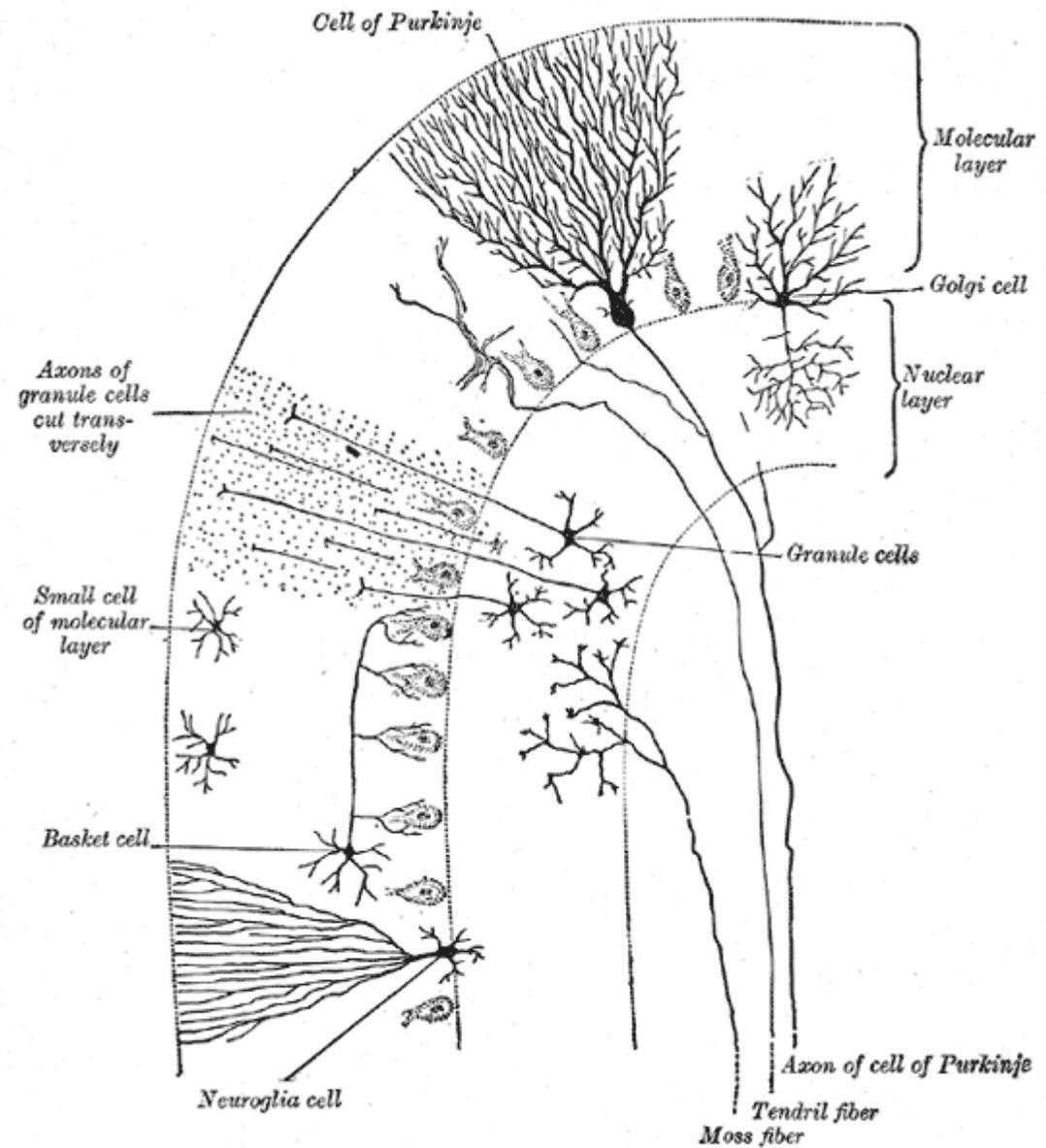
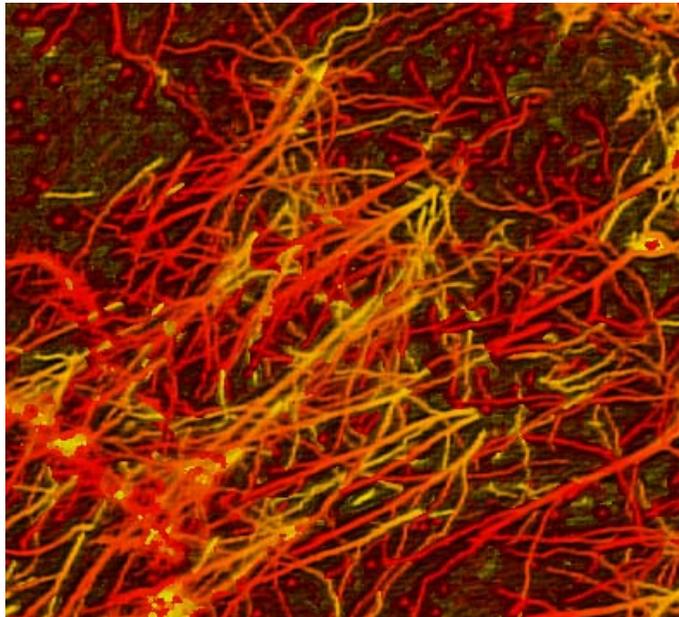


2. The neuron



Transverse section of a cerebellar folium.

http://en.wikipedia.org/wiki/Purkinje_cell

Brain cells: neurons and glial cells

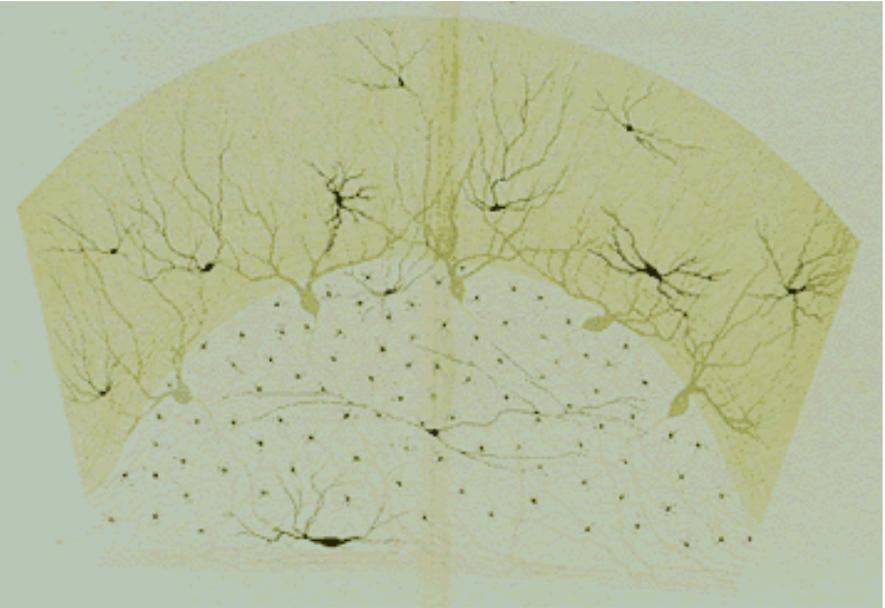
Neurons: the functional cells of the nervous system. See below.

Glial cells (neuroglia): make up 90% of the brain cells

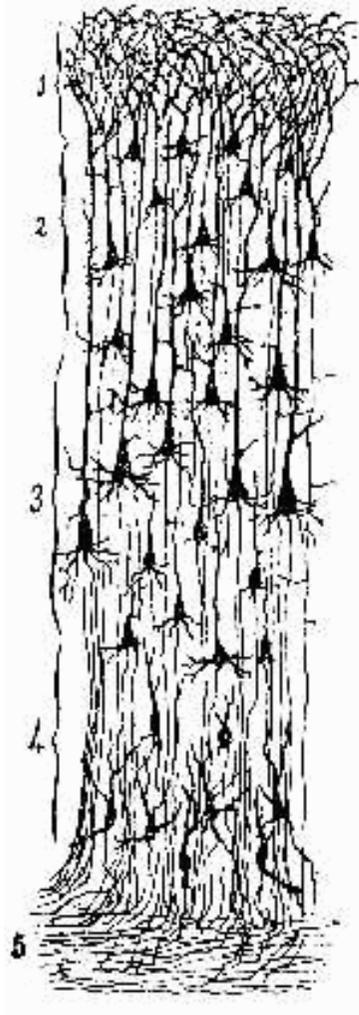
- a) **astrocytes** - these cells anchor neurons to blood vessels, regulate the micro-environment of neurons, and regulate transport of nutrients and wastes to and from neurons.
- b) **microglia** - these cells are phagocytic to defend against pathogens. They may also monitor the condition of neurons.
- c) **ependymal cells** - these cells line the fluid-filled cavities of the brain and spinal cord. They play a role in production, transport, and circulation of the cerebrospinal fluid.
- d) **oligodendrocyte** - produce the myelin sheath in the CNS which insulates and protects axons.
- e) **Schwann cells** - produce the myelin sheath in the PNS. The myelin sheath protects and insulates axons, maintains their micro-environment, and enables them to regenerate and re-establish connection with receptors or effectors.
- f) **satellite cells** - surround cell bodies of neurons in ganglia. Their role is to maintain the micro-environment and provide insulation for the ganglion cells.

http://webanatomy.net/anatomy/neuro_notes.htm

Camillo Golgi (1843-1926)

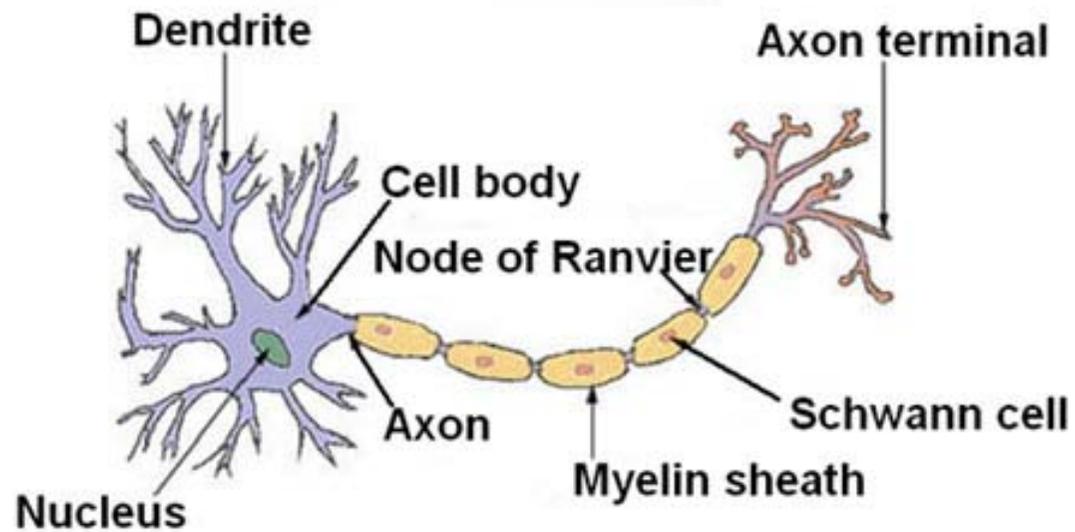


Santiago Ramón y Cajal (1852-1934)



independent neurons, or nerve cells, are the building blocks of the central nervous system

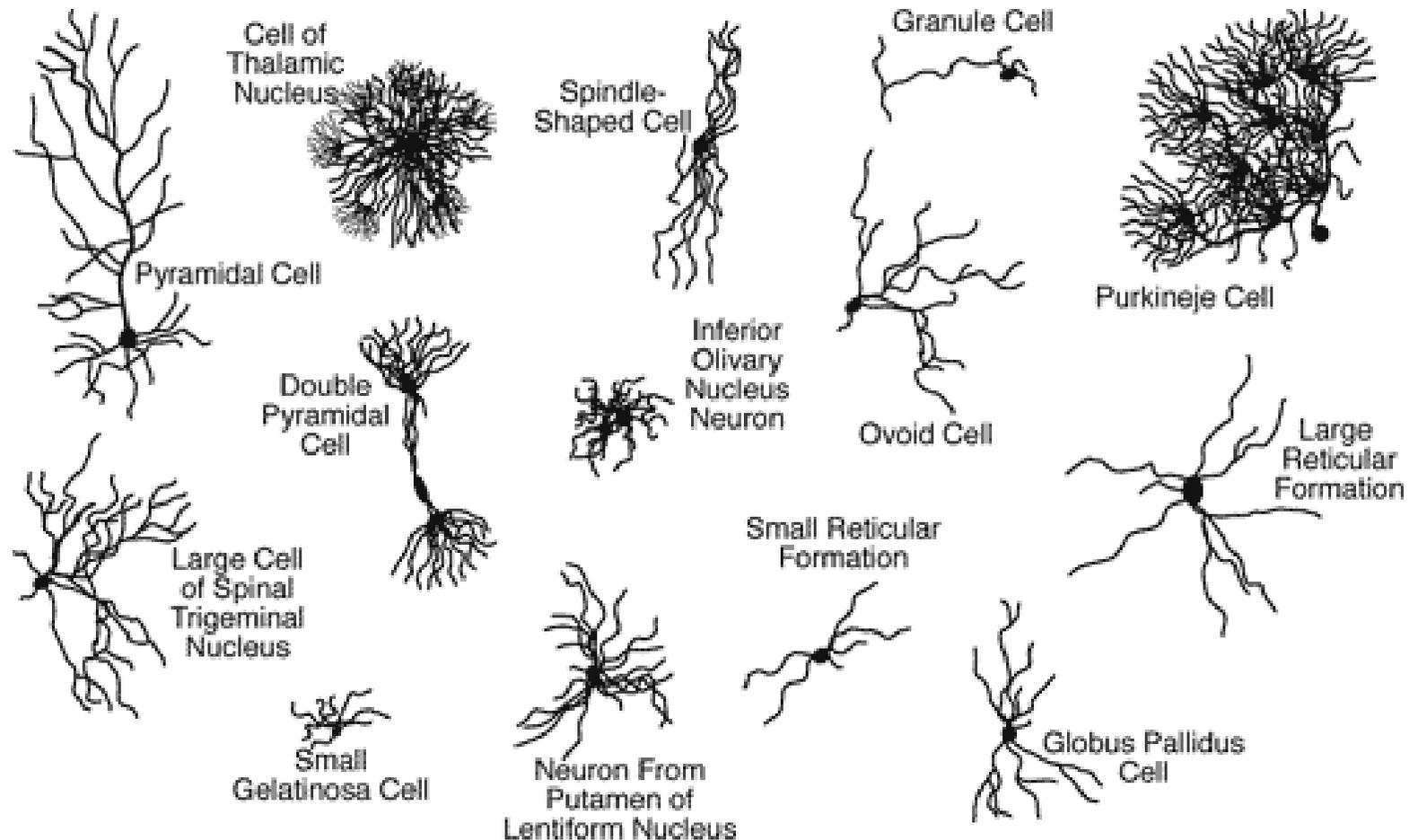
Structure of a Typical Neuron



Diameter: 4 – 100 μm

Length: an inch to several feet

10,000 specific types of neurons in the human CNS
various shapes and sizes
100-200 billion neurons in a brain



The drawings made by Cajal

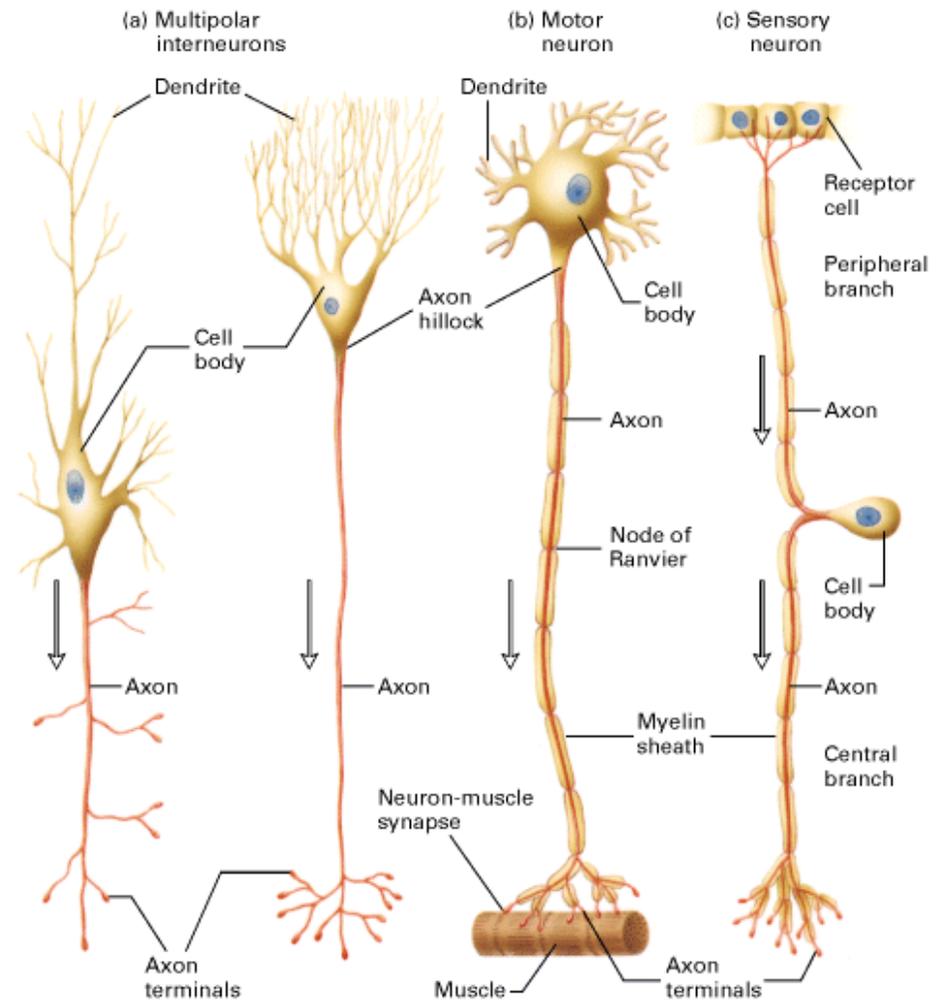
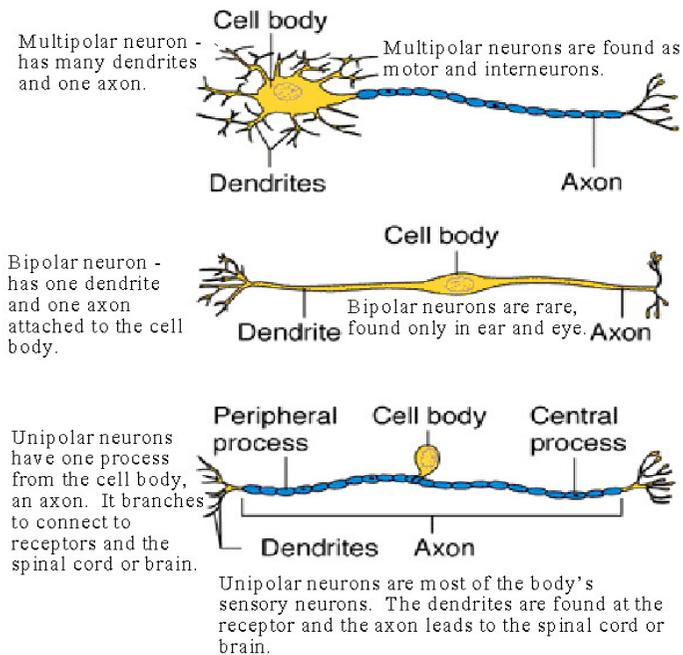
Neurons: 3 basic types

Multipolar: single axon and many dendrites, most neurons

Bipolar: two extensions from the cell body

Unipolar: single extension from the cell body
includes many primary sensory neurons

Structural Classes of Neurons



Active Conduction

Unmyelinated Axons

Many voltage gated Na^+ channels in proximity

Action potential and passive conduction of the depolarizing current

Opening of the nearby Na^+ channels to generate another action potential

Repeated until the action potential reaches the terminal

Myelinated Axons

Jumping of action potentials from node to node called saltatory conduction

axons covered with myelin sheath

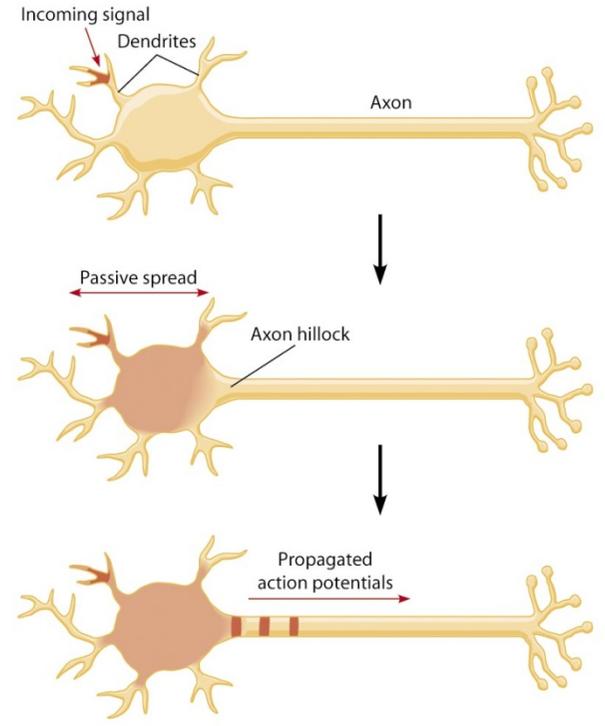
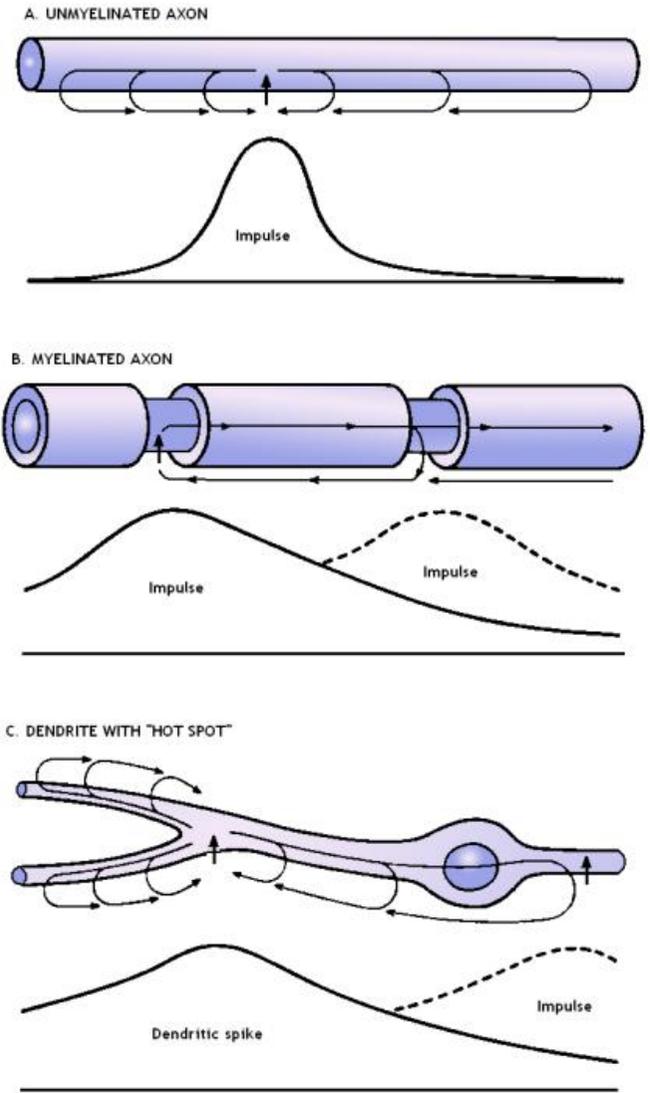
(in the form of Schwann cells in the PNS or oligodendrocytes in the CNS)

Myelin prevents current leakage by increasing resistance in the axon

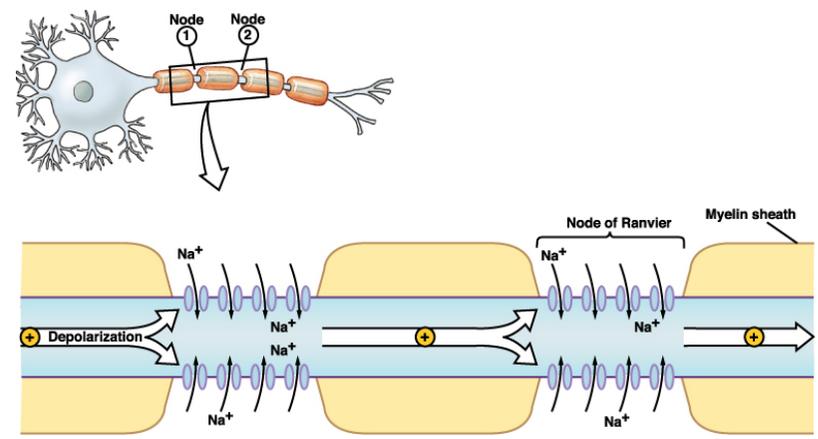
Passive current to the gaps between the myelin sheaths (Nodes of Ranvier)

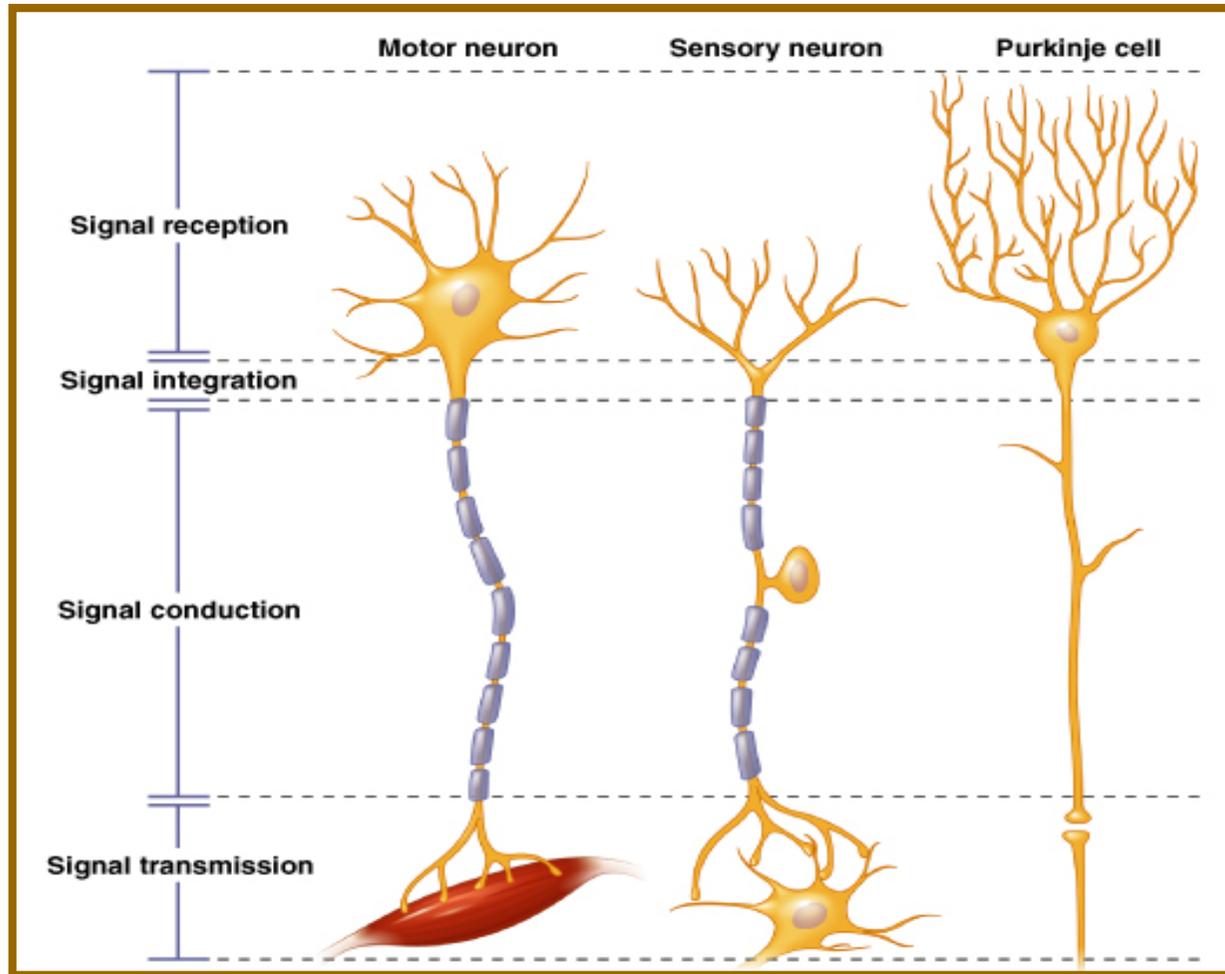
The Nodes of Ranvier contains Na^+ channels, which fire another action potential upon depolarization from the passive current

Passive & Saltatory conduction



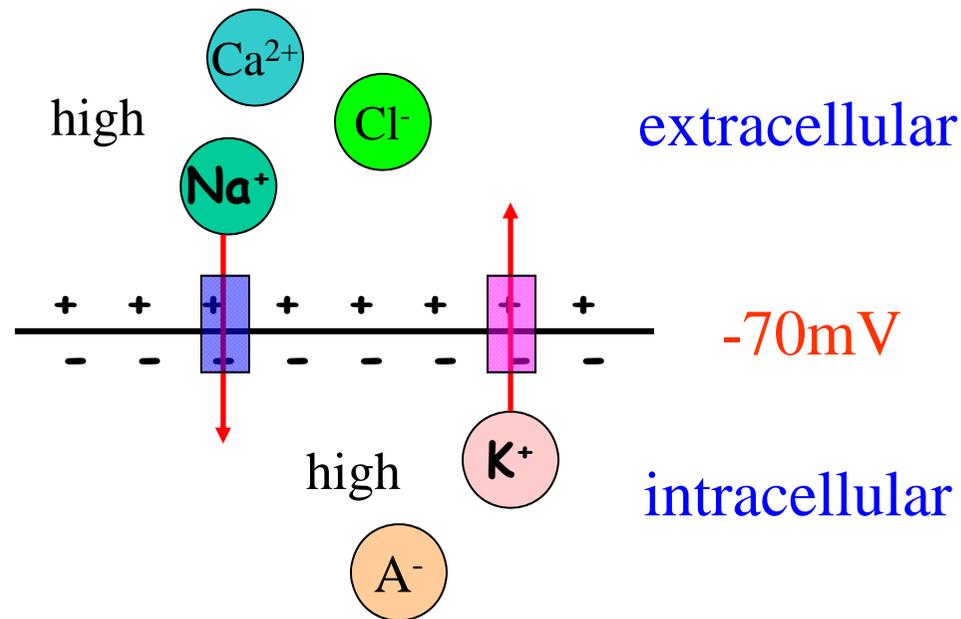
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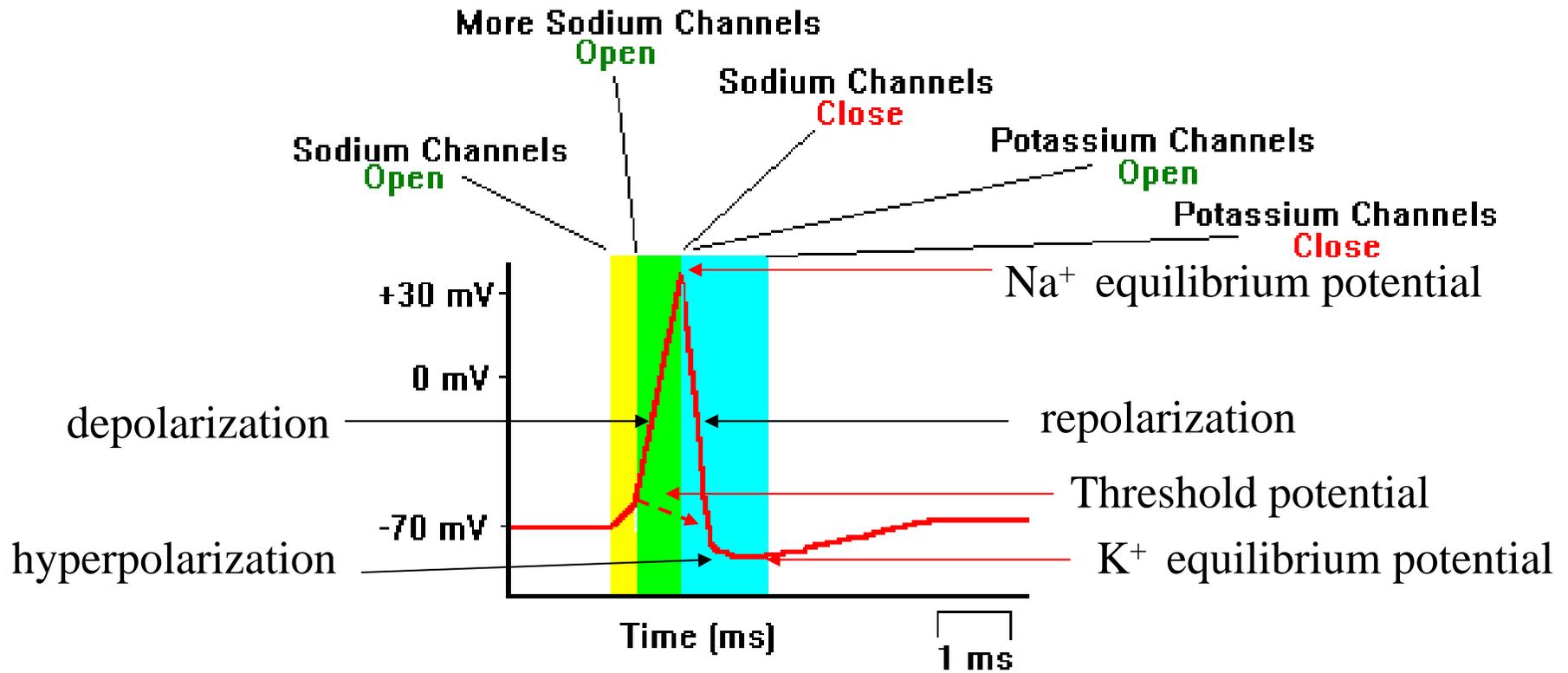




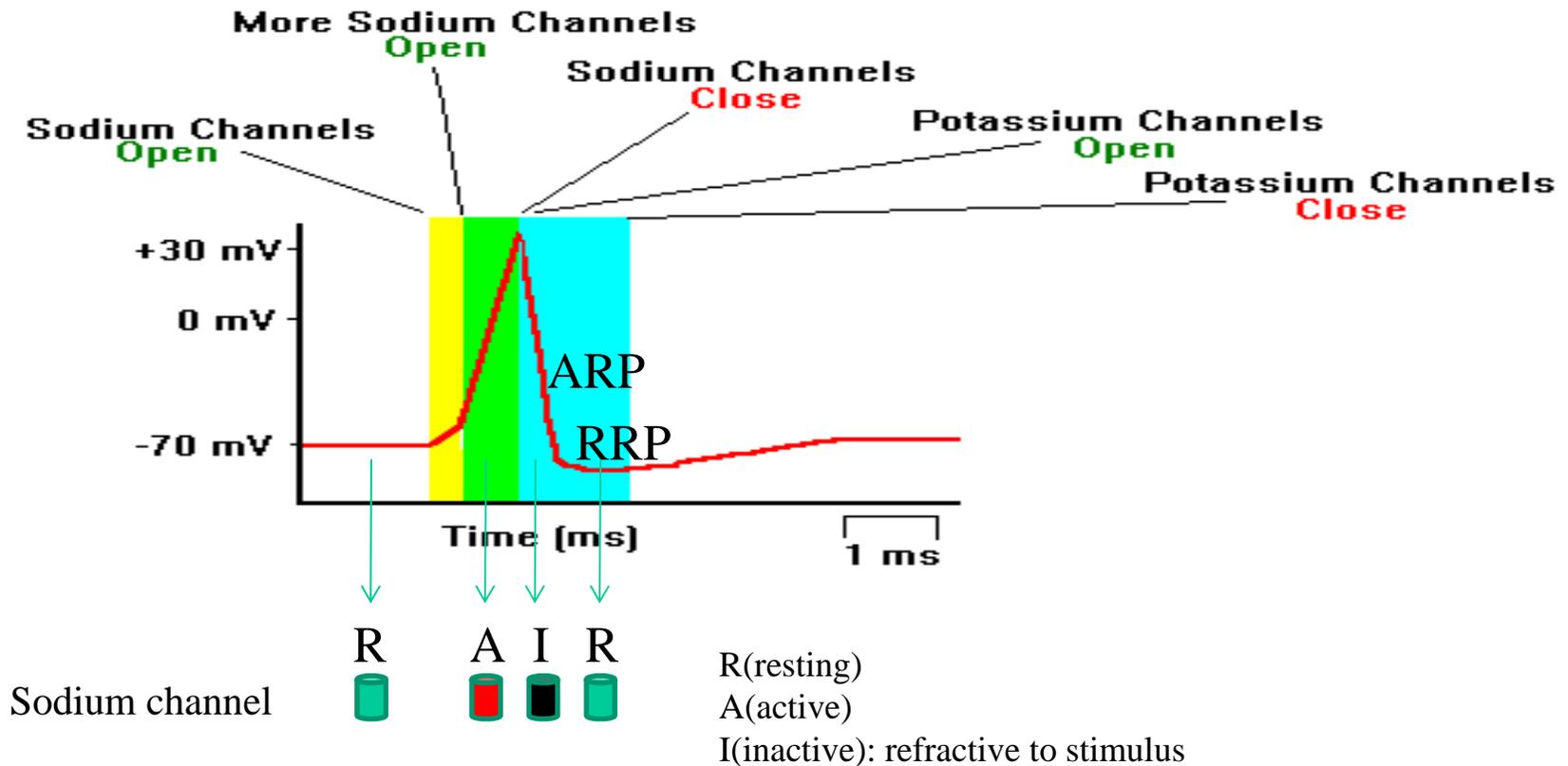
Action potential

<http://faculty.washington.edu/chudler/ap.html>





Voltage sensitive Na⁺ channel: counteraction by voltage sensitive K⁺ channel



When there is a touch,

Mechanical sensitive Na^+ channel is open

If a sense is weak (meaning small amount of Na^+ influx): local potential

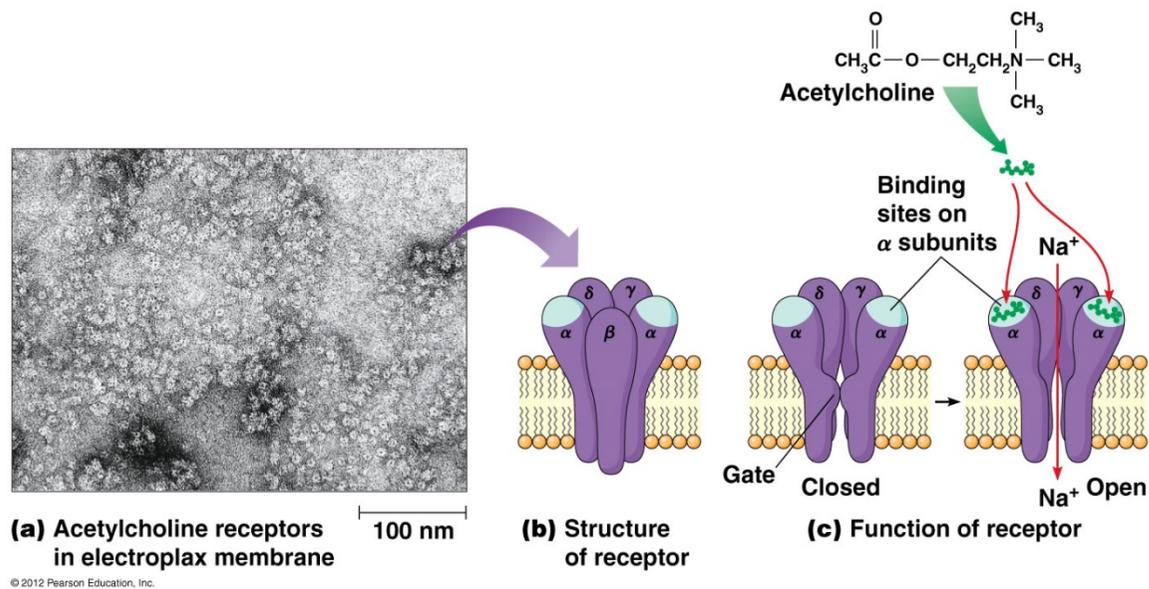
Leaky K^+ channel, which is constitutive, negates the potential difference

If a sense is strong to overcome the threshold potential (-60 mV): action potential

Voltage Na^+ channel is open (conformational change)

Ligand gated sodium channel

They are found e.g. in the [neuromuscular junction](#) as [nicotinic receptors](#), where the ligands are [acetylcholine](#) molecules. Most channels of this type are permeable to potassium to some degree as well as to sodium.



The [acetylcholine receptor](#): a ligand-gated sodium channel that binds two molecules of acetylcholine to open. <http://www.mun.ca/biology/desmid/brian/BIOL2060/BIOL2060-13/CB13.html>

Signal intensity

Repeated action potential: normally 30-100 Hertz or up to 500

Signal speed: depends on two

axon diameter

myelin sheath (electrical insulator: no ion transport): saltatory conduction

up to ~100 m/sec: 0.25 m/sec in case of unmyelinated neuron

Myelinated cells are sheathed multiply either by Schwann cells (peripheral nerves)

or oligodendrocytes (central nerves)

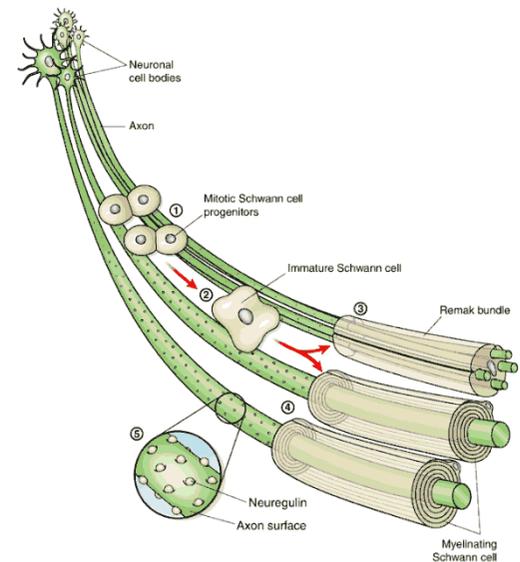
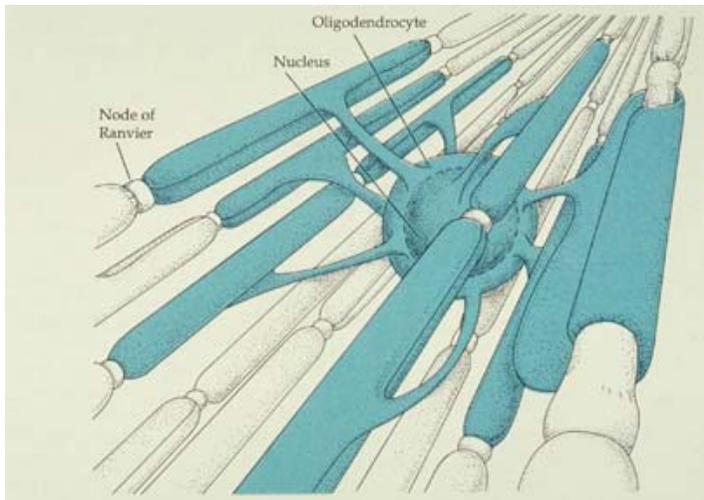
Even unmyelinated cells are even associated with Schwann cells (not multiple layer)

Totally unmyelinated cells are in disease state

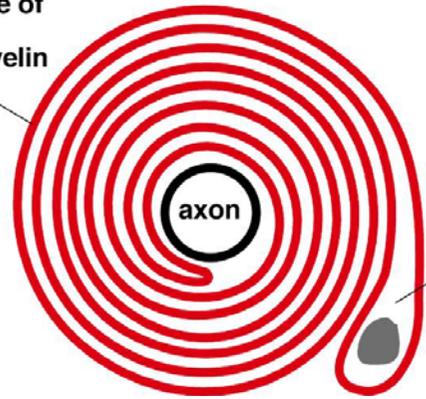
Ex.

Multiple sclerosis (central nervous system): the myelin sheath around the axons of brain and spinal cord are damaged

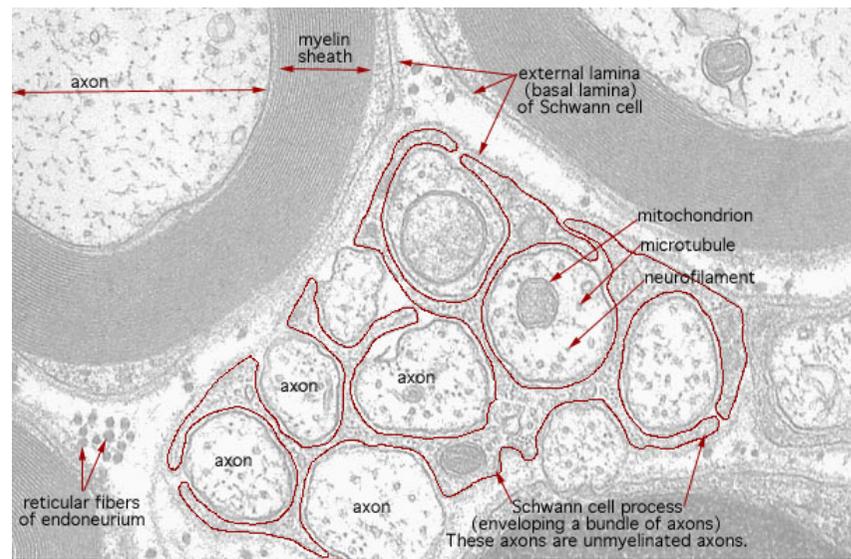
Peripheral demyelinating diseases (peripheral nervous system)



cell membrane of Schwann cell containing myelin



Schwann cell



Synapse

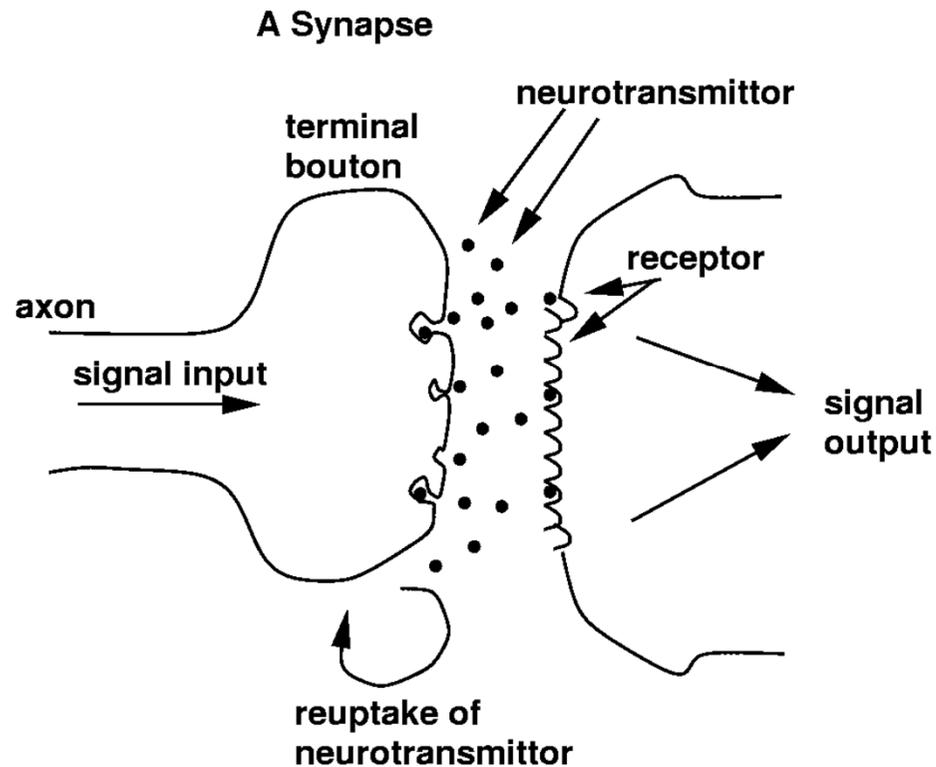
A gap between neurons (axon terminal and dendrite)

Suggested by Cajal

Demonstrated by EM in 1950s

How the signal is transmitted?

translation of electrical signal to chemical signal



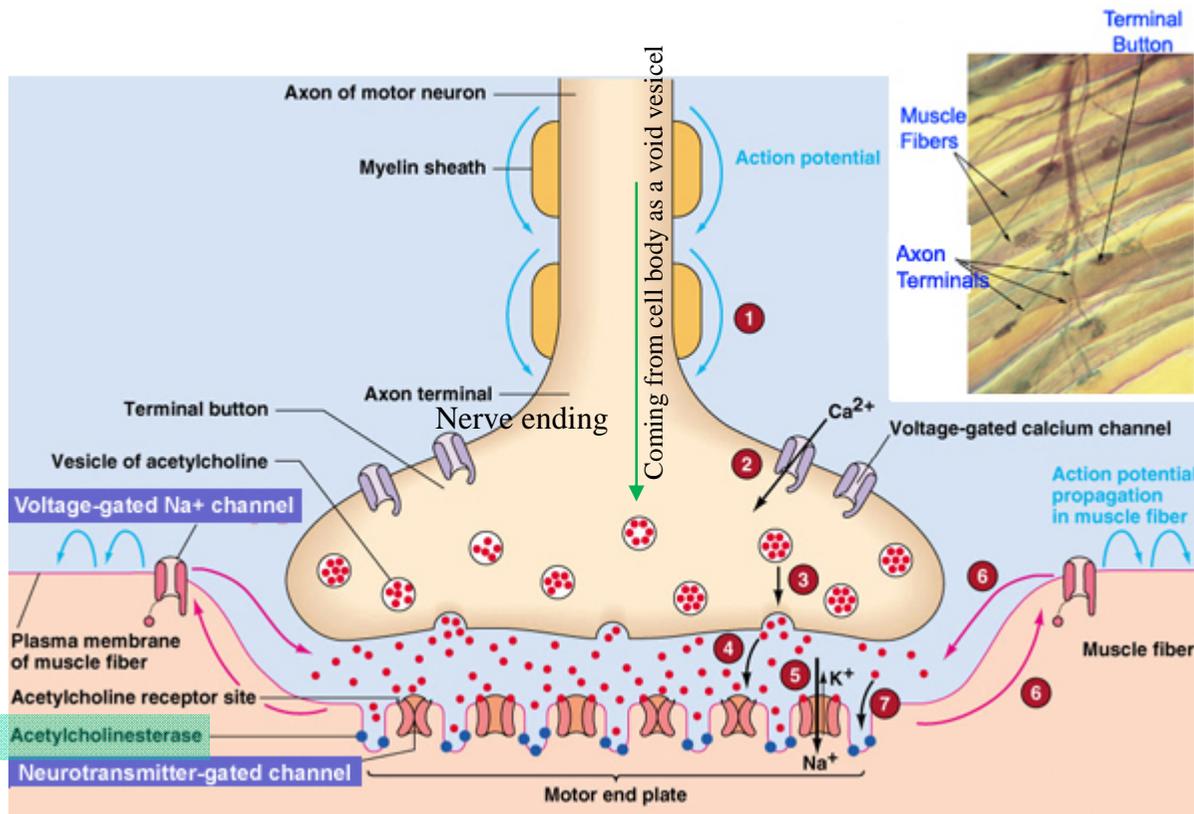
Neuromuscular junction: neuromuscular transmission

Synapse

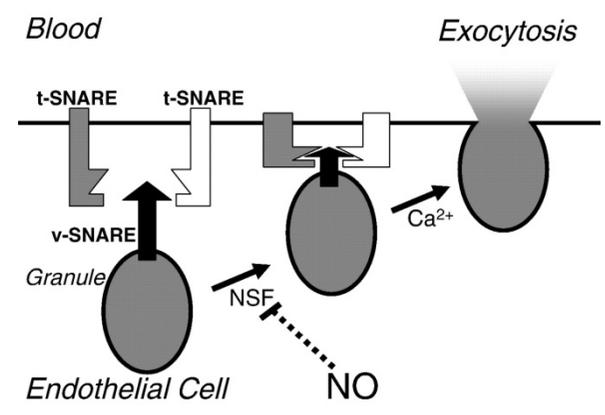
Presynaptic membrane

Postsynaptic membrane

The Neuromuscular Junction



Choline acetyltransferase
Acetylcholinesterase



Local potential leads to endplate potential (EPP), which is a sum of miniature EPP (very small EPP due to very small influx of ACh)

Chemical Synapses Can Be Excitatory or Inhibitory

Excitatory neurotransmitters

Open cation channels

Cause an influx of Na^+ that depolarizes the postsynaptic membrane for firing an action potential

Acetylcholine, *glutamate*, and *serotonin* are used as excitatory transmitters:

Glutamate mediates most of the excitatory signaling in the vertebrate brain

Inhibitory neurotransmitters

Open either Cl^- channels or K^+ channels

Suppresses firing by making it harder for excitatory influences to depolarize the postsynaptic membrane

γ -aminobutyric acid (GABA) and *glycine* are used as inhibitory transmitters.

Many transmitters can be either excitatory and inhibitory,

depending on where they are released,

what receptors they bind to,

and the ionic conditions that they encounter.

Acetylcholine can either excite or inhibit, depending on the type of acetylcholine receptors it binds to.

Chemical provides nerve communication

Curare: nerve toxin suggested by Claud Barnard
acetylcholine receptor blocker
muscle contraction is inhibited

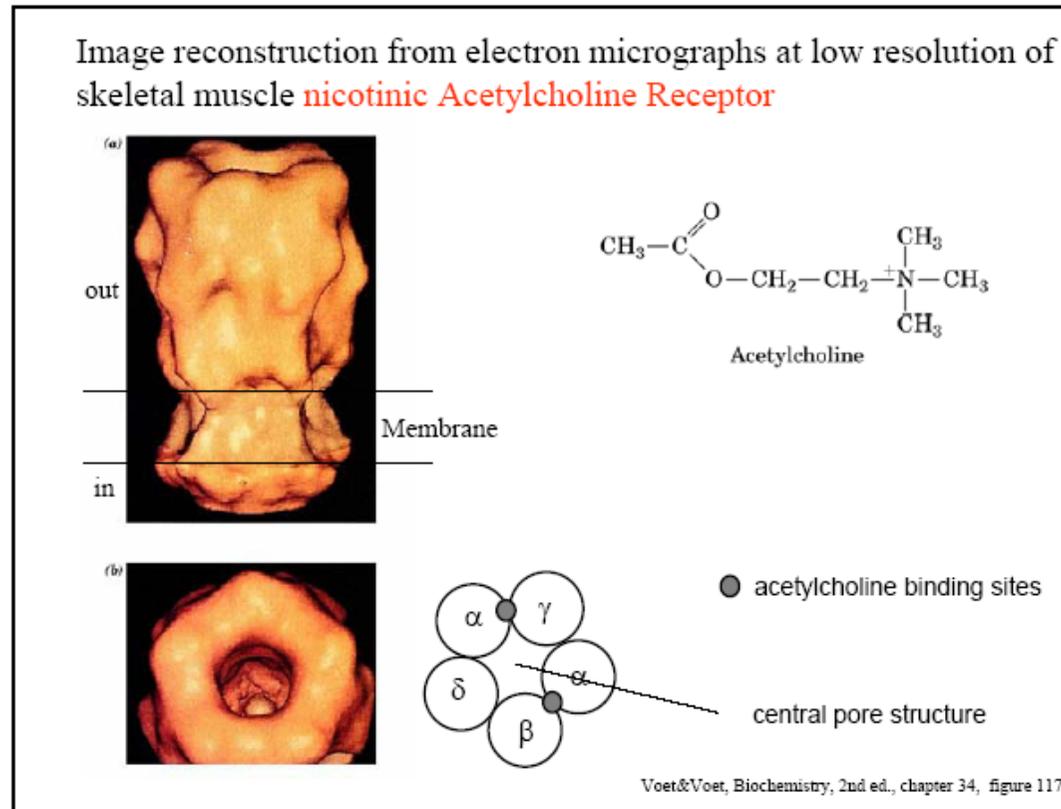
Discovery of the first neurotransmitter by Otto Loewi in 1929

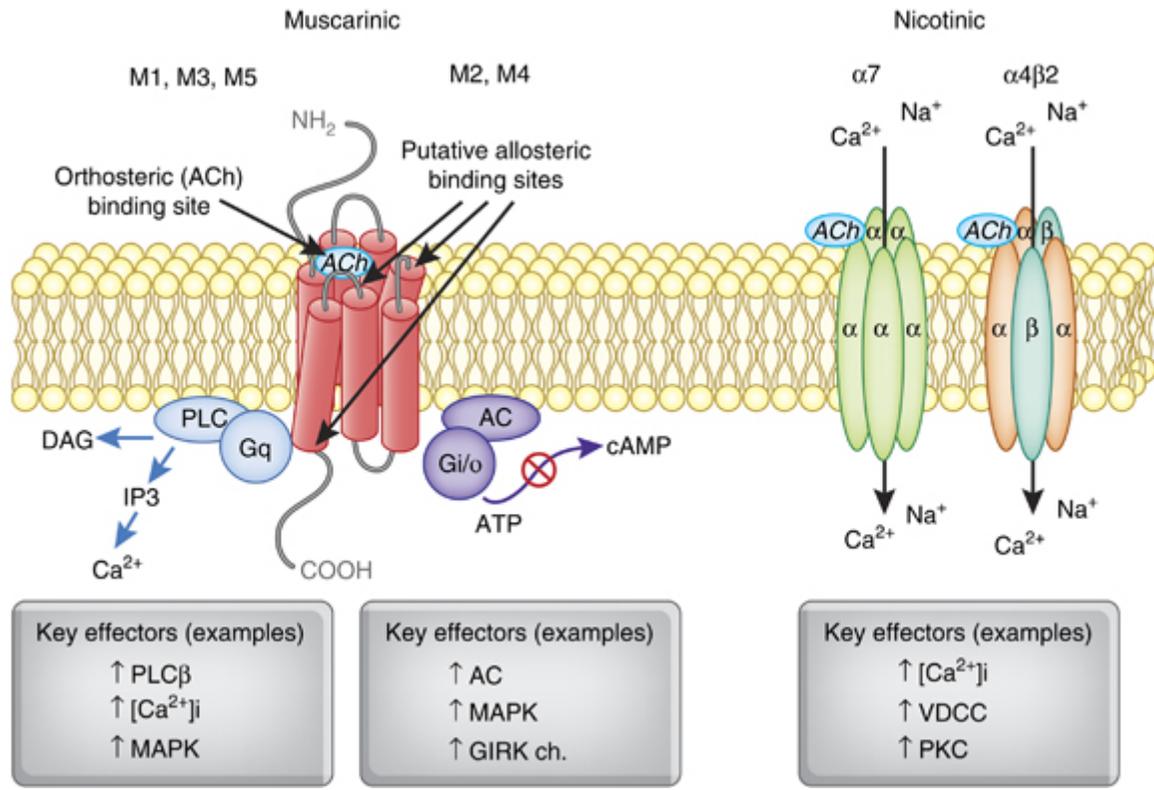
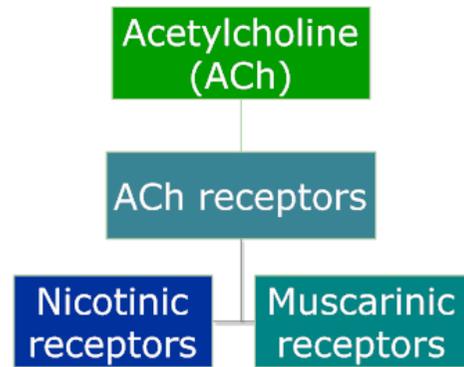
<http://faculty.washington.edu/chudler/chnt1.html>

acetylcholine

Release of acetylcholine into the synapse
the higher the signal the more acetylcholine released

Specific receptor molecules
Opening of ion channel





Nicotinic acetylcholine receptor (nAChR)

Ligand-gated ion channels

Found at the edges of junctional folds at the neuromuscular junction on the postsynaptic side

Activated by acetylcholine

Diffusion of Na⁺ and K⁺ across the receptor causes depolarization

Opening voltage-gated sodium channels

Firing of the action potential

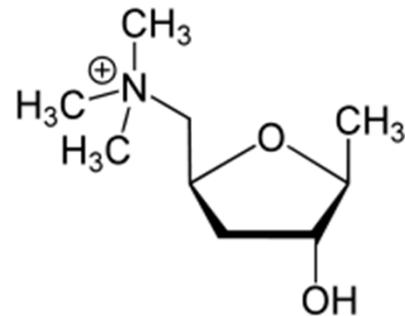
Muscular contraction

Muscarinic acetylcholine receptor (mAChR)

G-protein-coupled receptors

Activate other ionic channels via a second messenger cascade

Muscarine: a natural product in mushrooms



Iontropic receptor & Metabotropic receptors

Iontropic: ion channels

- Ligand-gated ion channels
- Voltage-gated ion channels
- Stretch-activated ion channels

Metabotropic: indirectly linked with ion channels through signal transduction

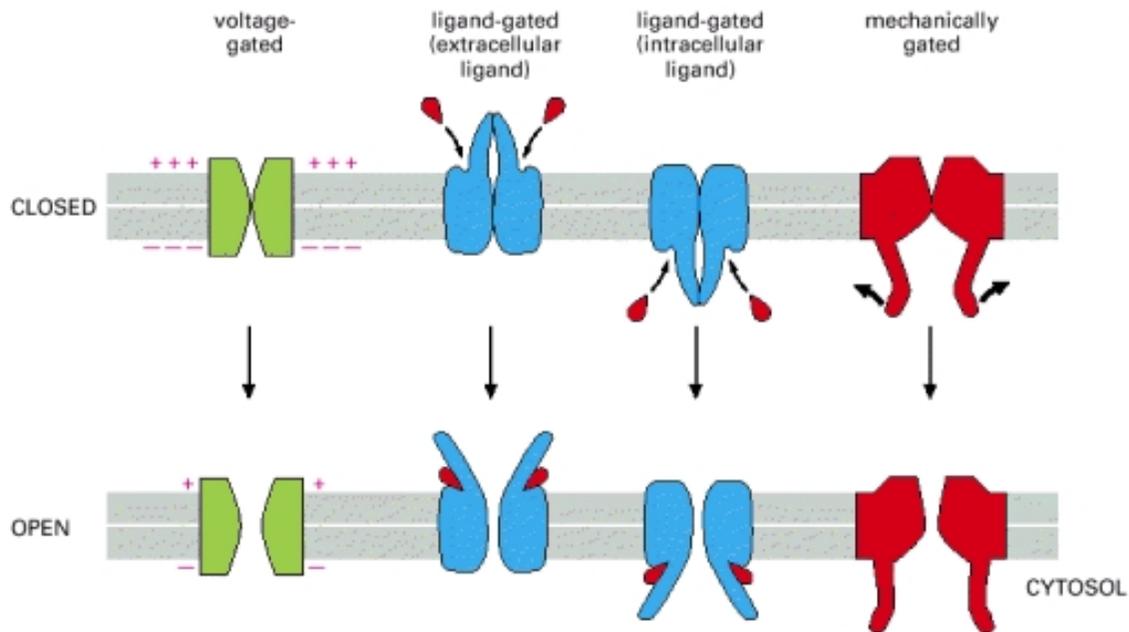
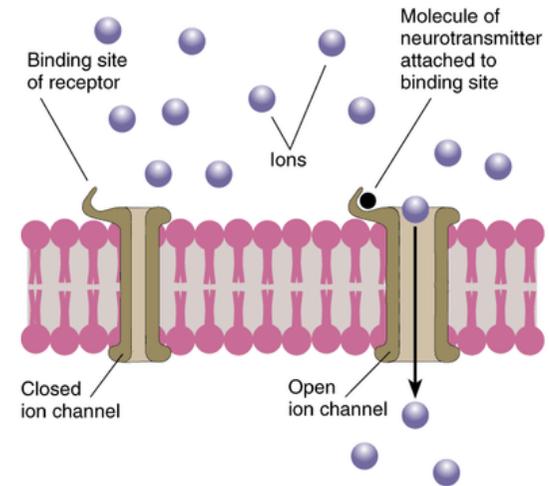
- G protein-coupled receptors
- Tyrosine kinases
- Guanylyl cyclase receptors

Signaling mediated by ion channels is generally immediate, simple, and brief

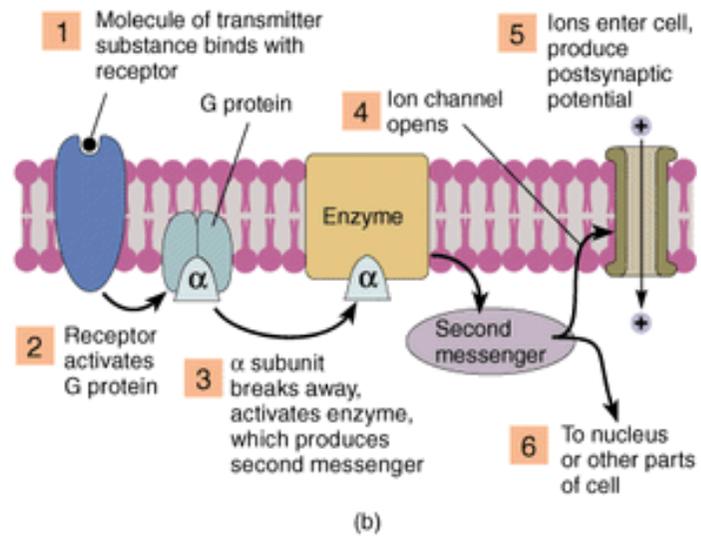
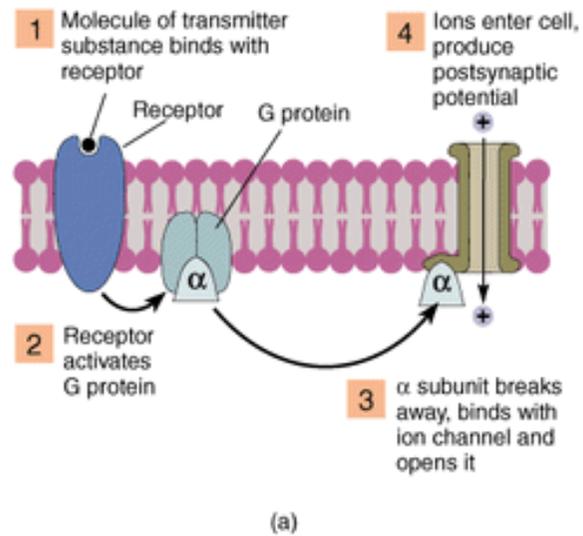
Signaling mediated by metabotropic receptors tends to be far slower and more complex, and longer lasting in its consequences.

Ion channels

► Ionotropic Receptors



► Metabotropic Receptors



How many synapses?

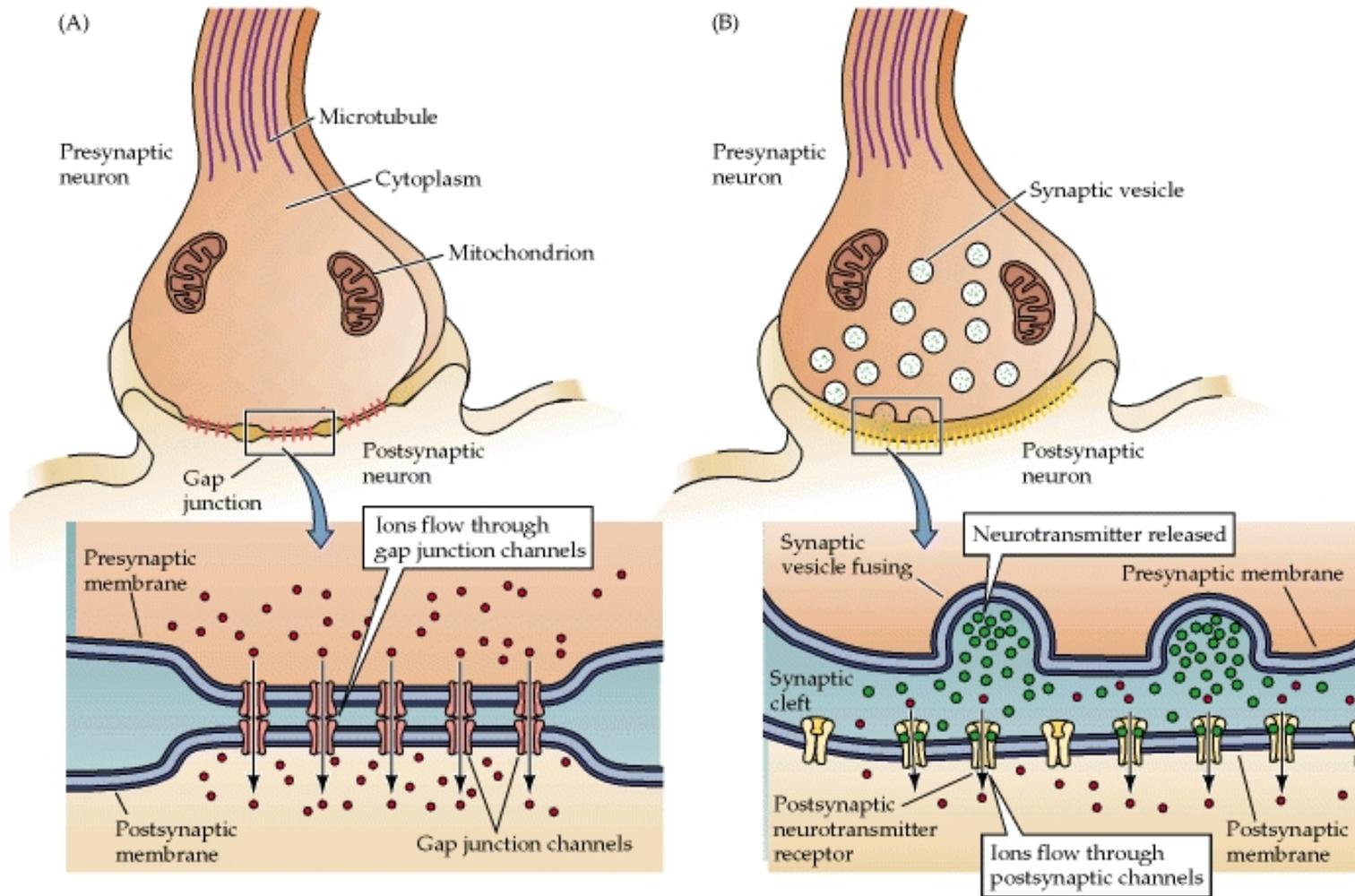
100-200 billion neurons in a brain

Each connected to 5000 and 200000 other neurons
(trees in the Amazon jungle and leaves in the trees)

Rapid removal of released neurotransmitters
transporters and degrading enzymes

Chemical synapse & electrical synapse
electrical synapse has an advantage of time and energy
but the majority are chemical synapse

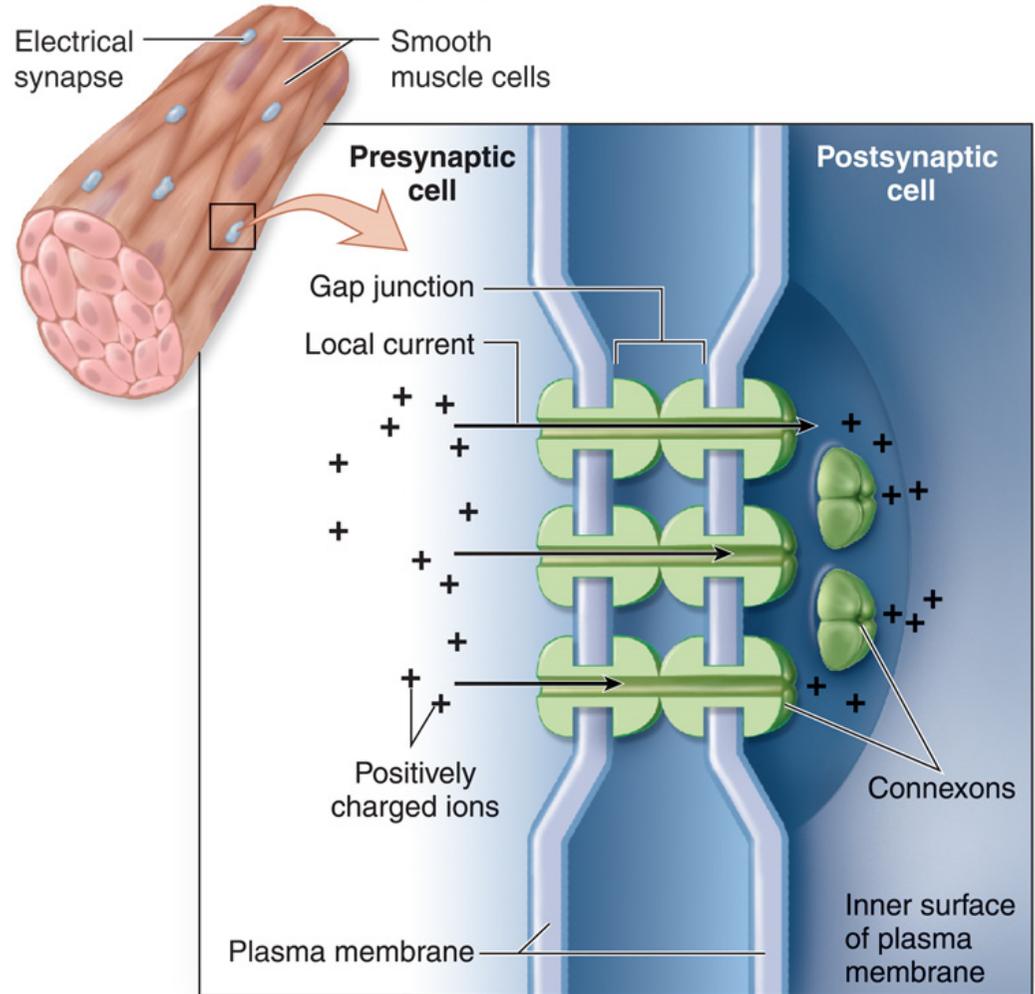
Chemical synapse & electrical synapse



Because passive current flow across the gap junction is virtually instantaneous, communication can occur without the delay that is characteristic of chemical synapses.

A more general purpose of electrical synapses is to synchronize electrical activity among populations of neurons. For example, certain hormone-secreting neurons within the mammalian hypothalamus are connected by electrical synapses. This arrangement ensures that all cells fire action potentials at about the same time, thus facilitating a burst of hormone secretion into the circulation. The fact that gap junction pores are large enough to allow molecules such as ATP and second messengers to diffuse intercellularly also permits electrical synapses to coordinate the intracellular signaling and metabolism of coupled neurons.

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(a) Electrical synapse

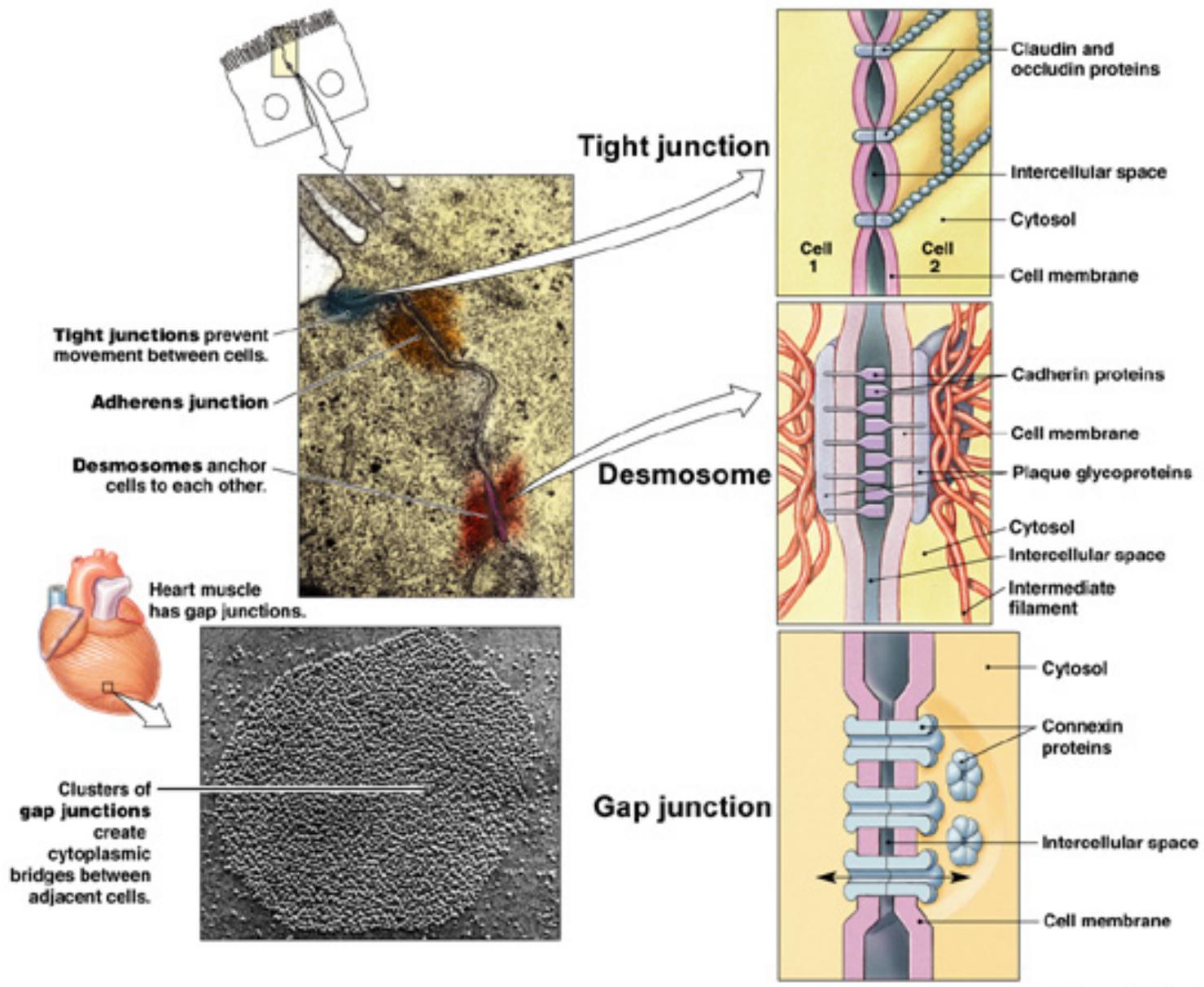


Fig. 3-21

Any advantage of chemical synapse?

Variable and diverse inputs

different concentrations (different extents)

different chemicals (different actions)

different times

even more subtle role in communication

neuromodulation: excitatory or inhibitory

<http://serendip.brynmawr.edu/bb/neuro/neuro98/202s98-paper2/Casasanto2.html>

Neuromodulatory transmitters secreted by a small group of neurons diffuse through large areas of the nervous system, having an effect on multiple neurons. Examples of neuromodulators include dopamine, serotonin, acetylcholine, histamine and others ([wikipedia](#)).

Enormous flexibility and versatility in the brain

using different combinations of transmitter chemicals

Volume transmission (extrasynaptic transmission): diffuse modulatory neurotransmitter systems

Cells of the central nervous system are able to communicate via a host of chemical signals that flow through the extracellular space. Volume transmission (VT) constitutes a novel and complementary communication system to classical synaptic transmission.

The new modality, which does not require specific connections between cells, leads to a reconsideration of the spatial relationships of neurons and glia, brings a new dimension to network modelling and is relevant to both short term interactions and long term tonic states of the brain.

Wiring and volume transmission (WT and VT)

WT is one-to-one transmission and includes classical synapses, gap junctions and membrane juxtapositions

VT is a one-to-many transmission and includes paracrine and endocrine-like transmissions in the brain extracellular space and cerebrospinal fluids.

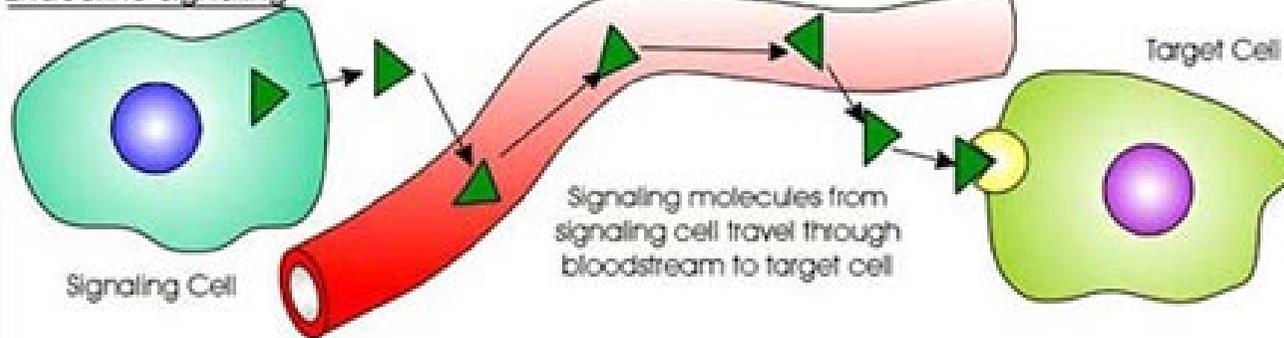
Any brain cell can participate in WT and VT and any kind of substance (e.g. ions, classical transmitters, peptides, neurosteroids) can be a signal in WT and VT.

These concepts are relevant for the pharmacokinetics and actions of neuropsychotropic drugs. These drugs can be regarded as exogenous VT signals in that they diffuse in the cerebral extracellular space and are constrained there by the same factors that influence migration of endogenous VT signals. In addition, neuropsychotropic drugs can better mimic and more effectively interact with the relatively unconstrained VT-type transmissions than with the rigidly constrained WT mechanisms, such as synaptic transmission.

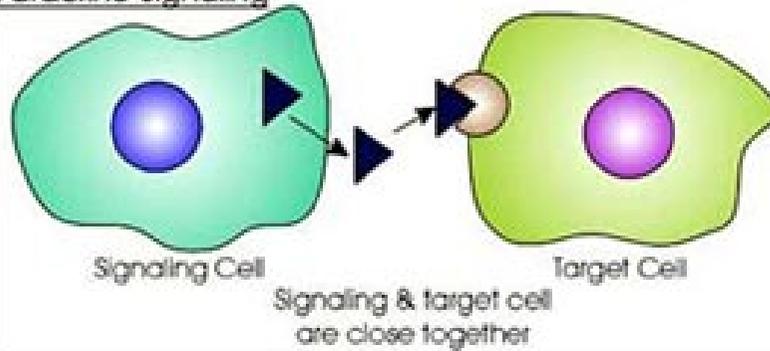
Trends in Pharmacological Sciences, [Volume 20, Issue 4](#), 142-150, 1 April 1999

Types of Intercellular Signaling

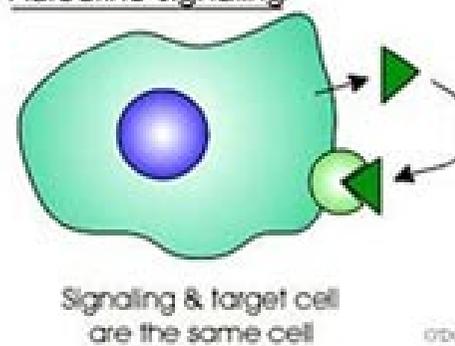
Endocrine Signaling



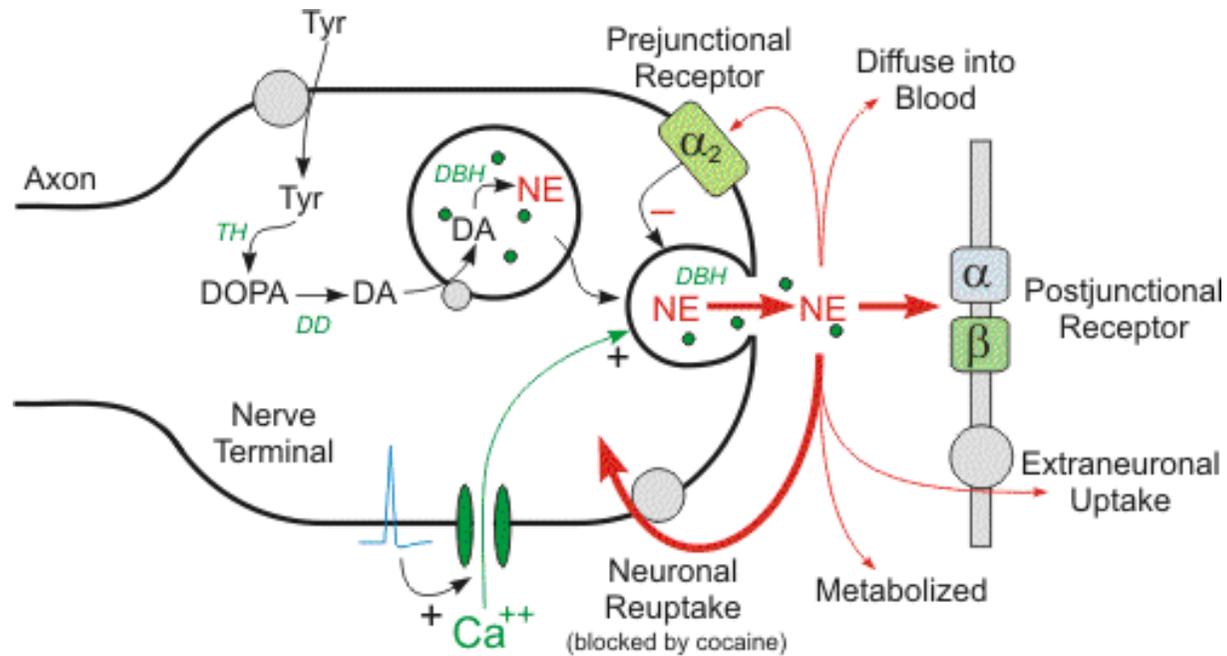
Paracrine Signaling



Autocrine Signaling



Neurotransmitter release



Tyr = tyrosine; TH = tyrosine hydroxylase; DD = DOPA decarboxylase;
DA = dopamine; DBH = dopamine β-hydroxylase; NE = norepinephrine

Voltage-dependent calcium channel (VDCC)

Brain & Computer

Chemical system & electrical system

Changing chemical composition & unchanging hardware

Novel response through learning to the same command

Thinking & logic (programmed)

Brain chemicals

Many brain chemicals

Highly specific targets and highly diverse ways of action

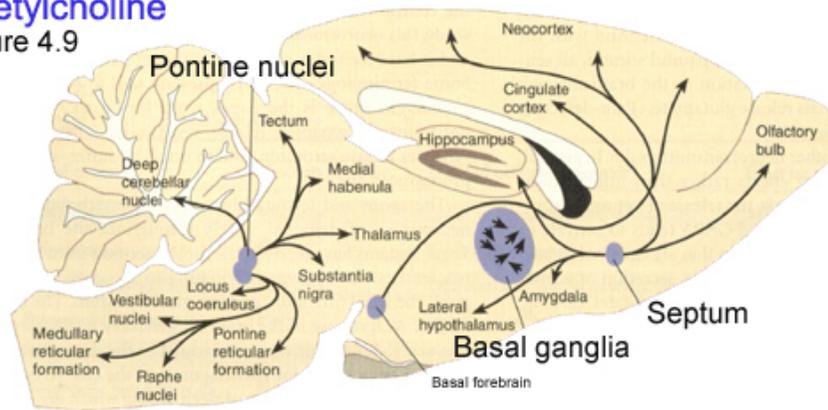
Common Neurotransmitters

Neurotransmitter	Action	Receptor Subtypes
Acetylcholine (ACh)	+/-	Nicotinic, Muscarinic
Norepinephrine (NE)	+	α_1 , α_2 , β_1 , β_2 , β_3
Dopamine (DA)	+/-	D ₁ , D ₂ (D ₃ , D ₄)
Serotonin (5-HT) (5 Hydroxytryptamine)	+/-	5-HT _{1A} , etc.
Glutamate (Glu)	+	NMDA, AMPA
GABA (Gamma-aminobutyric acid)	-	GABA _A , GABA _B
Enkephalins (Enk)	-	μ , κ , δ

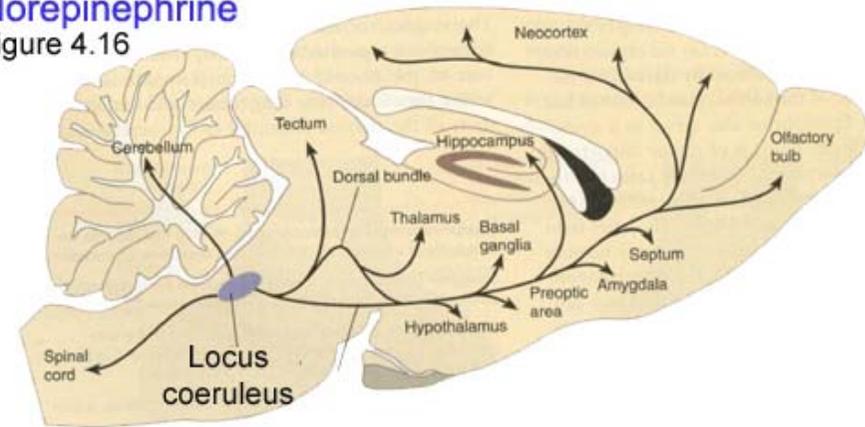
<http://www.colorado.edu/intphys/Class/IPHY3730/06neurotransmitters.html>

Major Brain Pathways

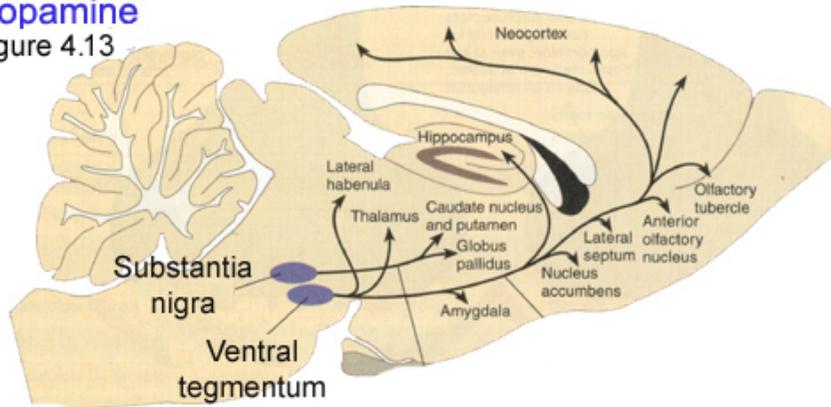
Acetylcholine
Figure 4.9



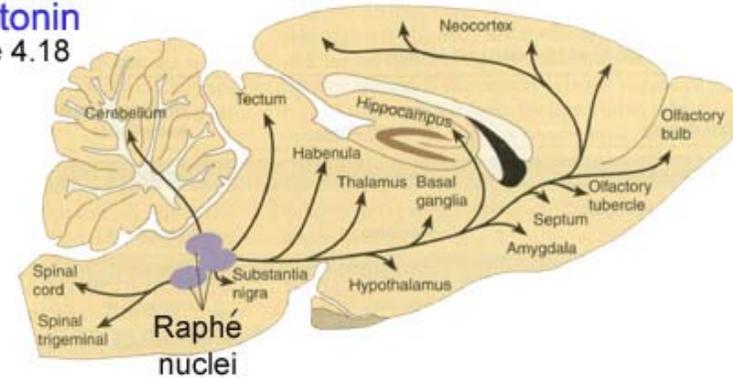
Norepinephrine
Figure 4.16



Dopamine
Figure 4.13



Serotonin
Figure 4.18



[See through brains](#)