Cellular Anatomy of the Nervous System

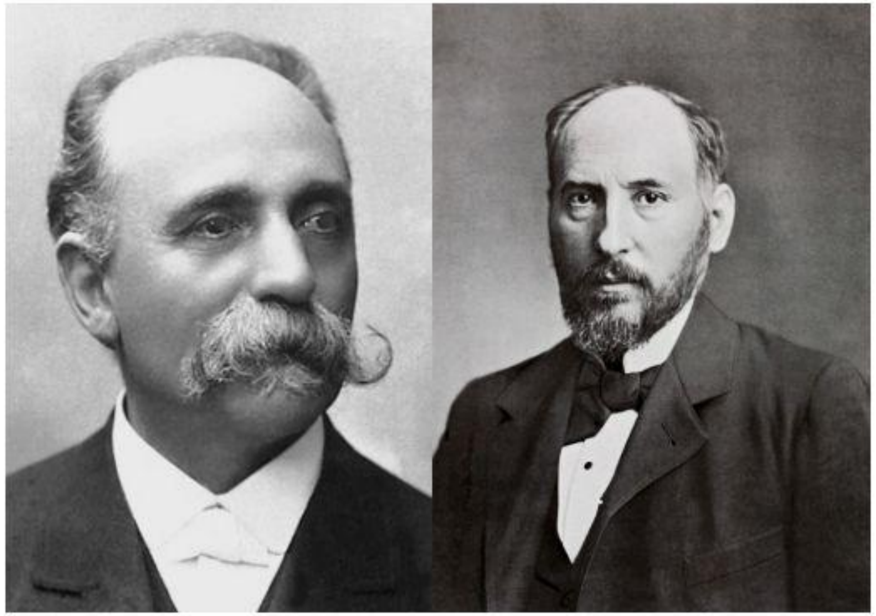
Chapter 3

History

- Autopsies (or post-mortem investigations) of gross structure of brain to see if noticeable differences existed and could be linked to the way the people died
- Mid-1600s - light microscopy - looking at biological substances (Antonie van Leeuwenhoek, Jan Swammerdam, & Robert Hooke); brain was complex and interesting
- Late 1800s - Camillo Golgi stain & reticular theory
  - The parts of the nervous system are all one very large, physically connected network
- About 10 years later, Santiago Ramon y Cajal repeated some of Golgi's staining experiments - neuron doctrine
  - Nervous system is a series of individual units that are physically separated from one another

Adversaries Share Nobel Prize

Figure 3.2 Camillo Golgi (left) and Santiago Ramon y Cajal (right) were both awarded the joint Nobel Prize in Physiology or Medicine in 1906.



"What a cruel irony of fate of pair, like Siamese twins united by the shoulders, scientific adversaries of such contrasting character!" - Cajal

More support for neuron doctrine with aid of modern techniques

Content

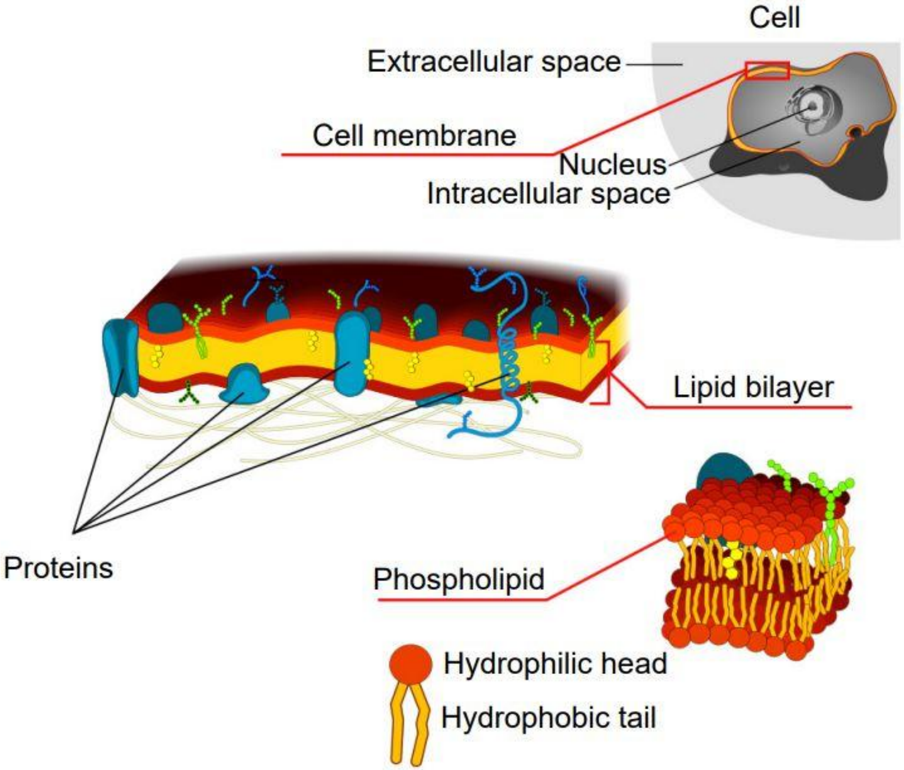
Characteristics of Neurons

- Neuron: basic unit of nervous system
- All basic features of typical mammalian cells (aqueous cytoplasm bounded by cell membrane & contain organelles like nucleus and mitochondria)
- Unique from other types of cells; variety of adaptations
- Best estimate on number of neurons in brain: 86 billion
  - Calculation is based on isotropic fractionator or "brain soup" technique
  - Developed by Suzana Herculano-Houzel
  - 0.2% of all cells in the body

Cell membrane

- AKA plasma membrane or lipid membrane
- Sheet of phospholipids
- Arranged into bilayer with hydrophobic tails touching each other and hydrophilic heads facing cytoplasm and extracellular space (which are mostly water)
- Effective and keeping ions and charged molecules separated and allowing small molecules like water and oxygen across the cell

Figure 3.3 The cell membrane is made up of a lipid bilayer, which consists of organized phospholipids.



Unique characteristics neurons have in common

1. Neurons are electroactive
2. Neurons are specialized for rapid communication
3. Neurons are "forever" cells
4. ...But, neurons can change

Details about electroactivity

Potential = Voltage

- Inside of most cells is negatively charged compared to solution outside
- Difference between charges is called membrane potential or transmembrane potential
- At rest, amplitude of the chard is -50 to -90 mV
- Often, say cell rests at about -70 mV

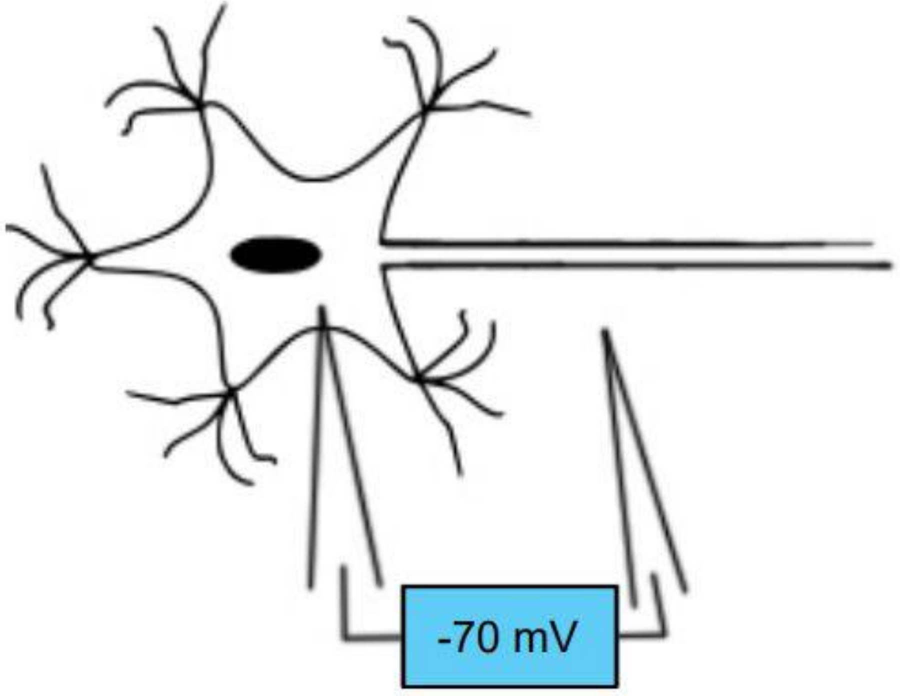


Figure 3.4 Compared to the extracellular space, the voltage of the neuron is generally negative.

More details about electroactivity

- Membrane potential is abbreviated as V_m
- When net positive charge enters cell, V_m becomes more positive
- Likewise, when net negative charge enters, V_m becomes more negative
- V_m can move from -70 mV to +45 mV and back to -70 mV in as little as 2 milliseconds

Details about rapid communication

- Many cells can send and receive chemical signals across long distances and time scales
- BUT Neurons communicate with a combination of electrical and chemical signals in a matter of milliseconds (consider this unit of measurement: milliseconds)
- Also, shape and organization of neurons makes them effective for directionality of signals
    - Many have incoming receiving end and outgoing sending end
    - Placement of one neuron next to correct partner is very important
- Many chemical signaling systems are in place to ensure developing nervous system is properly wired together

Details about "forever" cells

- Constantly replace non-neuronal cells (ex. Bone cells replace themselves at a rate of 10% each year; "new" skin each month, stomach cells are replaced about every week, & about 100 million new red blood cells are created every minute)
- BUT the mature nervous system generally does not undergo much neurogenesis (creation of new neurons)
- Neurons we have after development are kept until death; permanence of neuronal cell count is unique
- However, some areas (ex. olfactory system and hippocampus) display new nerve cell production

Details about changing neurons

- Even though most areas of brain do not create new neurons, existing ones have capability to change structure and function
- Some of the changes are thought to be everlasting
- Plasticity = ability for the brain to alter its morphology (Greek *plastikos*, meaning "capable of being shaped or molded"; think plastic surgery)
- Also, neurons can repair themselves to some extent (ex. PNS neurons injured or destroyed by trauma to body can regrow to connect once again with original partner)

Cellular anatomy of neurons

- Communication usually moves in one direction, and that pathway is used when discussing anatomical structures of neurons
- Basic anatomy
  - Dendrites
  - Soma (cell body)
  - Axon
  - Synapse

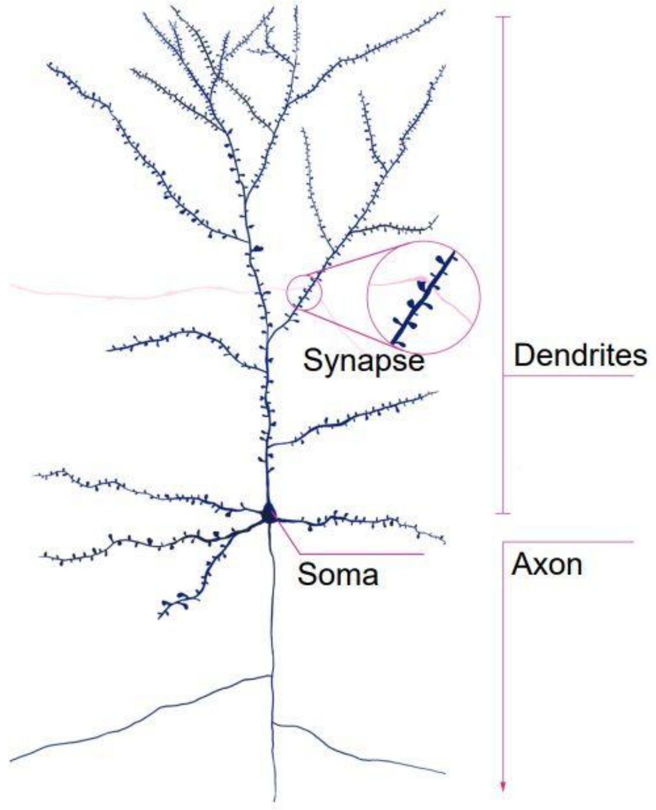


Figure 3.6 The basic anatomy of a neuron.

Dendrites

- Branch-like extensions that protrude from cell body
- Greek dendro-, meaning "tree" (think rhododendron)
- Considered to be where information first enters the neuron
- Generally, get thinner as you look farther away from the cell body
- May have protrusions or bumps, which are called spines (classified based on approximate shape)
- Each spine may represent an input site of communication (where chemical signals released by other cells are received by the dendritic spine)
- Dendritic plasticity is thought to underlie learning or maintaining memories
- Note that not all cells have spines, but they are still capable of changing; the input site may be anywhere along the dendrite or even at the cell body

Classification of spines

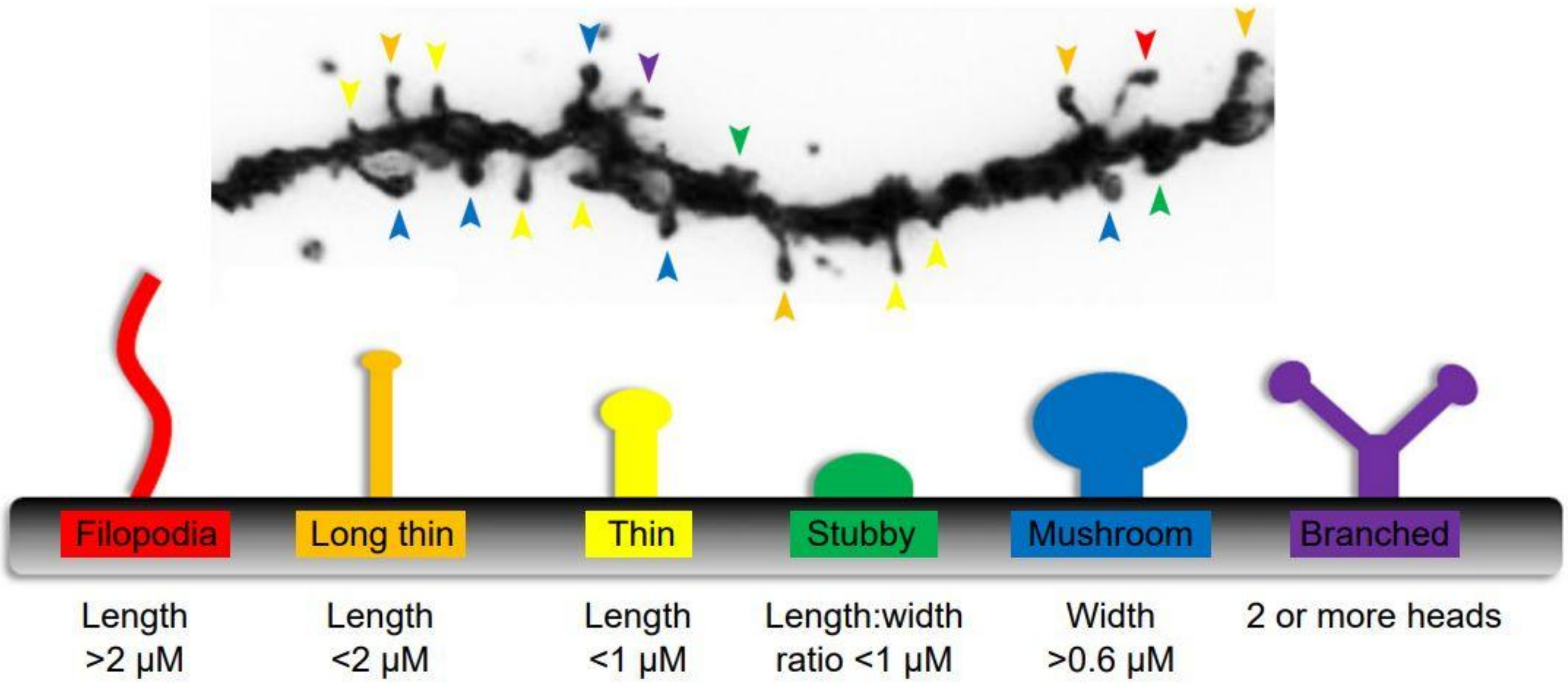


Figure 3.8 Tiny extensions of the cell membrane on dendrites are called spines. They can be classified based on their shapes and sizes.

Cell body

- AKA soma
- Somata (plural) vary in size (maybe 4 microns or µm - upwards of 100 microns in diameter)
  - Betz cells found in M1 have largest diameter (in M1)
  - Granule cells of cerebellum have smaller diameter
- Contains many organelles
  - Nucleus - houses DNA and other genetic material
  - Endoplasmic reticulum (ER)
  - Ribosomes – read the mRNA and translate code into proteins
  - Golgi apparatus - layers of folded plasma that help with transport

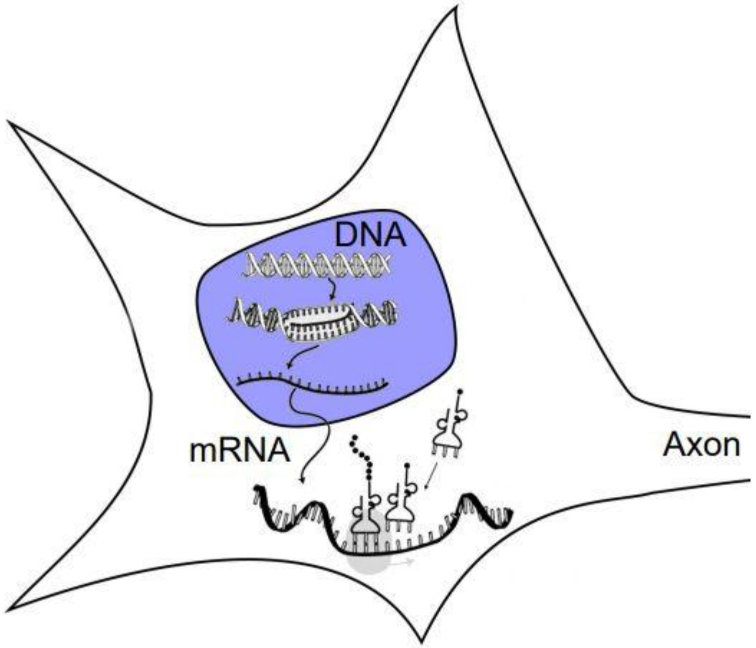


Figure 3.9 Like non-neuronal cells, DNA is housed in the nucleus (purple). DNA is transcribed into mRNA and exported out of the nucleus, where it can be translated into protein.

Axon

- Main output extension
- One per neuron
- One axon can branch several times after exiting soma; can communicate with many other neurons
- Usually thinner than dendrites (some being only a micron in diameter)
- Axon hillock - works as the integrative center (deciding whether to pass signal to next cell after considering incoming signals: excitatory, inhibitory, and modulatory signals); where action potential originates
    - Action potential: all-or-nothing change in electrical potential that neurons use to send a signal down the axon
- Axon terminal or terminal bouton - specialized for production and release of neurotransmitters
    - Active zone - where variety of proteins important to process of neurotransmitter release are embedded

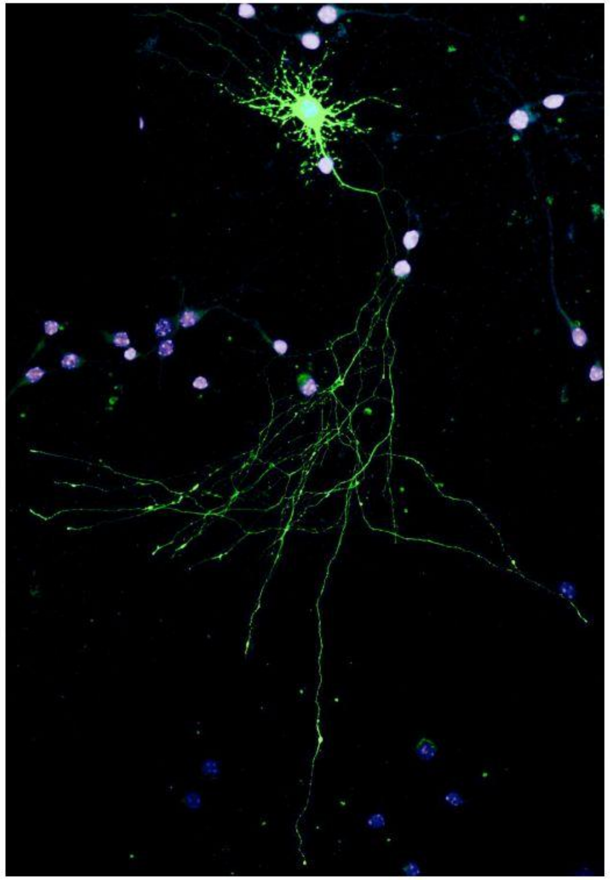


Figure 3.11 Neurons (green) extend a single axon from the soma, which can branch extensively.

Inside the axon

- Microtubules - organelle; molecular railway for proteins
- Motor-like proteins carry other proteins along the microtubules
- Anterograde transport - substances are moved away from the cell body
- Retrograde transport - substances are moved towards the cell body
- Neurofilaments – organelle; made up of several different proteins serving as cellular "scaffolding" that helps keep structure of axon intact
- Vesicles - within terminal; small spherical "packages" made of cell membrane and coated in special proteins; changes in electrical change cause these vesicles to fuse with inner membrane of neuron and allowing contents to be released

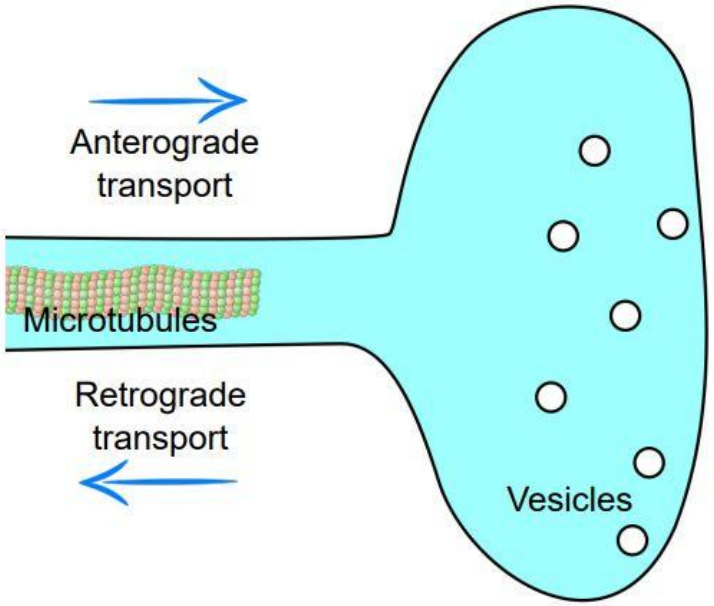
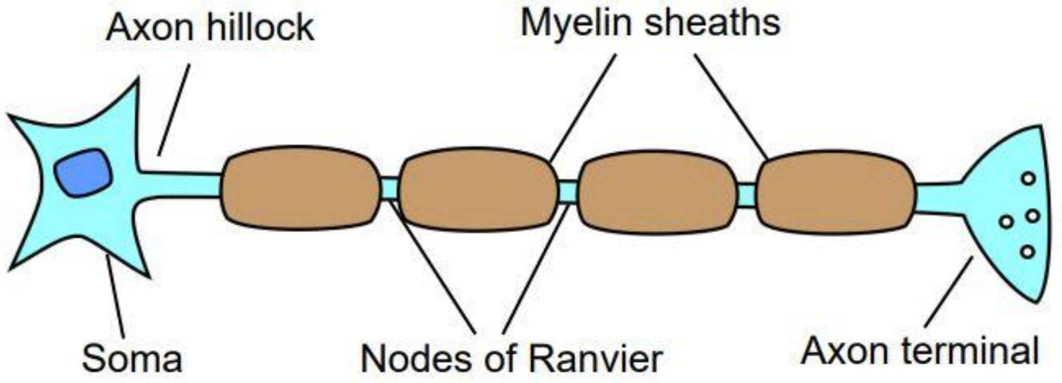


Figure 3.12 Diagram of an axon terminal, showing microtubules and vesicles.

Outside the axon

- Myelin sheath - special modification on some neurons; comprised of tightly-wrapped layers of cell membrane over a short section of the axon
  - Nodes of Ranvier - exposed axon between sections of myelin; on average, ~1 micron long
- Myelin - increases speed of transmission of electrical signal
  - Some heavily myelinated axons are able to send signals up to 120 meters per second (almost 270 miles per hour)
- Myelin - increases thickness of cell membrane; in doing so, acts as an insulator and causes signals to more reliably be passed down

Figure 3.13 Myelin sheaths are made up of layers of cell membranes that surround small sections of axons. The nodes of Ranvier are the exposed sections of axons between the myelin.



Synapse

- Physical distance separating two neurons
- Cajal's **neuron doctrine** - nervous system is a series of neurons in close proximity, separated by a gap of extracellular space
- Distance can vary
- Electrical synapse may be < 5 nanometers apart; neurons share cytoplasm but have separate cell membranes
- Chemical synapse may be ~15-40 nm; neurons do not share cytoplasm

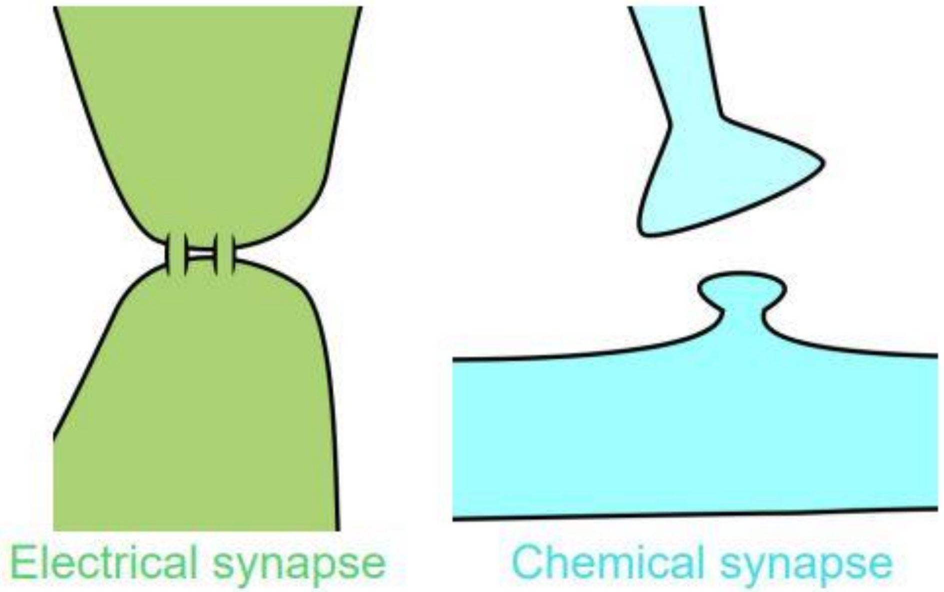


Figure 3.14 Electrical synapses physically share cytoplasm (left) while chemical synapses use neurotransmitters to communicate (right).

Clinical connection: Multiple sclerosis (MS)

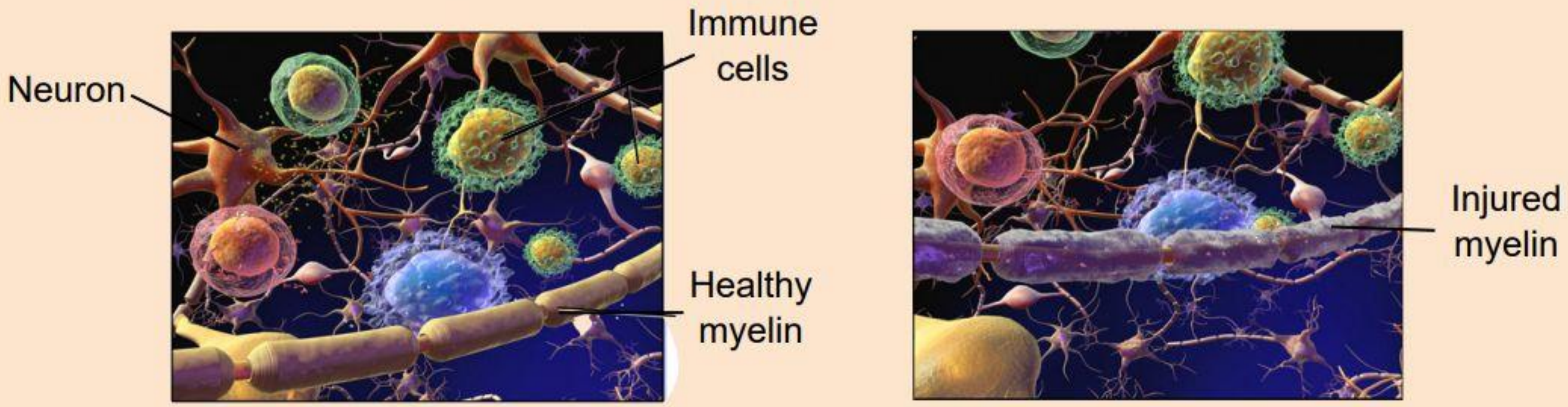


Figure 3.15 Multiple sclerosis is a disease resulting from the destruction of myelin, which hinders the ability for neurons to communicate properly.

- Results from destruction of myelin in CNS
- Signals do not reliably propagate from brain to body, from body to brain, or between brain areas
- Symptoms:
  - muscle weakness, poor balance, muscle spasms, (as a result of damaged myelin on efferent motor neurons)
  - numbness, pain, (as a result of damaged myelin on afferent neurons)
  - cognitive impairment, vision loss, and changes in affect leading to depression (brought on by neuronal signaling within brain)

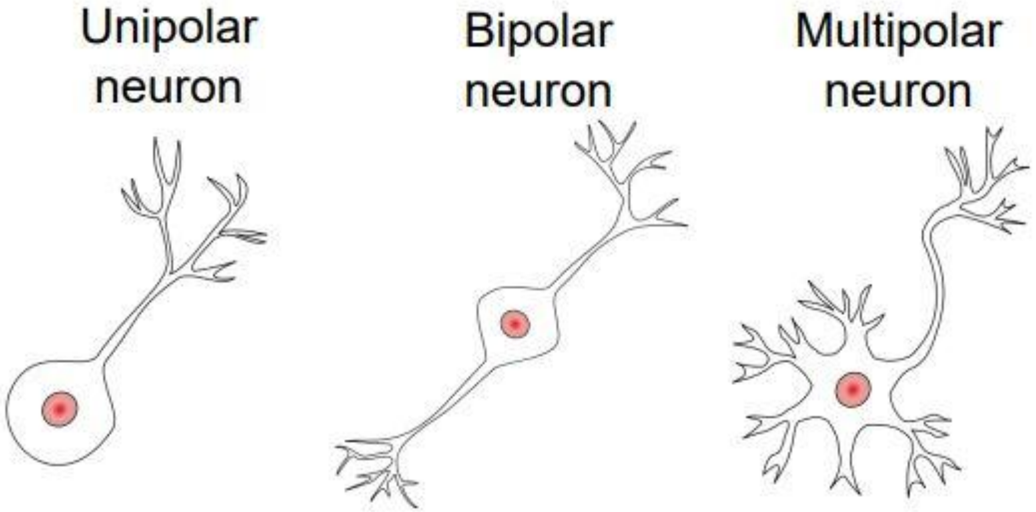
Multiple sclerosis continued

- Common, affecting some 2.5 million people worldwide
- Typically presents between 20-50 years old
- No known cure
- Therapy is focuses on slowing progression of disease, helping patients recover after an attack, or decreasing severity of symptoms
- Debilitating, but not lethal (decrease in life expectancy is 5-10 years)
- One leading theory about cause is faulty immune system (autoimmune disorder)
- Neurodegenerative aspects
- Very high incidence rate in Canada

Classification of neurons by **morphology**

- Wide variety of shapes and sizes with roughly three different classes based on morphology
  1. Unipolar cell - singular extension off soma acts as both receiving and sending end; very common in invertebrates; however, not found in humans
  2. Bipolar cell - single dendrite & single axon; not common, but found in sensory systems
  3. Multipolar cell - several dendrites & single axon; most common neuron type for humans

Figure 3.16 Neurons can be classified based on their morphology.



Classification of neurons by **functions**

- Also classified based on functions
  1. Sensory – afferent (variety of functions leading to variety of shapes and structures)
  2. Motor – efferent; 2 main types (somatic motor neurons [skeletal] & autonomic motor neurons [smooth muscles, cardiac muscles, & glands])
  3. Interneuron - relay between sensory or motor neurons and CNS or between each other; important to reflex circuits

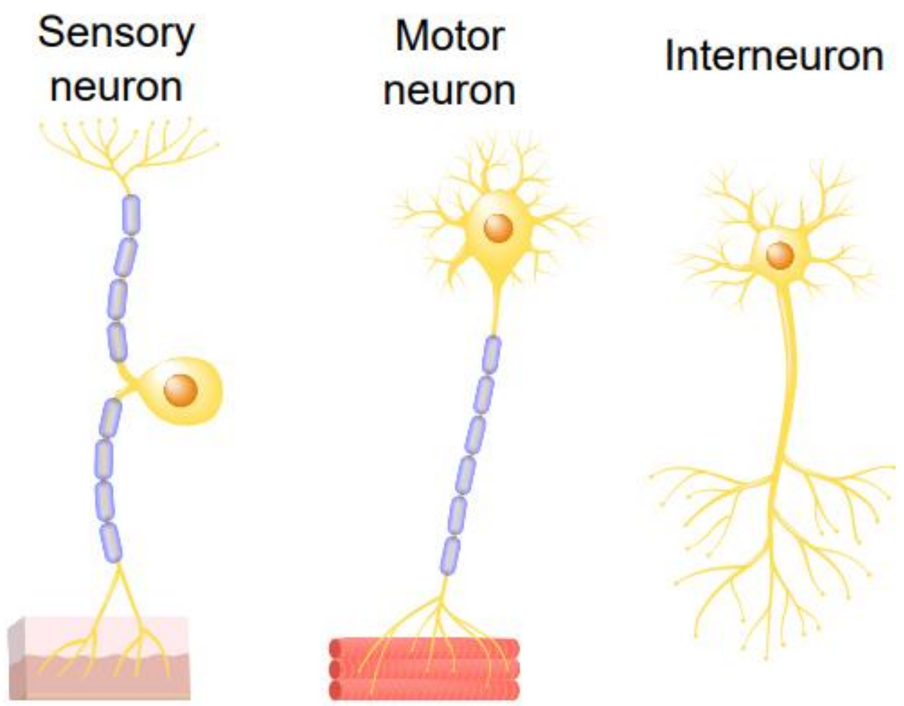


Figure 3.18 Neurons can also be classified based on their function.

Visualizing the synapse

- Electron microscopy (EM)
- Beam of electrons aimed at sample in vacuum & reflection of those electrons is collected with computer
- Electrons have shorter wavelength than visible light so we can see objects as small as 50 picometers (more than 10,000,000x magnification

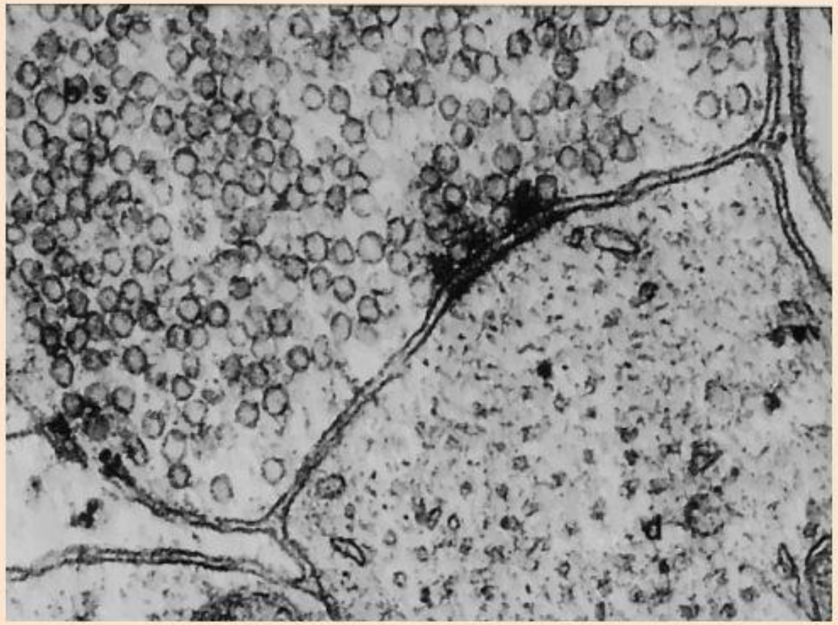


Figure 3.17 Electron microscope image showing a synapse at ultrastructural resolution (less than 100 nm).

Units in perspective…

Prefix	Symbol for Prefix		Scientific Notation
exa	E	1 000 000 000 000 000 000	10^{18}
peta	P	1 000 000 000 000 000	10^{15}
tera	T	1 000 000 000 000	10^{12}
giga	G	1 000 000 000	10^{9}
mega	M	1 000 000	10^{6}
kilo	k	1 000	10^{3}
hecto	h	100	10^{2}
deka	da	10	10^{1}
----	--	1	10^{0}
deci	d	0.1	10^{-1}
centi	c	0.01	10^{-2}
milli	m	0.001	10^{-3}
micro	µ	0.000 001	10^{-6}
nano	n	0.000 000 001	10^{-9}
pico	p	0.000 000 000 001	10^{-12}
femto	f	0.000 000 000 000 001	10^{-15}
atto	a	0.000 000 000 000 000 001	10^{-18}

Cellular functions of glia

- Umbrella classification of cells in the nervous system that are not neurons
- Historically viewed as providing structure, gluing neurons together
- Glia – Latin for glue
- Estimate is equal number of glial cells and neurons (86 billion of each)
- Many different classes of glia, but focus on these five:
    1. Astrocytes
    2. Oligodendrocytes
    3. Schwann cells
    4. Microglia
    5. Ependymal cells

Astrocytes

- Named for star-shaped morphology
- Dense expression of glial fibrillary acidic protein (GFAP) - which gets used as a marker to differentiate astrocytes from other cell populations
- One main function: help maintain blood-brain barrier (BBB)
- At end of extensions are "endfeet" which often wrap around endothelial cells surrounding blood vessels
- Endfeet release biological compounds that allow endothelial cells to remain healthy as they function in maintaining BBB
- Closely associated with synapses
- Have a dense expression of proteins that can transport glutamate inside astrocyte; act a glutamate sponge and decrease strength of glutamate signal

Astrocytes continued

- Similar uptake mechanism affecting extracellular concentration of ions such as potassium
- Tripartite synapse - refers to three components of synapse: presynaptic neuron, postsynaptic neuron, and astrocyte
- Astrocytes also synthesize and produce a variety of trophic factors (helper molecular signals)

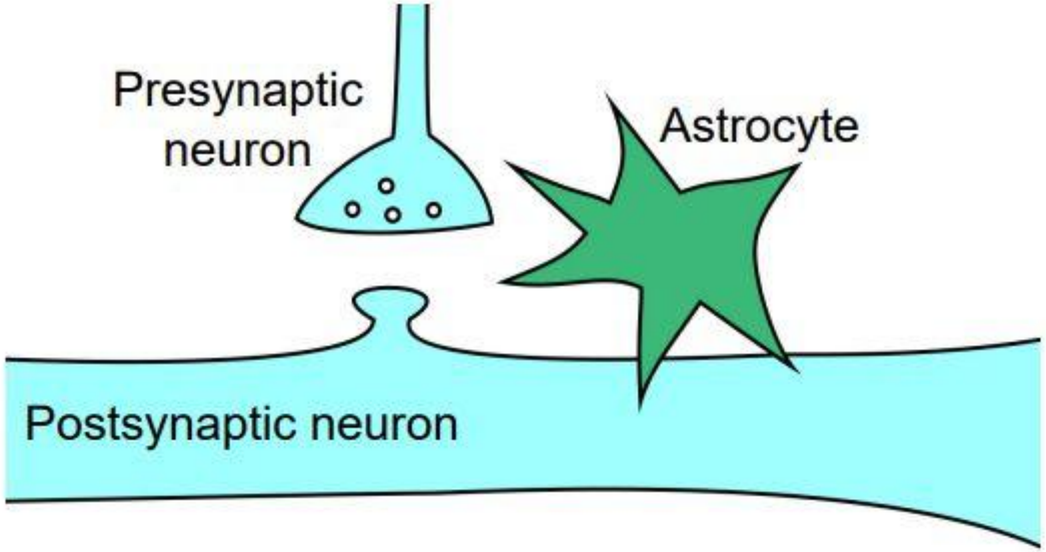


Figure 3.20 Astrocytes can modify communication between two neurons and are therefore part of the tripartite synapse.

Oligodendrocytes

- Only exist in CNS
- Name derives from morphology (oligo- refers to "small number" and dendro- refers to "tree"; each oligodendrocyte has a few branches that reach away from the cell body
- Function: add a layer of myelin around axons of nearby CNS neurons
- One oligodendrocyte can myelinate up to 50 segments of axons
- Responsible for increasing conduction speed of nearby neurons as they send signals
- Believed to have highest metabolic rate of any cell in brain

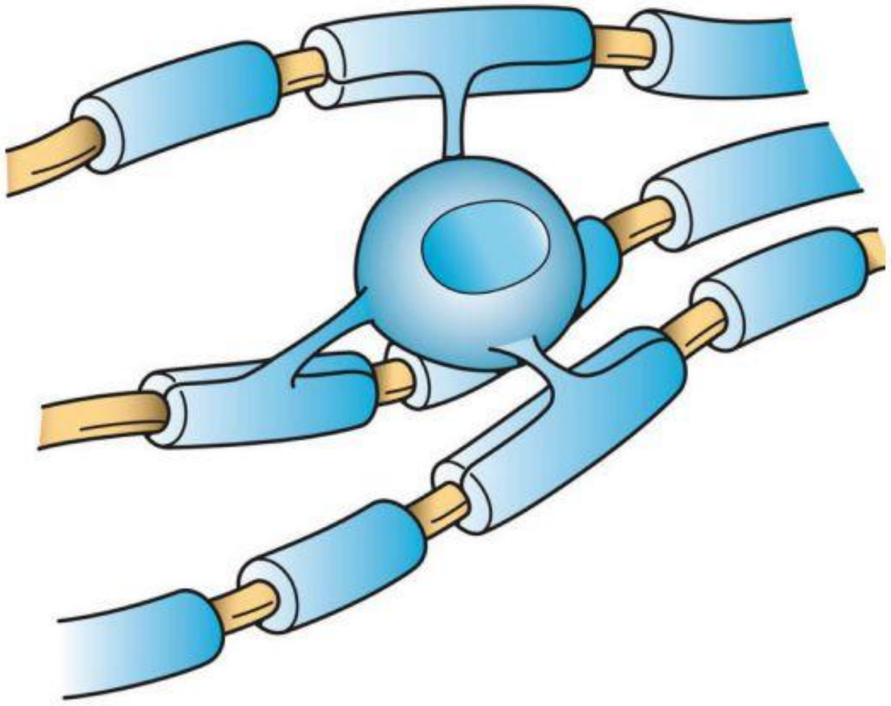


Figure 3.21 Oligodendrocytes are capable of myelinating multiple axon segments at once.

Schwann cells

- Named after German biologist who first described them
- Nerve cells that wrap around the axons of neurons that project towards muscles
- Only found in PNS
- Myelin sheath in PNS (function like oligodendrocytes)
- Produce only a single section of myelin
- Also function in regeneration of injured axons

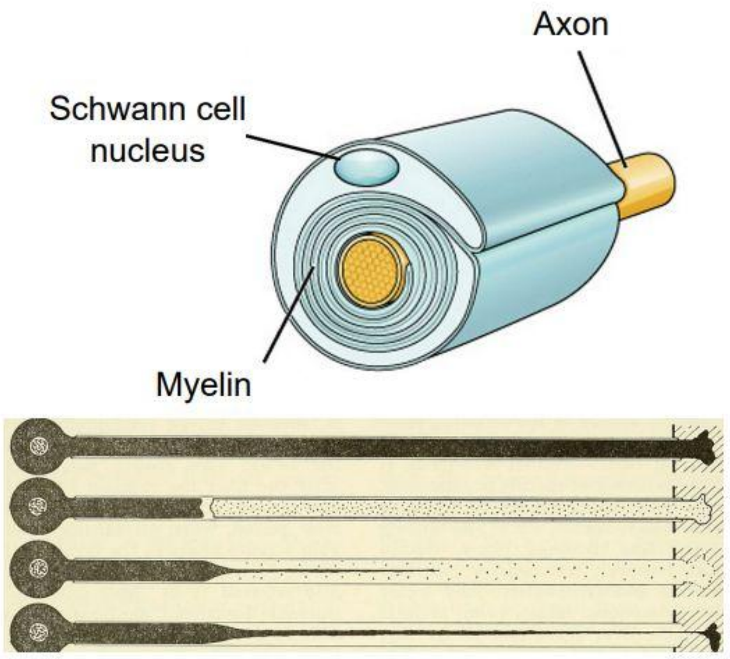


Figure 3.22 Schwann cells myelinate a single segment of an axon in the PNS (top). They also contribute to regeneration of injured nerves (bottom).

Microglia

- More immune cells, rather than neural
- Act as cellular scavengers travelling throughout the brain and spinal cord
- Estimated that they make up 10-15% of all cells in brain
- Identify and destroy clumps of proteins, dead / dying cells, or foreign pathogens that enter brain
- After injury to CNS, microglia rapidly react to the area (marker: lba1)

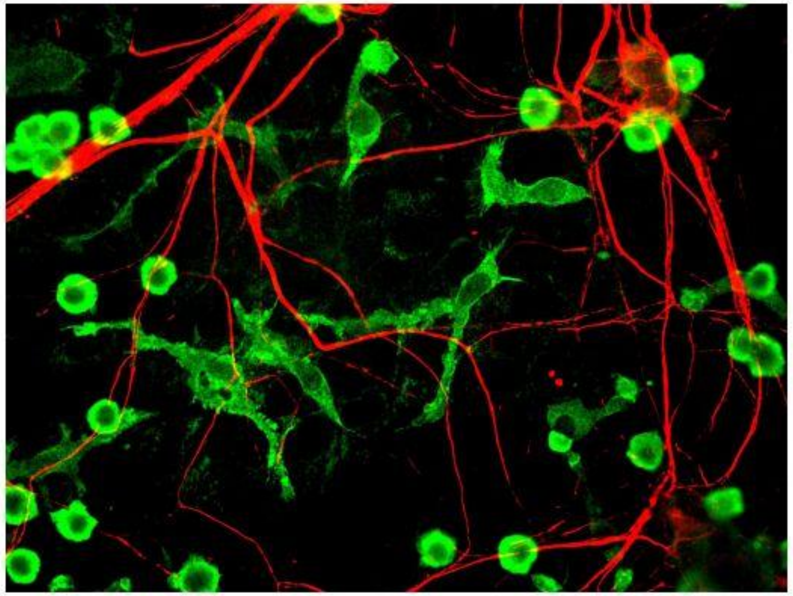


Figure 3.23 Microglia (green) are much smaller than neurons (red). They are neural immune cells that exhibit morphological changes when performing cellular cleaning.

Ependymal cells

- Along the inside of the ventricles
- Columnar with cilia that extend into ventricles and into central canal of spinal cord
- Produce cerebrospinal fluid (CSF)
  - Body produces ~0.5 L (2 cups) of CSF daily
- Part of structure called choroid plexus, a network of blood vessels and cells that form a boundary between blood and CSF

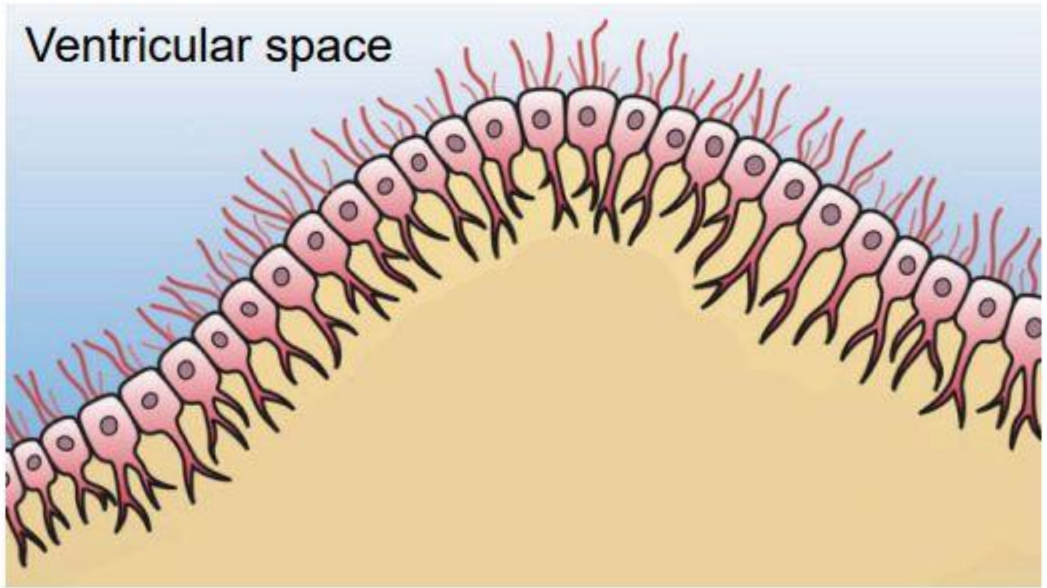


Figure 3.24 Ependymal cells line the inside of the ventricles and produce cerebrospinal fluid.