1. **Lecture: Cells of the nervous system**
2. **Practical: Investigating neurons and glia** *(2MDL)*
3. **Clinical presentation on Multiple Sclerosis** *(Dr Paolo Muraro – G16 lecture theatre)*

The Brain: a true supercomputer

100,000,000,000 cells

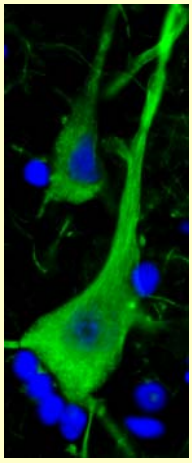
3,200,000 kilometres of wires

1,000,000,000,000,000 synaptic connections

All packed into 1.5 litres

INTRODUCTION

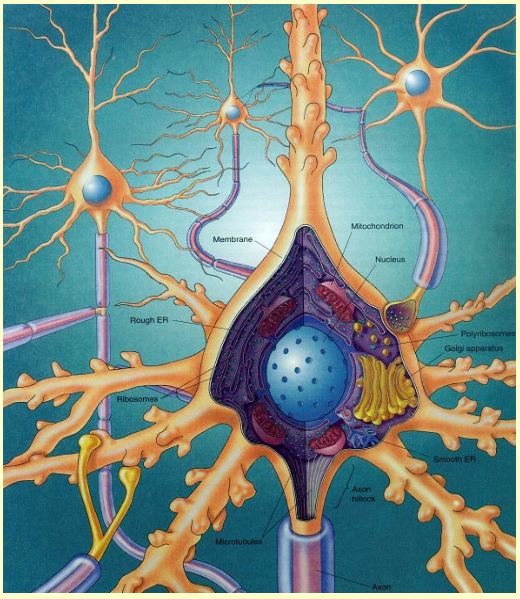
The Neuron



- basic structural and functional unit of the nervous system
- information processing unit.
- responsible for the generation and conduction of electrical signals
- communicate with one another via chemicals released at the synapse.
- supported by neuroglia, comprising several different cell types.

NEURONAL STRUCTURE

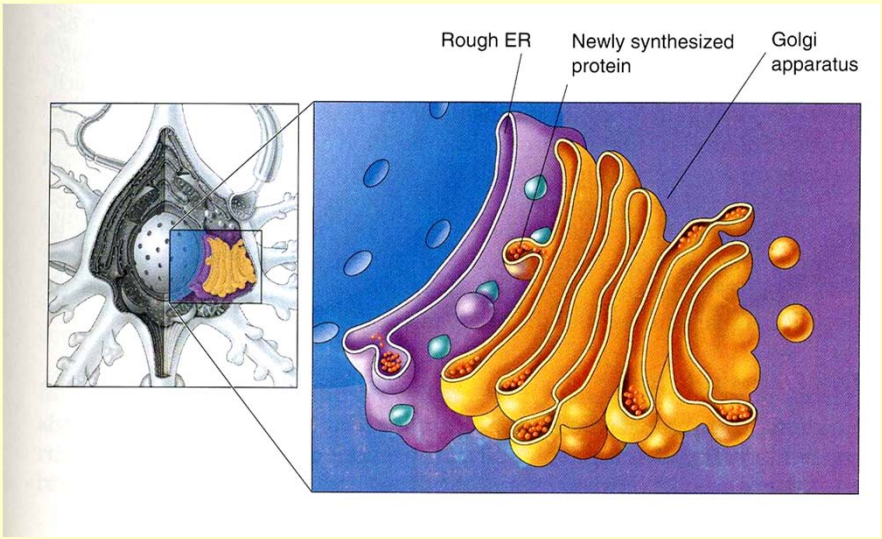
- Cellular structure of all neurons is similar.
- Diversity is achieved by differences in the number and shape of their processes.



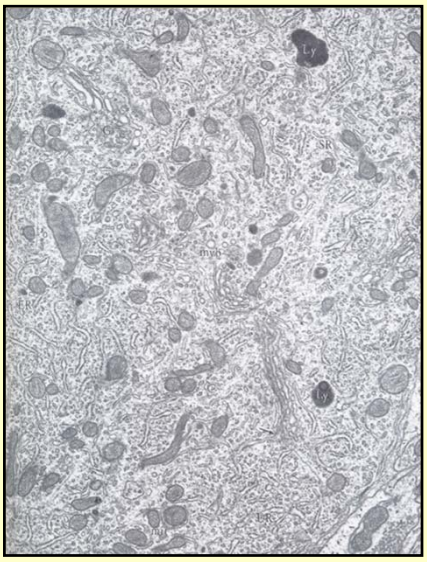
CELLS OF THE NERVOUS SYSTEM

- **large nucleus**
- **prominent nucleolus**
- **abundant rough ER**
- **well developed Golgi**
- **abundant mitochondria**
- **highly organised cytoskeleton**
- ***HIGHLY ORGANISED METABOLICALLY ACTIVE CELL***

A neuron is a highly organised, metabolically very active secretory cell



CELLS OF THE NERVOUS SYSTEM

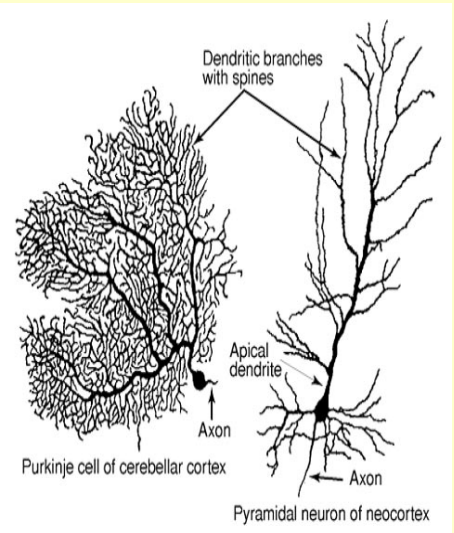


Neurons possess extensive rough endoplasmic reticulum and free ribosomes. An extensive Golgi apparatus is in keeping with high amounts of protein trafficking via the secretory pathway.

CELLS OF THE NERVOUS SYSTEM

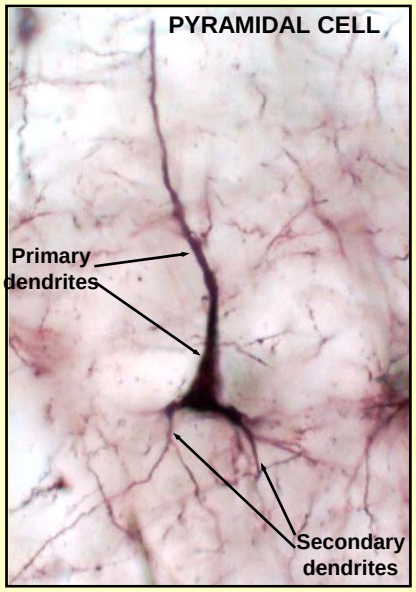
DENDRITES (input)

- **major area of reception of incoming information**
- **spread from cell body and branch frequently**
- **greatly increase the surface area of the neuron**
- **often covered in protrusions called spines**
- **dendritic spines receive the majority of synapses**
- **large pyramidal neurons may have as many as 30,000/40,000 spines**

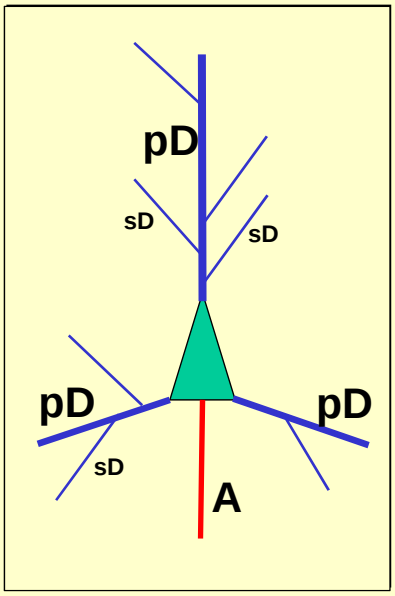


CELLS OF THE NERVOUS SYSTEM

DENDRITES



Light microscope

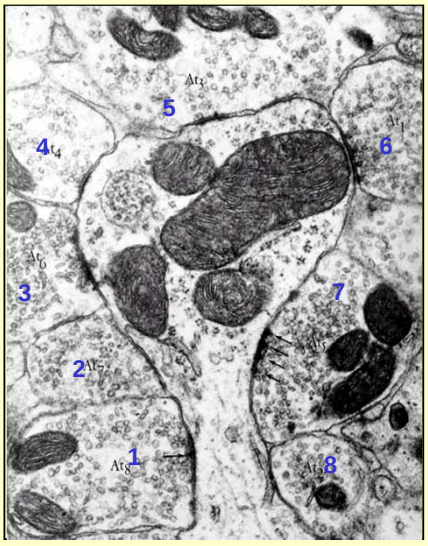


CELLS OF THE NERVOUS SYSTEM

DENDRITIC SPINES

One of the most plastic elements of the nervous system

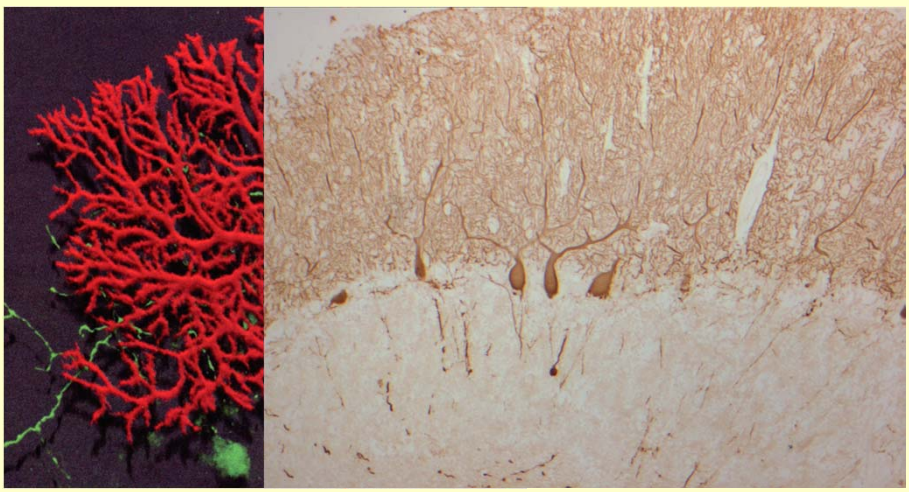
Light microscope - Golgi preparation



Electron microscope

CELLS OF THE NERVOUS SYSTEM

Purkinje neurons of the cerebellum

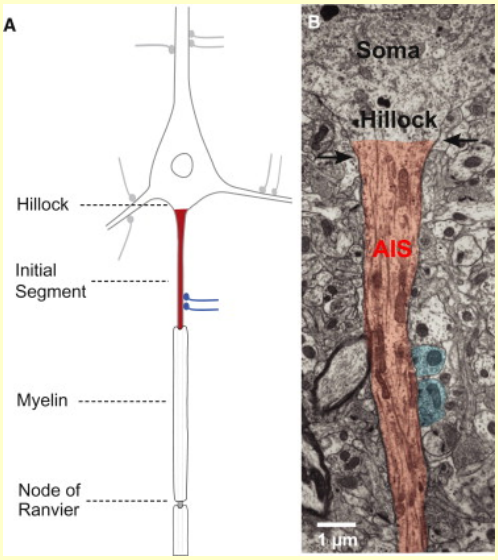


- **dendrites have an enormous number of spines (> 80,000/ cell)**
- **human cerebellum has approx 15 mill Purkinje cells.**

CELLS OF THE NERVOUS SYSTEM

AXONS - output

- **conduct impulses away from cell body**
- **emerge at the axon hillock**
- **usually only one per cell**
- **may branch after leaving cell body and at target**
- **prominent micro-tubules and neurofilaments**



CELLS OF THE NERVOUS SYSTEM

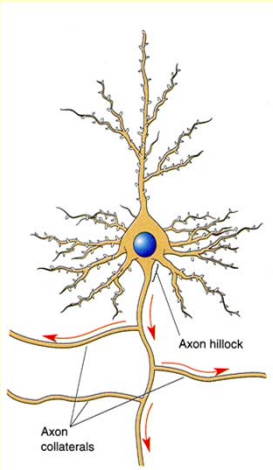
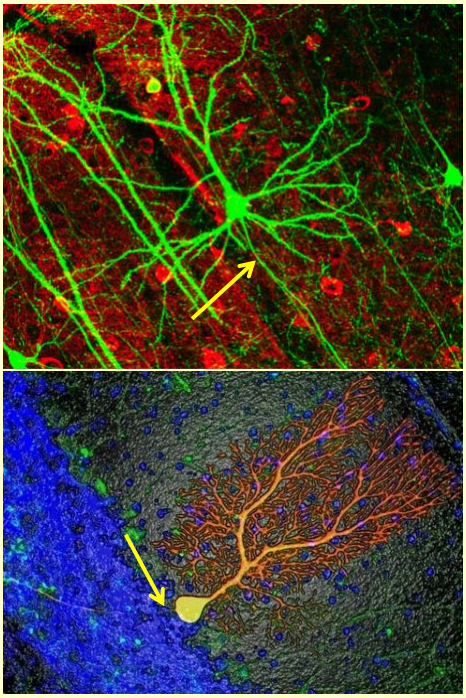
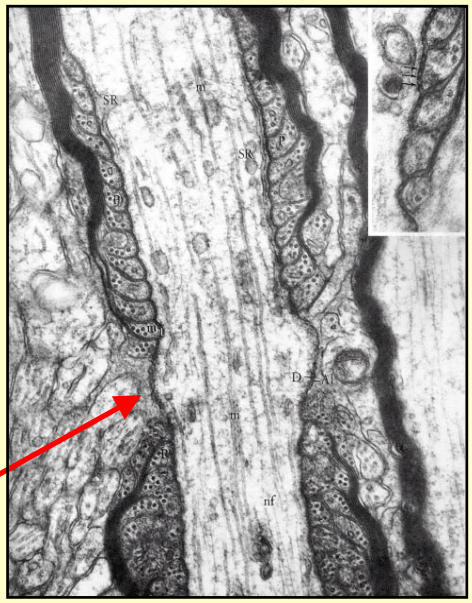


Figure 2.14
The axon and axon collaterals. The axon functions like a telegraph wire to send electrical impulses to distant sites in the nervous system. The arrows indicate the direction of information flow.

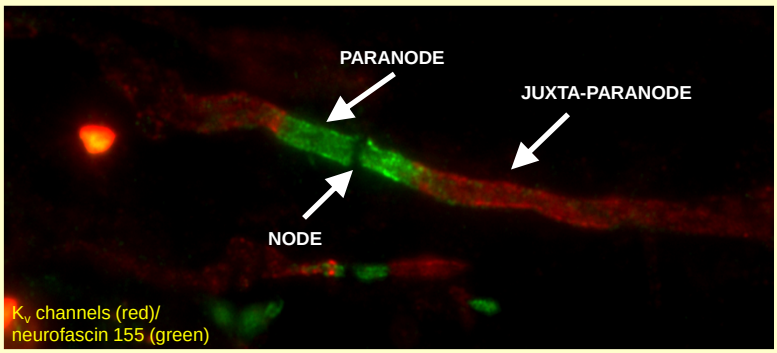


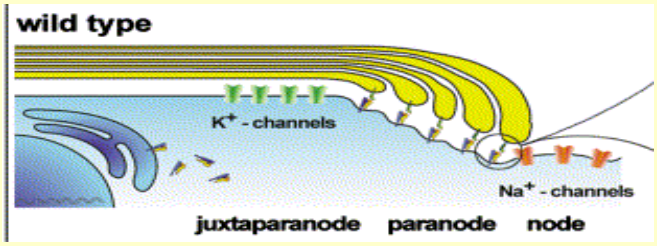
AXONS

- axons contain abundant intermediate filaments and microtubules
- axons can be myelinated or unmyelinated
- axonal membrane of myelinated fibre only exposed at node of Ranvier
- cable properties



The molecular composition of the axon is organised into domains





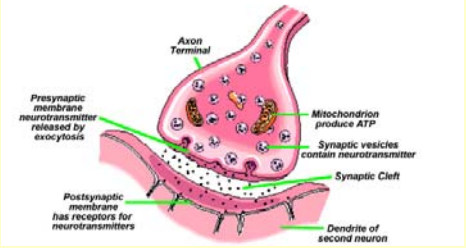
AXON TERMINALS

- axons often branch extensively close to target (terminal arbor)

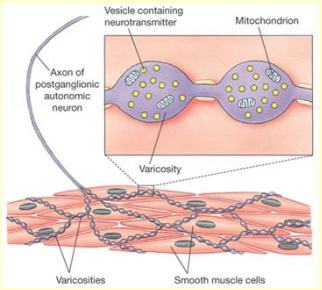
- form synaptic terminals with target

- boutons or varicosities

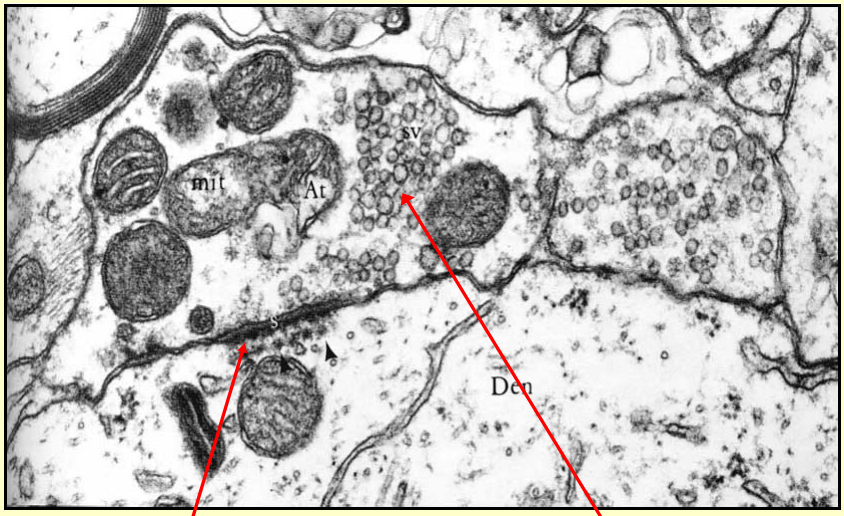
BOUTON *A SYNAPSE*



VARICOSITIES



SYNAPTIC STRUCTURE



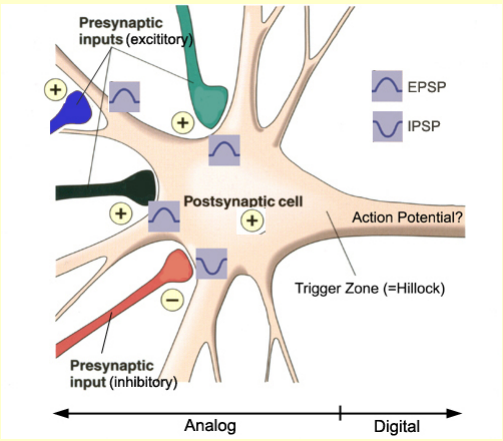
Synaptic density **Synaptic vesicles**

SYNAPTIC STRUCTURE

- synaptic vesicles, packaged in the Golgi and shipped by fast anterograde transport
- specialised mechanisms for association of synaptic vesicles with the plasma membrane
- abundant mitochondria - ~ 45% of total energy consumption is required for ion pumping and synaptic transmission - sensitivity to O_2 deprivation

SYNAPTIC ORGANISATION

- **neurons receive multiple synaptic input**
- **neurons use a diversity of chemical transmitters, excitatory and inhibitory**
- **competing inputs are integrated in the postsynaptic neuron (*neuronal integration*)**



SYNAPTIC ORGANISATION

Types of synapse:

- **axo-dendritic** ***(often excitatory)***
- **axo-somatic** ***(often inhibitory)***
- **axo-axonic** ***(often modulatory)***

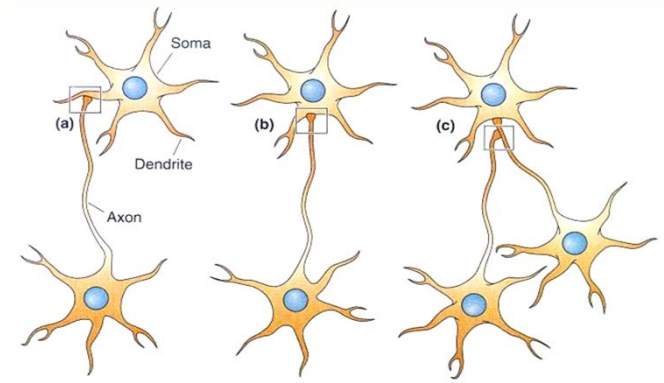
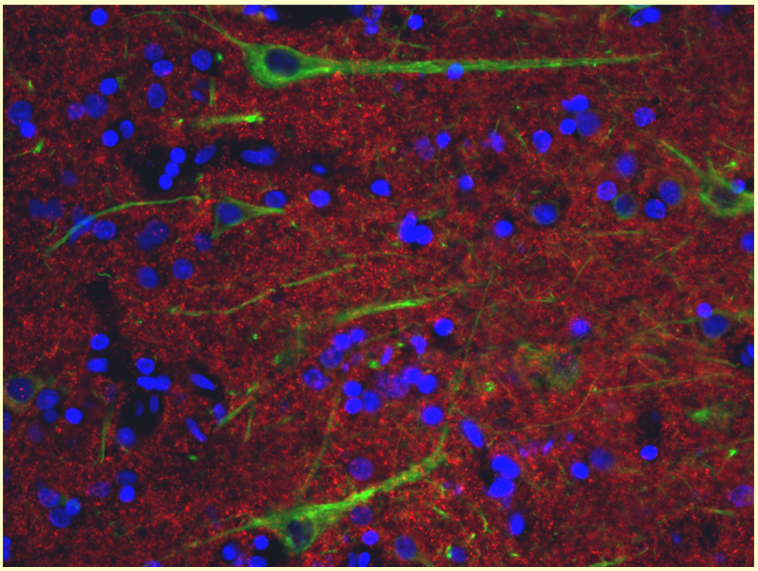


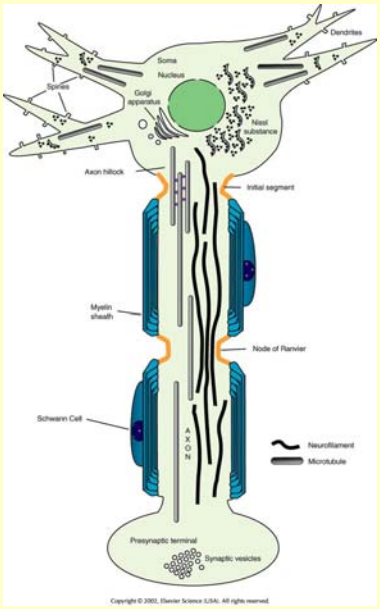
Figure 5.3
Synaptic arrangements in the CNS. (a) An axodendritic synapse, **(b)** an axosomatic synapse, and **(c)** an axoaxonic synapse.



Axo-dendritic synapses in the cerebral cortex

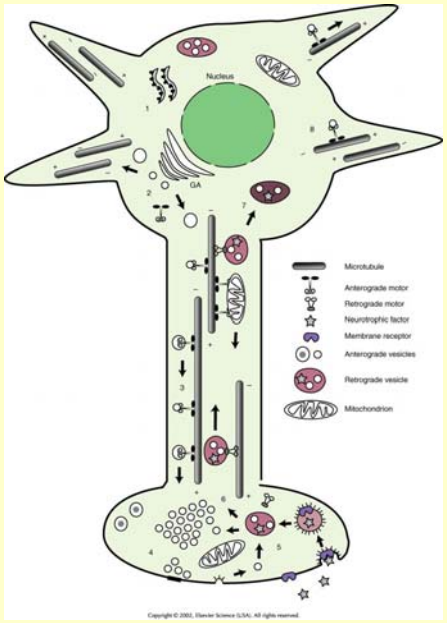
Neuronal cytoskeleton

- in the human adult axons range in length from micrometers to up to a meter
- highly organised cytoskeleton is required *(microfilaments, intermediate filaments, microtubules)*
- neurofilaments play a critical role in determining axon caliber
- microtubules are very abundant in the nervous system

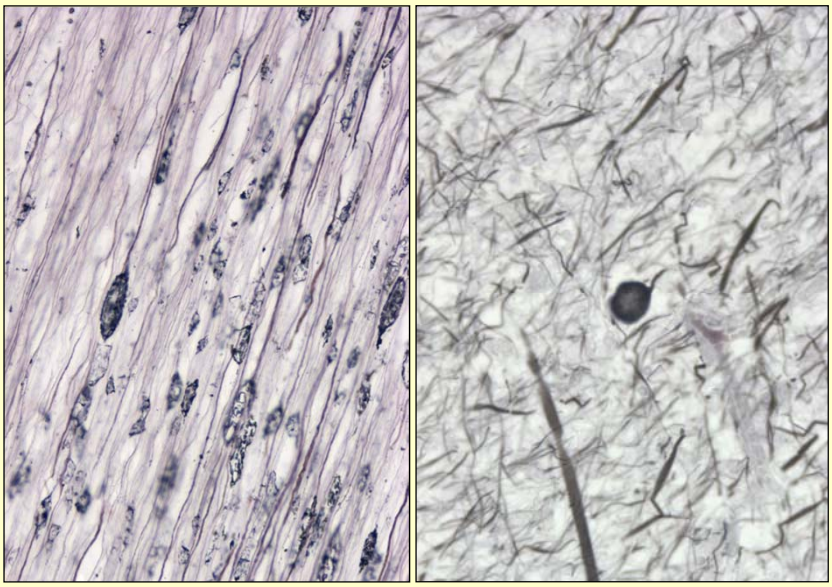


FAST AXONAL TRANSPORT

- transport of membrane associated materials
- vesicles with associated motors are moved down the axon at 100-400 mm per day
- different membrane structures targeted to different compartments
- retrograde moving organelles are morpholgically and biochemically distinct from anterograde vesicles



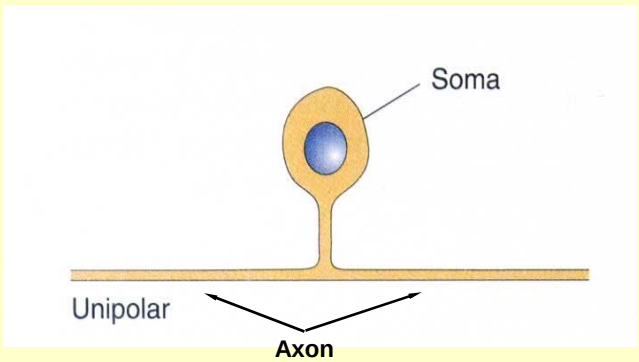
Axonal damage in Multiple Sclerosis

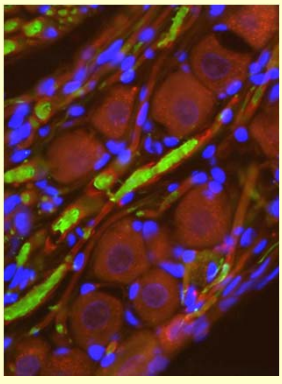


CELLS OF THE NERVOUS SYSTEM

MORPHOLOGICAL SUBTYPES OF NEURONS

1. Pseudounipolar
- sensory neurons have two fused processes which are axonal in structure.



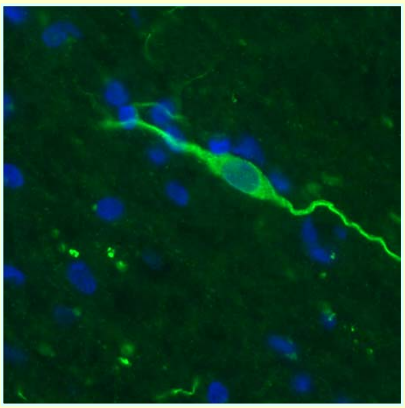


Dorsal root ganglion neurons

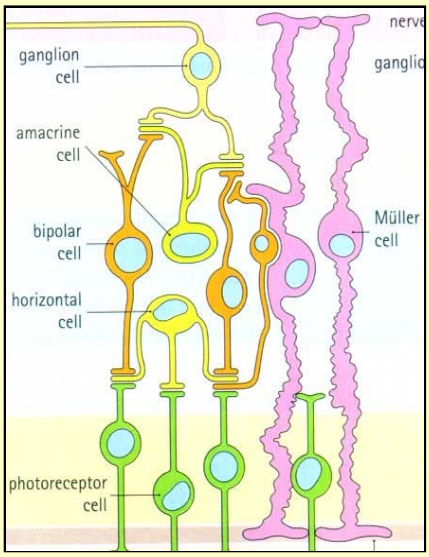
MORPHOLOGICAL SUBTYPES OF NEURONS

2. Bipolar

- retinal bipolar cells



cerebral cortex white matter



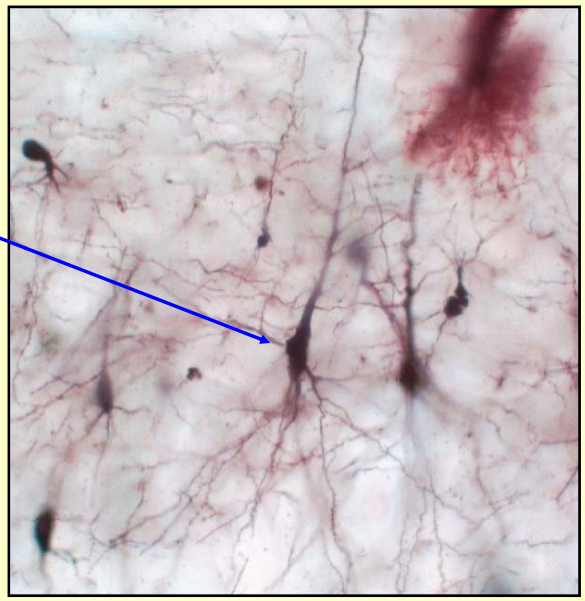
MORPHOLOGICAL SUBTYPES OF NEURONS

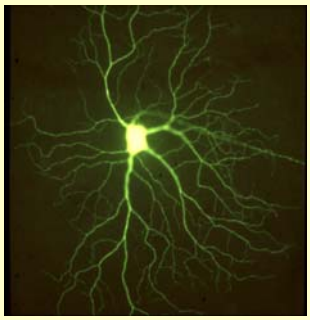
3. Golgi type I multipolar

- **highly branched dendritic trees**
- **axons extend long distances**
- **pyramidal cells of the cerebral cortex**
- **Purkinje cells of the cerebellum (15 mill)**
- **anterior horn cells of the spinal cord**
- **retinal ganglion cells**

3. Golgi type I multipolar

Pyramidal cell in the cerebral cortex





Retinal ganglion cell

MORPHOLOGICAL SUBTYPES OF NEURONS

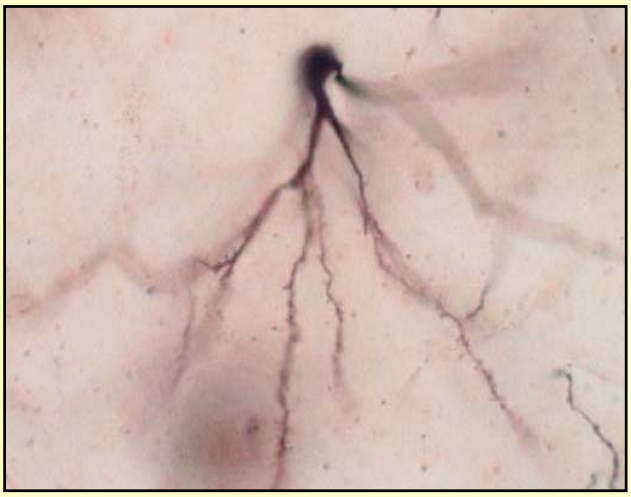
4. Golgi type II multipolar

- highly branched dendritic trees
- short axons
- axons terminate quite close to cell body of origin
- stellate cells of the cerebral cortex and cerebellum

CELLS OF THE NERVOUS SYSTEM 22.

MORPHOLOGICAL SUBTYPES OF NEURONS

4. Golgi type II multipolar - cerebral cortex



CELLS OF THE NERVOUS SYSTEM 23.

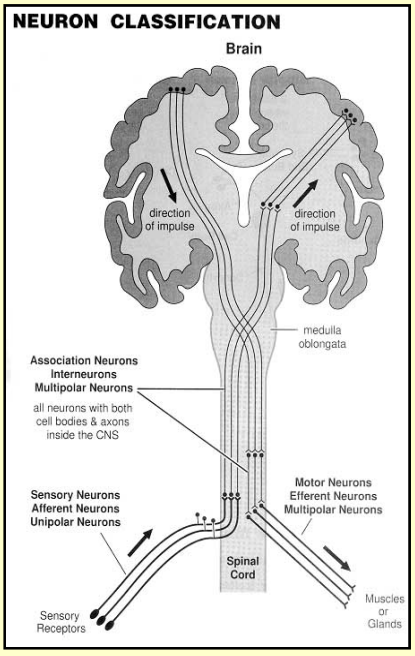
Functional classification of neurons

1. Sensory neurons

2. Motor neurons

3. Interneurons

- **responsible for modification, coordination, integration, facilitation and inhibition of sensory input.**



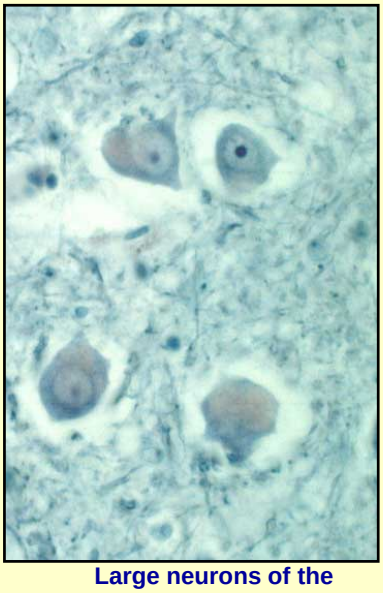
FUNCTIONAL ORGANISATION OF NEURONS

1. Nucleus

- group of unencapsulated neuronal cell bodies within the CNS.
- usually consist of functionally similar cells
- examples - brain stem nuclei (Raphe)
  deep cerebellar nuclei (Dentate)

1. Nucleus

Dentate nucleus of the cerebellum



Large neurons of the inferior olivary nucleus

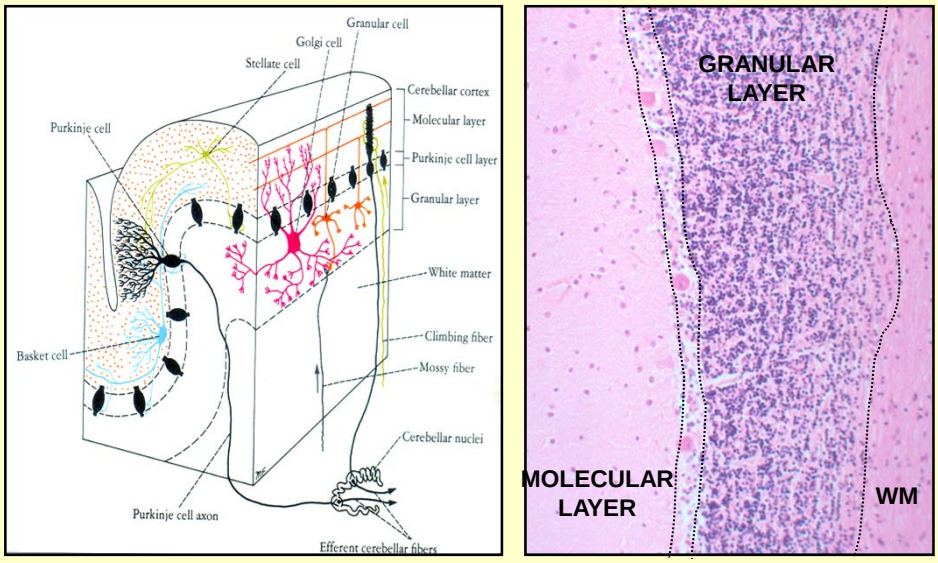
FUNCTIONAL ORGANISATION OF NEURONS

2. Laminae

- layers of neurons of similar type and function.

- examples - cerebral cortex grey matter
cerebellar gray matter

2. Laminae



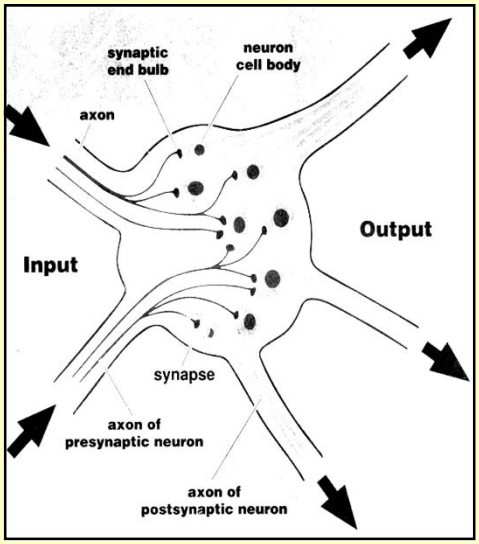
Neuronal organization in the cerebellum

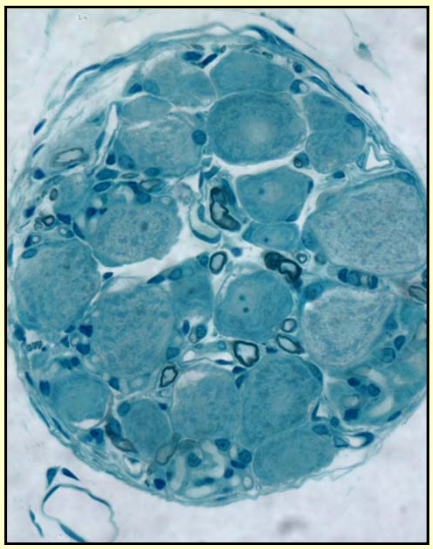
FUNCTIONAL ORGANISATION OF NEURONS

3. Ganglion

- group of encapsulated neuronal cell bodies in the peripheral nervous system
- examples - dorsal root ganglia
  - sympathetic ganglia

3. Ganglion





FUNCTIONAL ORGANISATION OF NEURONS

4. Fibre tracts

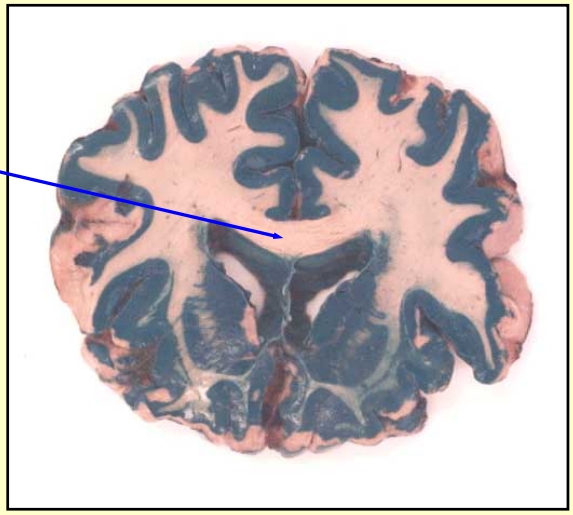
- groups or bundles of axons in the CNS

- mixture of myelinated and unmyelinated

- examples - corpus callosum
- internal capsule

FUNCTIONAL ORGANISATION OF NEURONS

4. Fibre tract

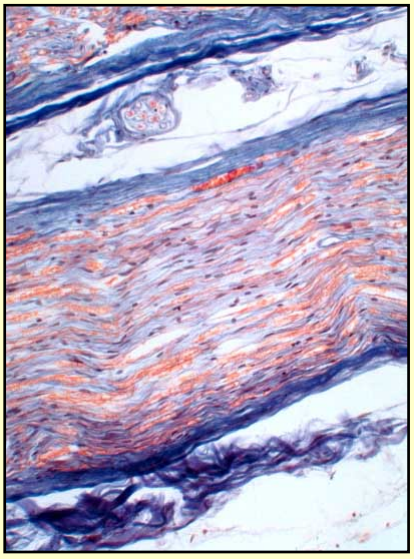


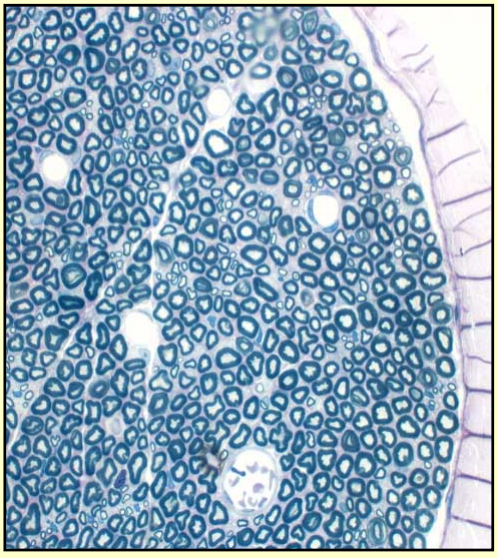
FUNCTIONAL ORGANISATION OF NEURONS

5. Nerve

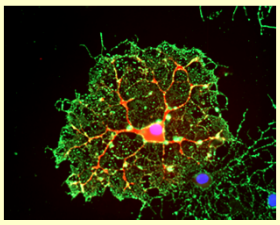
- discrete bundles of axons
- bring information to the CNS from sensory receptors and bring axons to effector organs
- often mixed sensory/motor
- usually part of the peripheral nervous system (except eg optic and olfactory nerves)

5. Nerve





CELLS OF THE NERVOUS SYSTEM

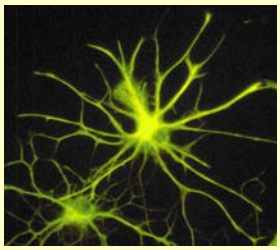


NEUROGLIA

- support cells of the nervous system
- astroglia, oligodendroglia, microglia, immature progenitors, ependymal cells, Schwann cells, satellite glia
- many and varied functions
- essential for the correct functioning of neurons

CELLS OF THE NERVOUS SYSTEM

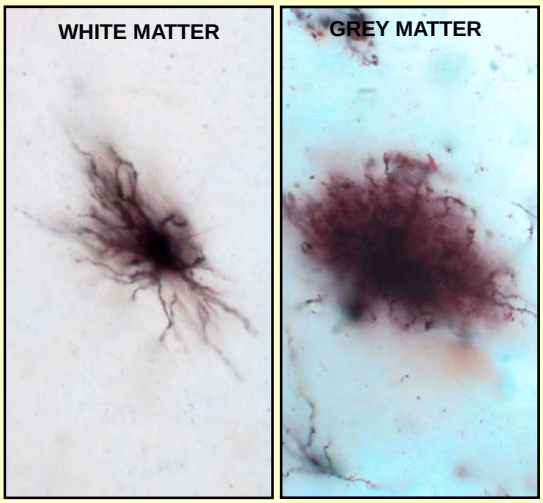
ASTROGLIA



- star shaped cells
- numerically the largest population of CNS glia
- intimate associations with other cell types
- several different types
  - fibrous astroglia *(WM)*
  - protoplasmic astroglia *(GM)*
  - radial astroglia

ASTROGLIA

- numerous intermediate filament bundles in cytoplasm of fibrous astroglia (GFAP)
- gap junctions suggest astroglia-astroglia signalling

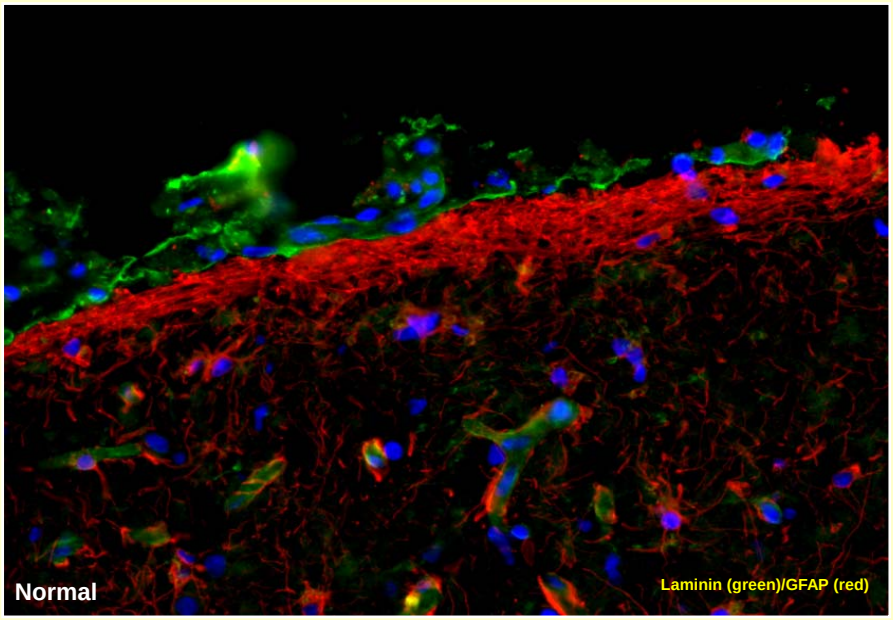


FIBROUS PROTOPLASMIC

ASTROGLIAL FUNCTIONS

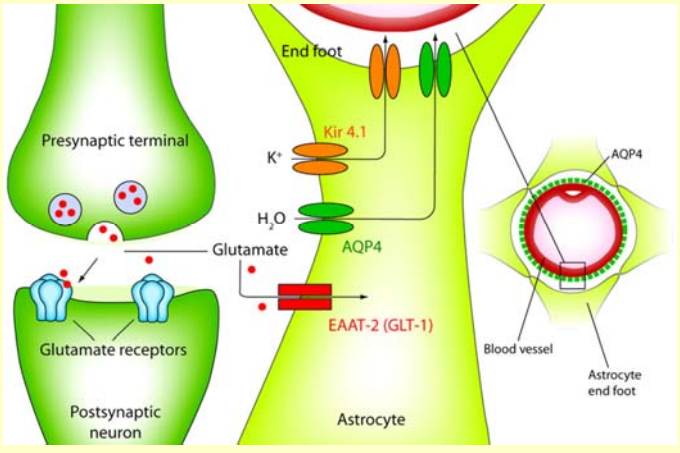
1. Scaffold for neuronal migration and axon growth during development.
2. Formation of blood-brain barrier.
3. Transport of substances from blood to neurons.
4. Segregation of neuronal processes (synapses).
5. Removal of neurotransmitters.
6. Synthesis of neurotrophic factors.
7. Neuronal-glial and glial neuronal signalling
8. Potassium ion buffering
9. Glial scar formation

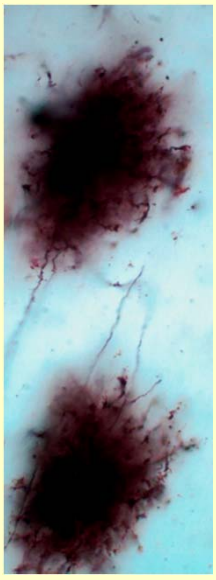
Barrier functions of astrocytes



CELLS OF THE NERVOUS SYSTEM

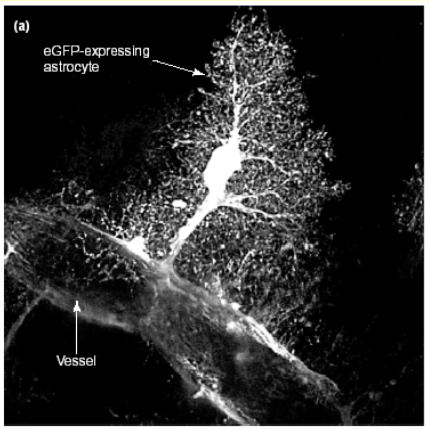
Removal of neurotransmitters, K^+ and H_2O.

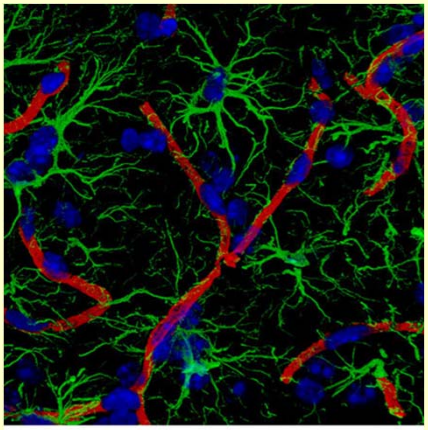




Astrocyte interaction with blood vessels

- ordered arrangement of astrocytes with minimal overlap
- each cell forms a specific territory that interfaces with microvasculature
- might include thousands of synapses





OLIGODENDROGLIA

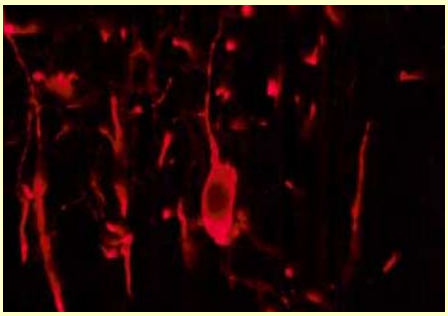
- the myelin forming cells of the CNS
  - interfasicular oligodendroglia
  - perineuronal oligodendroglia
- small spherical nuclei
- few thin processes
- prominent ER and Golgi
- metabolically highly active

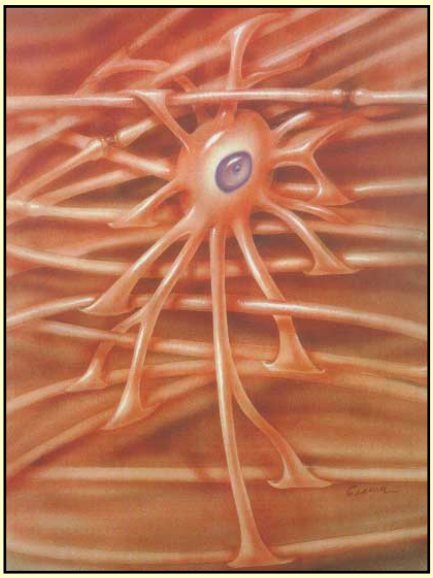
Electron micrograph of perineuronal oligodendroglia

CELLS OF THE NERVOUS SYSTEM

OLIGODENDROGLIAL FUNCTIONS

- production and maintenance of the myelin sheath
- each cell produces multiple sheaths (1-40)

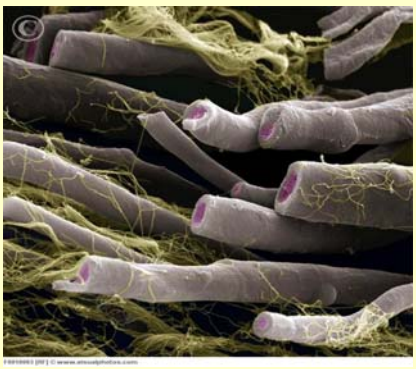


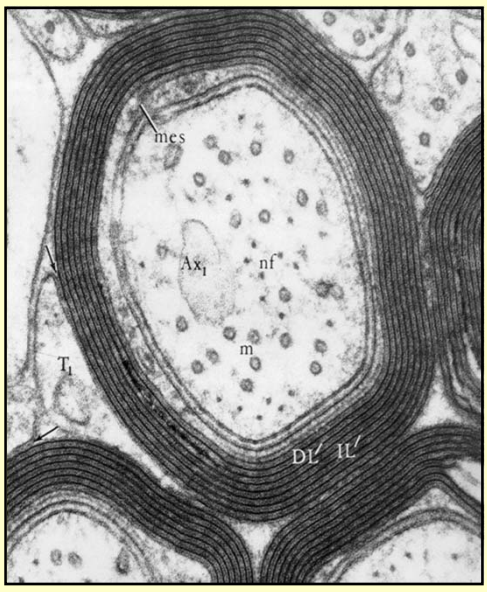


CELLS OF THE NERVOUS SYSTEM

MYELIN

- a lipid rich insulating membrane
- up to 50 lamellae
- dark and light bands seen at EM level

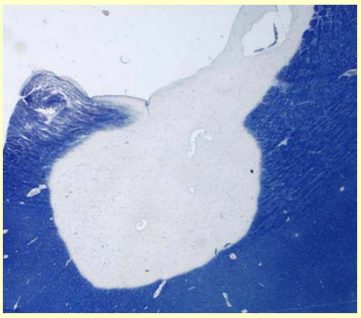




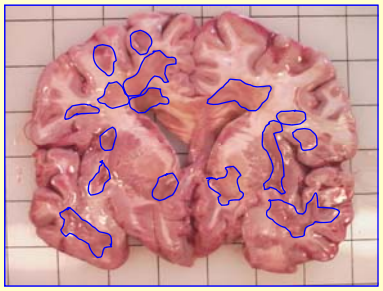
MYELIN

- loss of oligodendroglia and myelin has disastrous consequences

- myelin disease states
  - *Multiple Sclerosis (MS)*
  - *Adrenoleucodystrophy*



Luxol fast blue staining of an MS lesion



MICROGLIA

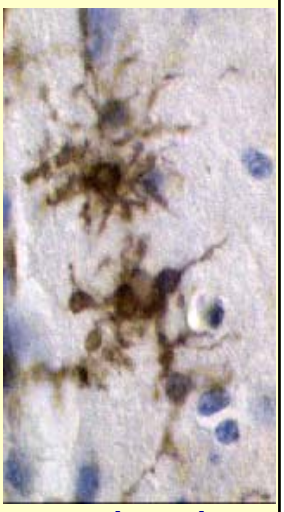
- derived from bone marrow during early development.
- resident macrophage population of the CNS
- involved in immune surveillance
- present antigens to invading immune cells
- first cells to react to infection or damage
- role in tissue modelling
- synaptic stripping

CELLS OF THE NERVOUS SYSTEM

MICROGLIAL MORPHOLOGY

Resting ramified

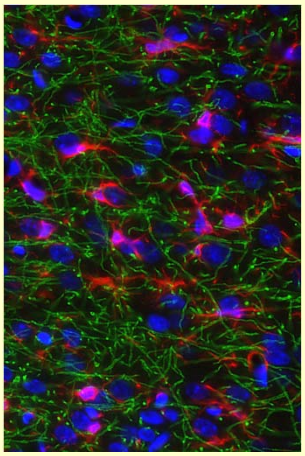
Rod-like

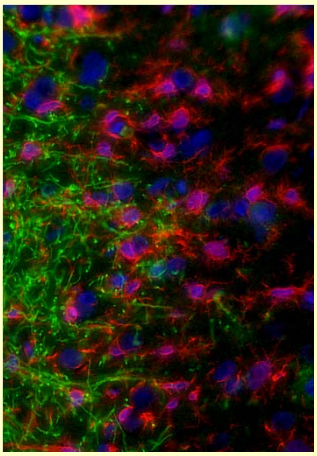


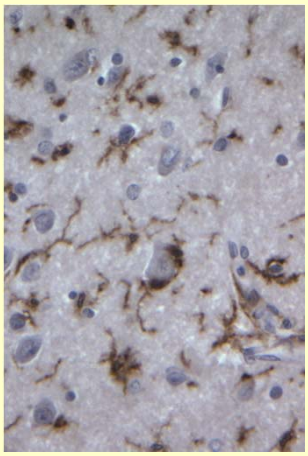
Activated

CELLS OF THE NERVOUS SYSTEM

MICROGLIA AND INFLAMMATION







PERIPHERAL GLIA

Schwann cells

- myelin producing cells of the PNS
- each Schwann cell produces only one myelin sheath
- surround unmyelinated axons
- promote axon regeneration

Schwann cells