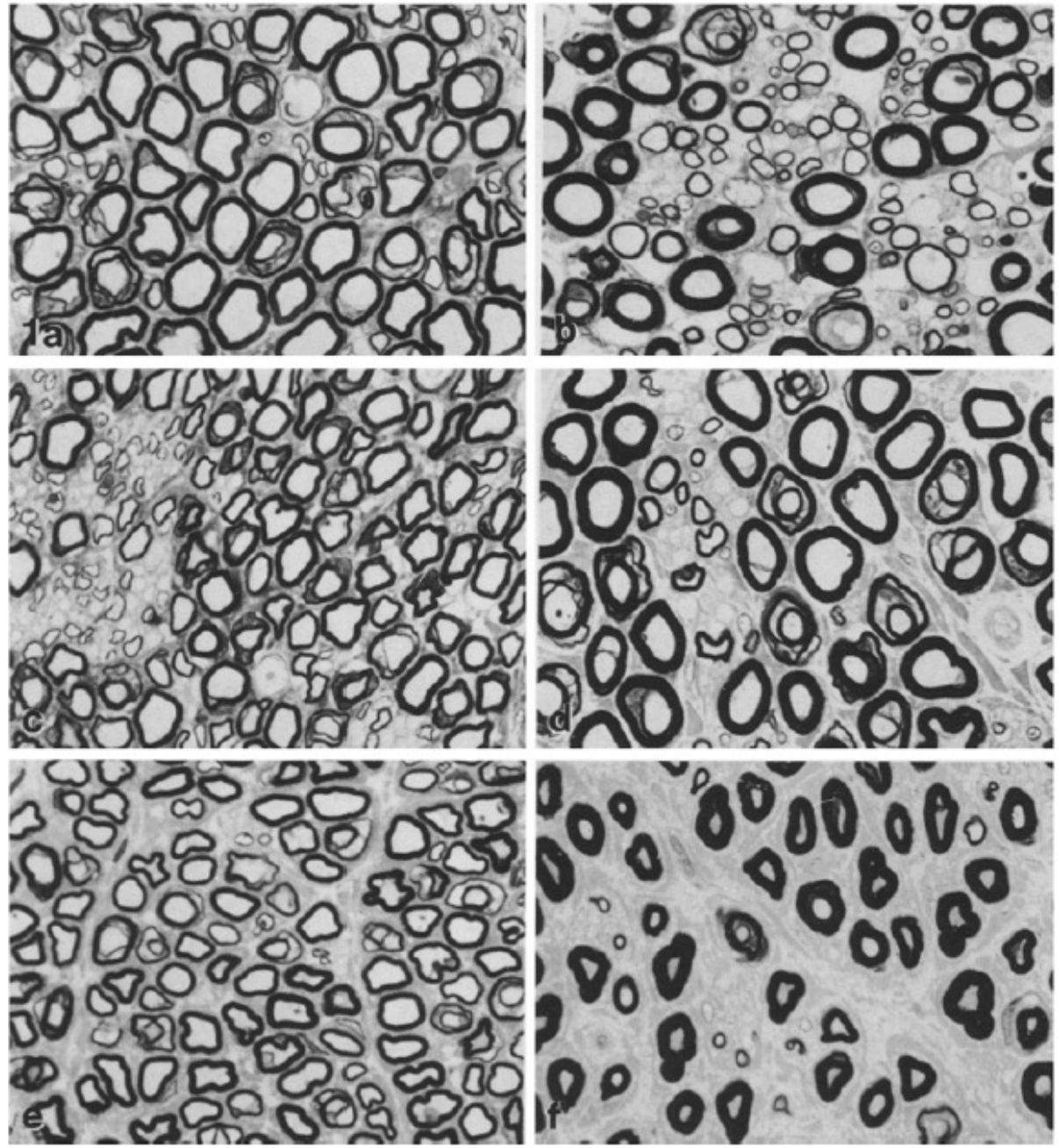




Myelin formation by Schwann cell circumnavigation

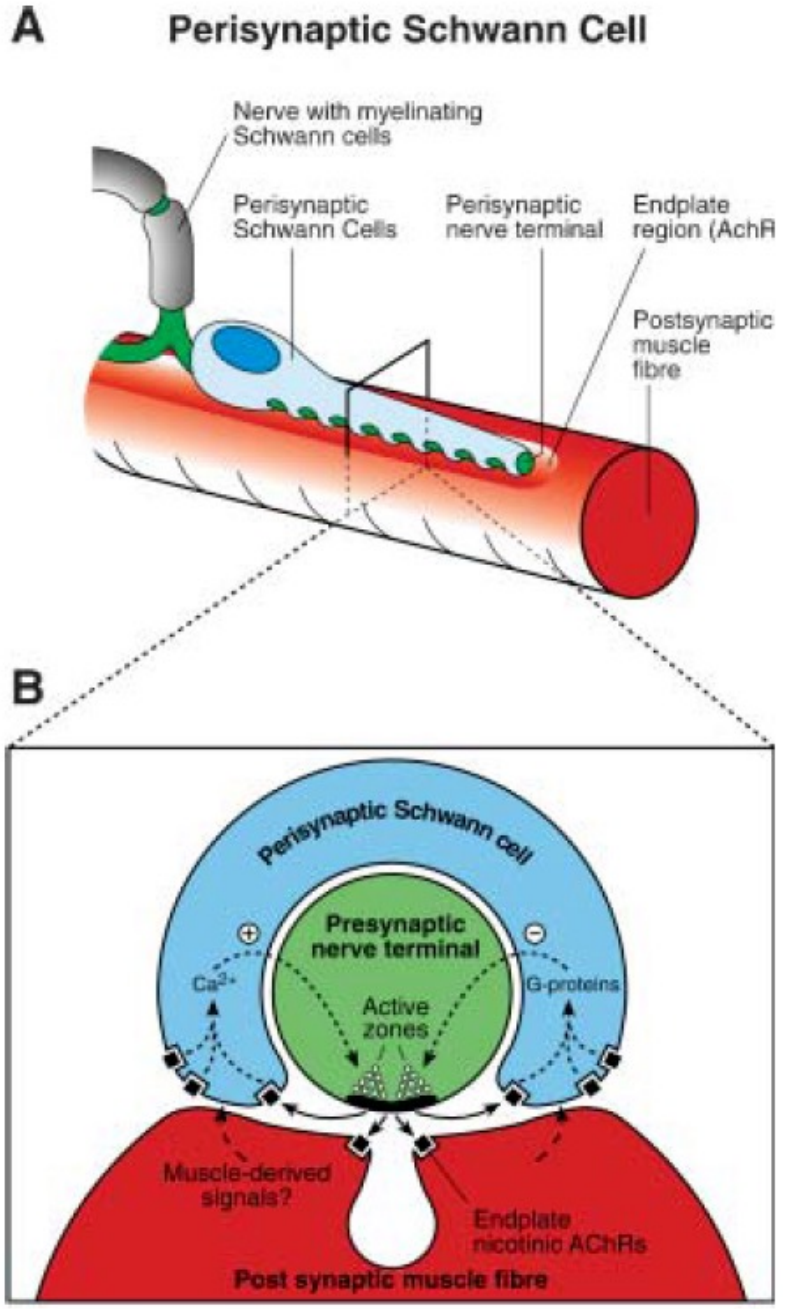


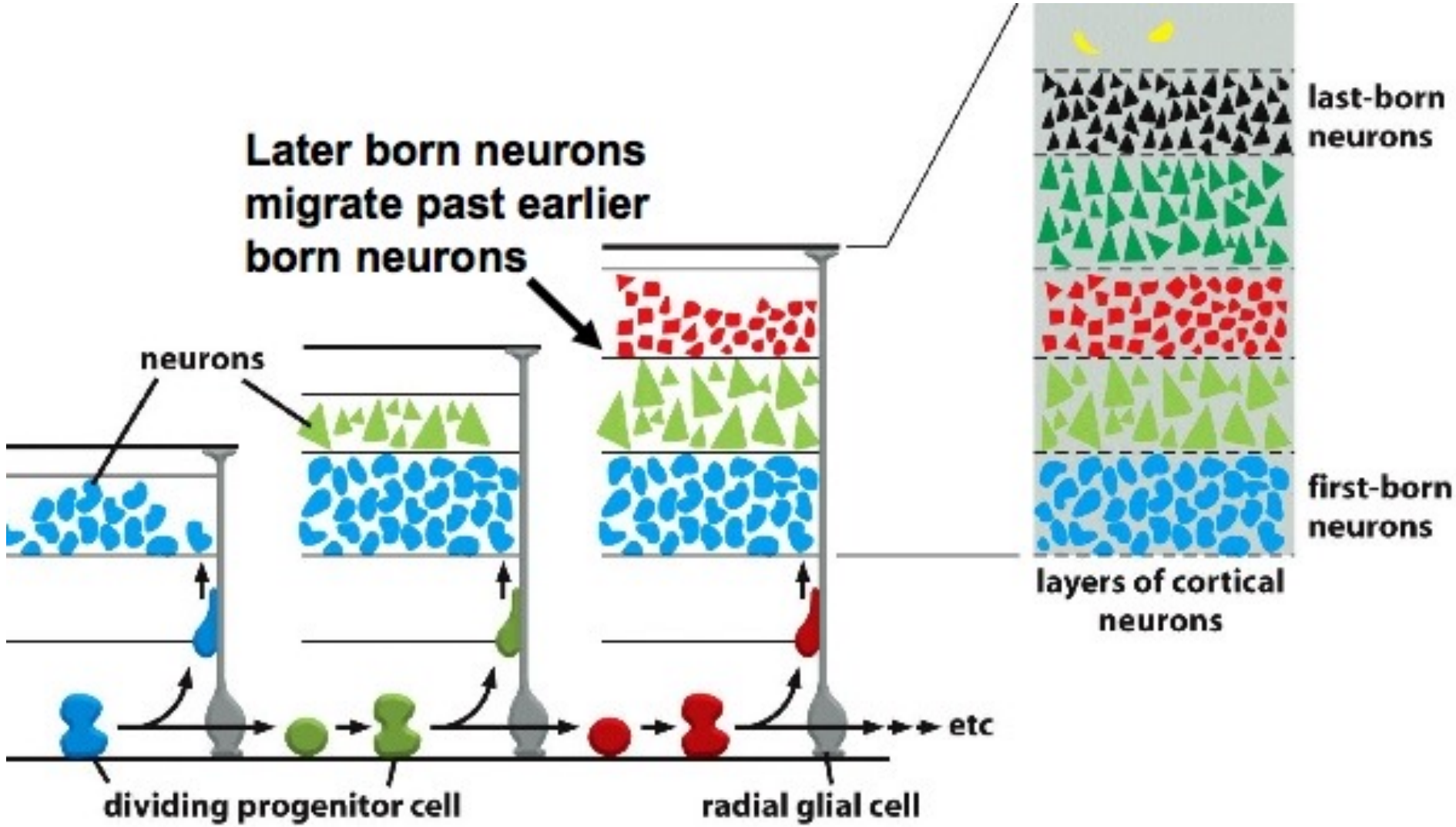
Myelin formation by progression of the inner lip

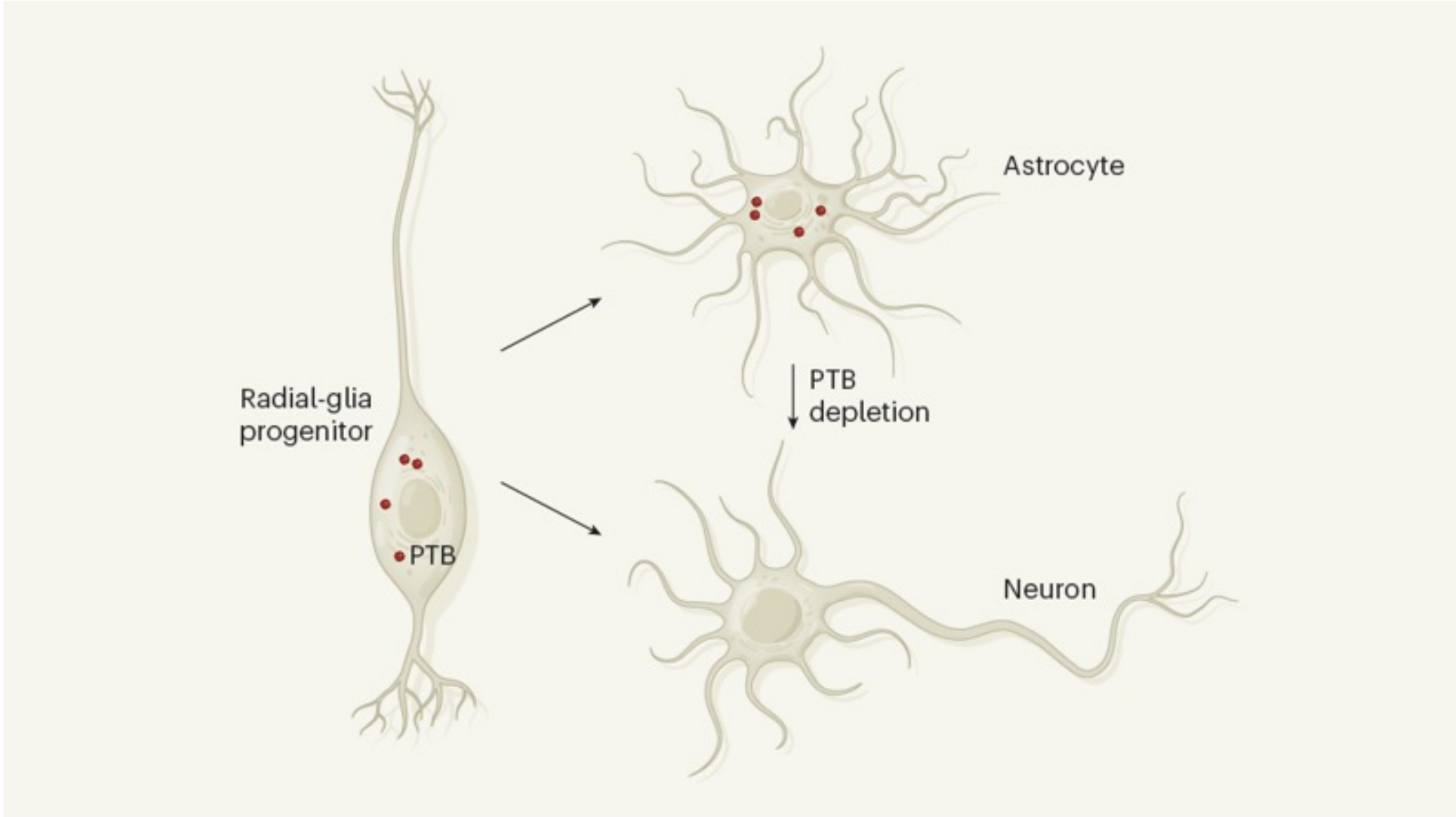

a
b
c
d
e
f

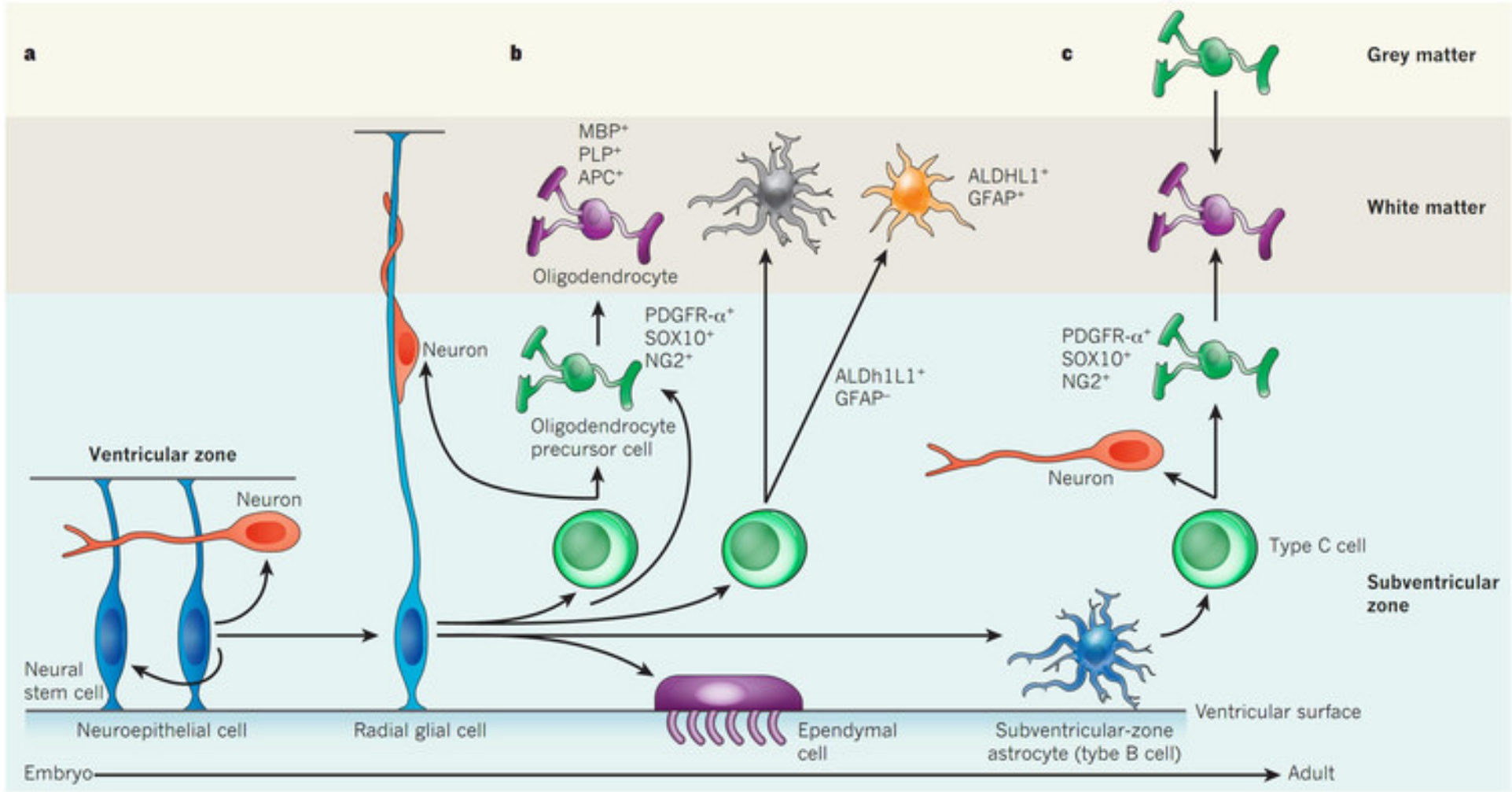
Terminal (Perisynaptic) Schwann cells

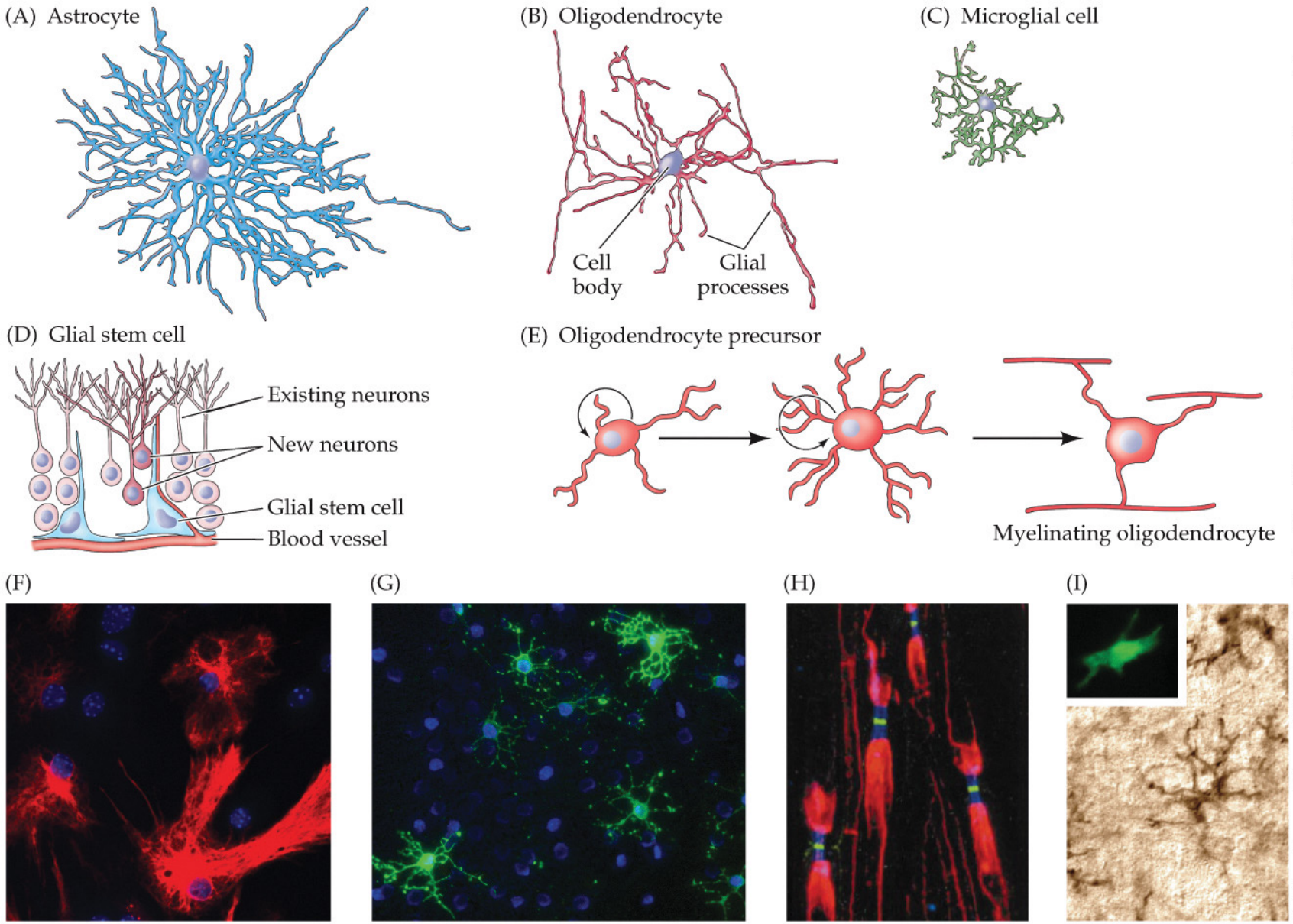
- Non-Myelinating Schwann Cells at Neuromuscular Junctions
- Axonal renervation of denervated endplates
- Enhance or decrease neurotransmission at NMJs




Later born neurons
migrate past earlier
born neurons
neurons
last-born
neurons
first-born
neurons
layers of cortical
neurons
etc
dividing progenitor cell
radial glial cell


Astrocyte
PTB
depletion
Radial-glia
progenitor
PTB
Neuron


a
b
c
Grey matter
White matter
MBP+
PLP+
APC+
Oligodendrocyte
ALDHL1+
GFAP+
PDGFR-α+
SOX10+
NG2+
Oligodendrocyte
precursor cell
Neuron
ALDh1L1+
GFAP–
PDGFR-α+
SOX10+
NG2+
Neuron
Ventricular zone
Neuron
Type C cell
Subventricular
zone
Neural
stem cell
Neuroepithelial cell
Radial glial cell
Ependymal
cell
Subventricular-zone
astrocyte (tybe B cell)
Ventricular surface
Embryo
Adult



A–C from Jones and Cowan (1983) *The Structural Basis of Neurobiology*. New York: Elsevier: 282–370. D, E from Nishiyama et al. (2009) *Nature Rev. Neurosci.* 10: 9–22. F,G courtesy of A.-S. LaMantia. H: From Bhat et al. (2001) *Neuron* 30(2): 369–383. I courtesy of A. Light. (inset) Courtesy of G. Matsushima.

***NEUROSCIENCE 6e*, Figure 1.5**