Behavioral Neuroscience A
3: Cells

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https://youtu.be/mPM5act57lg

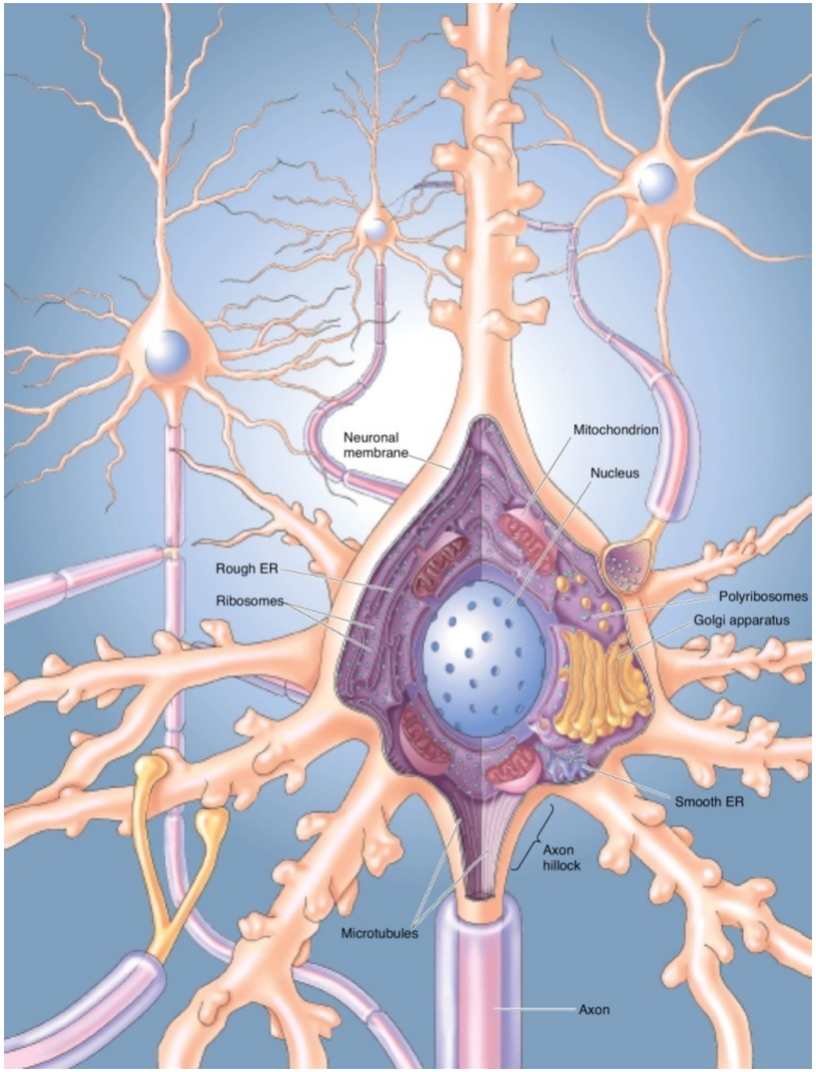
Lecture Video at above link.

Cells

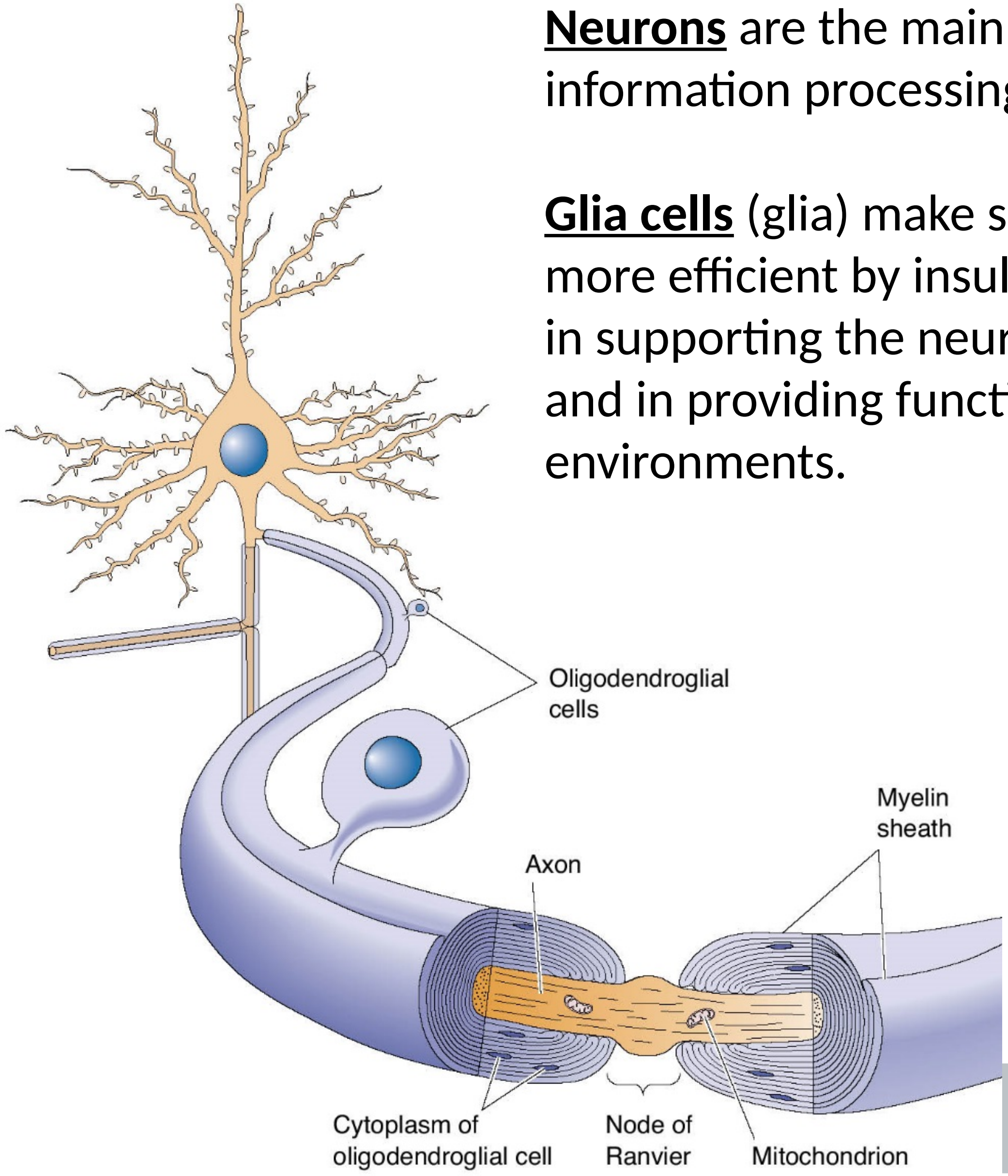
<u>Cells in the nervous system</u>

1) Neurons and glia
2) Histology
3) Neurons: structure, types, and arrangement
4) Adult Neurogenesis
5) Neural death - Parkinson’s disease
6) Glia
7) Damage to glia – Multiple sclerosis

8) How to study for this course..



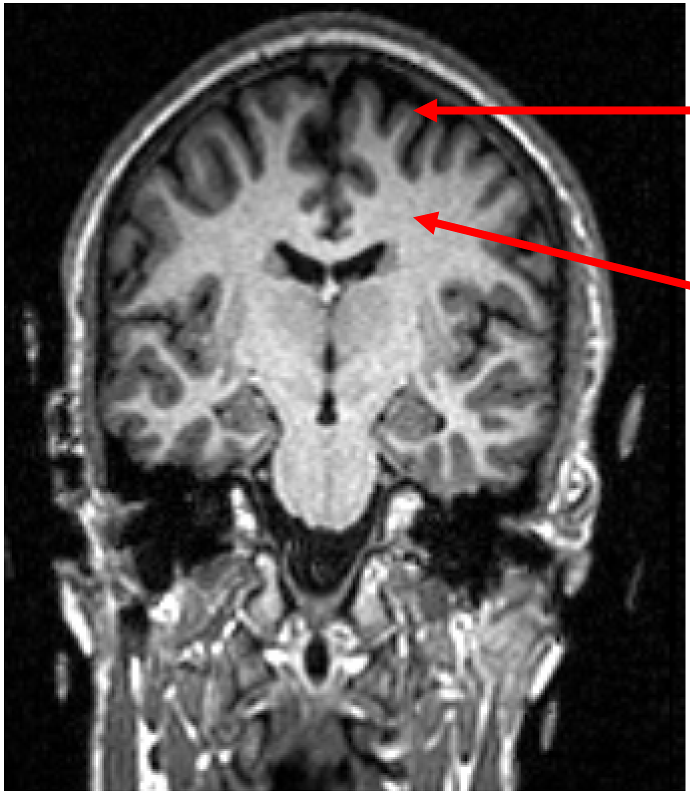
Neuronal Cells vs. Glial Cells



<u>Neurons</u> are the main elements for information processing in the brain.

<u>Glia cells</u> (glia) make signal transduction more efficient by insulation, and play a role in supporting the neurons in development and in providing functional extracellular environments.

“Grey” matter vs. “White” matter



Gray matter: consists mainly of cell bodies (neurons and glia)

White matter: consists of myelinated fiber tracks (connections) between neurons.

Myelin consists to a large degree of lipids and serves as insulation to improve signal transduction.

We can see the difference between these two tissue types on this T1-weighted magnetic resonance image (MRI).

Histology

Histology is the science of examining tissues under microscope.

Remember from last class:

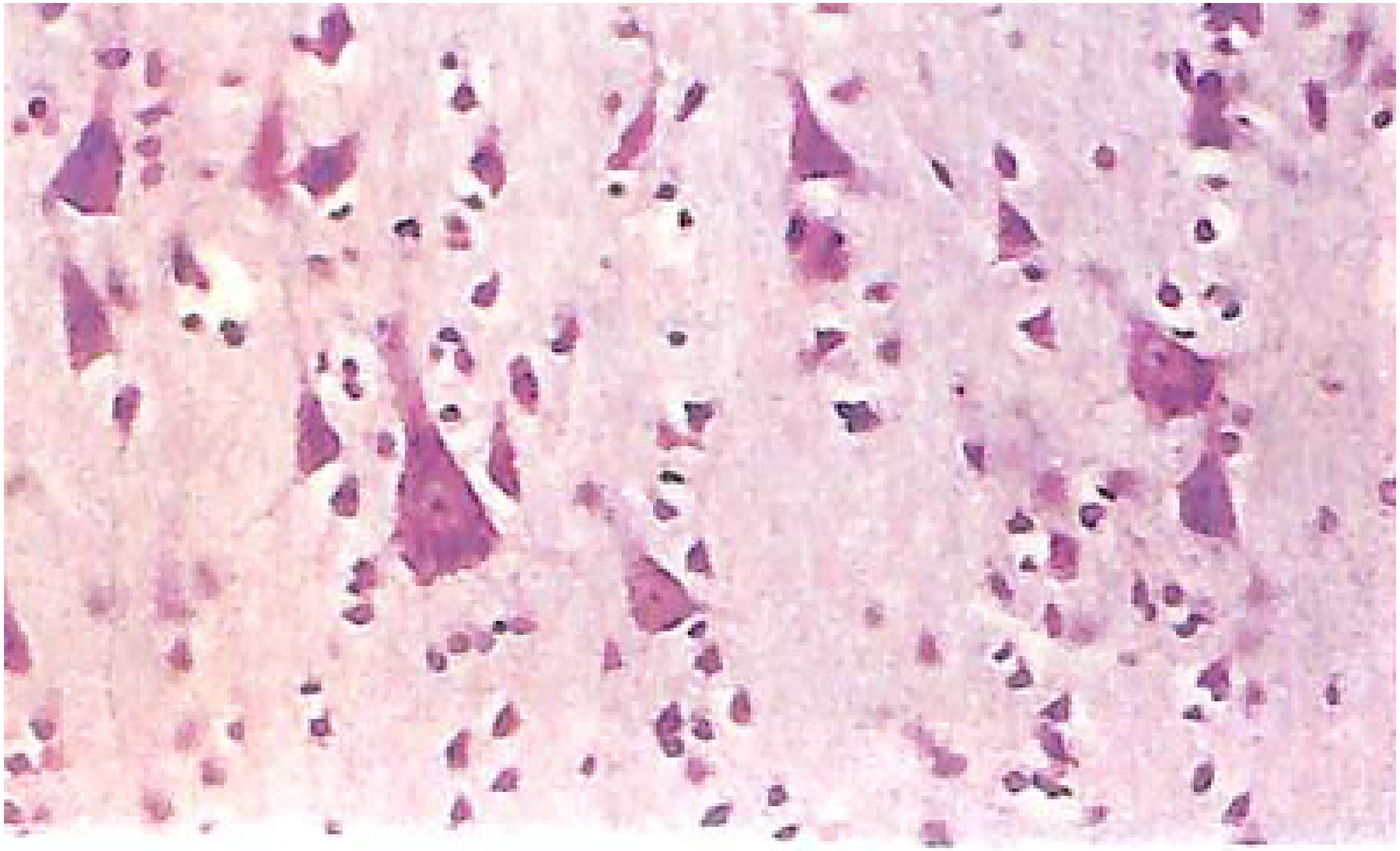
- We “slice” the brain into thin slices

- We “stain” the brain with chemicals to make some parts stand out

- We look at the slice under the microscope.

Nissl Stain

Nissl stain (late 19th century)

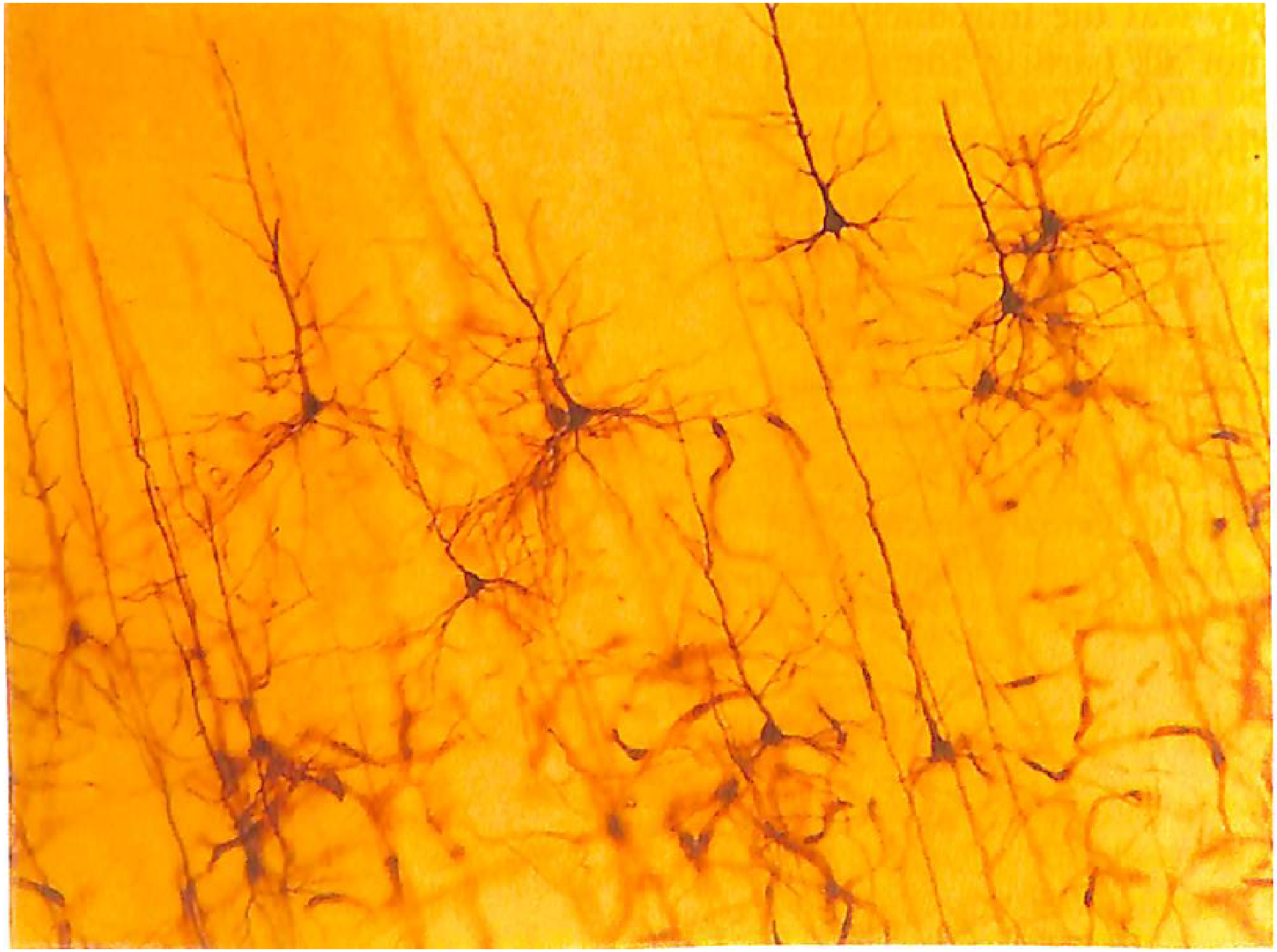


stains neurons' cell bodies (in particular the endoplasmatic reticulum of the cells)

Golgi Stain

Golgi stain (also late 19th century)

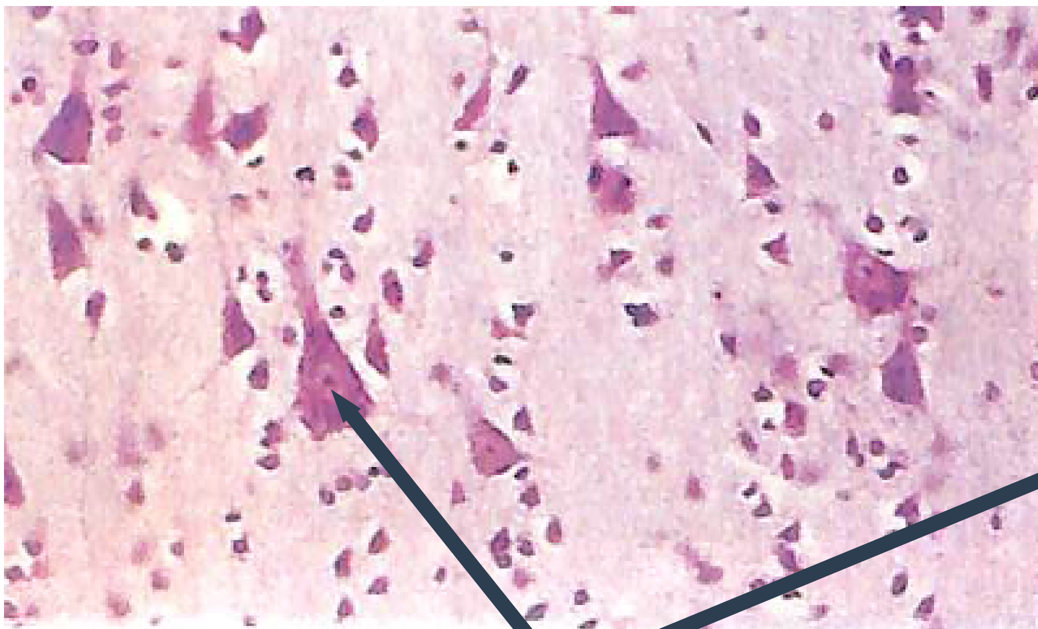
stains only few (~1/100) neurons
cell bodies + neurites (axons, dendrites)

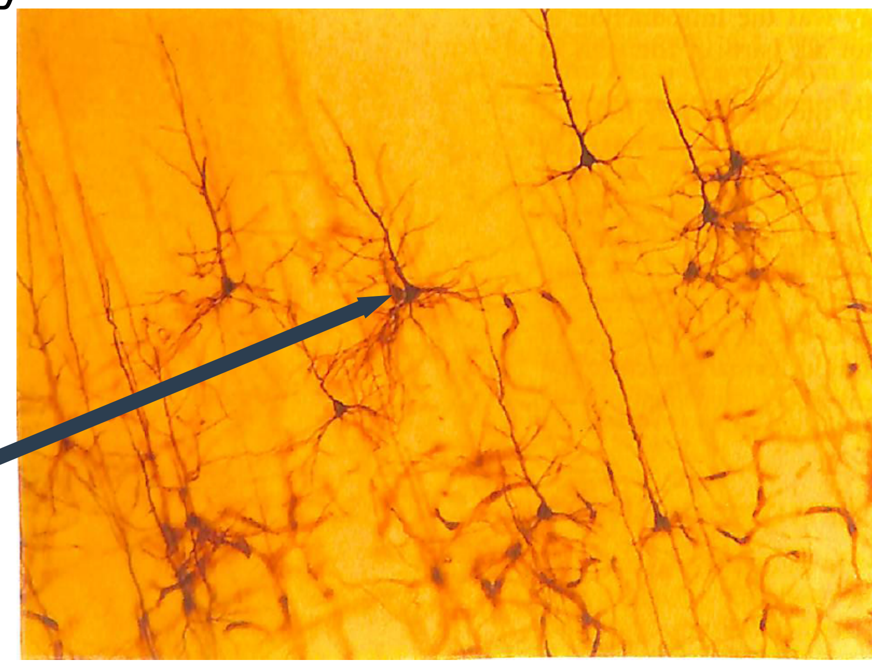


Bear, Neuroscience

What is a brain cell?

What if I told you that these are both **the same part of the brain**
→ They are just stained differently

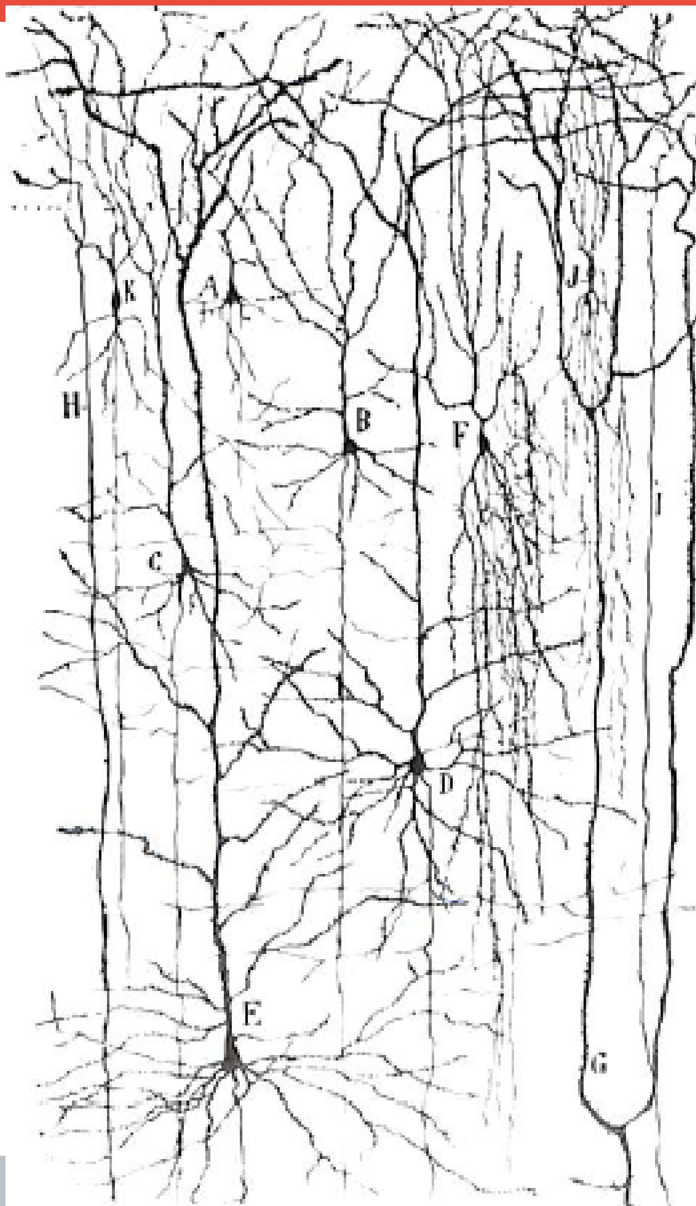




This might be a similar “object”

-They look different though!
-So what does a neuron (brain cell) “actually” look like?

What is a neural cell?



My man, Cajal.

FIGURE 2.5
Santiago Ramón y Cajal (1852–1934).
(Source: Finger, 1994, Fig. 3.26.)

<u>Neuron doctrine:</u>
Neurons communicate by contact, not continuity.
That means, neurons are individual cells (not a continuous web) and are the primary unit of information processing in the brain.

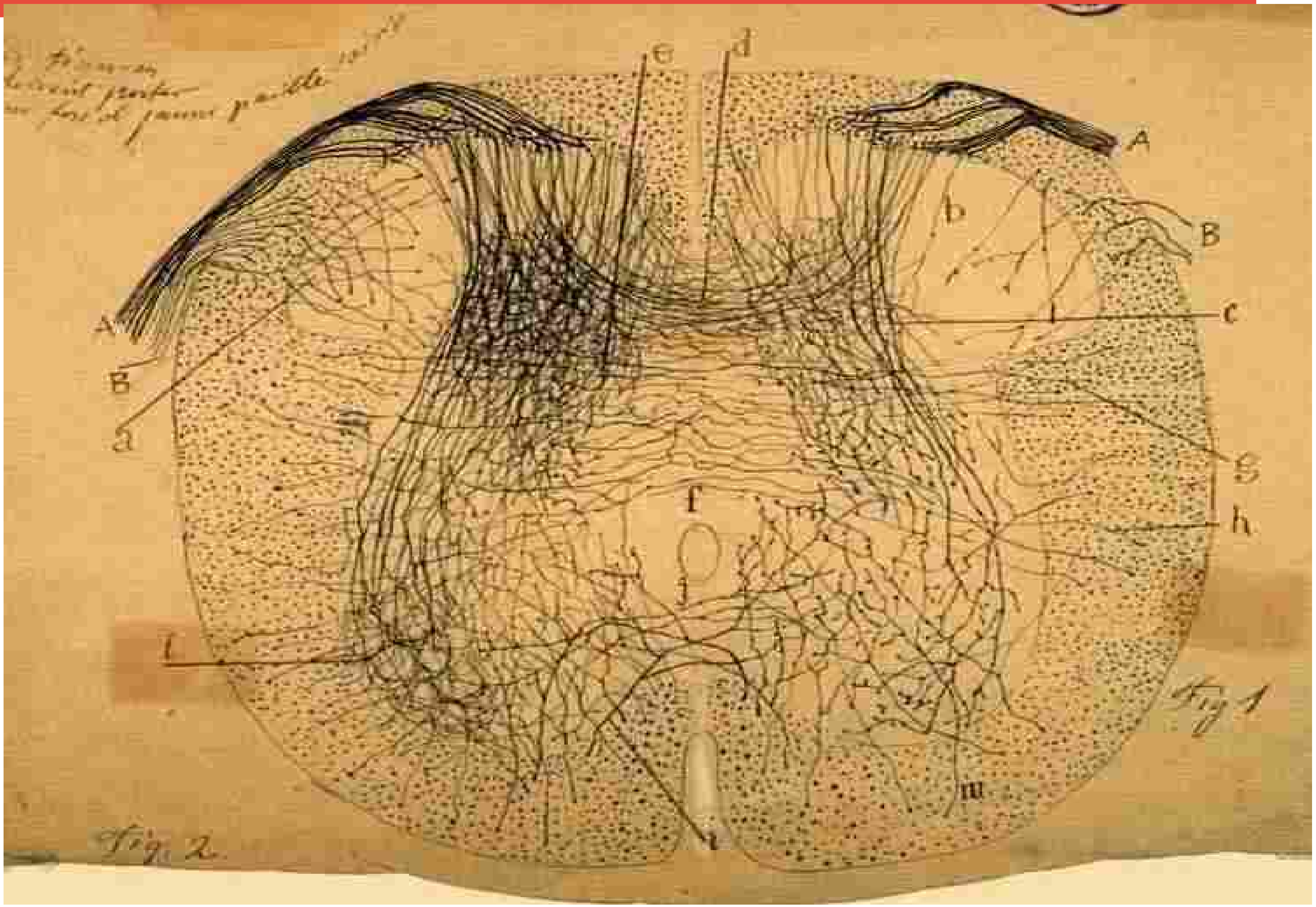
What is a neural cell?

It looks like a "web" (net).

What is the main "piece" to look at?

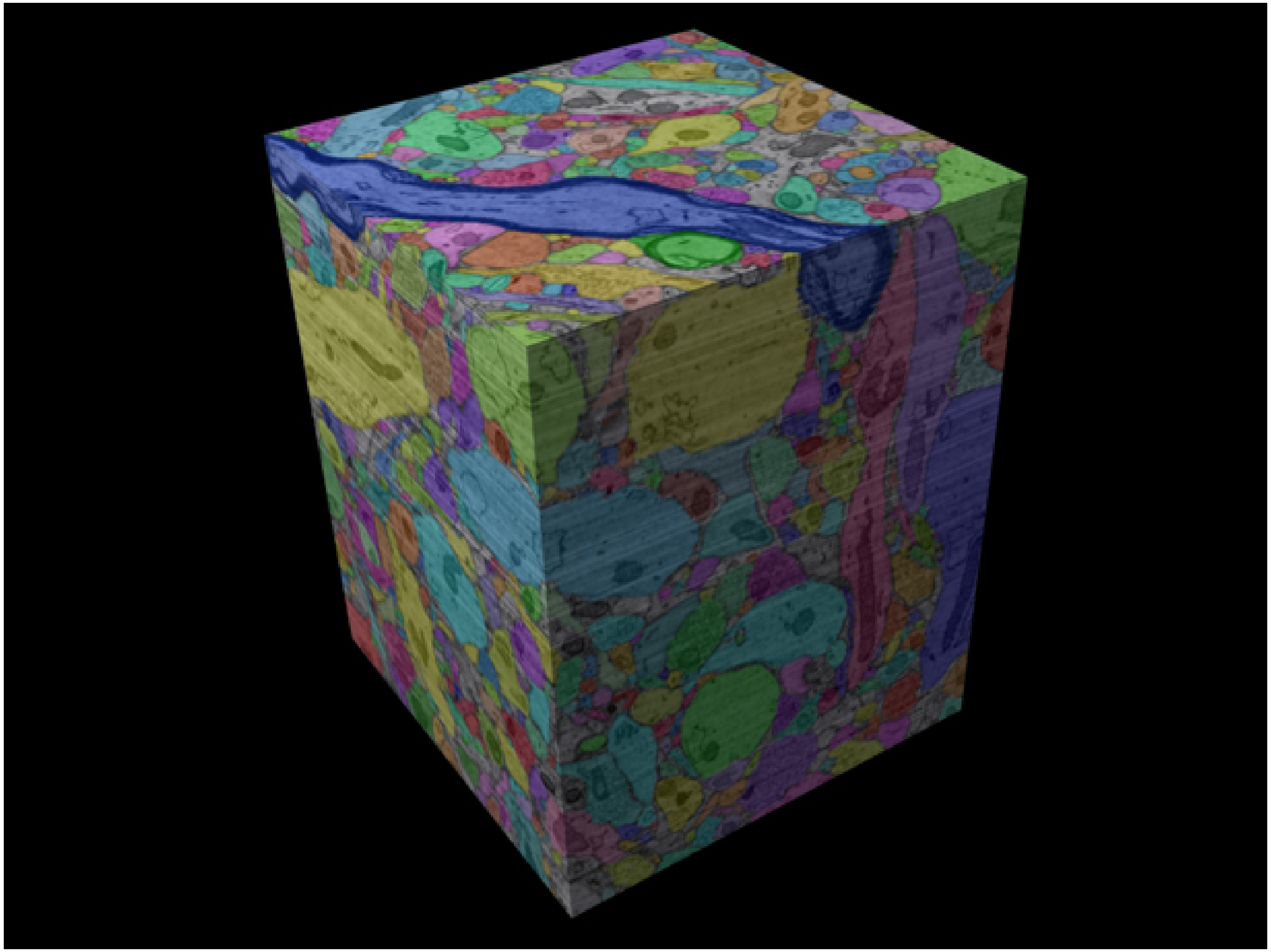
→ Is it all the connections between nodes (cells)?

→ Or are cells the main thing?



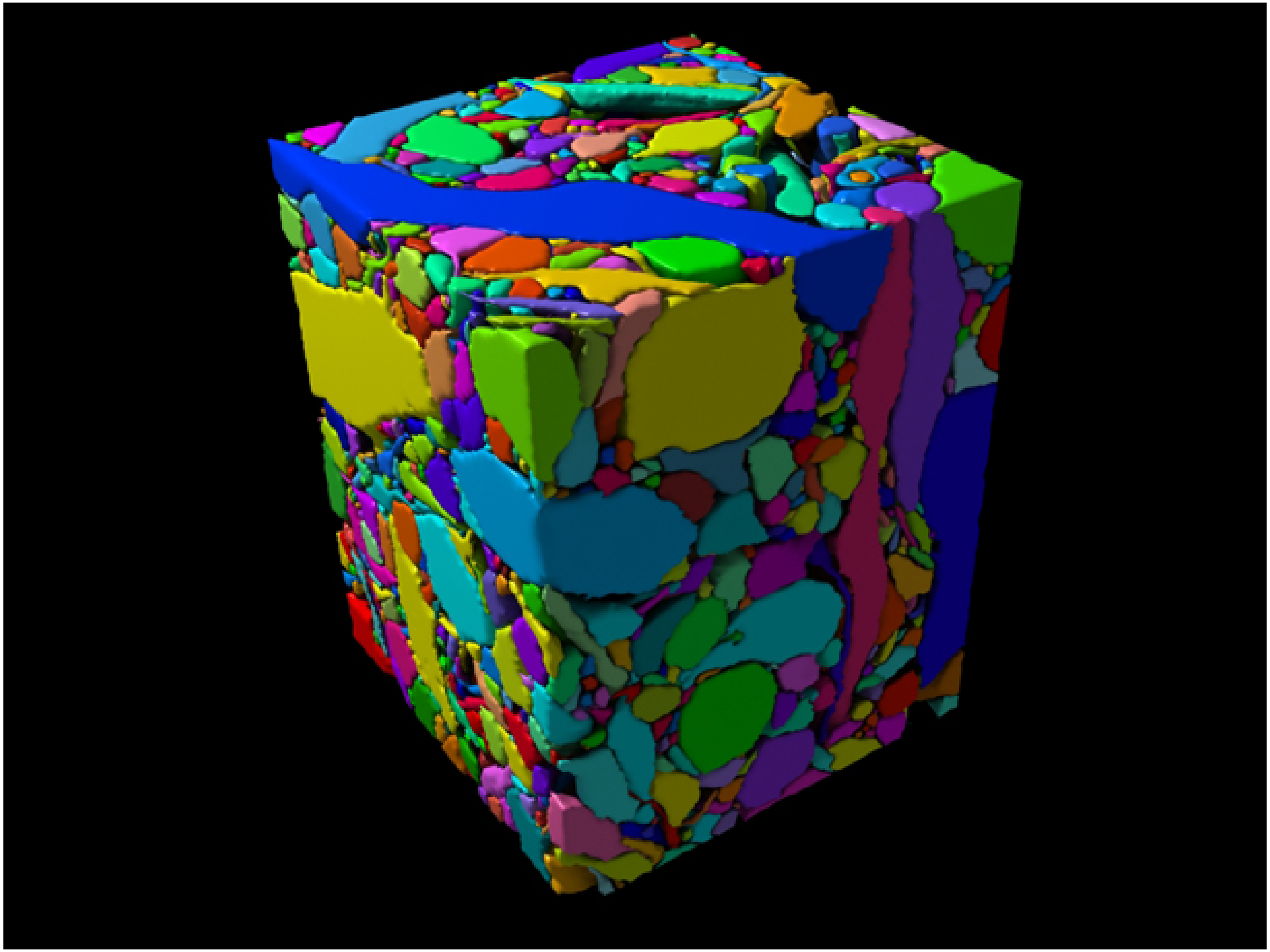
Modern neurons

Now we have electron microscopes....
We can see in much finer detail.



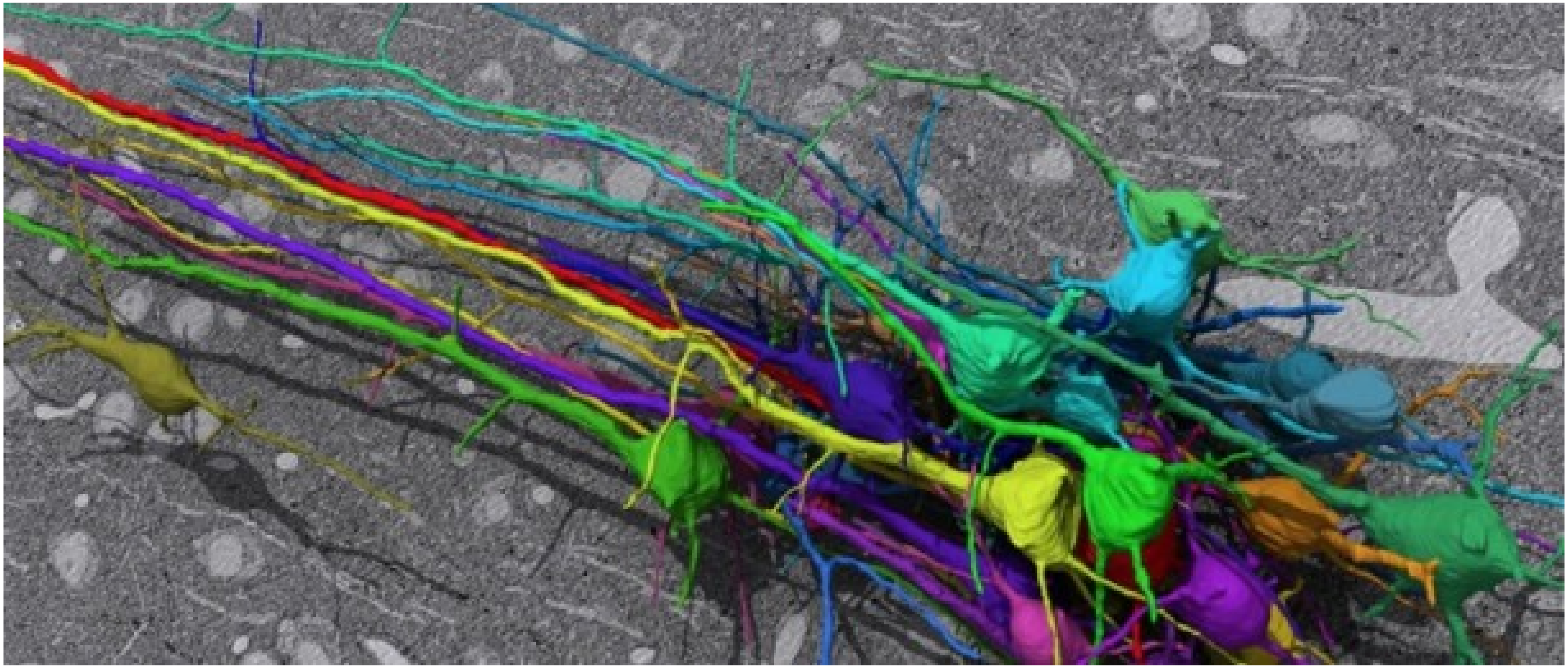
With electron microscopy, we achieve finer details.
In this image, manual labeling of cells was used to describe a small block of brain.

Modern neurons



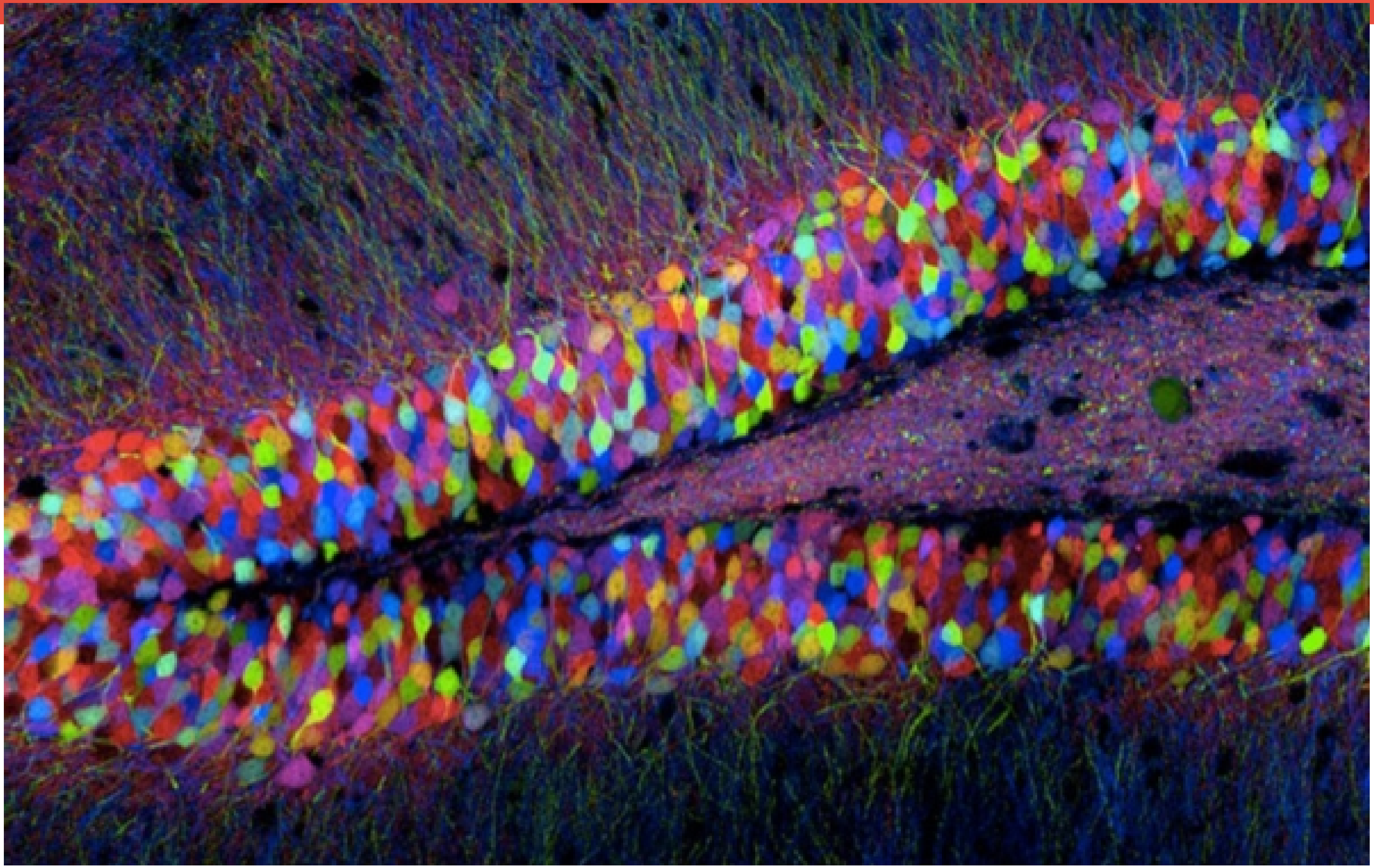
3-D segment the cells...

Modern Histology



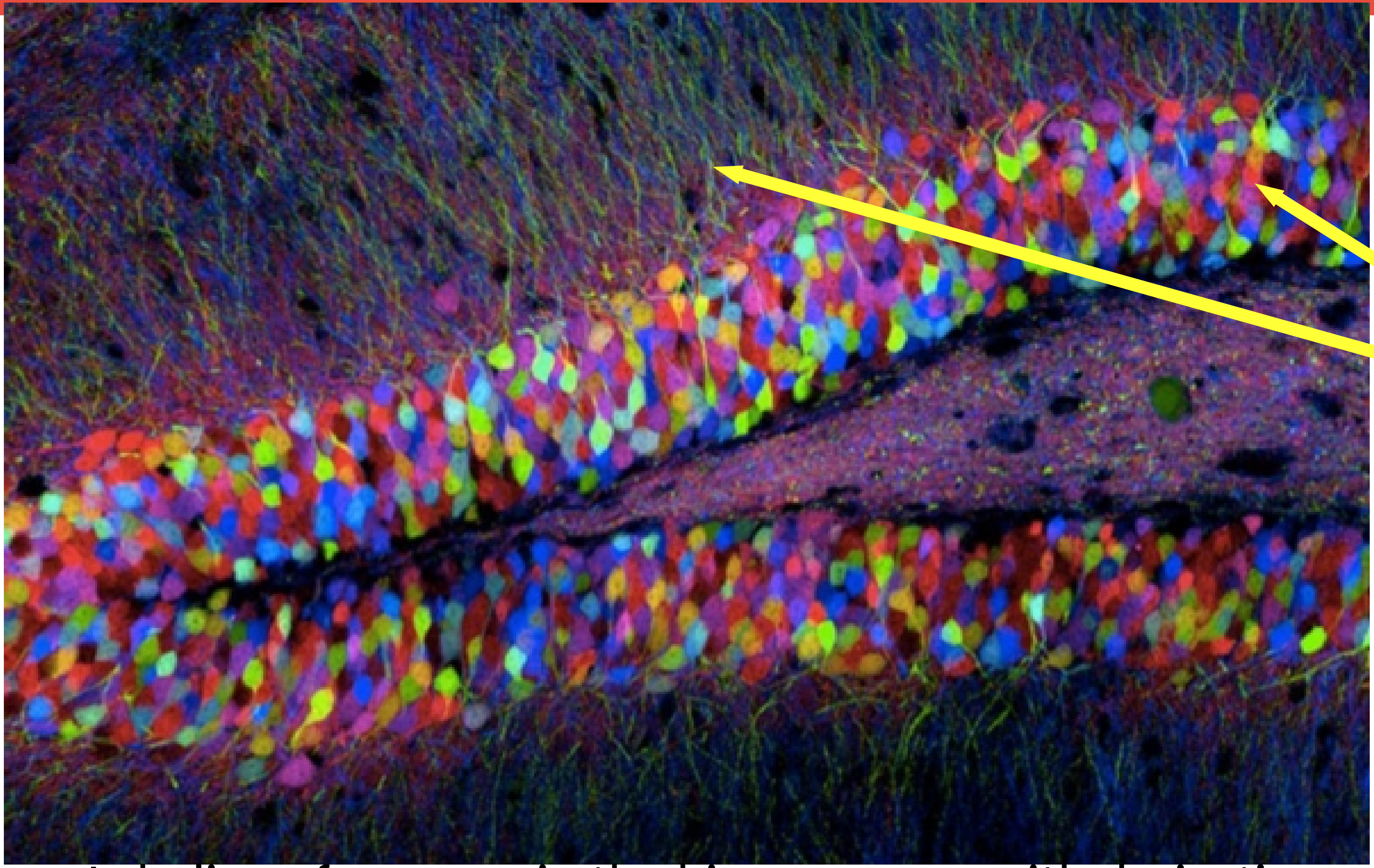
So now we can “see” what neurons actually look like in 3D by reconstructing them from very detailed microscope images.
→ This is very expensive and not used for daily research.

Modern Histology



Labeling of neurons in the hippocampus with derivatives of green fluorescent protein (GFP)-> each individual neuron has its own color.

Modern Histology



Can see "cell bodies" and "fibers"

Labeling of neurons in the hippocampus with derivatives of green fluorescent protein (GFP)-> each individual neuron has its own color.

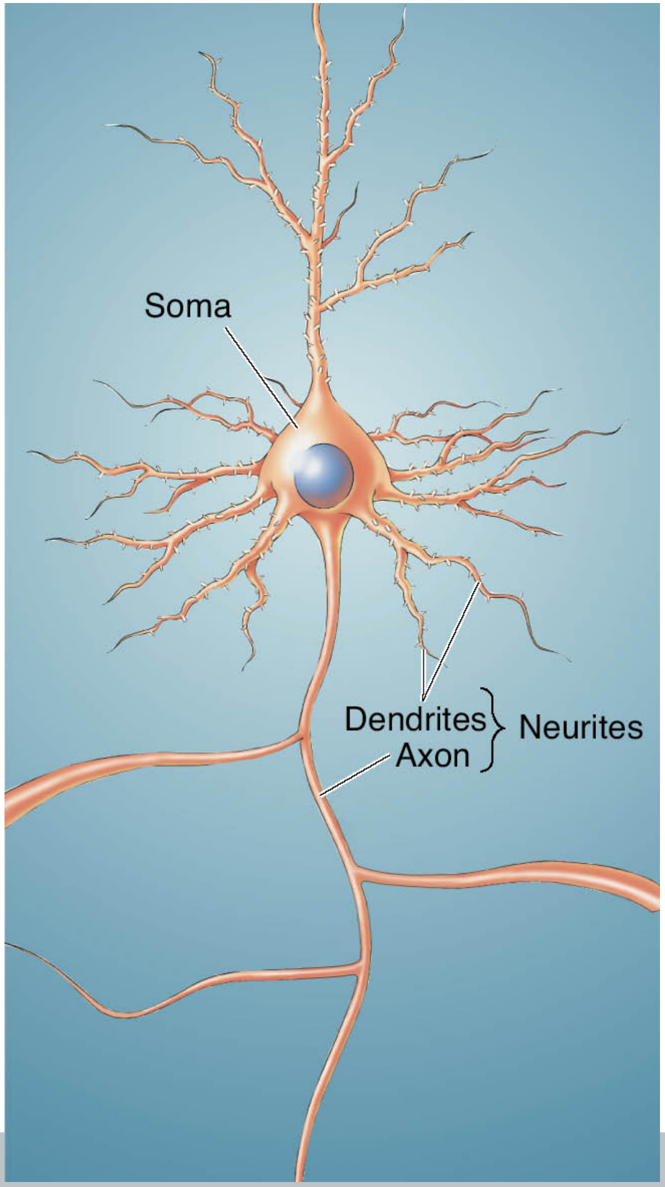
Jeff Lichtman: Brainbow

Cells

So...now we saw the shape.

But what *is* a neuron?

Neural Cells (Neurons) Structure

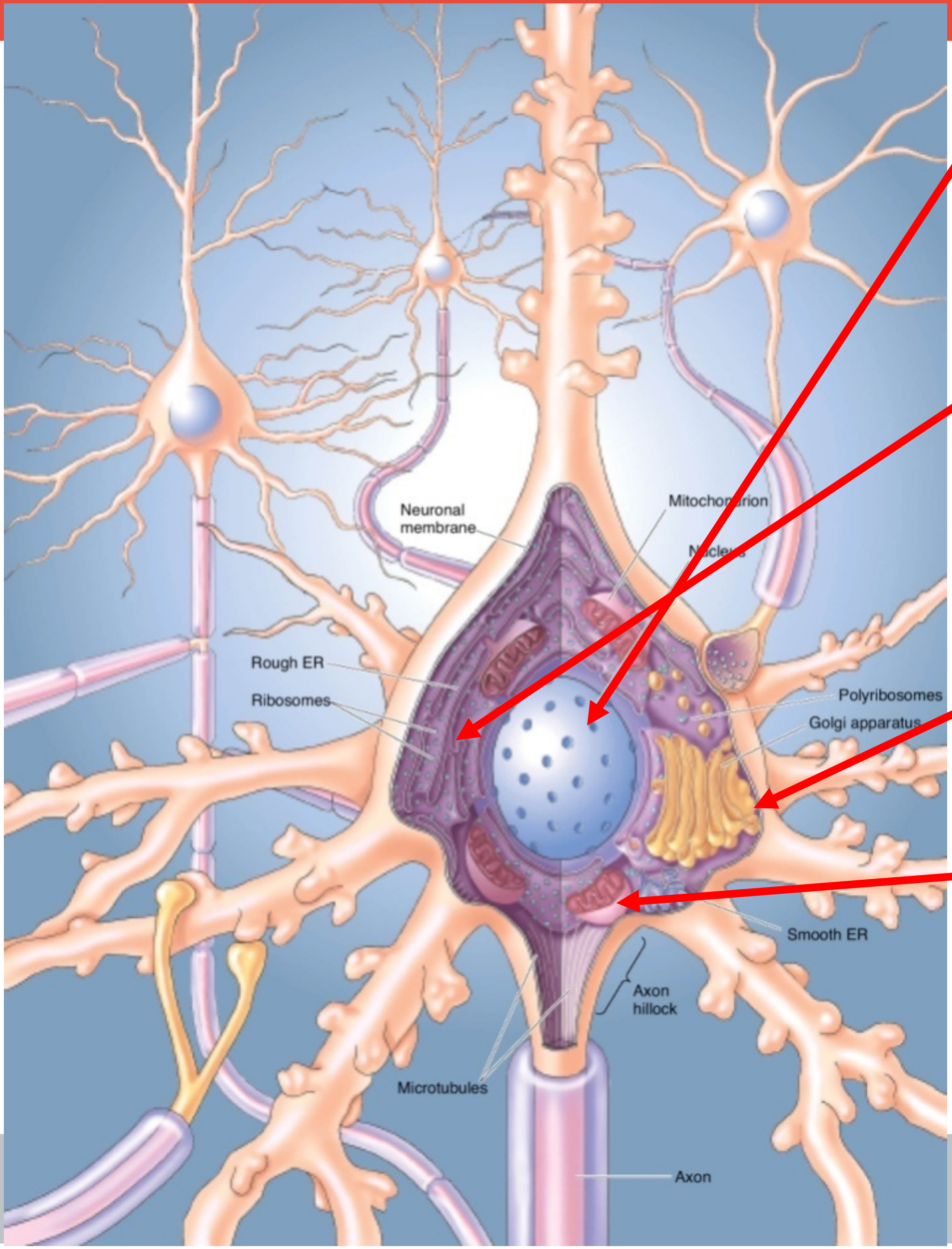


Dendrites: Signal input

Axon: Signal Output

Bear, Neuroscience

Neural Cell Structure: Inside



Nucleus

contains chromosomes

DNA transcription -> messenger RNA (mRNA)

Rough endoplasmic reticulum

contains ribosomes

translation: mRNA -> protein

Golgi apparatus

protein processing

preparation for transport

Mitochondrion

cellular respiration

-> adenosine triphosphate (ATP) = energy source

Bear, Neuroscience

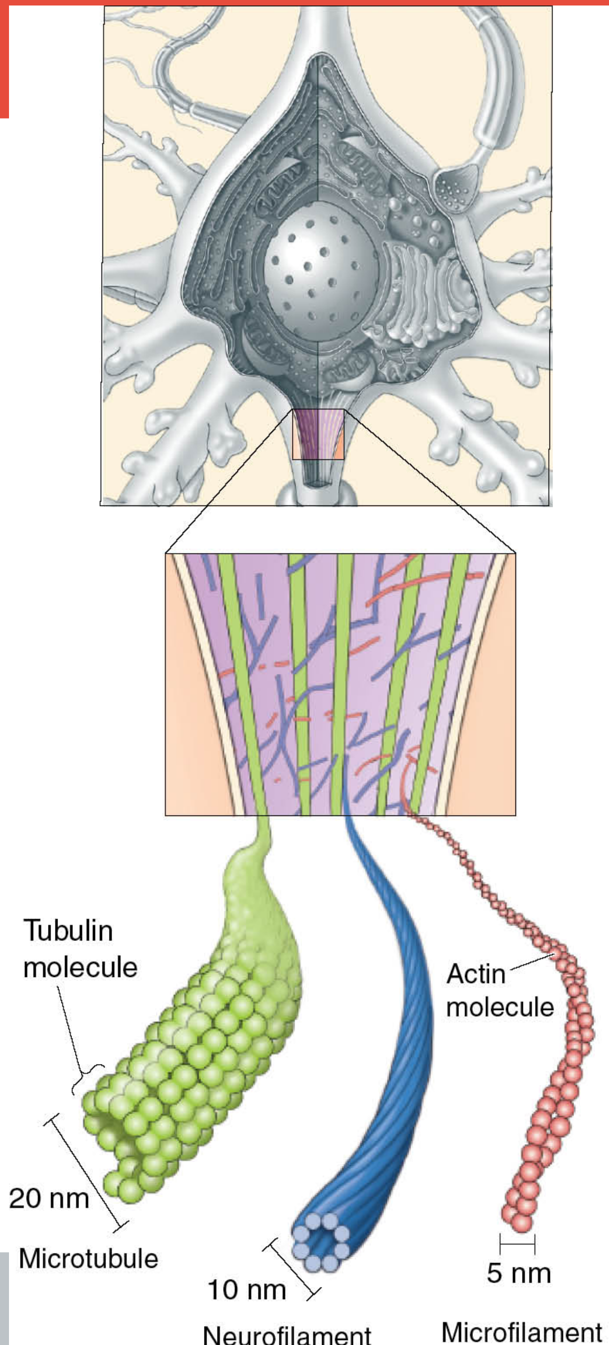
Neuron Cell Cytoskeleton

Neural cells have a "cytoskeleton" (cell skeleton)

Consists of different filaments:
-microtubules
-neurofilaments
-microfilaments

Purpose:

-Scaffolding (support)
-Intracellular transport (special proteins "walk along" the scaffolds to move)
-Axon growth

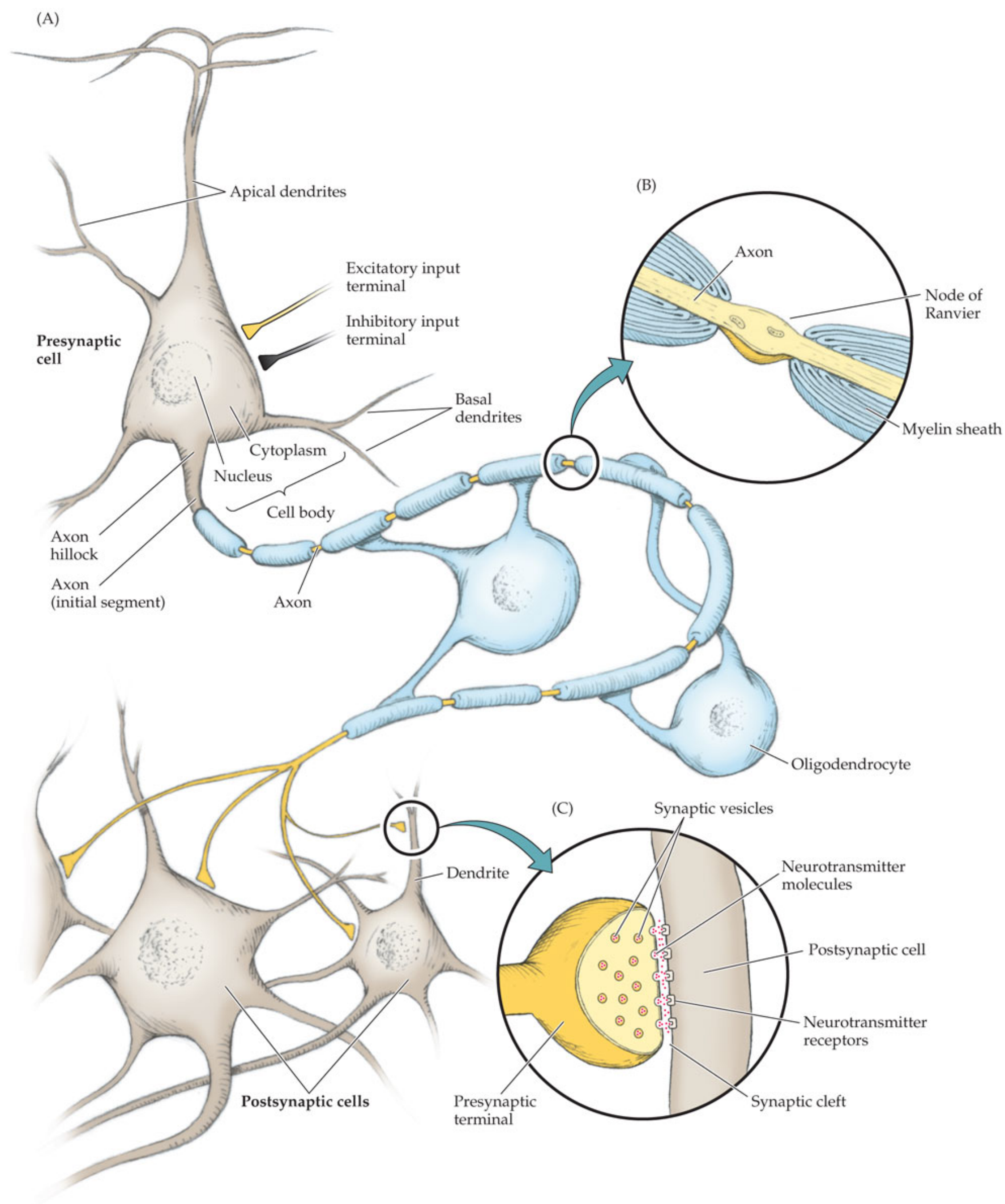


Synapses

How do cells connect?

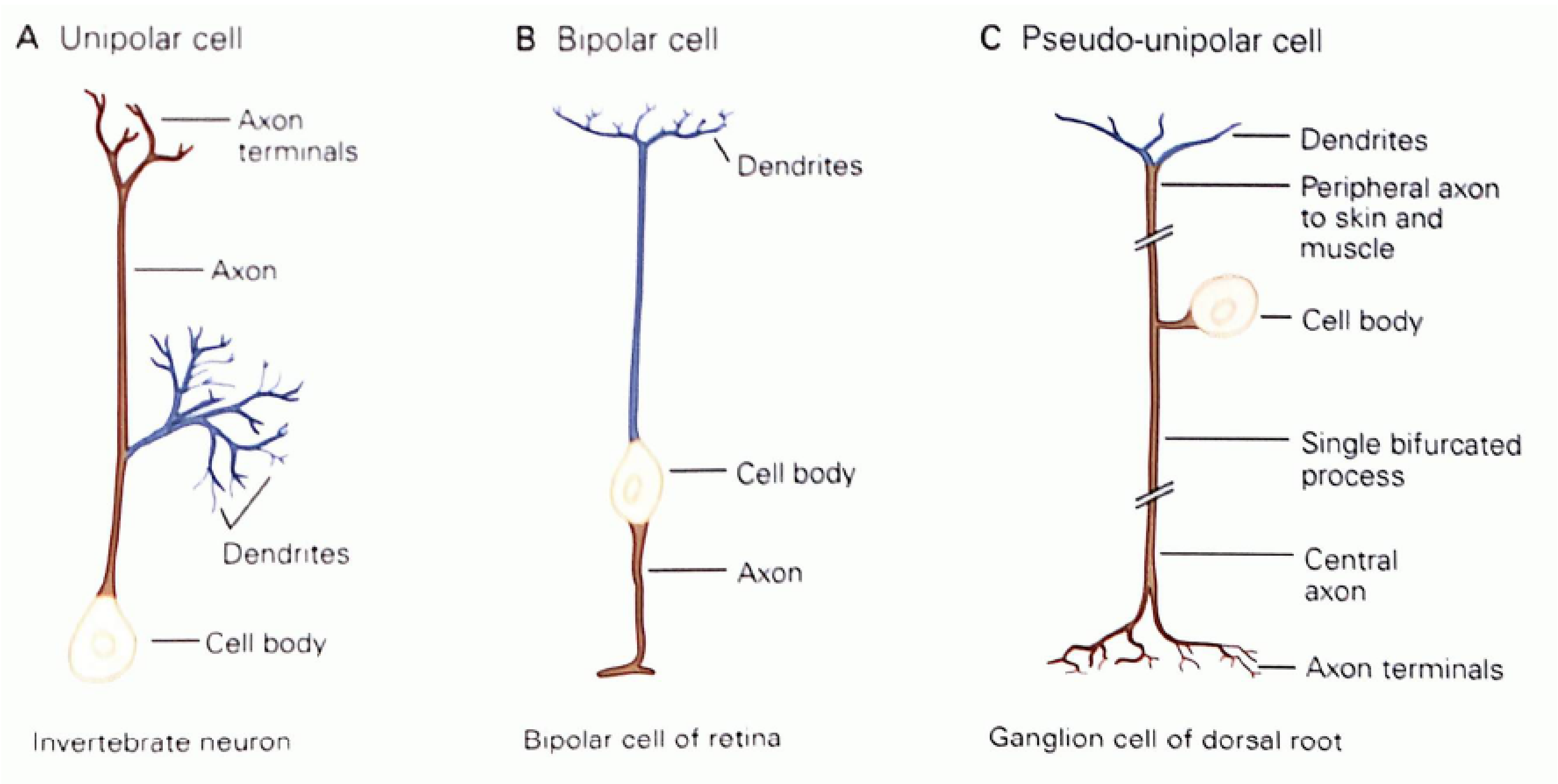
Neurons contact each other with synapses: small clefts which are bridged by chemicals (neurotransmitters).

Information transmission along the neurites (dendrites and axons) is electrical.



Blumenfeld, Neuroanatomy through clinical cases

The many shapes of cells

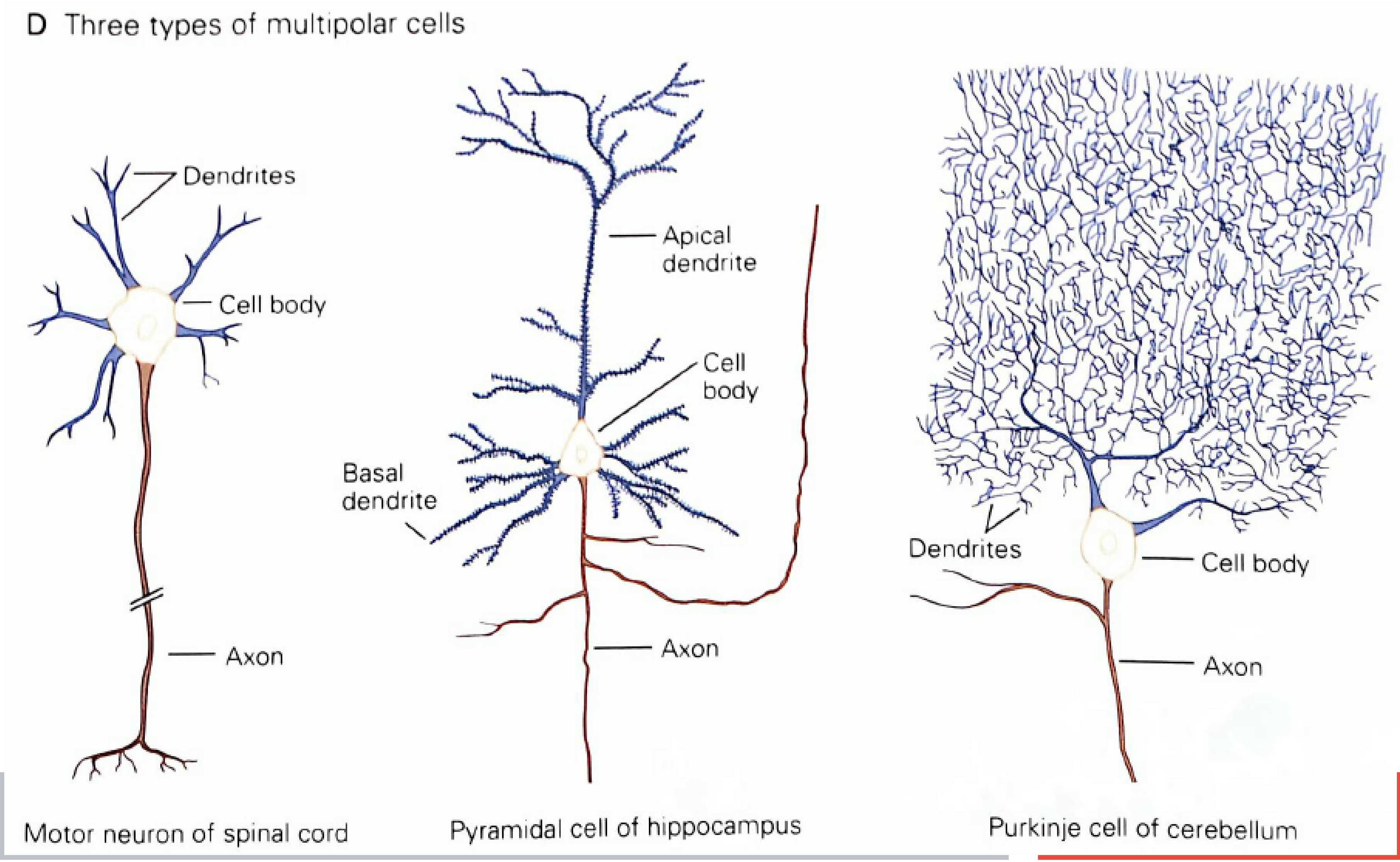


Many, many shapes of cells.

Kandel, Principles of Neural Science

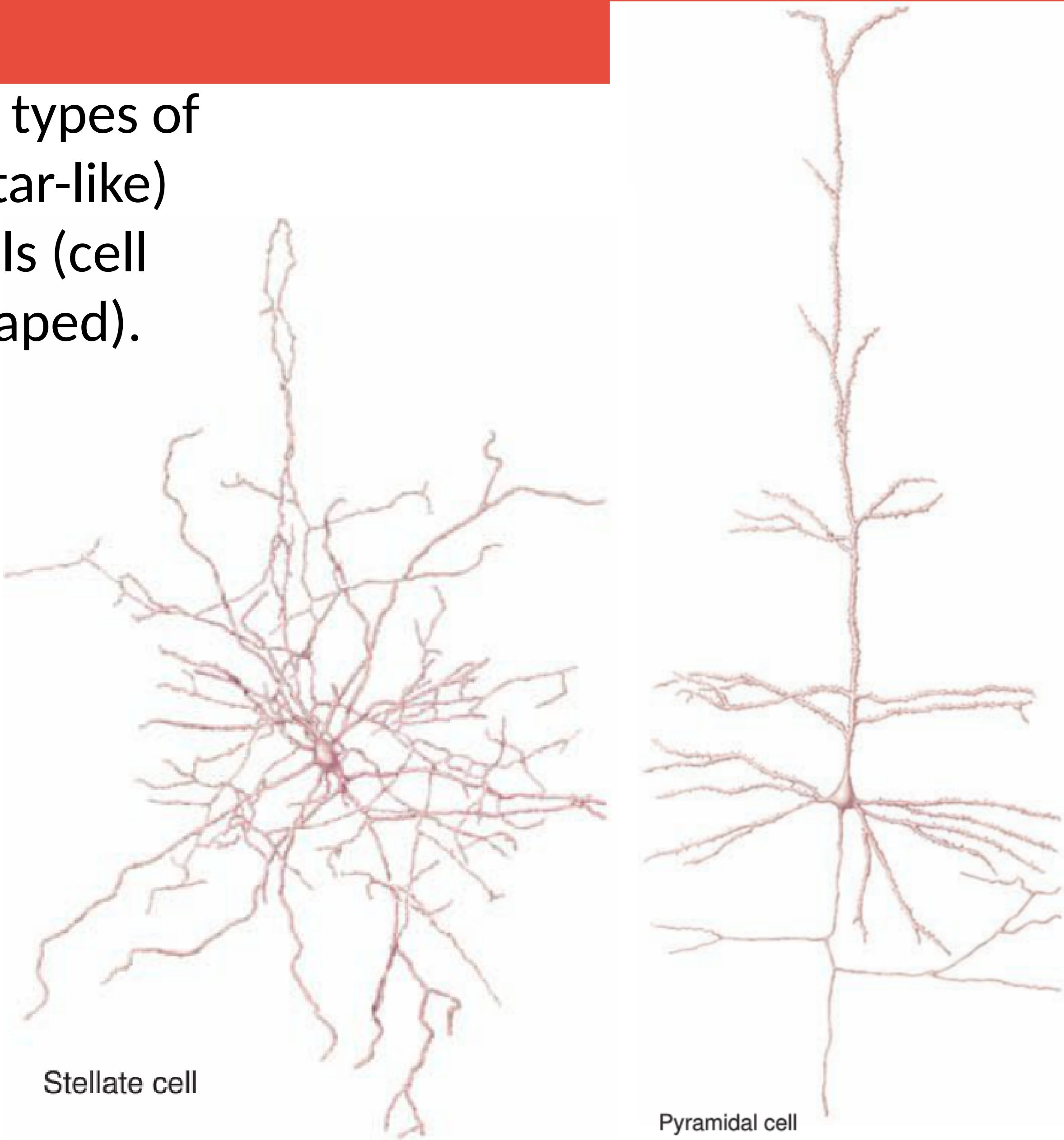
The many shapes of cells

For example, spinal cord motor neurons (left) receive around 10,000 synaptic inputs, cerebellar Purkinje cells (right) up to 1,000,000.



In cortex…

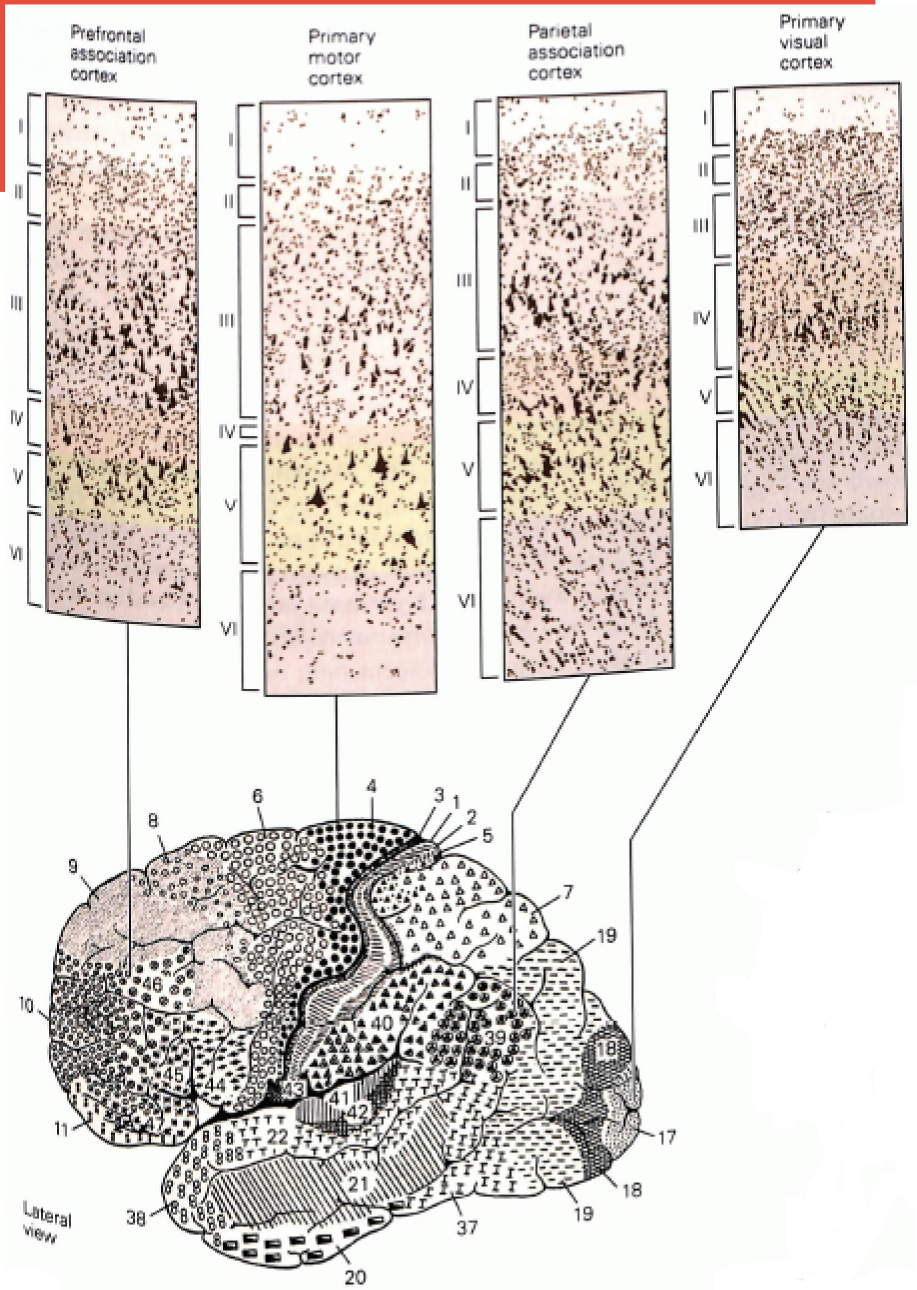
In cerebral cortex, two types of neurons are stellate (star-like) cells and pyramidal cells (cell bodies are pyramid-shaped).



Bear, Neuroscience

Brodmann Areas (BA)

The six cortical layers are numbered I-VI.
Layer I: dendrites
Layer II/III: connections to other cortical areas
Layer IV: input from thalamus
Layer V: output to brain stem, spinal cord.
Layer VI: output to thalamus



Last class we talked about *Brodmann Areas*

You can find different shapes/types of cells depending on the layer and function (and brain region).

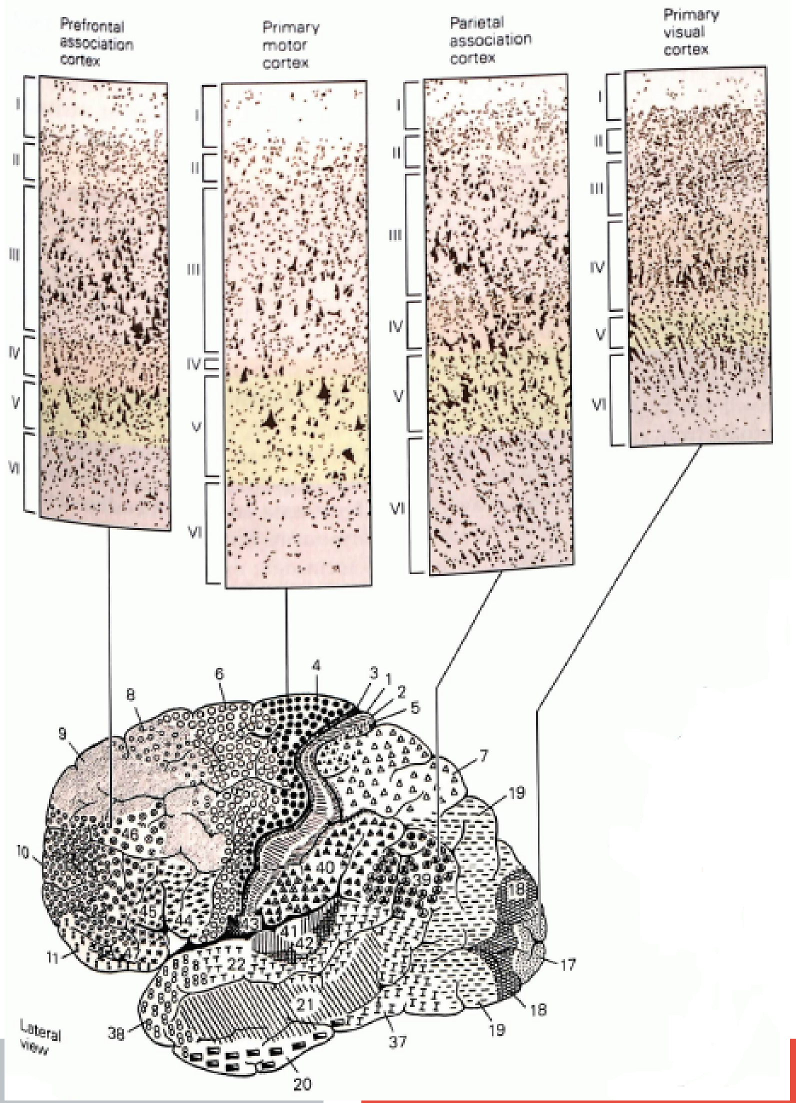
Kandel, Principles of Neural Science

Cytoarchitecture based on region

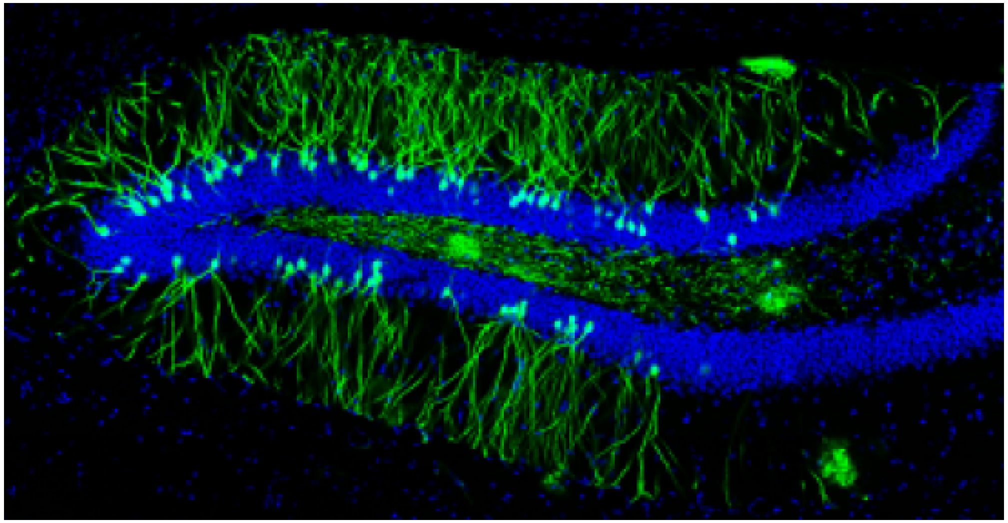
2) Primary motor cortex
Thick output layer V with large pyramidal cells to spinal cord (motor neurons).

4) Primary visual cortex
Thick thalamic input layer IV, important for a sensory area.

Overall thickness also varies from 1-4.5mm
e.g., Area 3 (Somatosensory): < 2mm
Area 4 (Motor cortex): 4mm



Neurogensis in Adults?

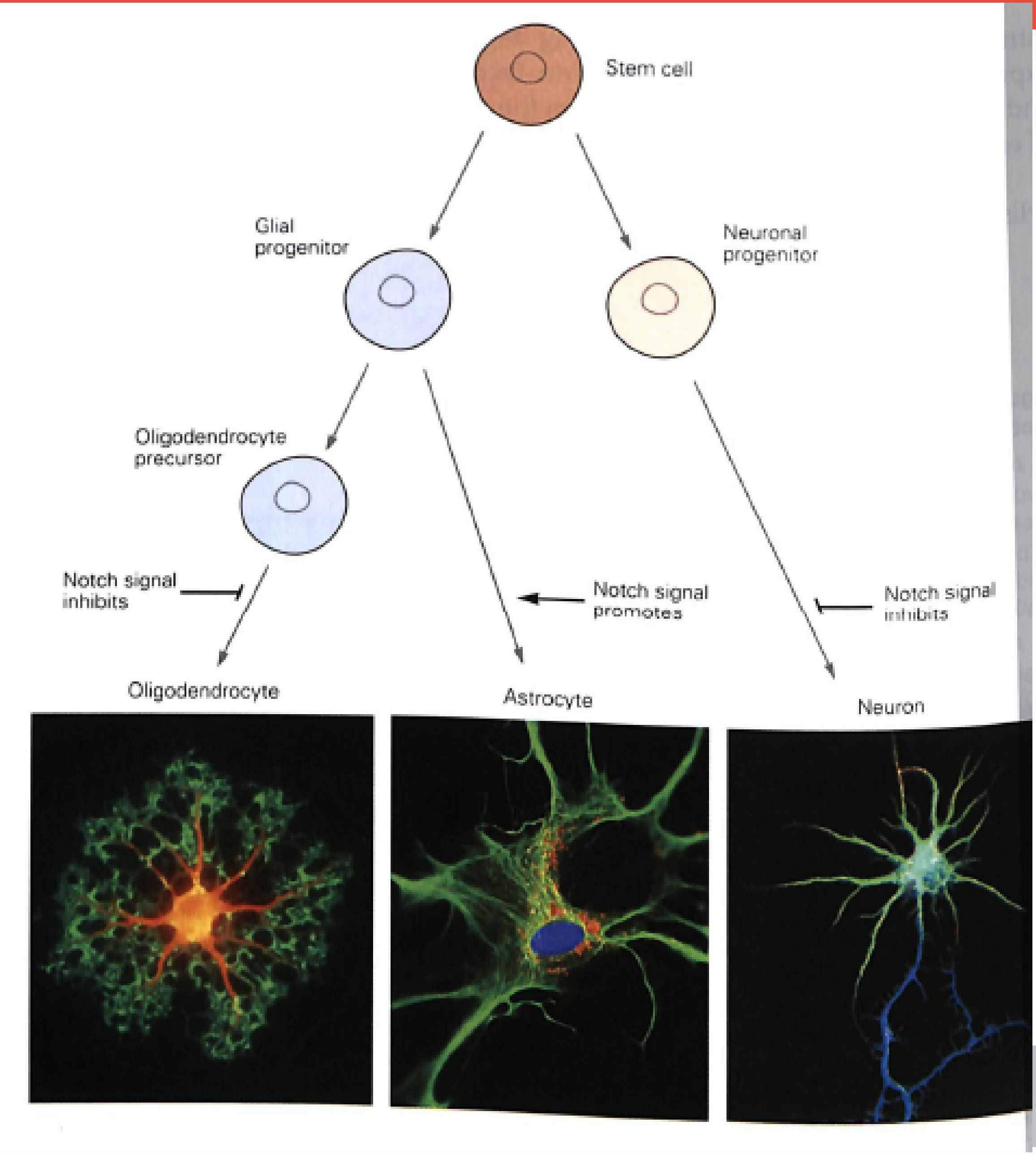


Cell death in the brain underlie various diseases, can new cells form and replace lost cells in adults?

-> Is adult neurogenesis possible?

-> If yes, is it the underlying mechanism for recovery from stroke or persistent vegetative state?

New neurons in adult brain?



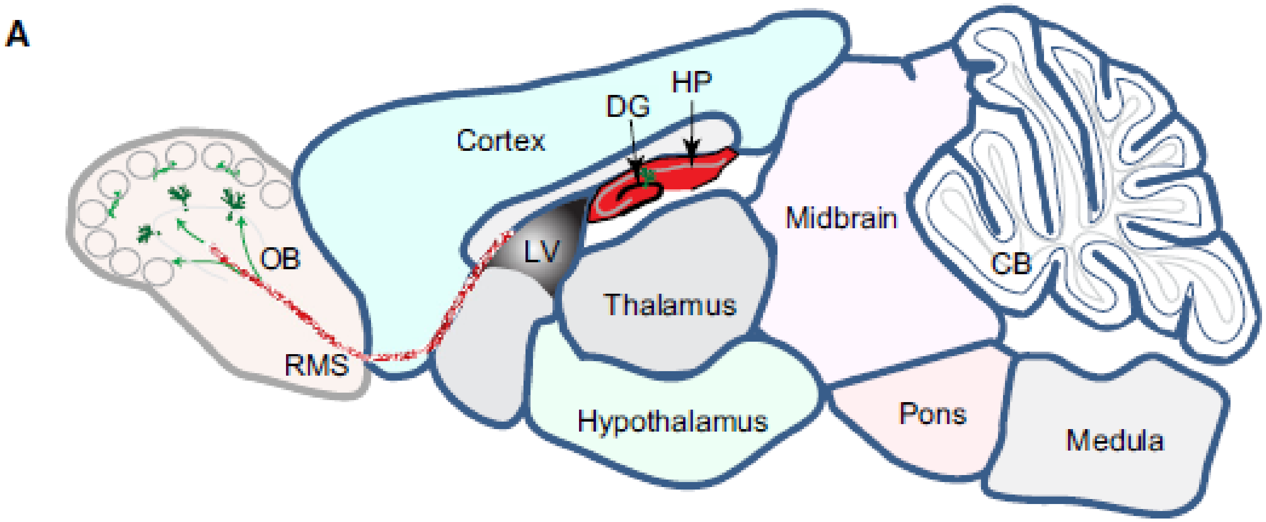
Yes, we now know that to some degree new neurons can form in **hippocampus**
and an area called the **subventricular zone**.

Neurons are formed by cell division of neuronal progenitor cells .

Kandel, Principles of Neural Science

New neurons in adult brain?

In the adult rodent brain, new neurons can mainly form in hippocampus (HP and DG below) and the subventricular zone (close to LV: lateral ventricle) from which they migrate to the olfactory bulb (OB).



Ming and Song, Neuron, 2011

Forum TRENDS in Neurosciences Vol.24 No.10 October 2001 617

Science and Society

Environment complexity stimulates visual cortex neurogenesis: death of a dogma and a research career

Michael S. Kaplan

Introduction by the Editor

Over the past few years, the classic idea that no new nerve cells are born in the adult mammalian brain has finally and conclusively been refuted by the scientific community. Yet, the first indications that

The beginning: a few lucky breaks and the first hints of things to come

My interest in this controversial topic got off of to a flying start when in 1970 as an undergraduate student at Tulane University (1970–1975), I worked closely

humans who are exposed to culture, supportive family or excellent teachers would flourish in enriched environments, and why should this not involve neurogenesis[3]?

I submitted this undergraduate

In the mid/late 70's Michael Kaplan described neurogenesis in rat visual cortex.

However, the dogma at that time was "no neurogenesis in the adult brain", or at least the adult primate brain.

Accordingly, an eminent researcher, Pasko Rakic, found no neurogenesis in macaque monkeys.

The dogma led to Kaplan not being able to pursue his research – even though he wanted to continue to show neurogenesis in humans. He abandoned research for a clinical career.

A decade later, others conducted the human trials and found neurogenesis in adult human hippocampus!

1998 Nature America Inc. • http://medicine.nature.com

ARTICLES

Neurogenesis in the adult human hippocampus

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In human stroke patients...

Stroke can induce neurogenesis at the damaged site (Ming and Song, Neuron, 2011), but it may not be enough to repair the brain.

Other mechanisms might include a recovery from swelling/inflammation, or a rebalancing of neural excitation/ inhibition, or that other brain structures take over functions.

Voss et al. (Journal of Clinical investigation, 2007) described a patient who after a car accident was in coma for 1-2 weeks and then progressed to a minimally conscious state for a 19-year period. He then recovered his ability to communicate (first word “mom”) and move his left arm.

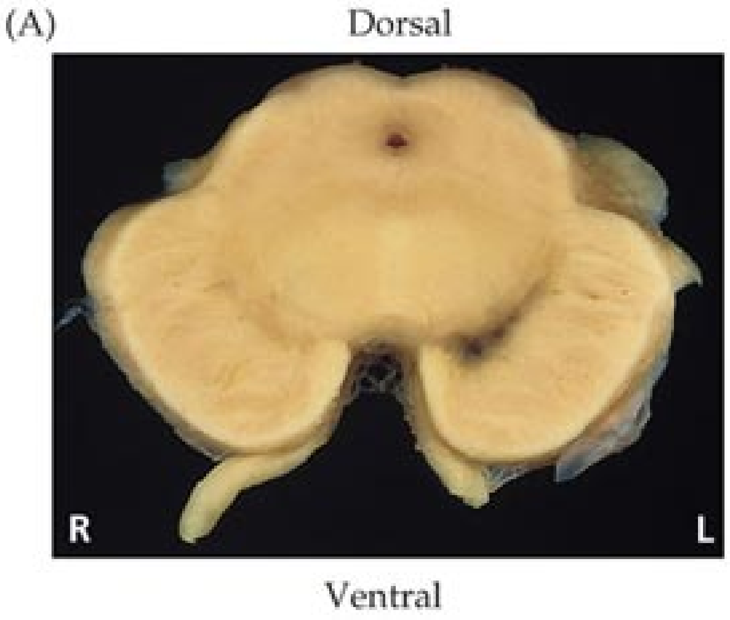
In human stroke patients...

Stroke can induce neurogenesis at the damaged site (Ming and Song, Neuron, 2011), but it may not be enough to repair the brain.

His recovery was accompanied by a possible reorganization of axonal fiber tracts, in particular in parietal/occipital areas (picture: fiber tracts depicted with diffusion tensor imaging).

What happens when cells die...?

Parkinson's disease is an example of a disease caused by neural cell loss. It is characterized by a loss of dopaminergic neurons in the substantia nigra.



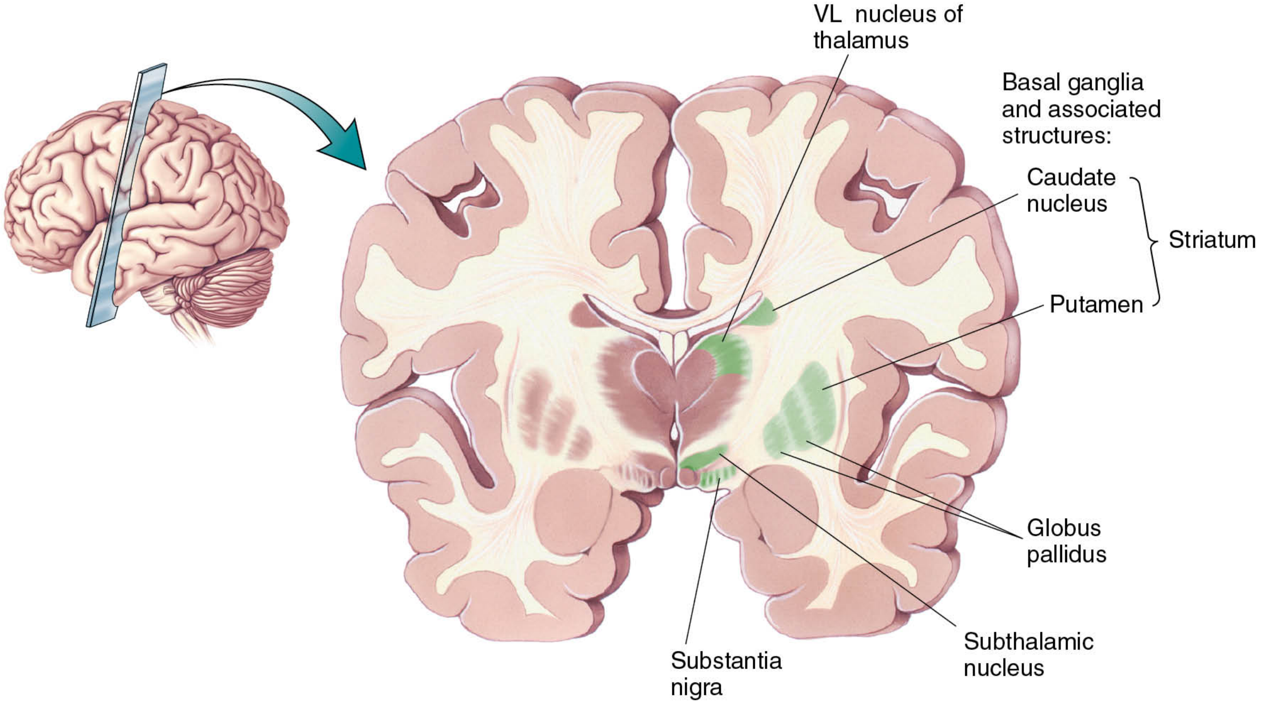
In this midbrain section, we see less "black substance" in the right side of the brain (R) -> cell loss in the substantia nigra.

Blumenfeld, Neuroanatomy through clinical cases

Parkinson's

<u>Symptoms</u>: resting tremor (shaking)
bradykinesia (slowed movements)
rigidity (increased resistance to passive movements)
unsteady gait

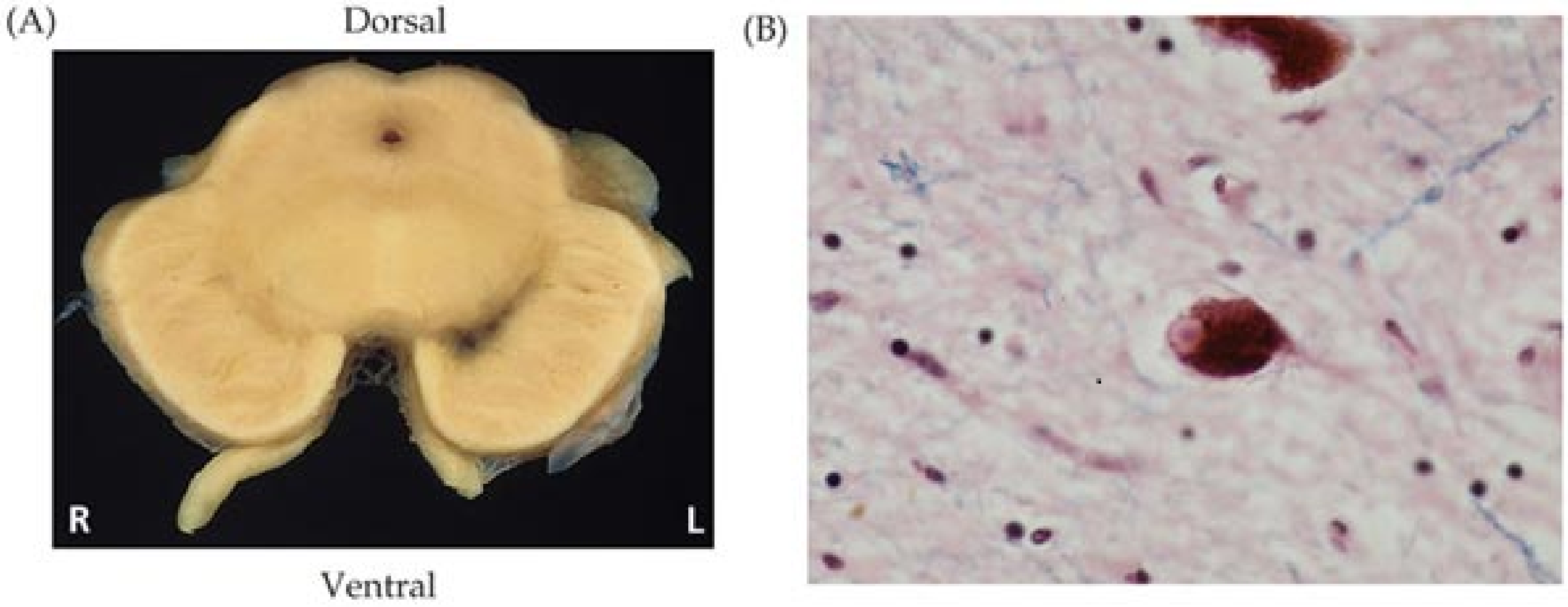
Usual onset: 40-70 years
Above 65 years: ~1% of individuals



Bear, Neuroscience

Parkinson’s

Remaining dopaminergic neurons exhibit Lewy bodies – accumulations of the protein α-synuclein.

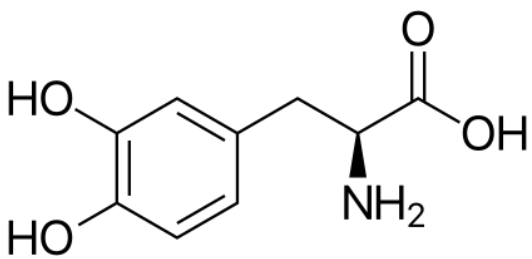


Blumenfeld, Neuroanatomy through clinical cases

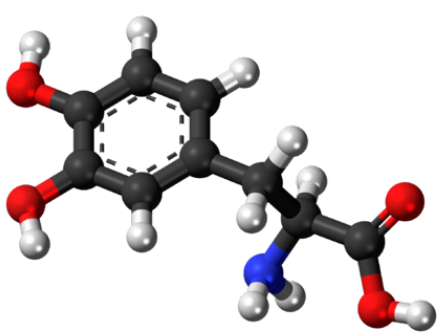
Parkinson’s

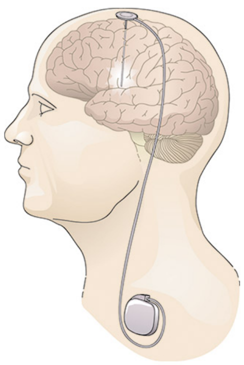
Parkinson’s disease is often accompanied by mild cognitive impairment, affecting executive functions (e.g., planning, behavioral inhibition), attention, and possibly visuospatial functions.
Treatment is mostly a life-long replacement of dopamine by administering a dopamine precursor (L-DOPA).

Extreme cases, e.g. young patients, may receive more invasive treatments – e.g. DBS



L-DOPA





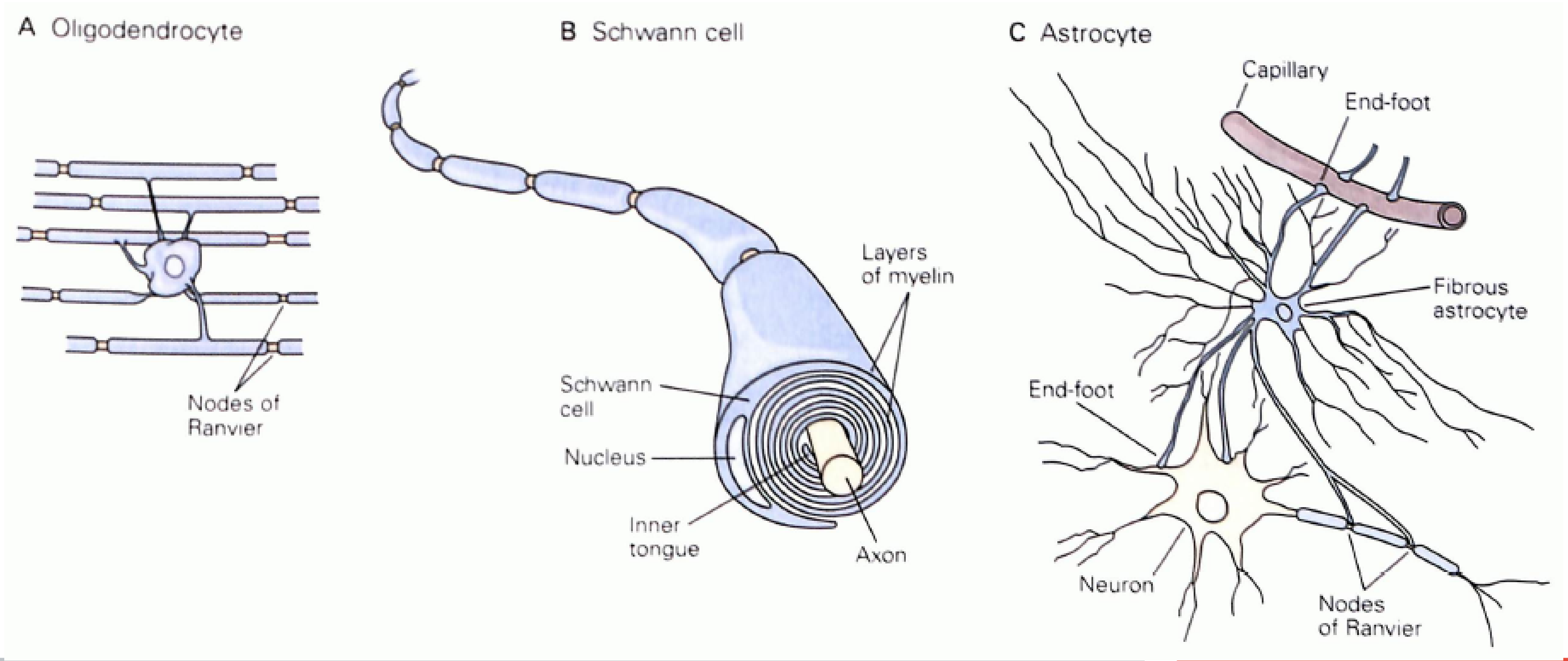
DBS

ninds.nih.gov

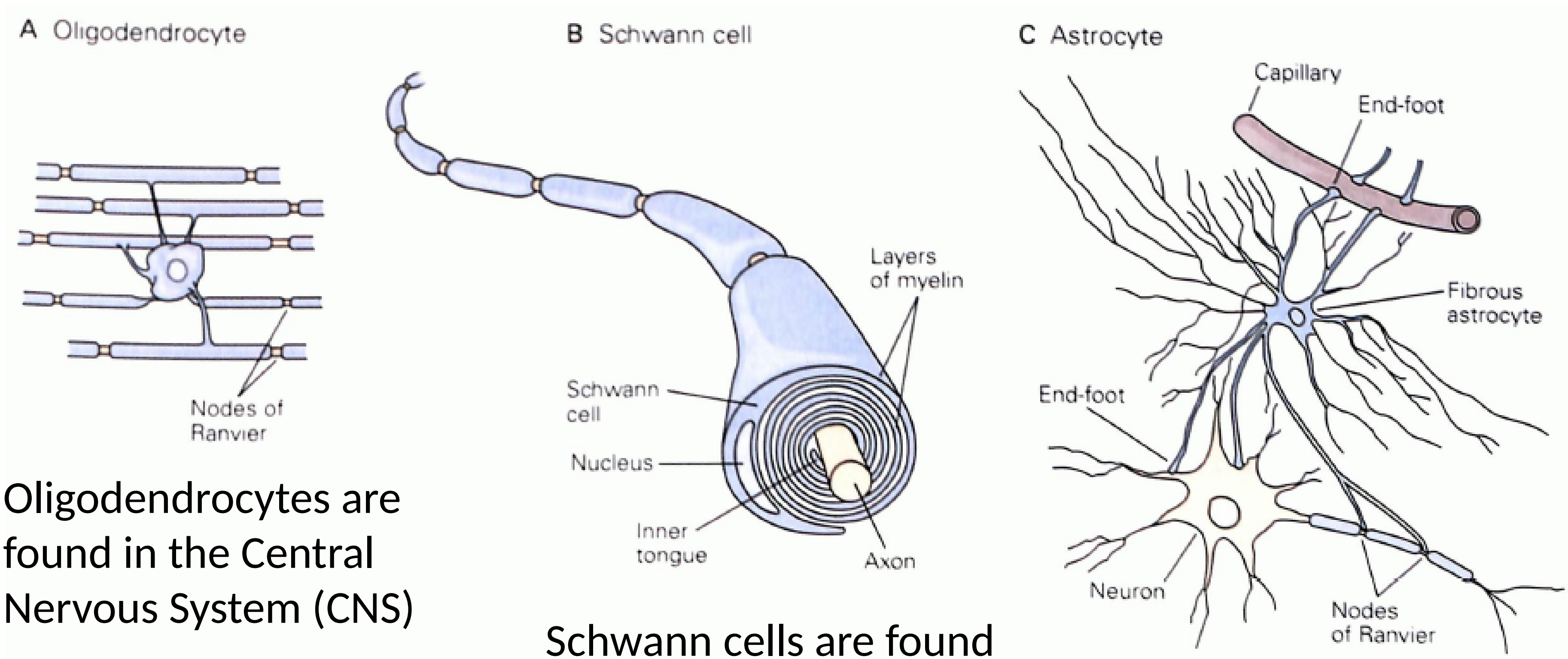
Glial Cells

There is other stuff in the brain besides just neurons!

→ Glial Cells



Glial Cells - Types

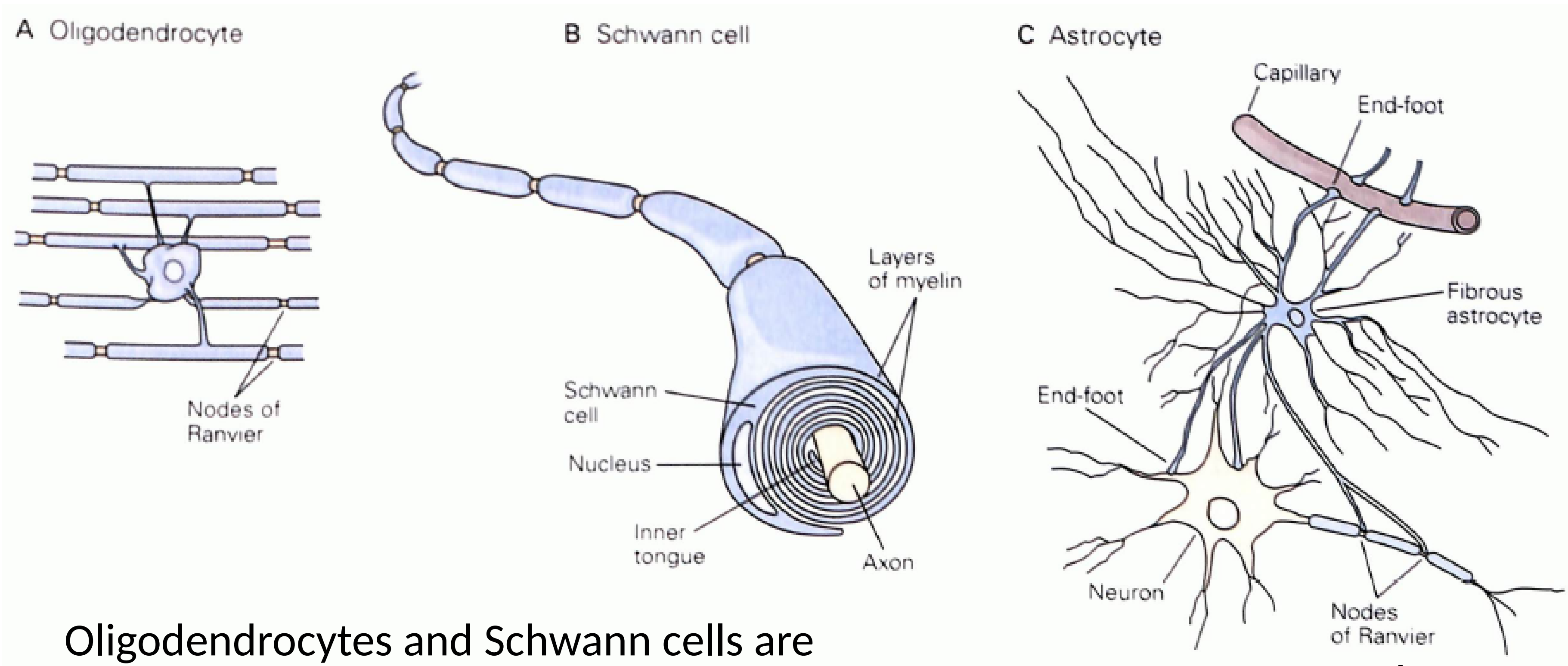


Oligodendrocytes are found in the Central Nervous System (CNS)

Schwann cells are found in the Peripheral Nervous System (PNS)

Astrocytes (star-like cells) are the most numerous glia cells and fill the space between neurons in CNS

Glial Cells - Function

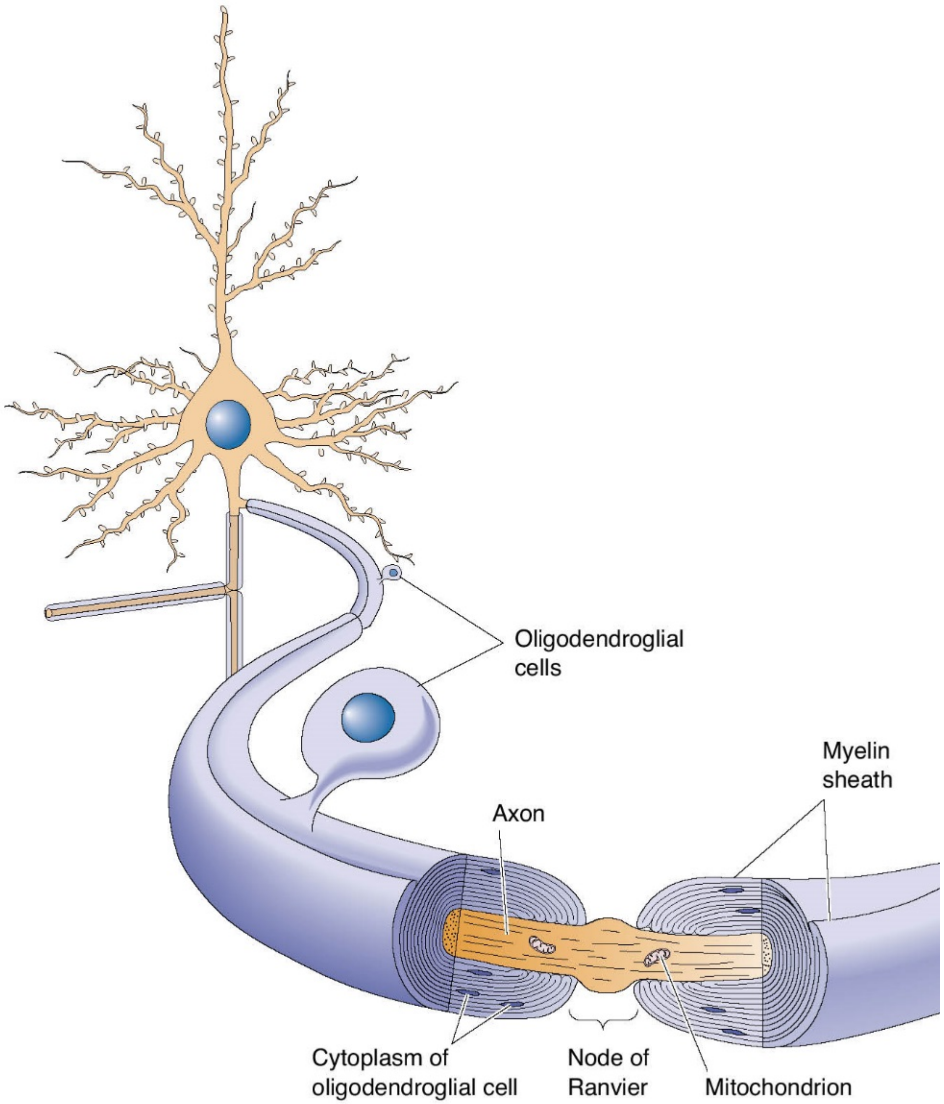


Oligodendrocytes and Schwann cells are myelinated to improve neurons' signal transduction

Astrocytes: regulate chemical extracellular environment, signaling

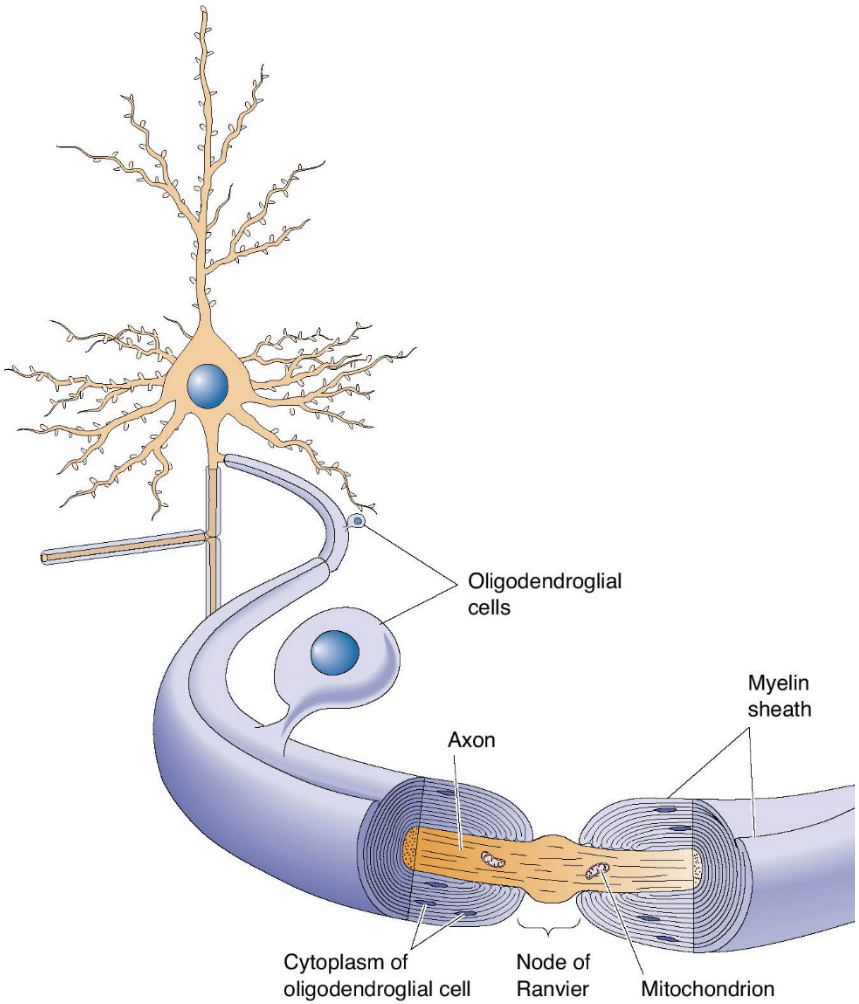
Myelin

The myelin sheaths of the oligodendrocytes are wrapped around the axon many times to ensure good insulation (ions cannot escape from the neuron) and efficient signal transduction.



Bear, Neuroscience

Multiple Sclerosis (MS)



Multiple sclerosis is an autoimmune disease affecting central nervous system myelin.
Myelin in the periphery is not affected.

Plaques form in multiple locations that lead to sclerotic scars.

Symptoms: e.g., muscle weakness, spasticity, sensory impairments, bladder/ bowel dysfunction

Peak age of onset: 20-40 years

Prevalence: 1-100 per 100,000 people

Multiple Sclerosis

Magnetic resonance imaging scan of brain of patient with multiple sclerosis. White lesions in white matter (arrow) caused by destruction of myelin sheaths

Murray, bmj, 2006, Diagnosis and treatment of multiple sclerosis

Review and Summary

- Neurons and glia are the major cell types in the nervous system.

- Neurons are the main actors for signal transmission and processing, glial cell mainly facilitate electrical signaling and provide scaffolding and support.

- Central nervous disease can arise as an effect of neural cell death – e.g., Parkinson's disease – but also glial damage – e.g., multiple sclerosis.