Excitable Tissue: Nerve

The human central nervous system (CNS) contains about10^{11} (100 billion) **neurons.** It also contains (10-50) times this number of **glial cells.**

Glial Cells

There are two major types of glial cells in the vertebrate nervous system: microglia and macroglia

Microglia

are scavenger cells that resemble tissue macrophages and remove debris resulting from injury, infection, and disease. Microglia arise from macrophages outside of the nervous system and are physiologically and embryologically unrelated to other neural cell types.

Macroglia

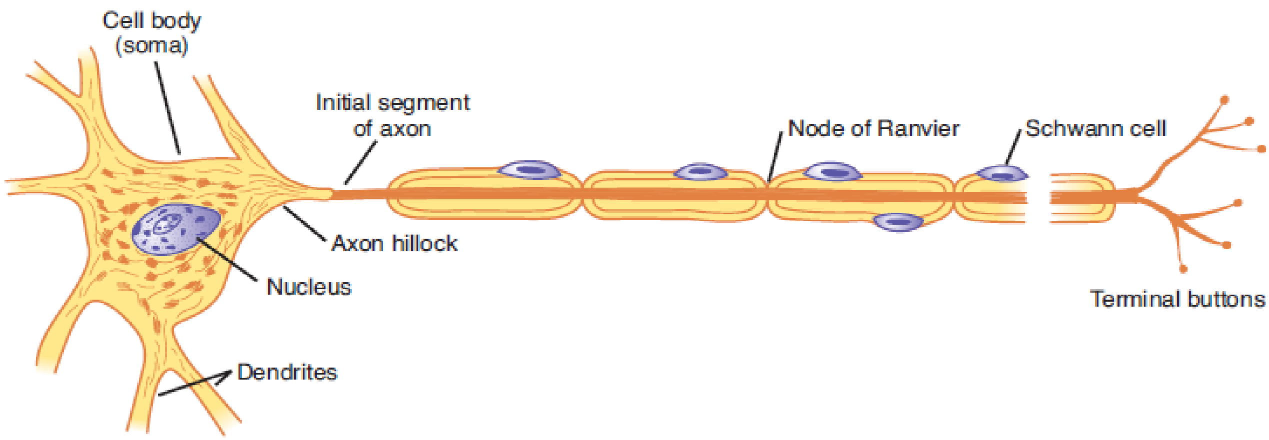
are of three types: oligodendrocytes, Schwann cells, and astrocytes. Oligodendrocytes and Schwann cells are involved in myelin formation around axons in the CNS and peripheral nervous system, respectively. Astrocytes**,** which are found throughout the brain, are of two subtypes.

Fibrous astrocytes: which contain many intermediate filaments, are found primarily in white matter.

Protoplasmic astrocytes : are found in gray matter and have a granular cytoplasm. Both types send processes to blood vessels, where they induce capillaries to form the tight junctions making up the **blood–brain barrier.** They produce substances that are tropic to neurons, and they help maintain the appropriate concentration of ions and neurotransmitters by taking up $K+$ and the neurotransmitters glutamate and γ-aminobutyrate (GABA).

Neurons

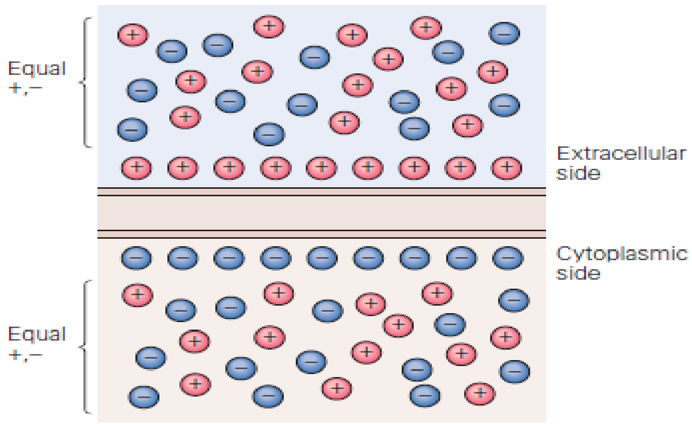
Neurons in the mammalian central nervous system come in many different shapes and sizes. Most have the same parts as the typical spinal motor neuron. The cell body (soma) contains the nucleus and is the metabolic center of the neuron. Neurons have several processes called Dendrites that extend outward from the cell body and arborize extensively. Particularly in the cerebral and cerebellar cortex, the dendrites have small knobby projections called dendritic spines. A typical neuron also has a long fibrous axon that originates from a somewhat thickened area of the cell body, the axon hillock. The first portion of the axon is called the initial segment. The axon divides into presynaptic terminals, each ending in a number of synaptic knobs which are also called terminal buttons. They contain granules or vesicles in which the synaptic transmitters secreted by the nerves are stored. Based on the number of processes that emanate from their cell body, neurons can be classified as unipolar, bipolar, and multipolar.



The axons of many neurons are myelinated, that is, they acquire a sheath of **myelin,** a protein -lipid complex that is wrapped around the axon. In the peripheral nervous system, myelin forms when a Schwann cell wraps its membrane around an axon up to 100 times. The myelin sheath envelops the axon except at its ending and at the **nodes of Ranvier,** Periodic 1-μm constrictions that are about 1 mm apart.

EXCITATION & CONDUCTION

Nerve cells have a low threshold for excitation. The stimulus may be electrical, chemical, or mechanical. Two types of physicochemical disturbances are produced: local, nonpropagated potentials called, depending on their location, **synaptic** and propagated potentials, the **action potentials** (or **nerve impulses**). These are the only electrical responses of neurons and other excitable tissues, and they are the main language of the nervous system.



This membrane potential results from separation of positive and negative <u>charges across the cell membrane.</u>

The excess of positive charges (red circles) outside the cell and negative charges (blue circles) inside the cell at rest represents a small fraction of the total number of ions present.

In neurons, the concentration of K+ is much higher inside than outside the cell, while the reverse is the case for Na+. This concentration difference is established by the Na+ -K+ ATPase. In response to a depolarizing stimulus, some of the voltage-gated Na+ channels become active, and when the **threshold potential** is reached (at 7–15 mV of depolarization (potential of –55 mV), the **firing level** is reached and an action potential occurs), the voltage-gated Na+ channels overwhelm the K+ and other channels and an action potential results. Although Na+ enters the nerve cell and K+ leaves it during the action potential, the number of ions involved is minute relative to the total numbers present. Other ions, notably Ca2+, can affect the membrane potential through both channel movement and membrane interactions. A decrease in extracellular Ca2+ concentration increases the excitability of nerve and muscle cells by decreasing the amount of depolarization necessary to initiate the changes in the Na+ and K+ conductance that produce the action potential. Conversely, an increase in extracellular Ca2+ concentration can stabilize the membrane by decreasing excitability.

DISTRIBUTION OF ION CHANNELS IN MYELINATED NEURONS

Voltage-gated Na+ channels are highly concentrated in the nodes of Ranvier and the initial segment in myelinated neurons. The initial segment and, in sensory neurons, the first node of Ranvier are the sites where impulses are normally generated, and the other nodes of Ranvier are the sites to which the impulses jump during saltatory conduction.

"ALL-OR-NONE" LAW

Once threshold intensity is reached, a full-fledged action potential is produced. Further increases in the intensity of a stimulus produce no increment or other change in the action potential as long as the other experimental conditions remain constant. The action potential fails to occur if the stimulus is sub-threshold in magnitude, and it occurs with constant amplitude and form regardless of the strength of the stimulus if the stimulus is at or above threshold intensity.

SALTATORY CONDUCTION

Depolarization in myelinated axons jumps from one node of Ranvier to the next, with the current sink at the active node serving to electrotonically depolarize the node ahead of the action potential to the firing level. This jumping of depolarization from node to node is called **saltatory conduction.** It is a rapid process that allows myelinated axons to conduct up to 50 times faster than the fastest unmyelinated fibers.

PROPERTIES OF MIXED NERVES

Peripheral nerves in mammals are made up of many axons bound together in a fibrous envelope called the **epineurium.** Potential changes recorded extracellularly from such nerves therefore represent an algebraic summation of the all-or-none action potentials of many axons. With subthreshold stimuli, none of the axons are stimulated and no response occurs. When the stimuli are of threshold intensity, axons with low thresholds fire and a small potential change is observed. As the intensity of the stimulating current is increased, the axons with higher thresholds are also discharged. The electrical response increases proportionately until the stimulus is strong enough to excite all of the axons in the nerve. The stimulus that produces excitation of all the axons is the **maximal stimulus,** and application of greater, **supramaximal** stimuli produces no further increase in the size of the observed potential.

Nerve fiber types in mammalian nerve.

Fiber Type	Function	Fiber Diameter (μm)	Conduction Velocity (m/s)
A			
α	Proprioception; somatic motor	12–20	70–120
β	Touch, pressure	5–12	30–70
γ	Motor to muscle spindles	3–6	15–30
δ	Pain, cold, touch	2–5	12–30
B	Preganglionic autonomic	<3	3–15
C			
Dorsal root	Pain, temperature, some mechano-reception	0.4–1.2	0.5–2
Sympathetic	Postganglionic sympathetic	0.3–1.3	0.7–2.3

[a]A and B fibers are myelinated; C fibers are unmyelinated.

In general, the greater the diameter of a given nerve fiber, the greater its speed of conduction.

NEUROTROPHINS

A number of proteins necessary for survival and growth of neurons. Some of these neurotrophins are products of the muscles or other structures that the neurons innervate (retrograde transport), but others are produced by astrocytes they foster the production of proteins associated with neuronal development, growth, and survival. Other neurotrophins are produced in neurons and transported in an anterograde fashion to the nerve ending, where they maintain the integrity of the postsynaptic neuron. The first neurotrophin to be characterized was Nerve growth factor (NGF), a protein growth factor that is necessary for the growth and maintenance of sympathetic neurons and some sensory neurons. It is present in a broad spectrum of animal species, including humans, and is found in many different tissues. (responsible for the growth and maintenance of cholinergic neurons in the basal forebrain and striatum)

Relative susceptibility of mammalian A, B, and C nerve fibers to conduction block produced by various agents.

Susceptibility to:	Most Susceptible	Intermediate	Least Susceptible
Hypoxia	B	A	C
Pressure	A	B	C
Local anesthetics	C	B	A