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Myelination in the CNS and PNS

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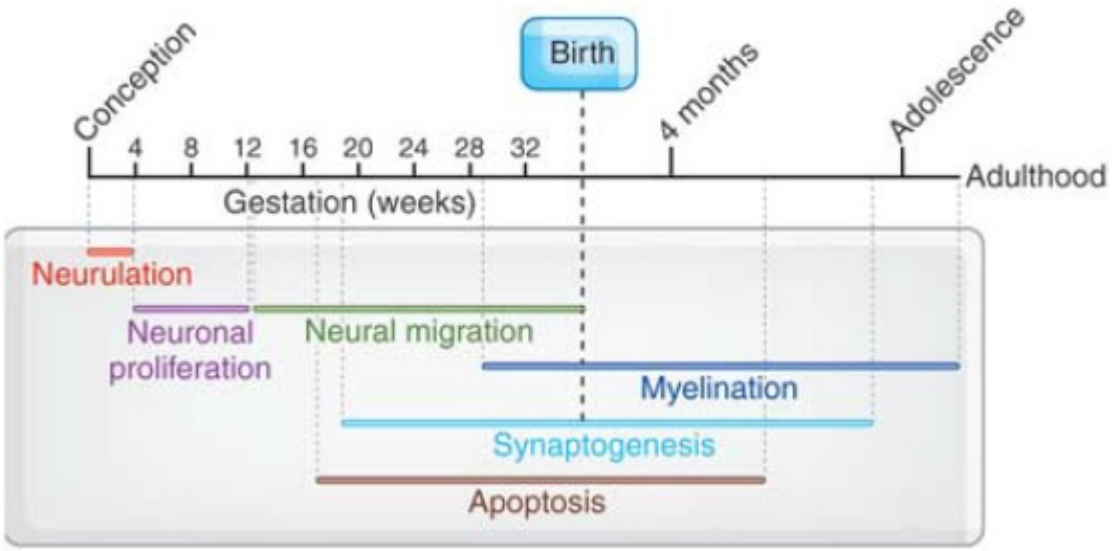
Myelination

Myelination refers to a process by which glia cells produce an insulation sheeth (myelin) that covers axons of some neurons

Myelin speeds up the transmission of neural impulses

Myelination occurs first in the spinal cord and then in the hindbrain, midbrain and forebrain



Myelination: Gradual Process

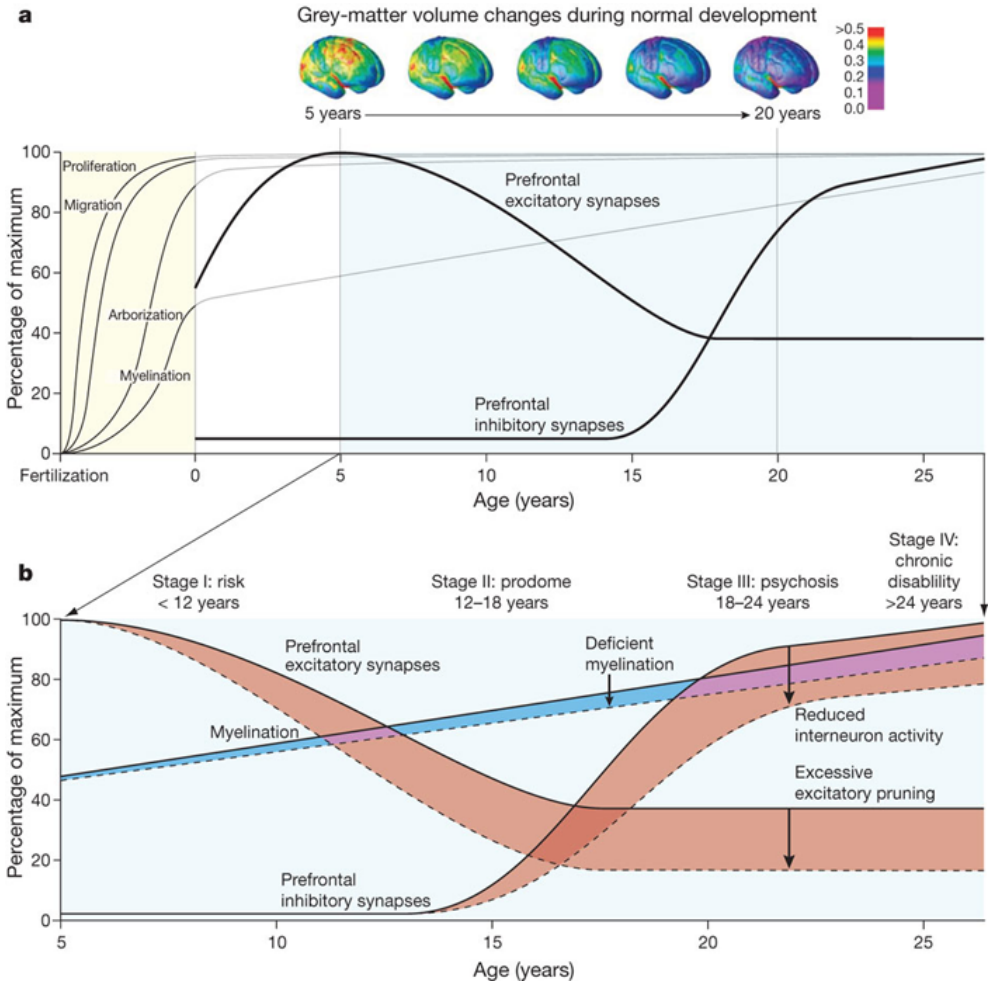
Myelination occurs late in development and continues during childhood and puberty

Myelination is the main cause of the increase in a child´s brain size

In the first four years of life, the brain increases to 80% of its adult weight

Malnutrition or prenatal and postnatal exposure to ethanol affects myelination (often irreversibly)

Myelination: Gradual Process

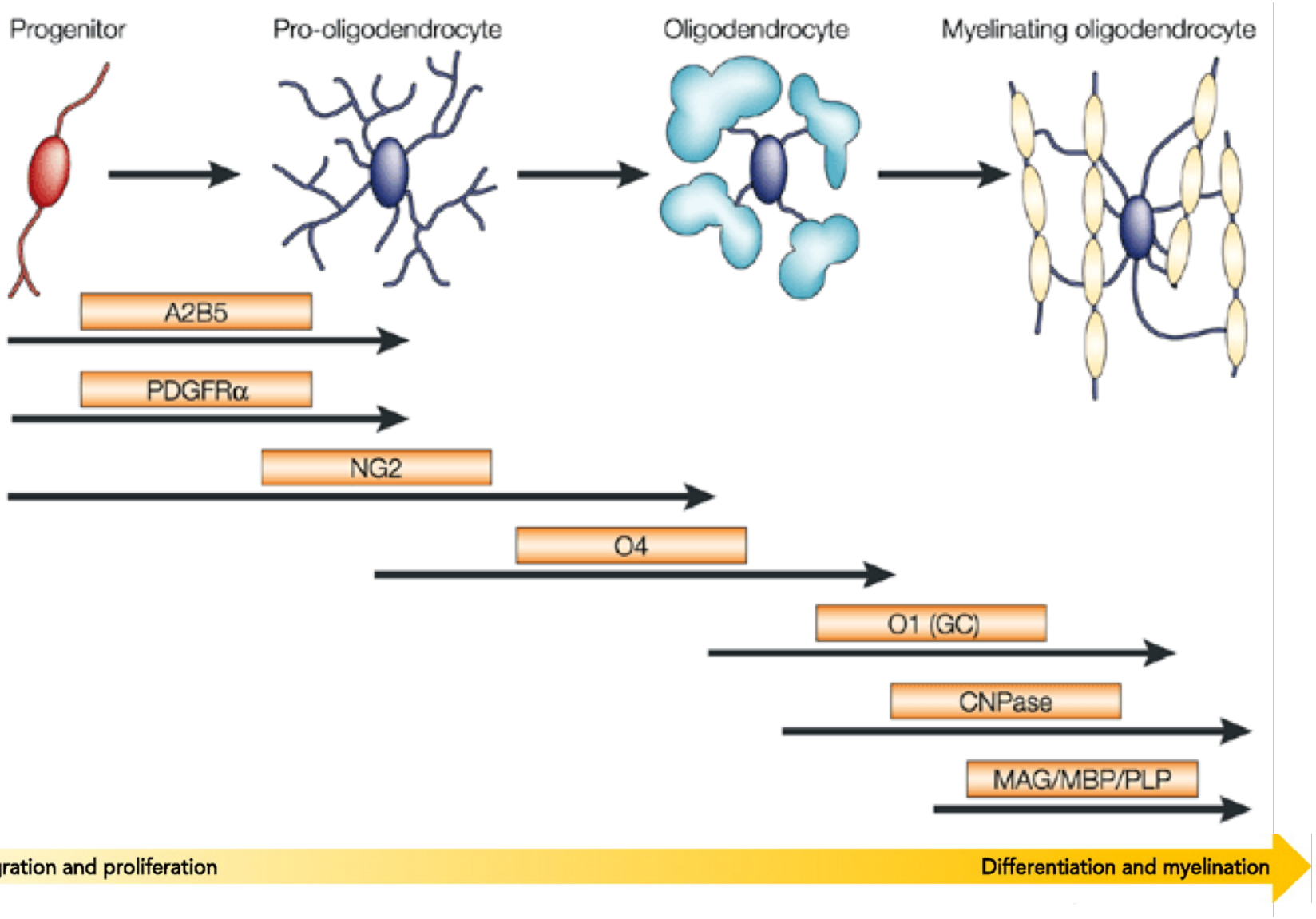


Impact of myelination:

Better judgement, impulse control, decision making, social interactions

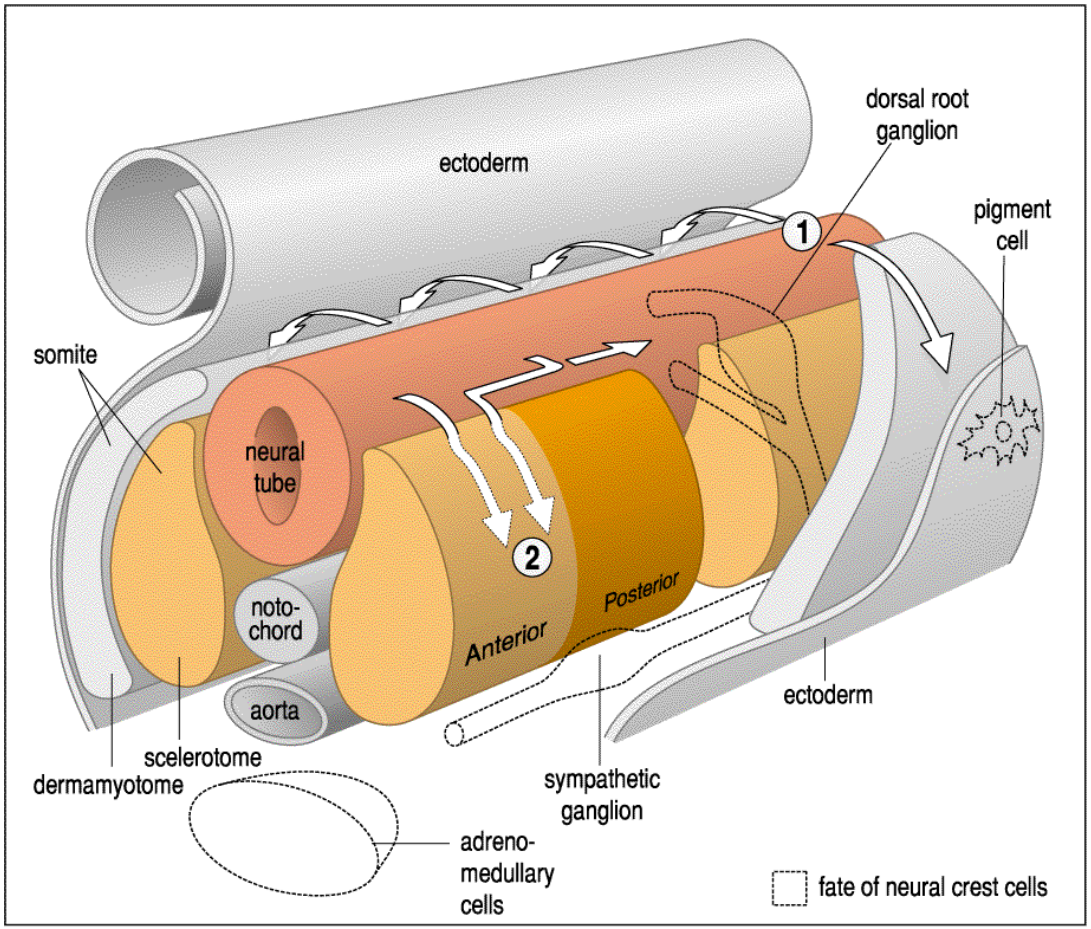
Frontal lobe development is slower than limbic system development (emotional response system) – possibly explains Impulsiveness and risky behavior in adolescents

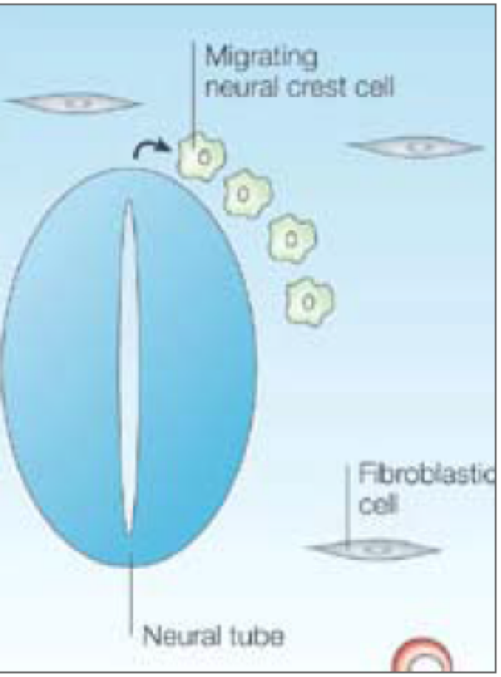
Oligodendrocyte Maturation and Myelination

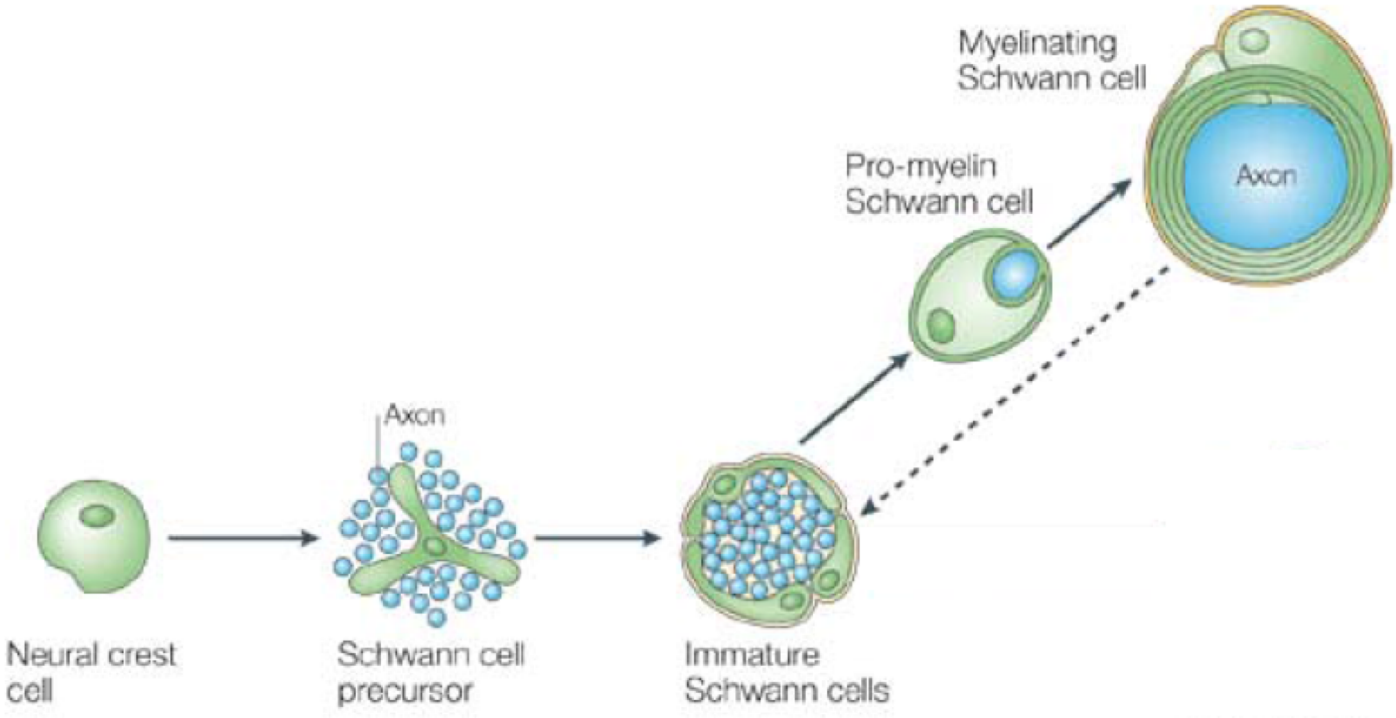


Schwann Cells

Neural crest-derived Schwann cell progenitors migrate over the surface of the neural tube, then through the anterior somites.



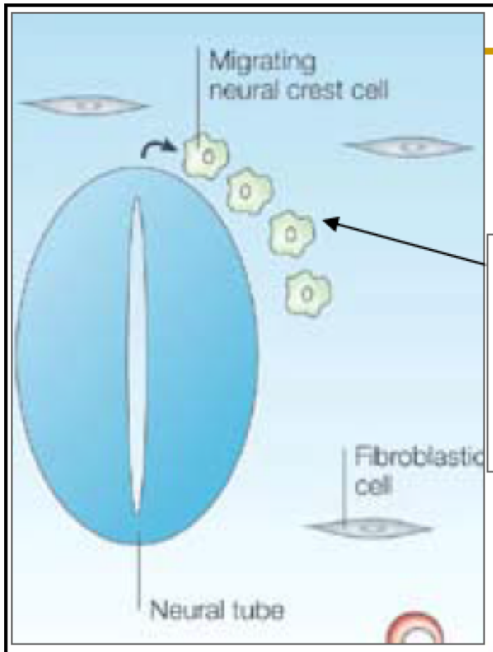




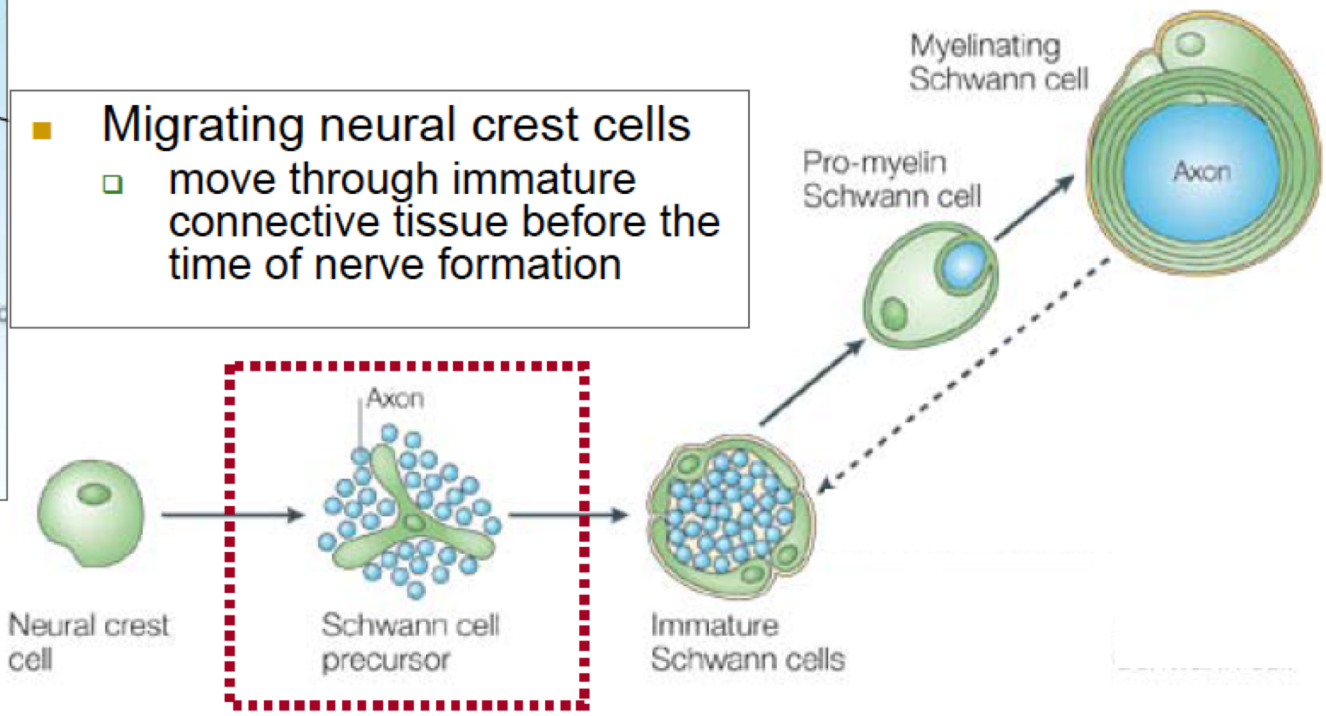
Schwann cell development - involves three transient cell populations

- Migrating neural crest cells
- Schwann cell precursors (SCPs).
- Immature Schwann cells

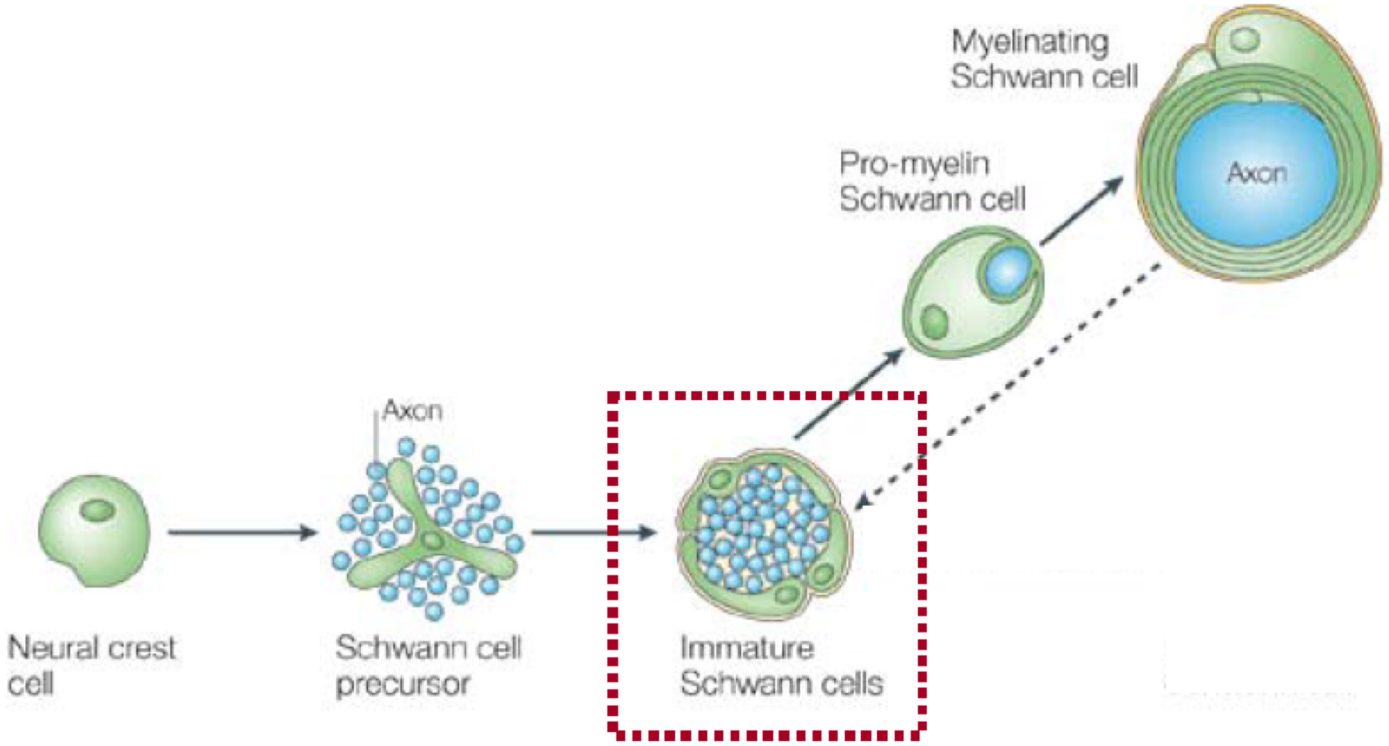
SCPs and immature Schwann cells, but not migrating neural crest cells, are intimately associated with neurons



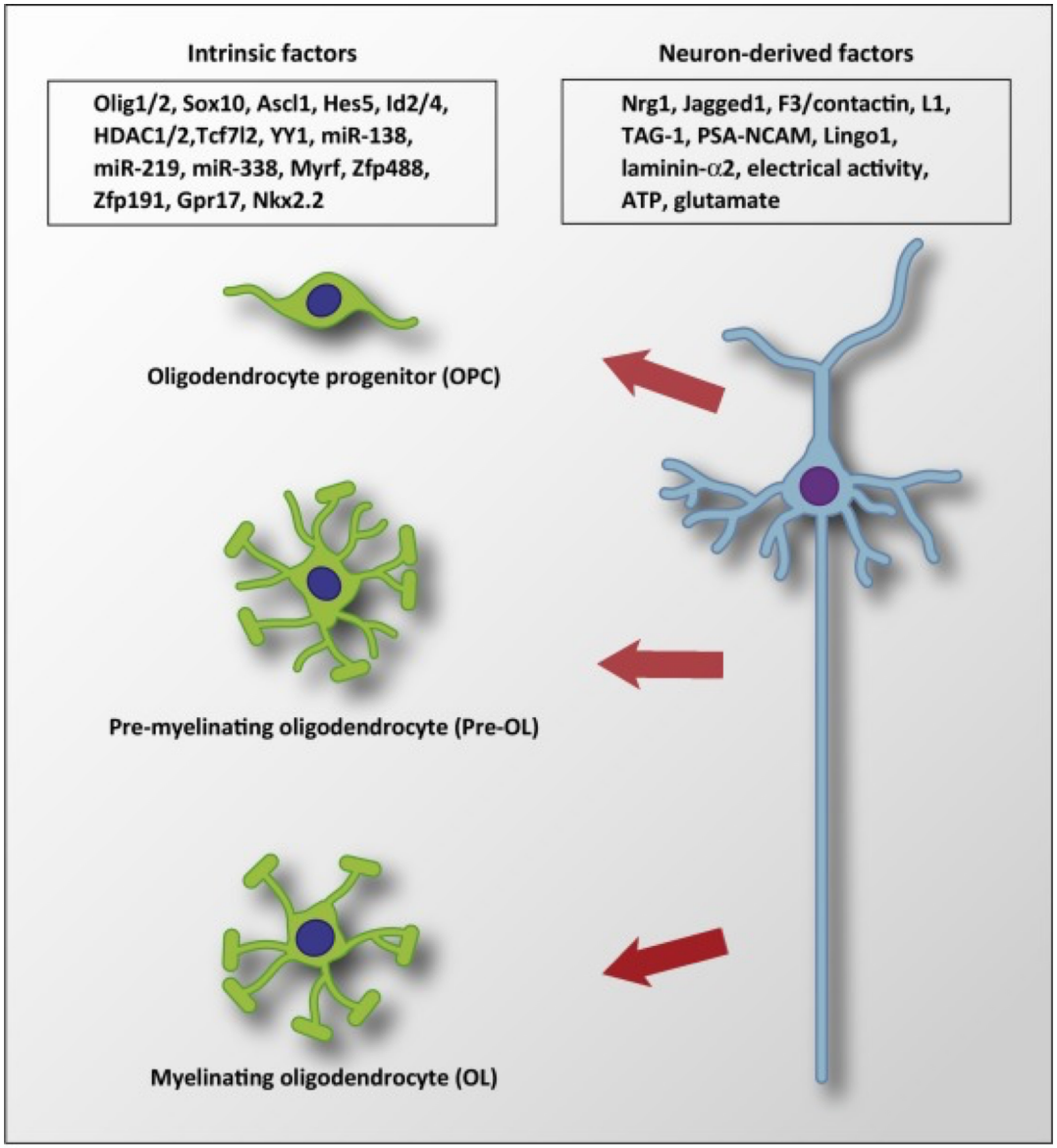
- Migrating neural crest cells
  - move through immature connective tissue before the time of nerve formation

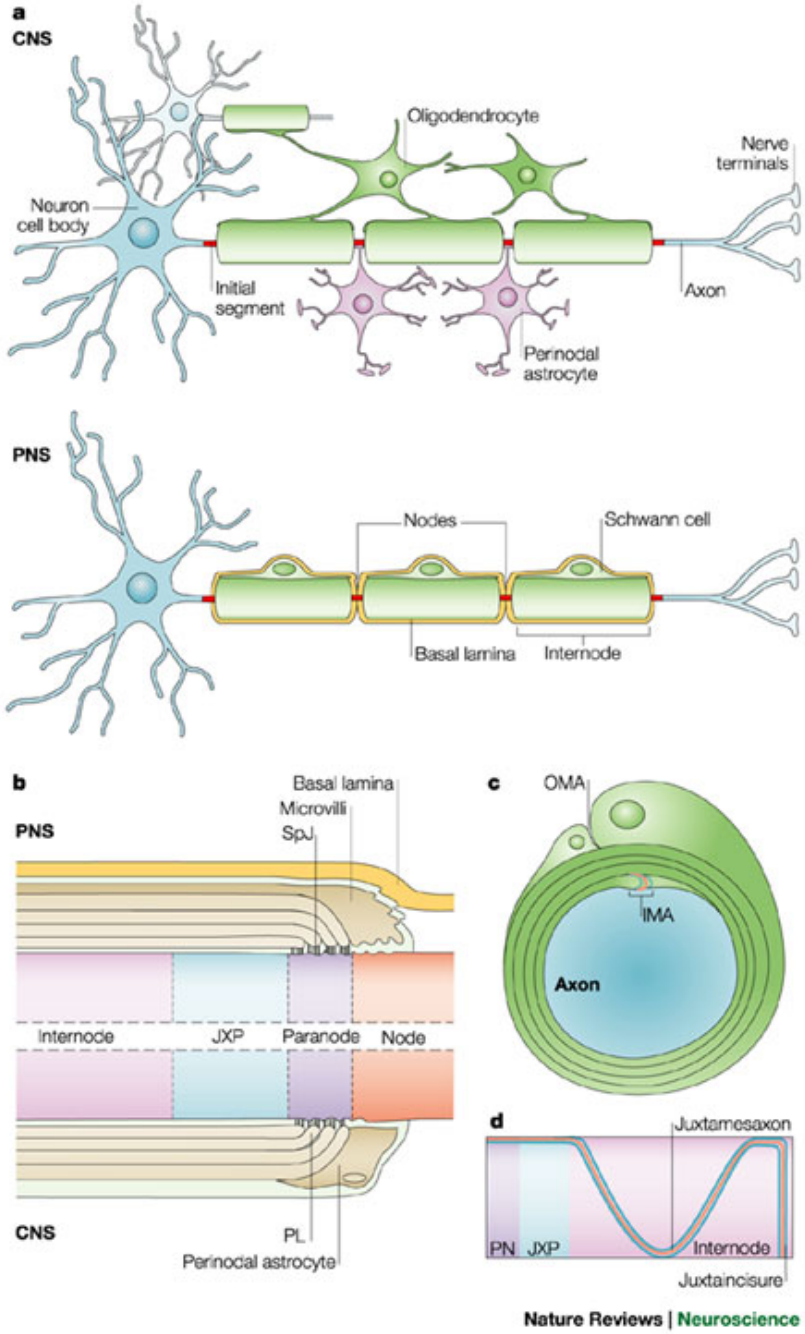


- **Schwann cell precursors** (SCPs).
  - Tightly associated with axons and are found in early nerves that are still compact
  - Express proteins not found in migrating neural crest cells, including



- **Immature Schwann cells**
  - Found in nerves that have acquired the basic tissue relationships of adult nerves
  - **Their fate is determined by the axons with which they associate**
  - Myelination occurs only in Schwann cells that by chance envelop large diameter axons
  - Schwann cells that ensheath small diameter axons progress to become mature non-myelinating cells.


Intrinsic factors
Olig1/2, Sox10, Ascl1, Hes5, Id2/4, HDAC1/2,Tcf7l2, YY1, miR-138, miR-219, miR-338, Myrf, Zfp488, Zfp191, Gpr17, Nkx2.2
Neuron-derived factors
Nrg1, Jagged1, F3/contactin, L1, TAG-1, PSA-NCAM, Lingo1, laminin-α2, electrical activity, ATP, glutamate
Oligodendrocyte progenitor (OPC)
Pre-myelinating oligodendrocyte (Pre-OL)
Myelinating oligodendrocyte (OL)

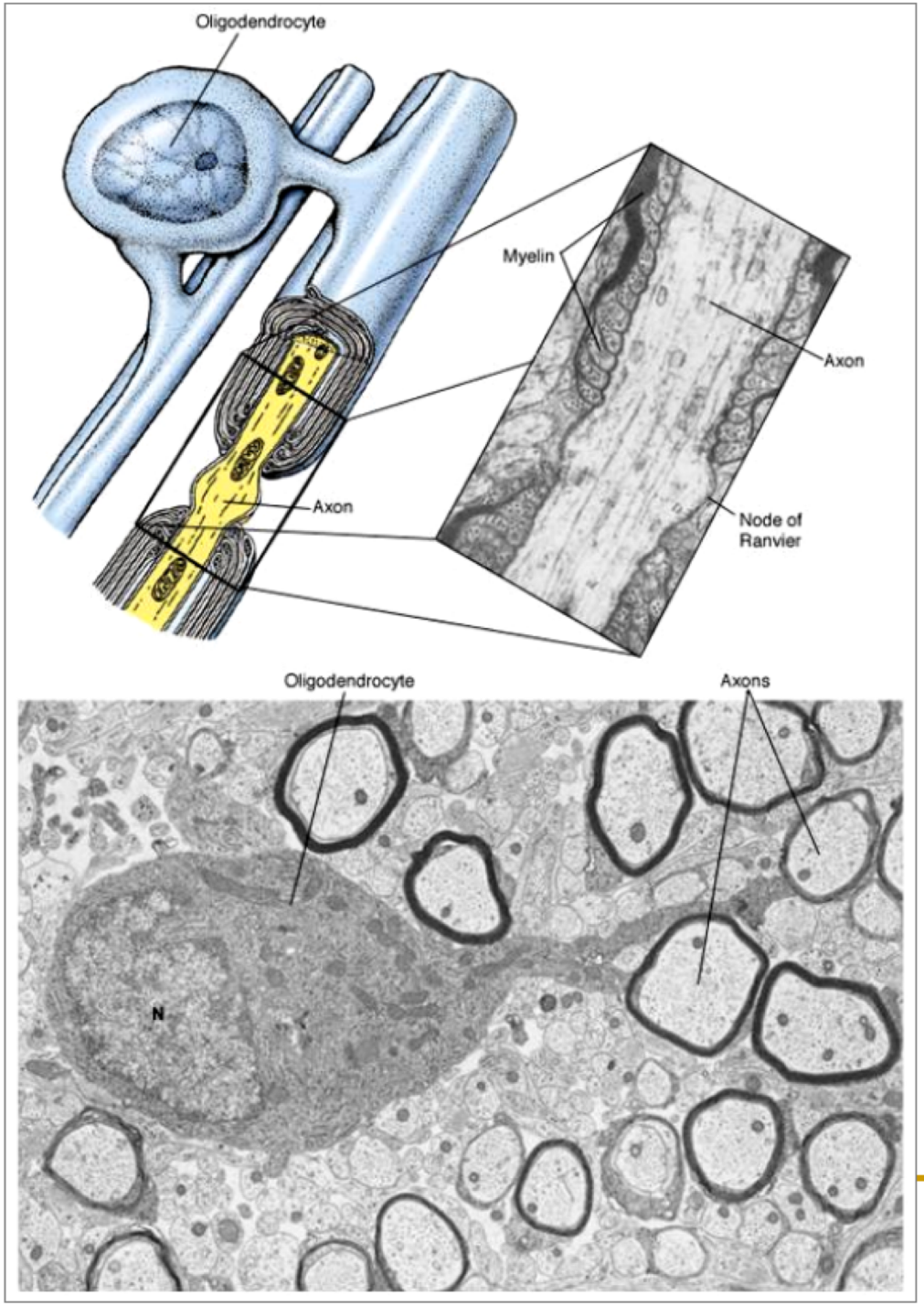


Oligodendrocytes in CNS

One can myelinate different axons and several internodes per axon

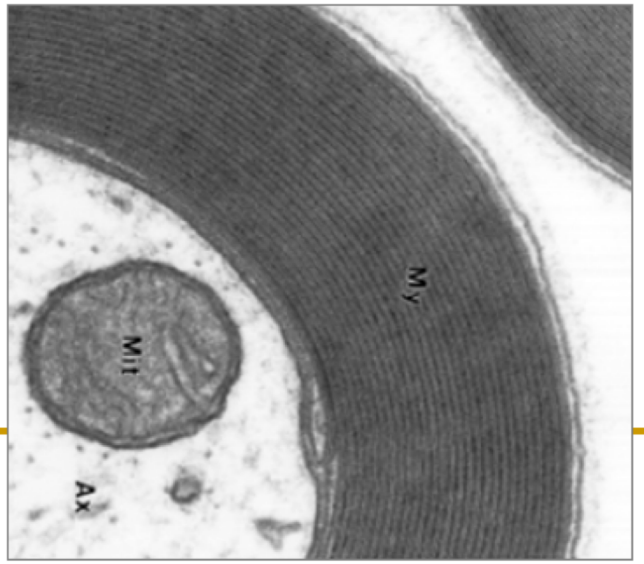
Schwann cells in PNS

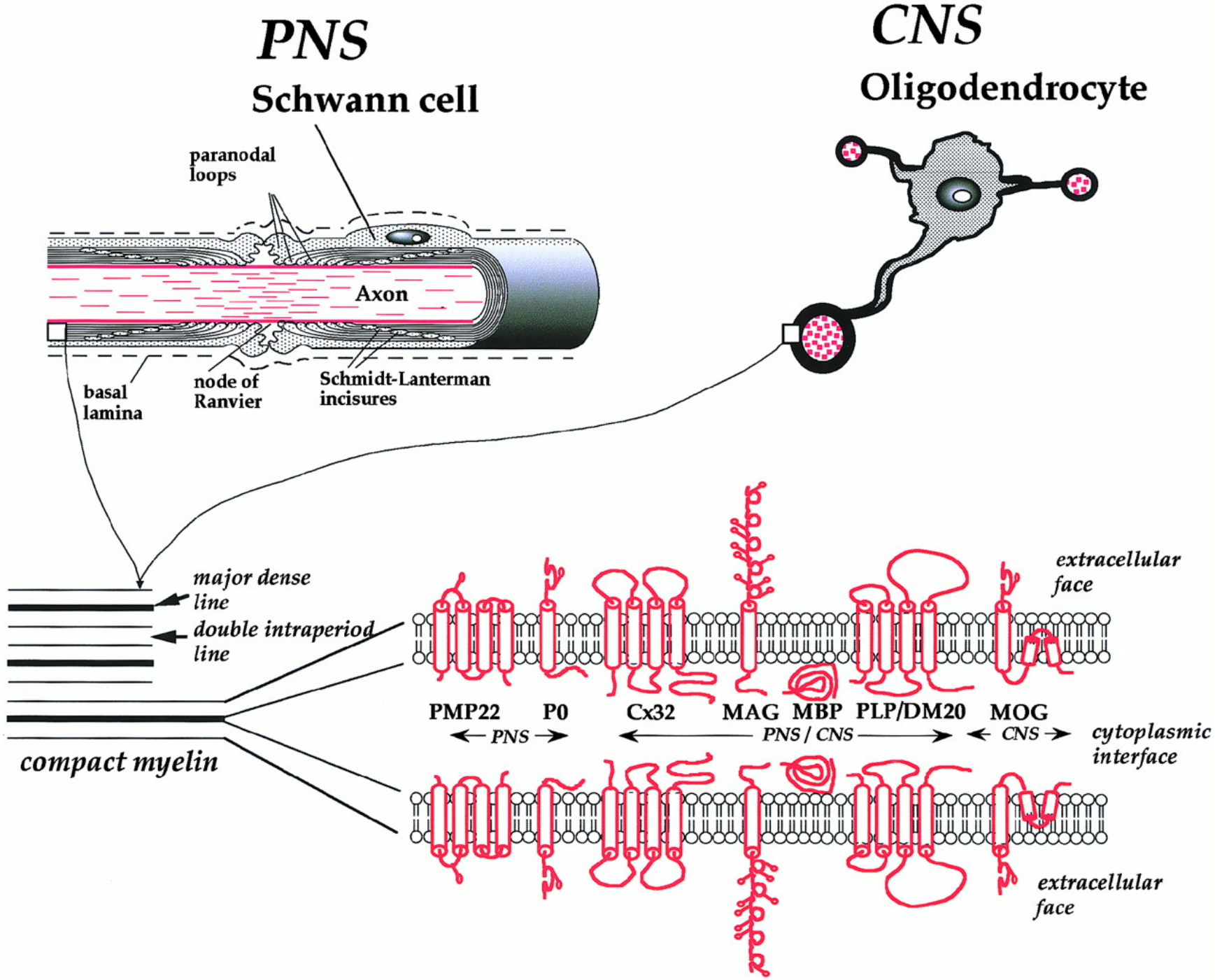
Myelinate a single internode in a single axon



Myelin

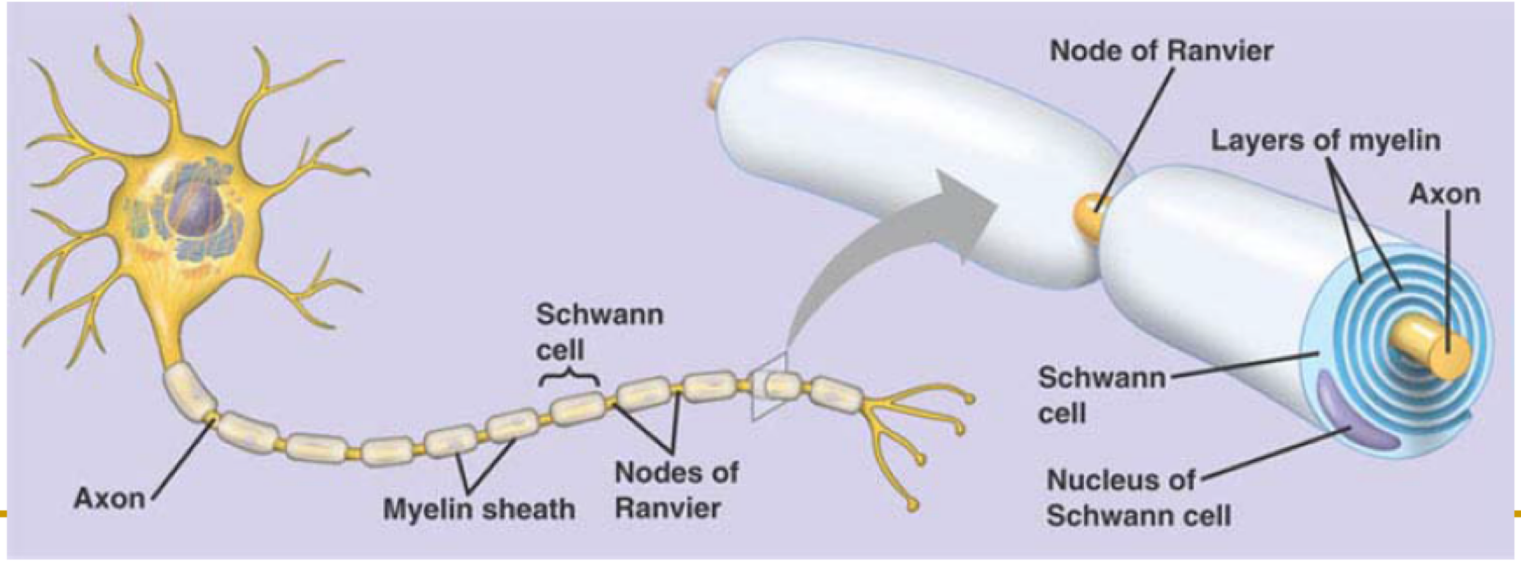
- **Glial cell wraps around axon many times**
  - very thin layers of membrane
  - very little cytoplasm
- **Very compact, so saves space for lots of neurons**
- **Greatly enhances the conduction of the electrical signal**

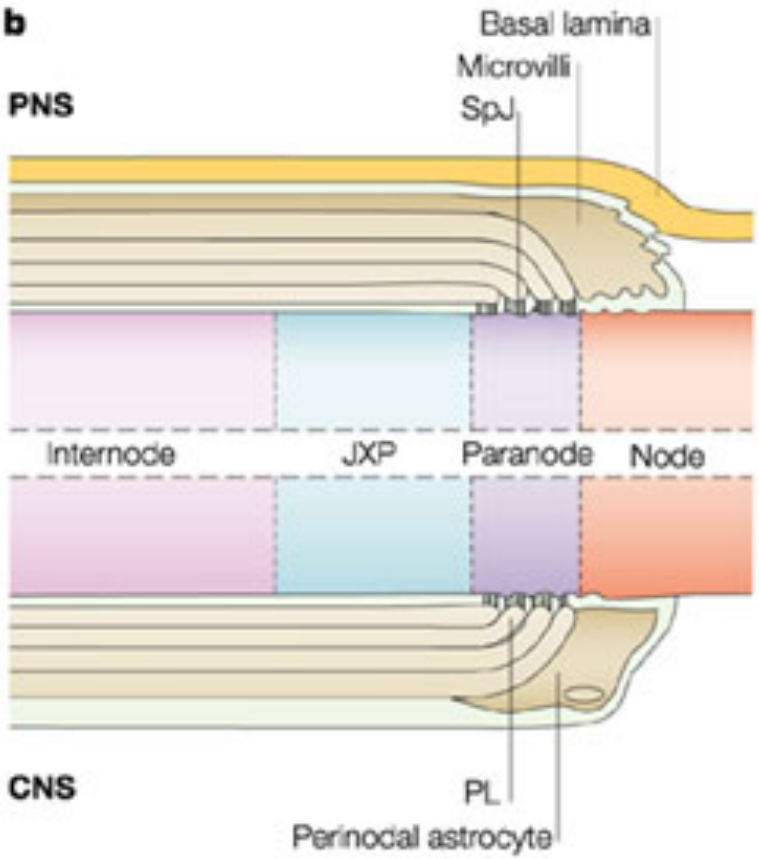



PNS
Schwann cell
CNS
Oligodendrocyte
paranodal loops
Axon
basal lamina
node of Ranvier
Schmidt-Lanterman incisures
major dense line
double intraperiod line
compact myelin
extracellular face
PMP22
P0
Cx32
MAG
MBP
PLP/DM20
MOG
PNS
PNS / CNS
CNS
cytoplasmic interface
extracellular face

Nodes of Ranvier

- **Gaps** between sections of myelination
- "**Booster stations**" to give strong depolarization
- Keeps action potential moving quickly along axon
- High concentration of **voltage-gated ion channels**
- Boosts conduction speed 100X
- Located at about 1 mm intervals

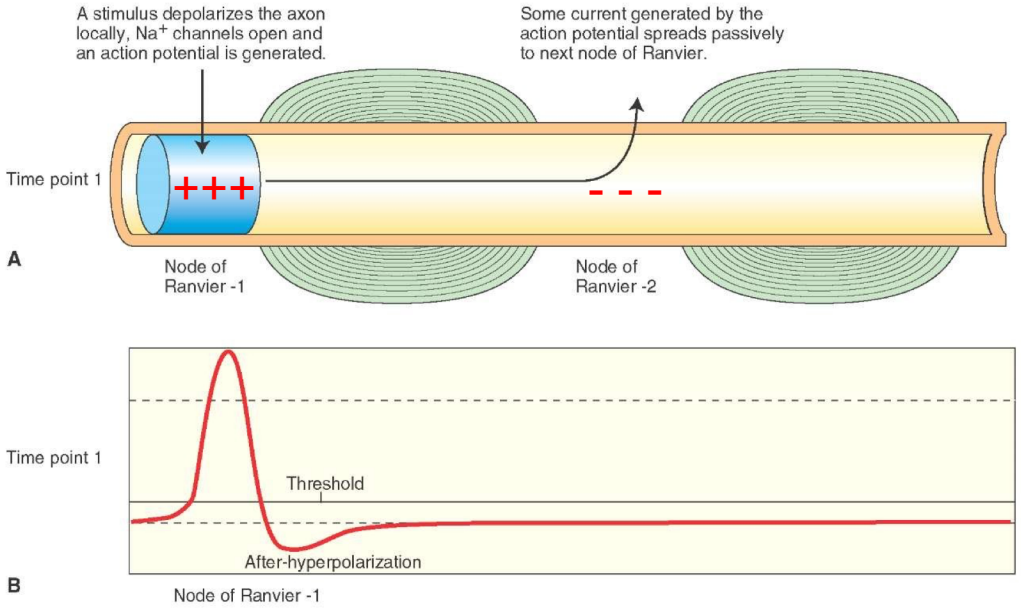


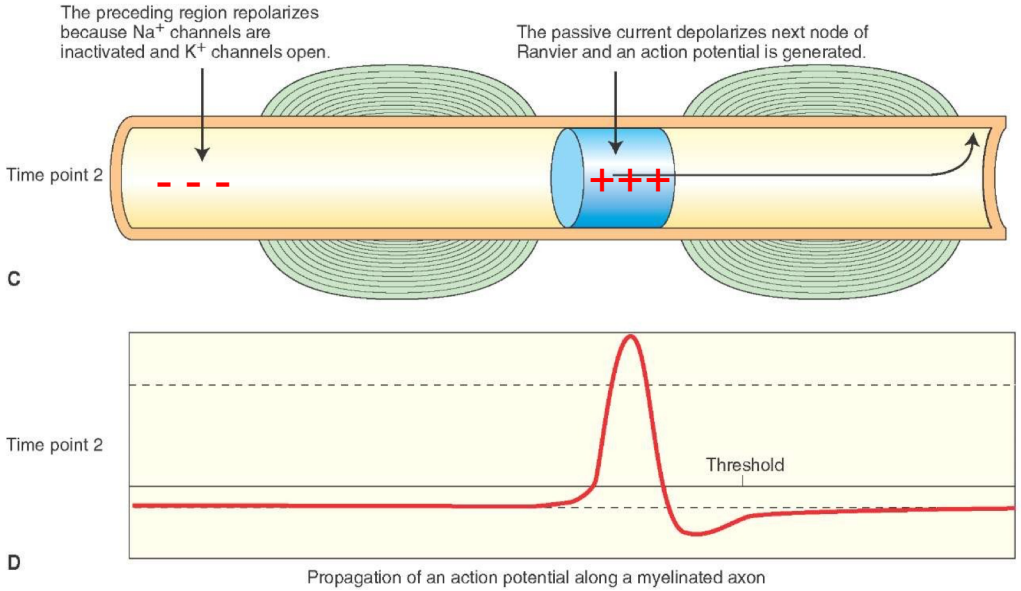


Schematic longitudinal cut of a myelinated fibre around the node of Ranvier showing:

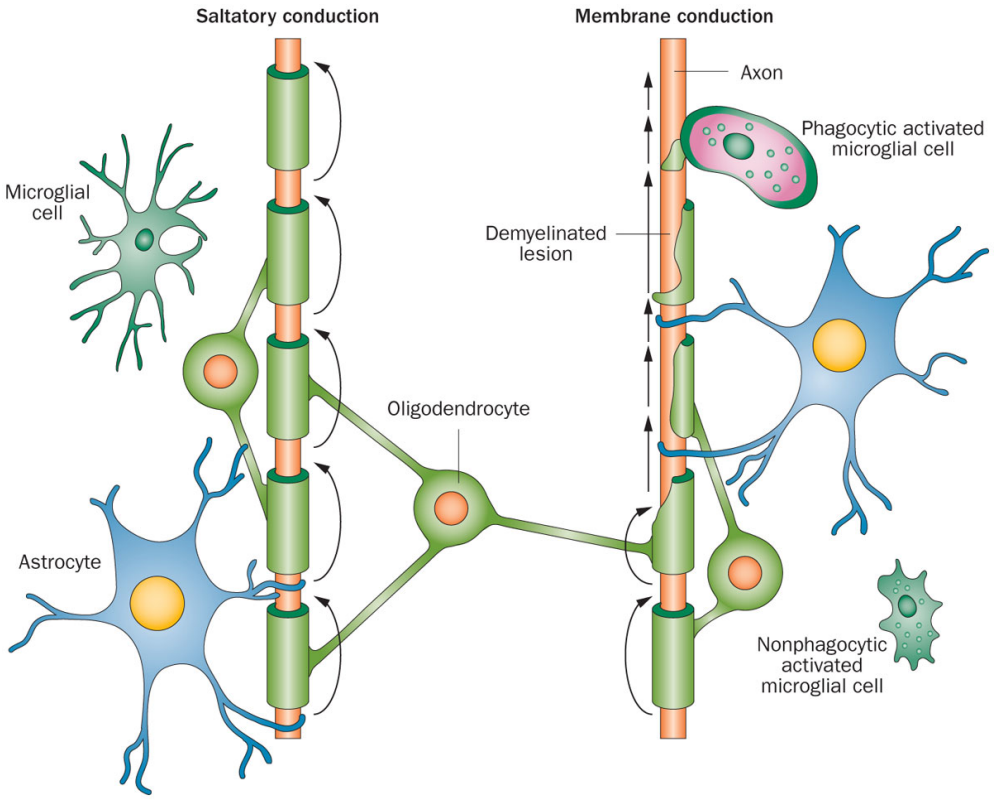
- The node, paranode, juxtaparanode (JXP) and internode are labelled.
- The node is contacted by Schwann cell **microvilli** in the PNS or by processes from **perinodal astrocytes** in the CNS.
- Myelinated fibres in the PNS are covered by a **basal lamina**.

Saltatory conduction velocity





Propagation of an action potential along a myelinated axon



Frohman, T. C. *et al.* (2013) Uhthoff's phenomena in MS—clinical features and pathophysiology *Nat. Rev. Neurol.* doi:10.1038/nrneurol.2013.98