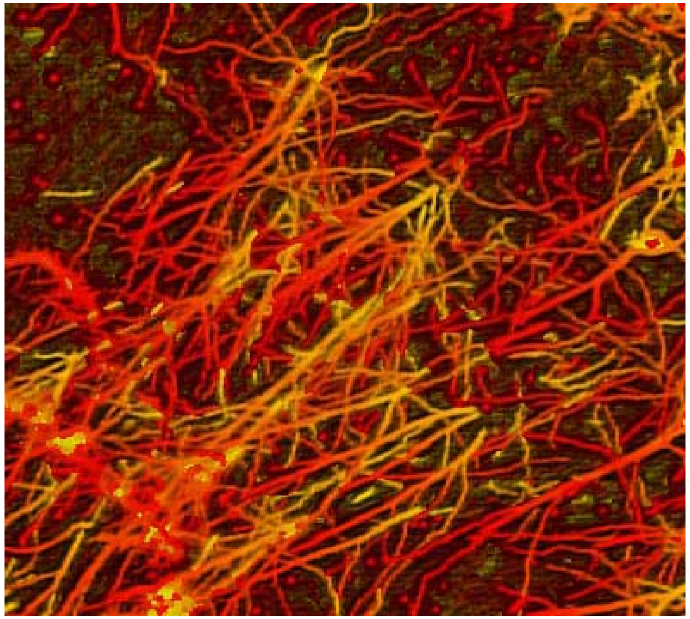
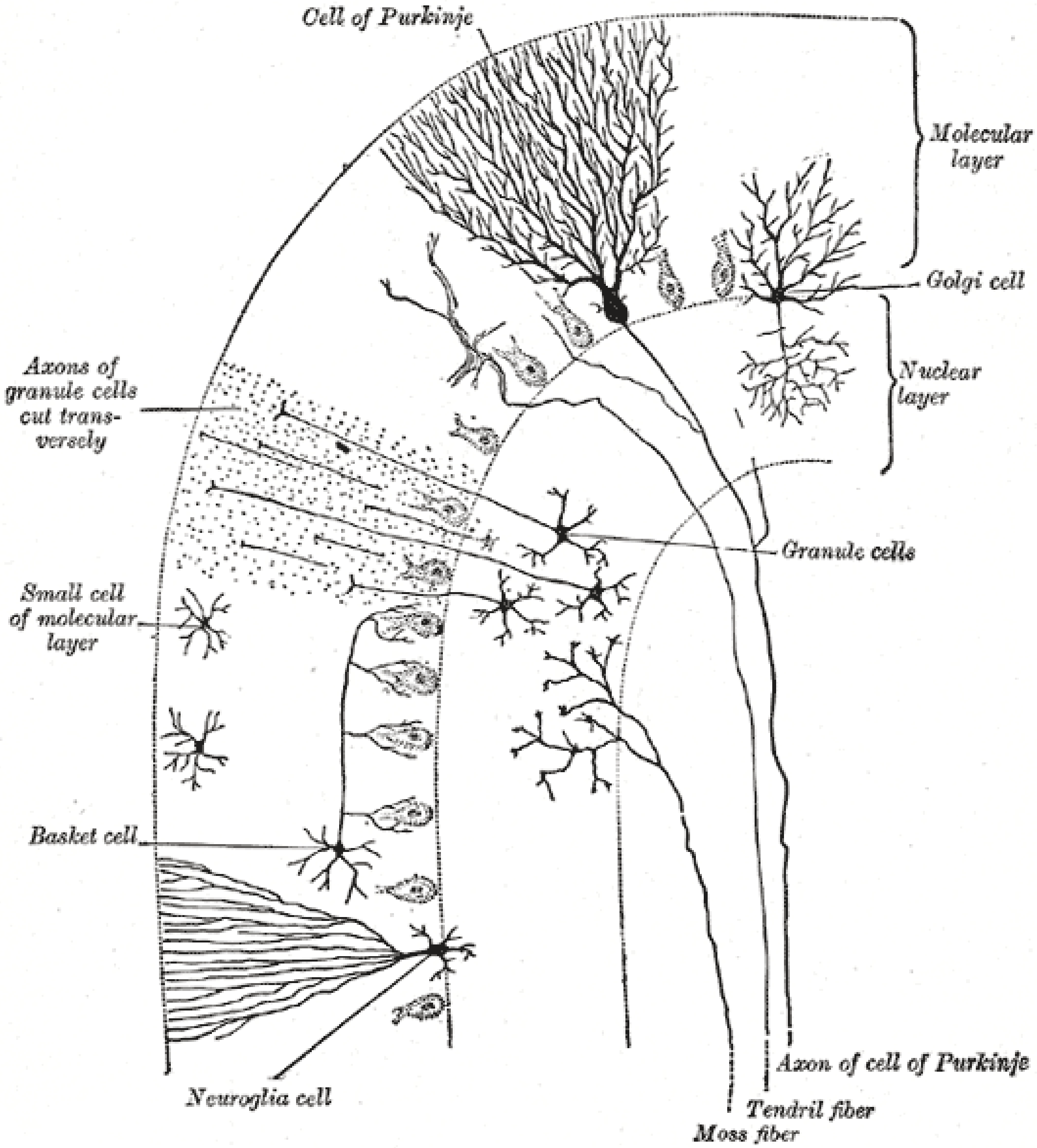
2. The neuron





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.

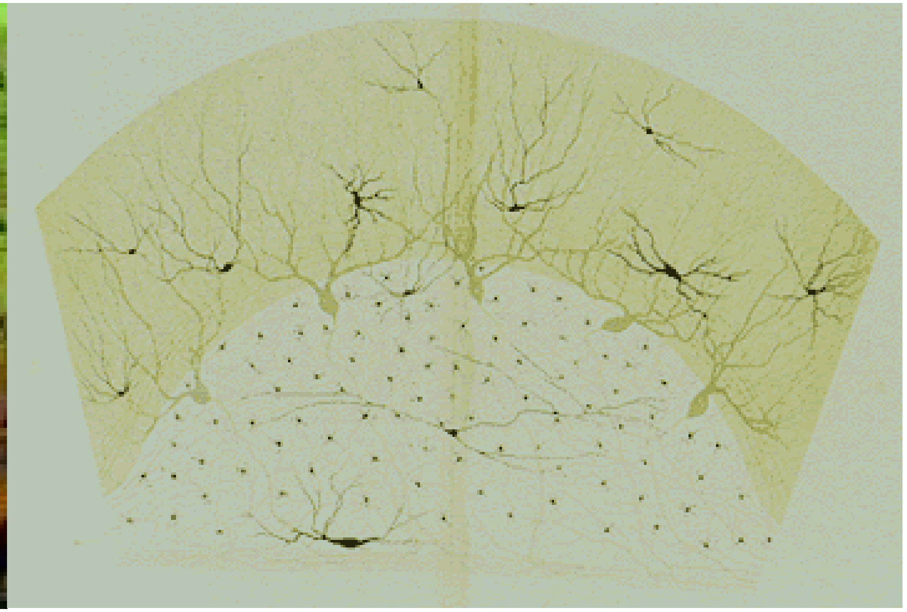
d) **oligodendrocyte -** produce the myelin sheath in the CNS which insulates and protects axons**.**

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.

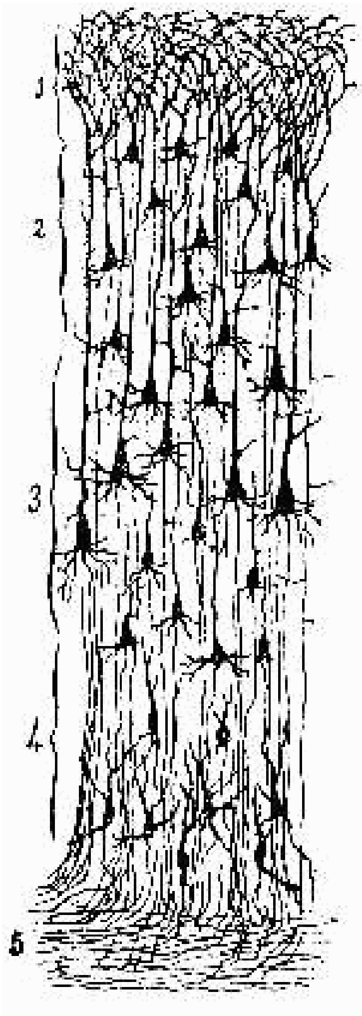
f) **satellite cells -** surround cell bodies of neurons in ganglia. Their role is to maintain the micro-environment and provide insulation for the ganglion cells.

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

Camillo Golgi (1843-1926)



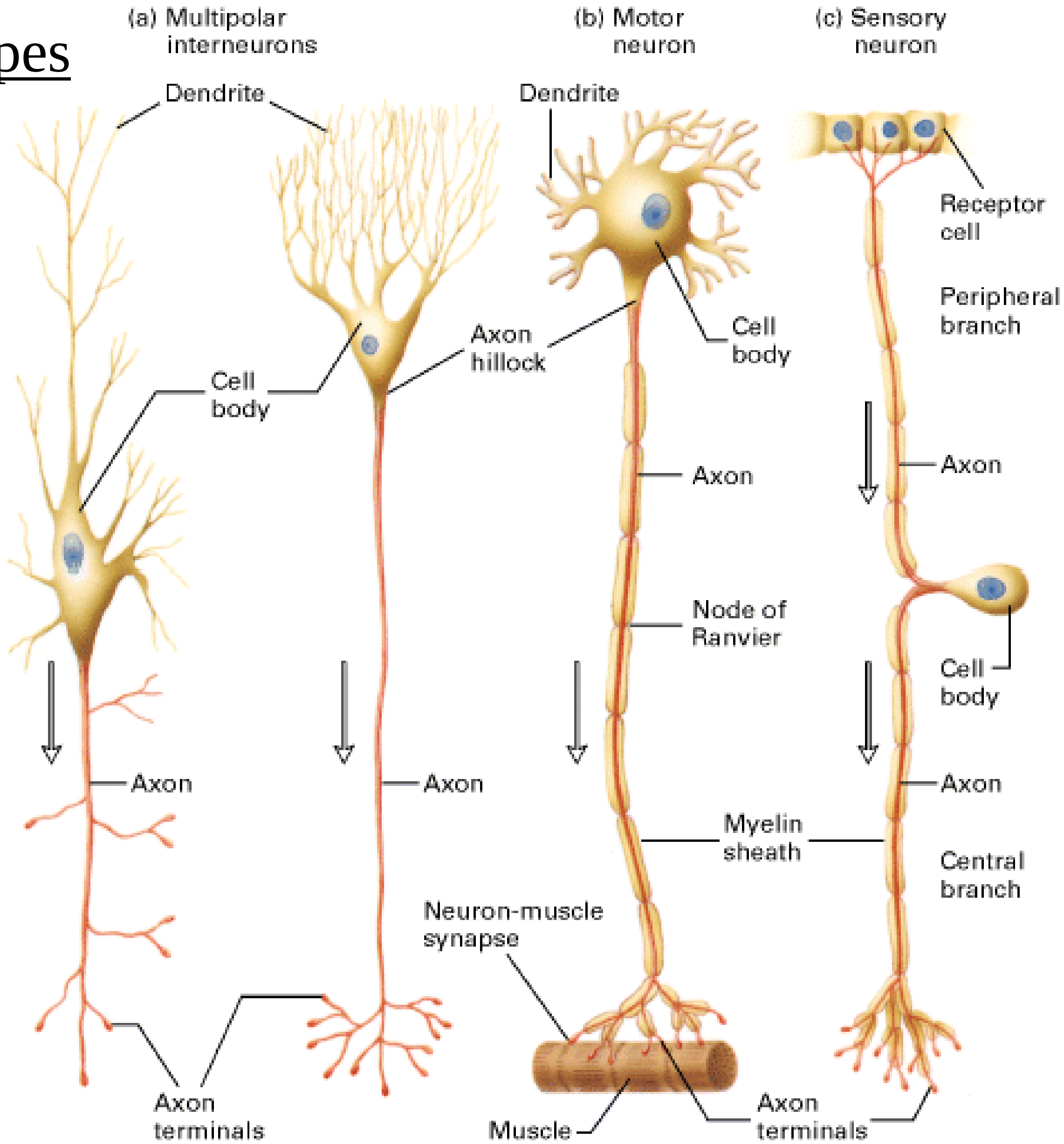
Santiago Ramón y Cajal (1852-1934)



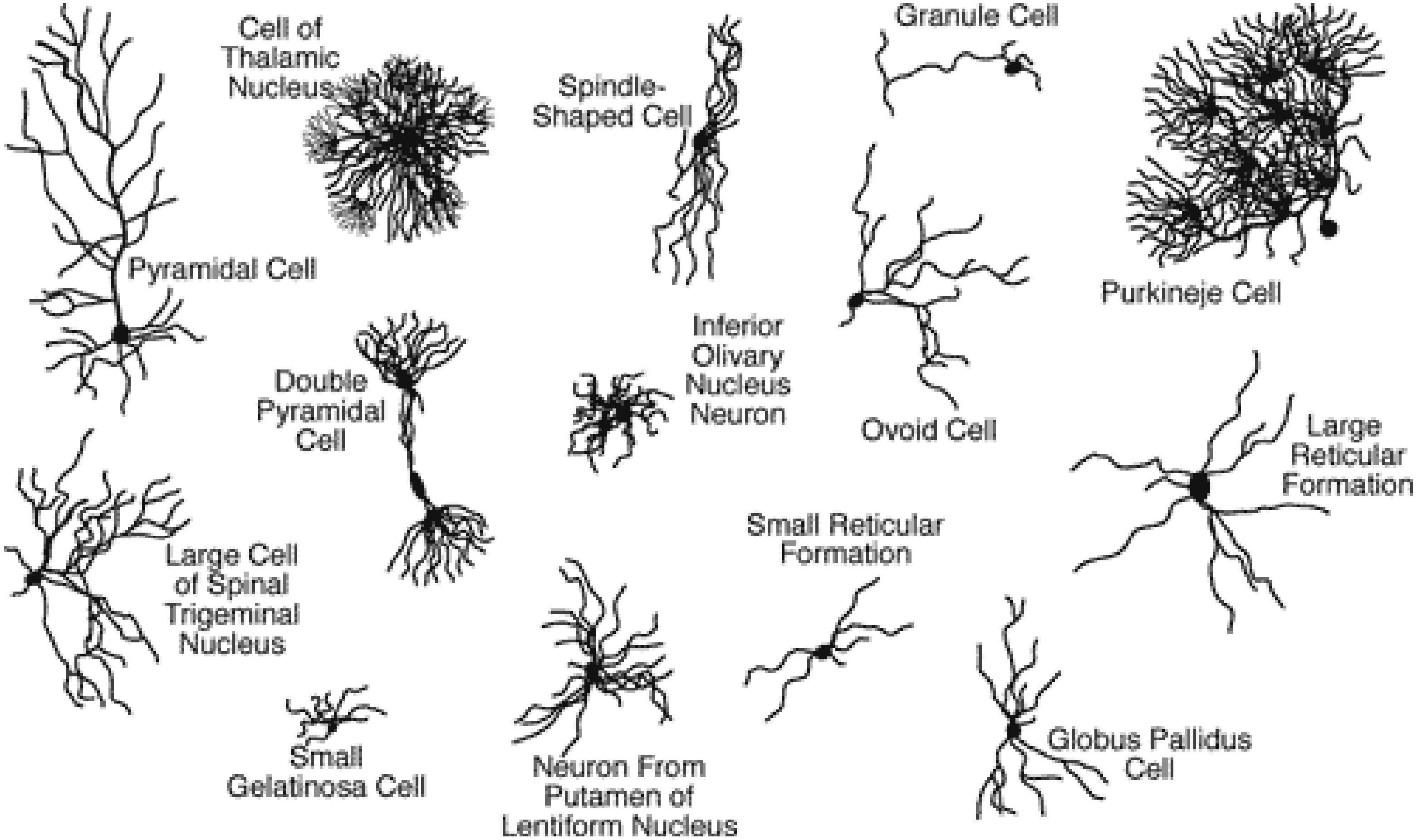
independent neurons, or nerve cells, are the building blocks of the central nervous system

Neurons: 3 basic types

Interneuron
Motor neuron
Sensory neuron

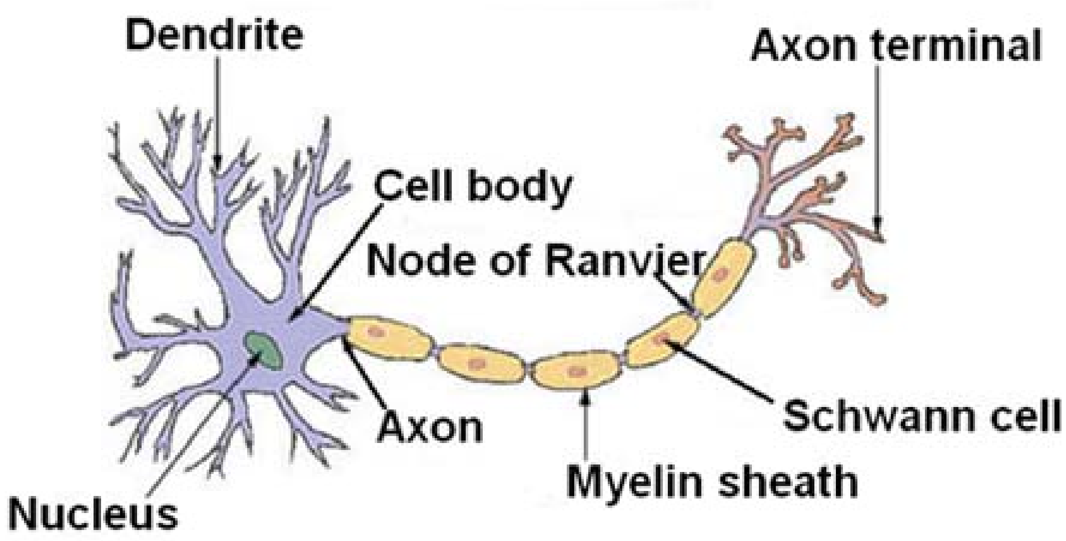


10,000 specific types of neurons in the human CNS
various shapes and sizes
100-200 billion neurons in a brain



The drawings made by Cajal

Structure of a Typical Neuron

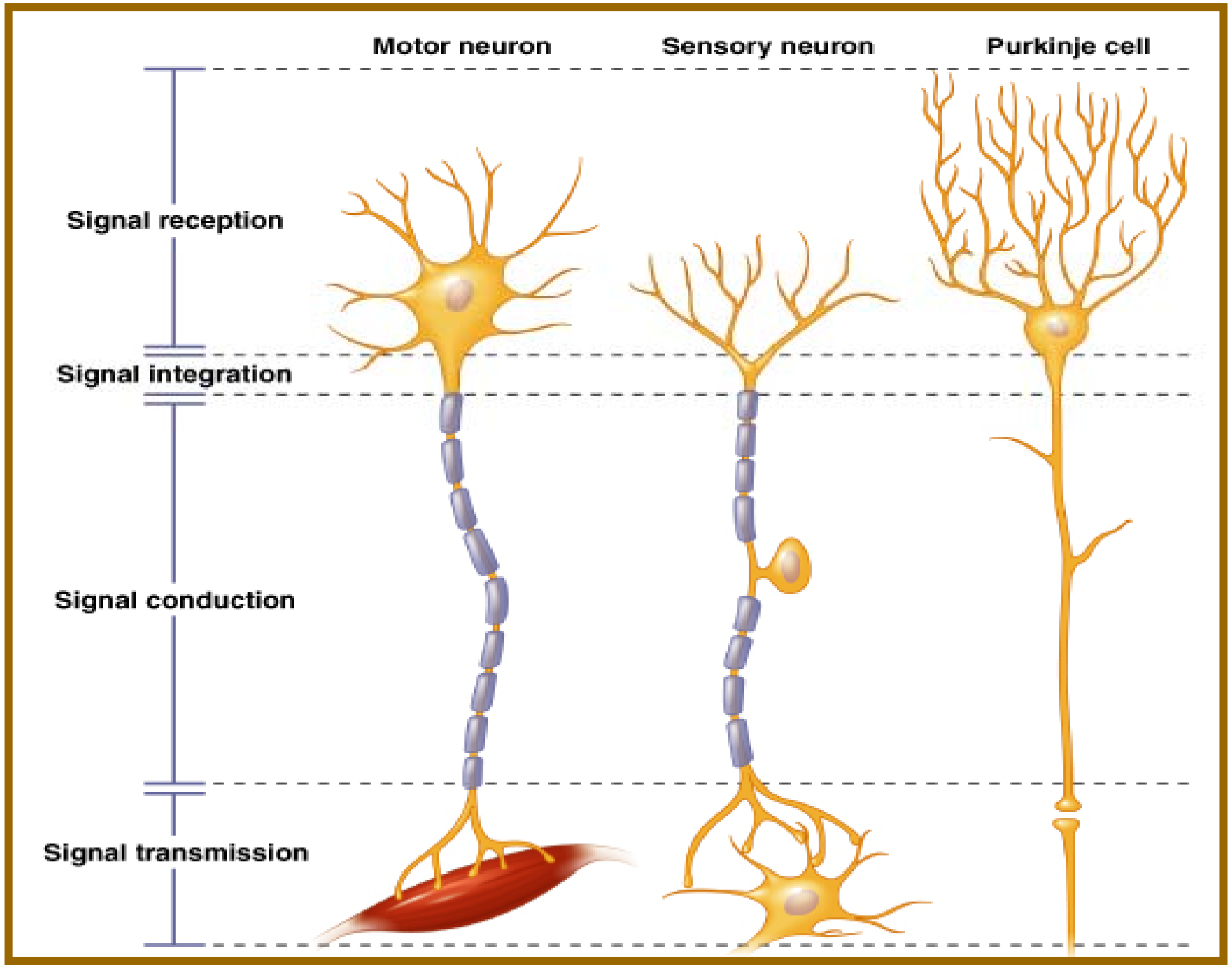


Diameter: 4 – 100 um
Length: an inch to several feet

Active Conduction

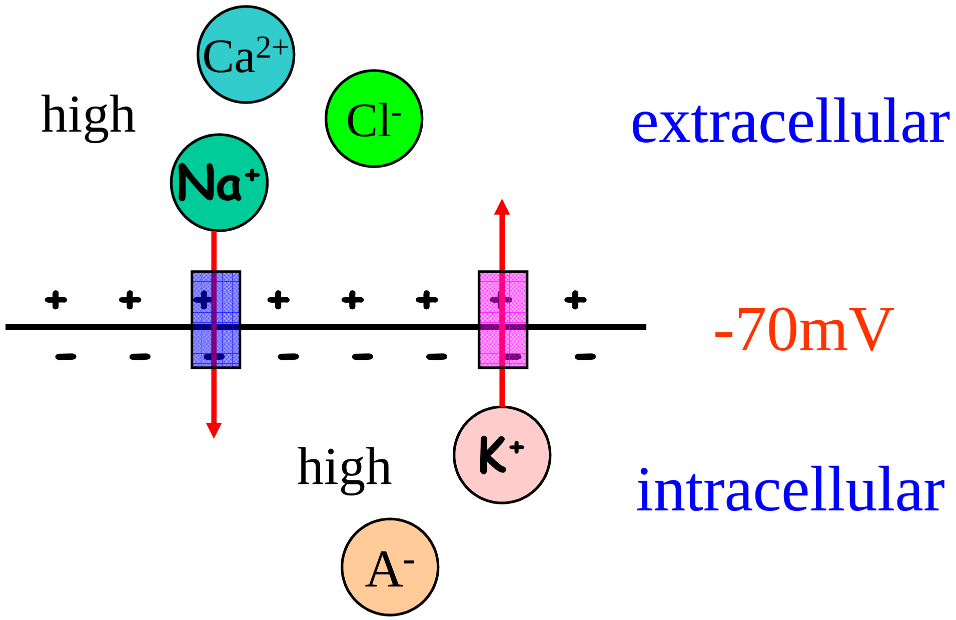
Unmyelinated Axons
many voltage gated Na^+ channels in proximity
action potential and passive conduction of the depolarizing current
opening of the nearby Na^+ channels to generate another action potential
repeated until the action potential reaches the terminal

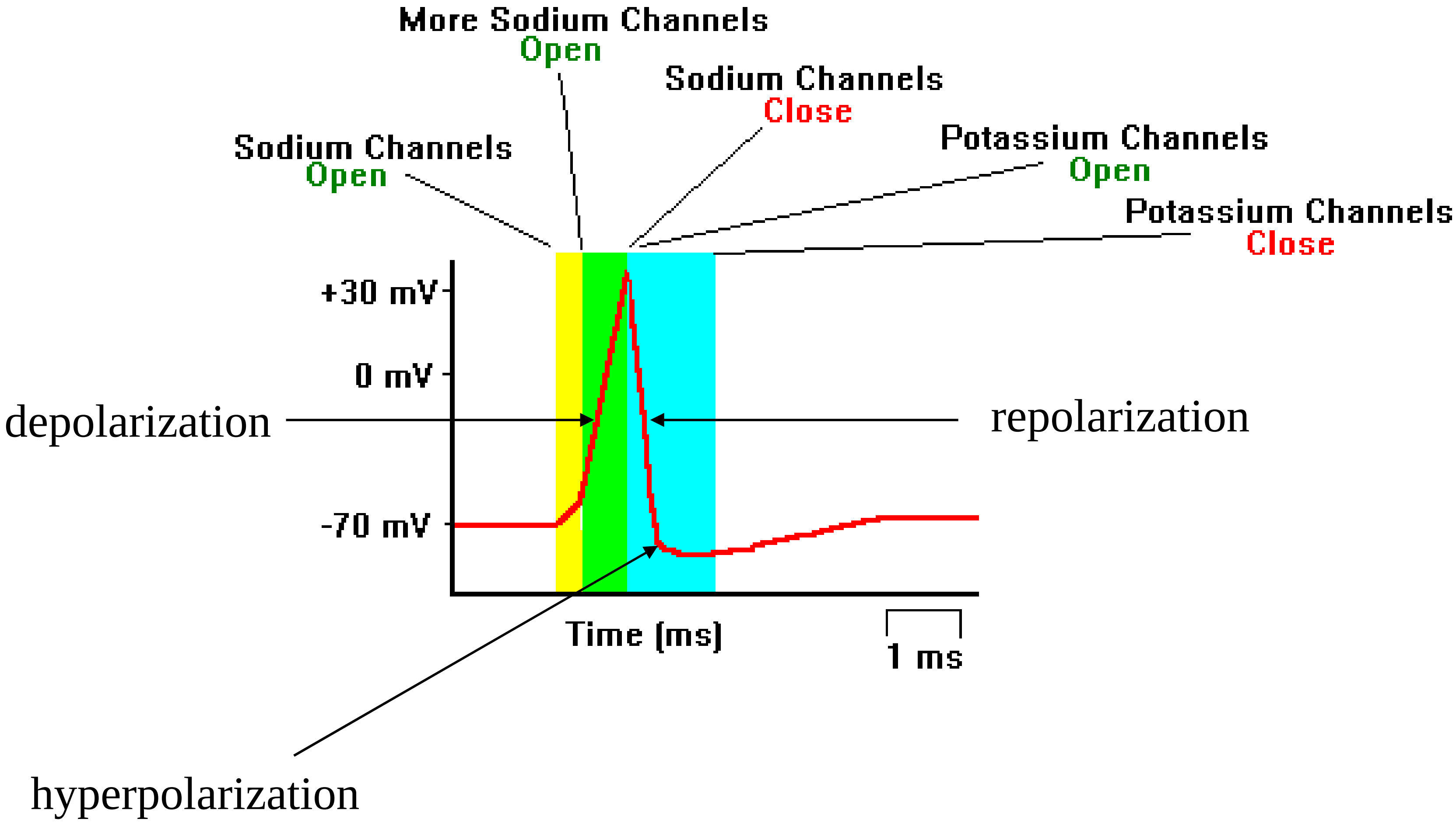
Myelinated Axons
jumping of action potentials from node to node called saltatory conduction
axons covered with myelin sheath
(in the form of Schwann cells in the PNS or oligodendrocytes in the CNS)
myelin prevents current leakage by increasing resistance in the axon
passive current to the gaps between the myelin sheaths (Nodes of Ranvier)
The Nodes of Ranvier contains Na^+ channels, which fire another action potential upon depolarization from the passive current


Motor neuron
Sensory neuron
Purkinje cell
Signal reception
Signal integration
Signal conduction
Signal transmission

Action potential

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



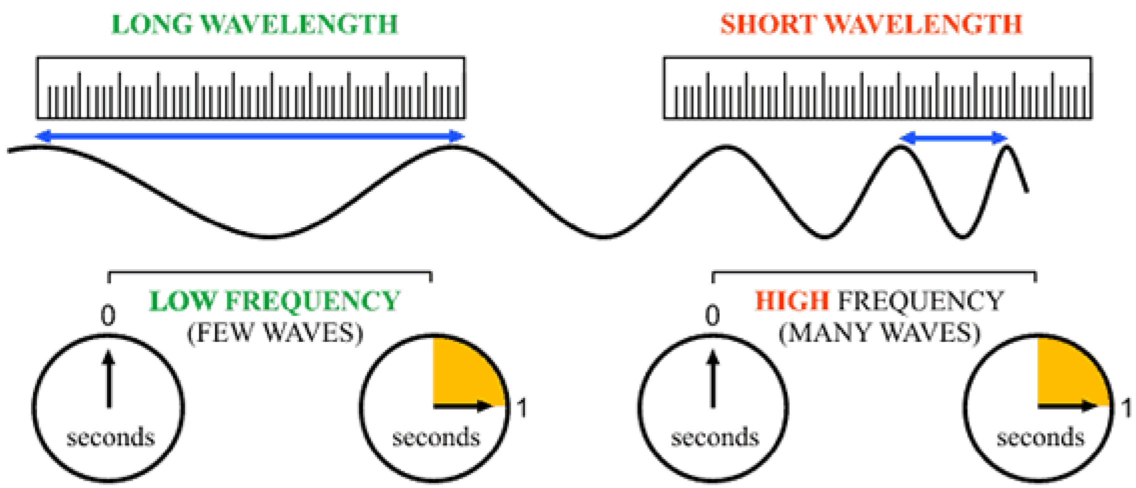

More Sodium Channels
Open
Sodium Channels
Close
Sodium Channels
Open
Potassium Channels
Open
Potassium Channels
Close
+30 mV
0 mV
-70 mV
depolarization
repolarization
hyperpolarization
Time (ms)
1 ms

Signal intensity

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

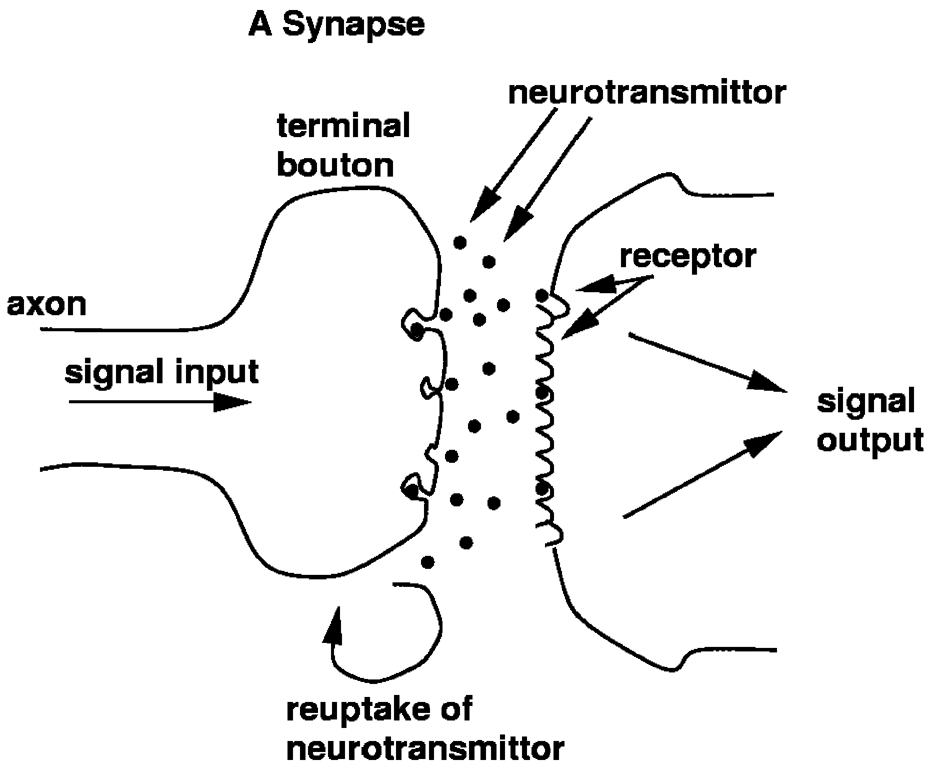
Signal speed

axon diameter
myelin sheath
up to 220 miles/h



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



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

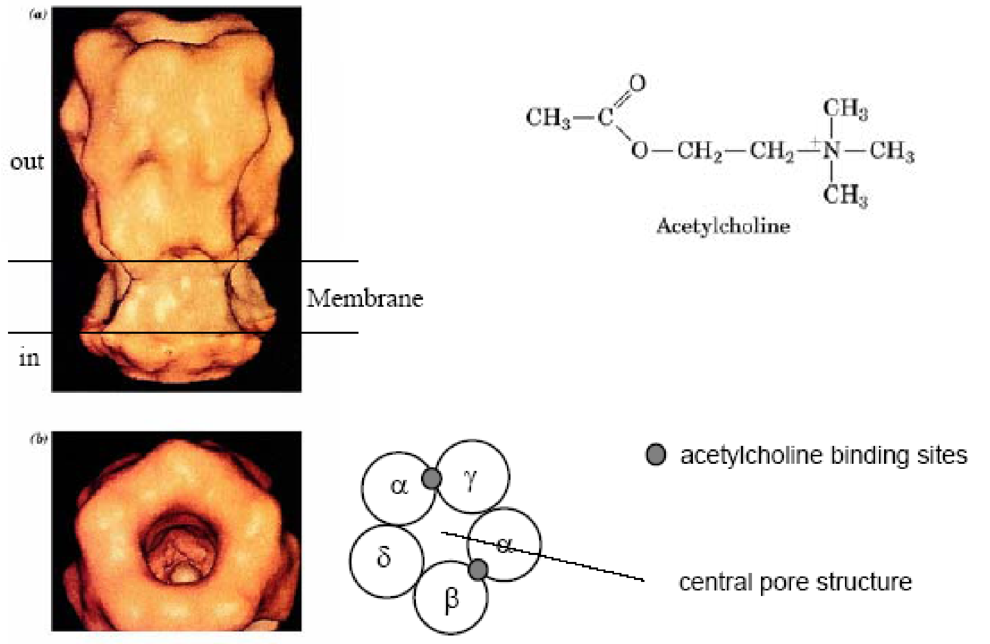
Release of acetylcholine into the synapse

the higher the signal the more acetylcholine released

Specific receptor molecules

Opening of ion channel

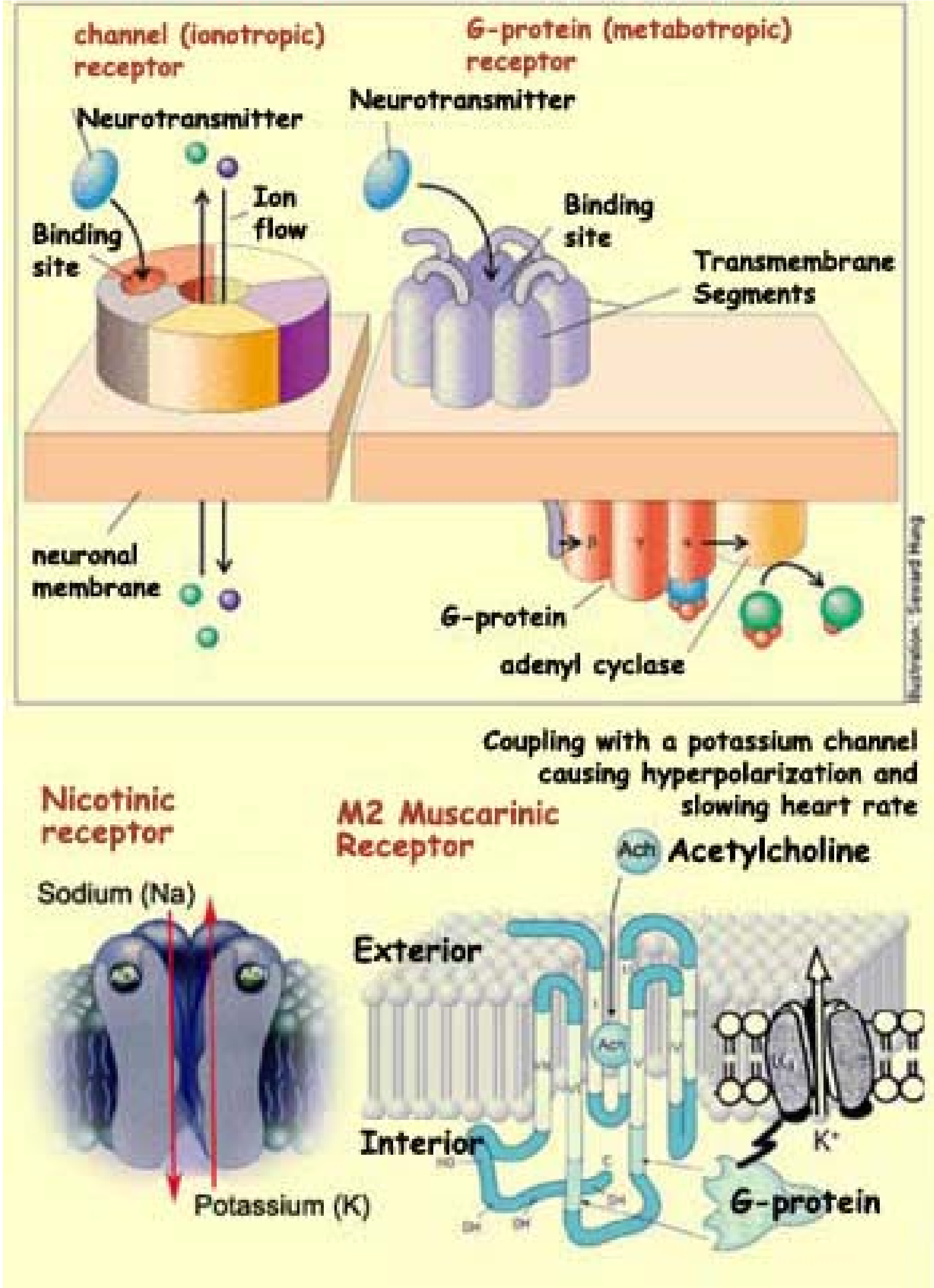
Image reconstruction from electron micrographs at low resolution of skeletal muscle nicotinic Acetylcholine Receptor



Voet&Voet, Biochemistry, 2nd ed., chapter 34, figure 117

Nicotinic acetylcholine receptors (*nAChR*, also known as “ionotropic" acetylcholine receptors) are particularly responsive to nicotine

Muscarinic acetylcholine receptors (*mAChR*, also known as “metabotropic" acetylcholine receptors) are particularly responsive to muscarine.



Neurotransmitter receptors: classified into two broad categories

Ionotropic receptors: form ion channel pore

quick response
effect in the immediate region of the receptor

Metabotropic: G protein-coupled receptors

indirectly linked with ion-channels on the cell membrane
through signal transduction mechanisms, often G proteins
slow response
effect can be widespread through the cell

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)

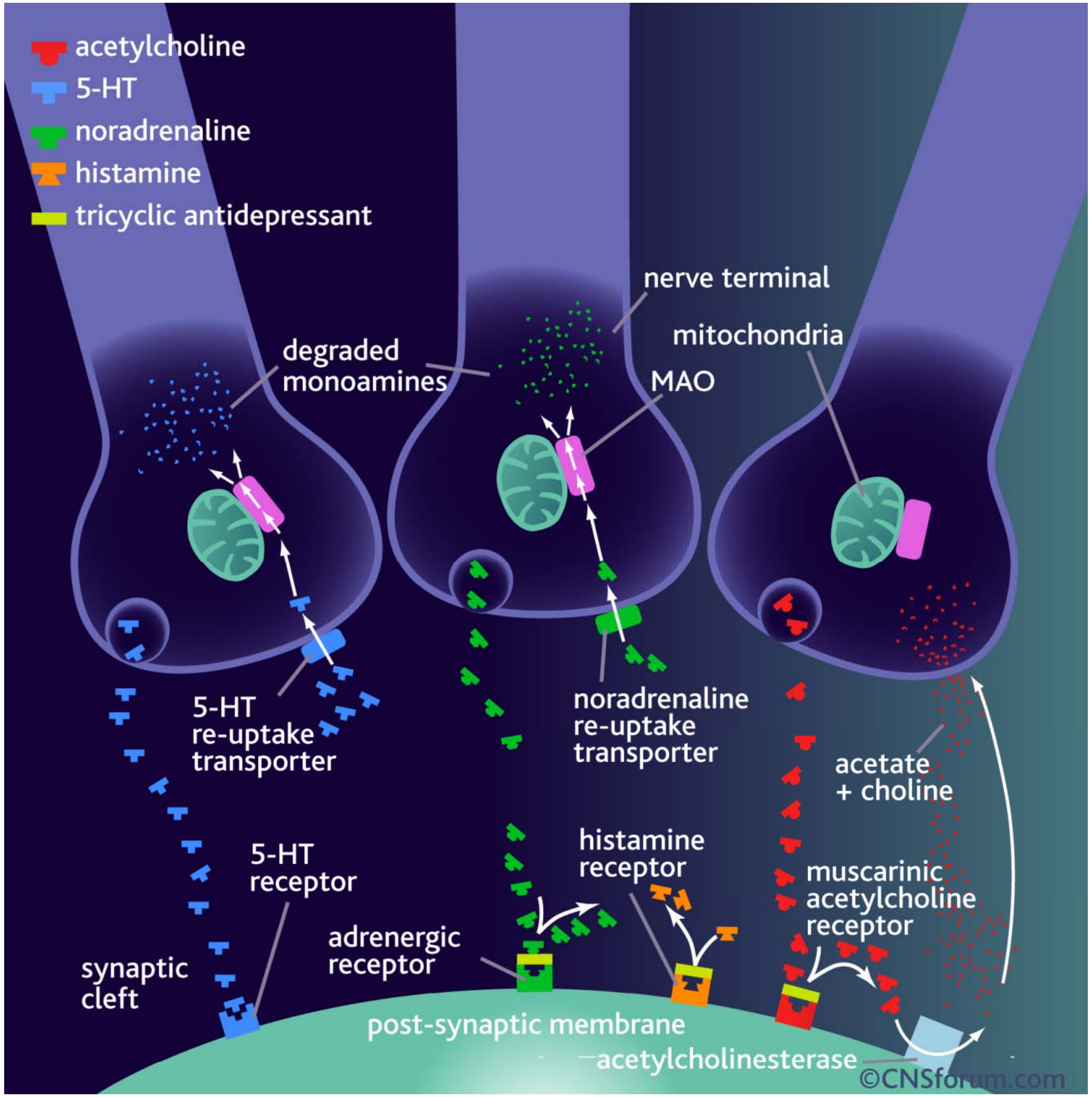
Rapid removal of released neurotransmitters

transporters and degrading enzymes

Chemical synapse & electrical synapse

electrical synapse has an advantage of time and energy

but the majority are chemical synapse


acetylcholine
5-HT
noradrenaline
histamine
tricyclic antidepressant
nerve terminal
mitochondria
degraded
monoamines
MAO
5-HT
re-uptake
transporter
noradrenaline
re-uptake
transporter
acetate
+ choline
5-HT
receptor
histamine
receptor
muscarinic
acetylcholine
receptor
adrenergic
receptor
synaptic
cleft
post-synaptic membrane
acetylcholinesterase
©CNSforum.com

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

Enormous flexibility and versatility in the brain

using different combinations of transmitter chemicals

Brain & Computer

Chemical system & electrical system
Changing chemical composition & unchanging hardware
Novel response through learning to the same command
Thinking & logic (programmed)

Homework: chemical structures

Brain chemicals

Many brain chemicals

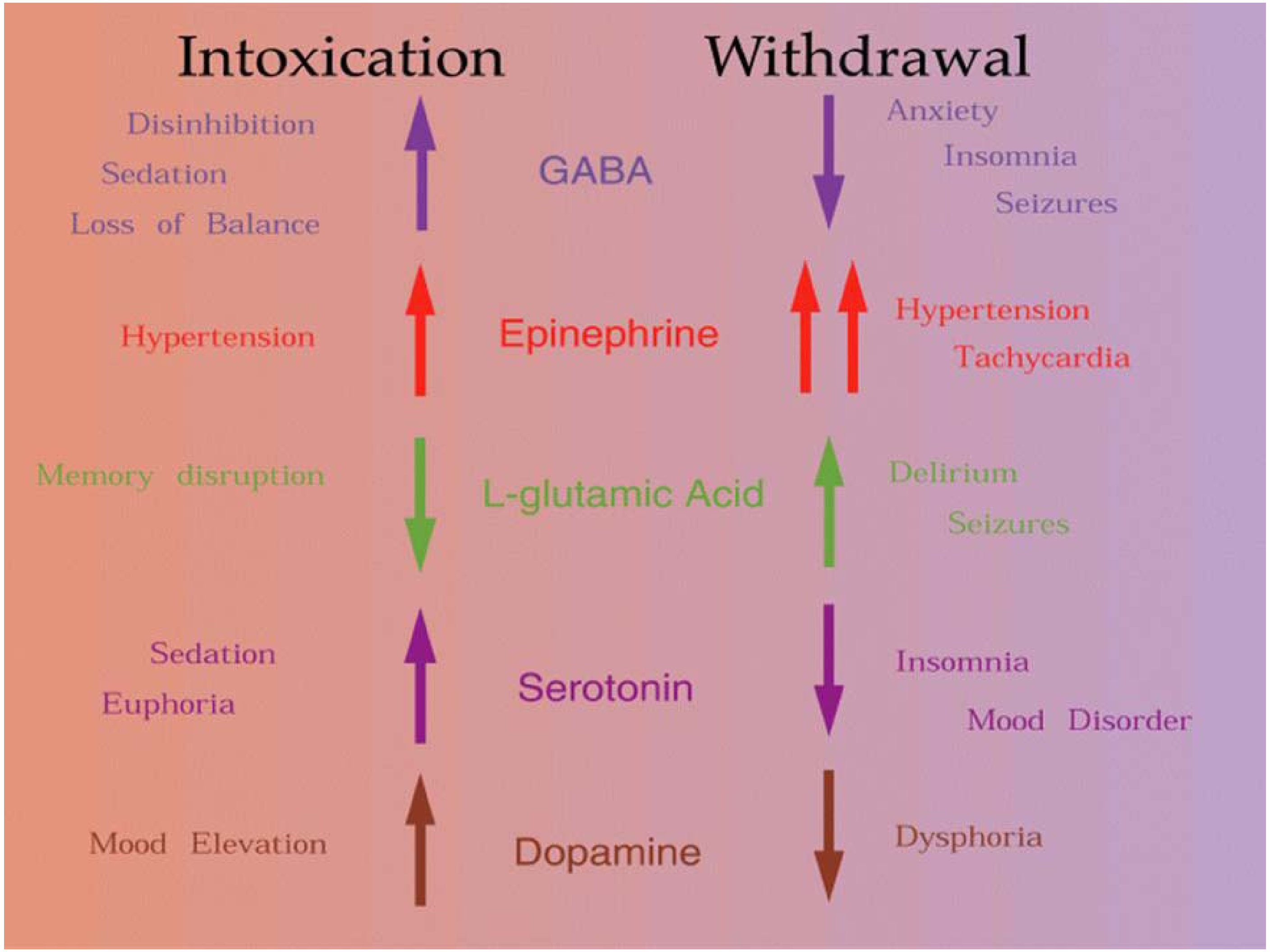
Highly specific targets and highly diverse ways of action

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-HT1_A, etc.
Glutamate (Glu)	+	NMDA, AMPA
GABA (Gamma-aminobutyric acid)	-	$GABA_A$, $GABA_B$
Enkephalins (Enk)	-	μ, κ, δ

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

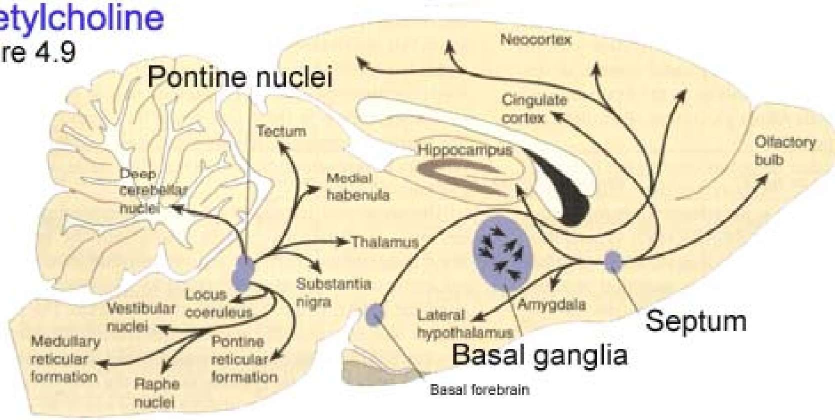
http://www.colorado.edu/intphys/Class/IPHY3730/06neurotransmitters.html


Intoxication
Withdrawal
Disinhibition
Sedation
Loss of Balance
GABA
Anxiety
Insomnia
Seizures
Hypertension
Epinephrine
Hypertension
Tachycardia
Memory disruption
L-glutamic Acid
Delirium
Seizures
Sedation
Euphoria
Serotonin
Insomnia
Mood Disorder
Mood Elevation
Dopamine
Dysphoria

Major Brain Pathways

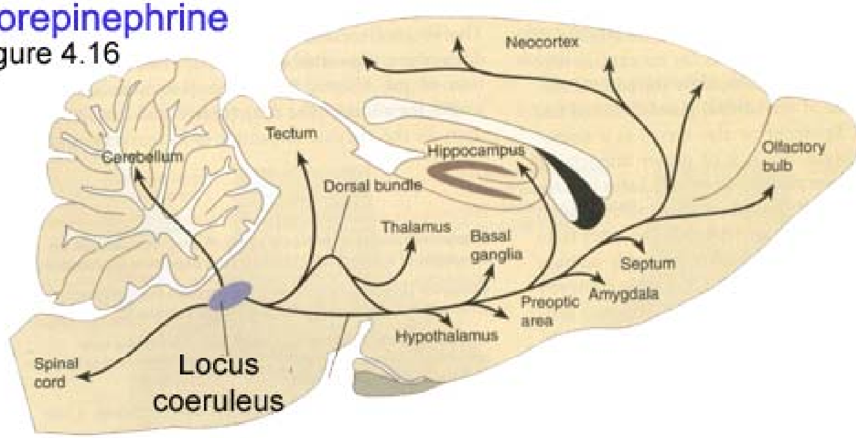
Acetylcholine

Figure 4.9



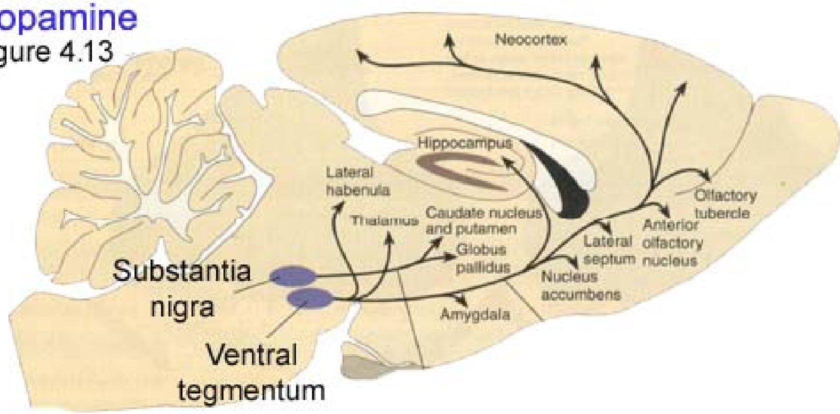
Norepinephrine

Figure 4.16



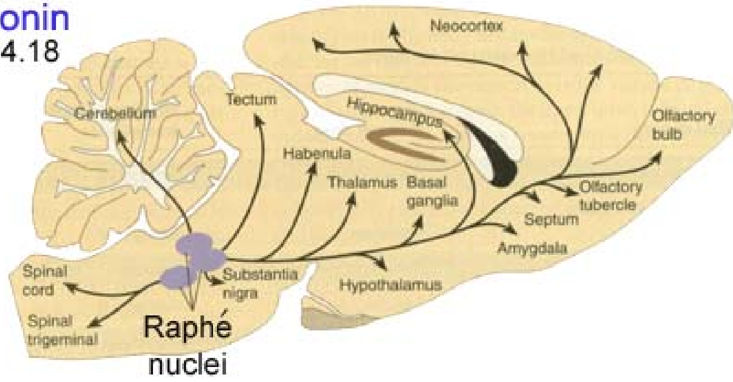
Dopamine

Figure 4.13



Serotonin

Figure 4.18



Drugs

influence on behavior by changing chemical communication
nicotine, morphine, cocaine, ecstasy

Nicotine

Agonist action on acetylcholine receptor
Stimulation is far higher than with acetylcholine

- long-term effects on brain: receptors become less sensitive and habituated
- need for the higher amounts: chemical basis of addiction

Nicotine works on one receptor type: one-sided effect

Body in alerted condition

Morphine

Heroin: chemically modified form of morphine

Effect on brain stem and slow down breathing
Relief from pain
feel pain but not bothered
Mimic natural transmitters (opioid peptides): enkephalin, endorphin, dynnorphin

Enkephalin blocker (naloxone) worsens pain & analgesic effects of acupuncture

Opioid peptide act locally but morphine or heroin acts on all brain

The excessive activation of receptors is similar to nicotine addiction

Cocaine and crack: smoking & snorting

Blocks noradrenaline removal
Sustained effects
Puts body into a false stress situation

Amphetamine (speed)
excess release of noradrenaline & dopamine
prevent their reabsorption

Dopamine, noradrenaline, acetylcholine: brain stem

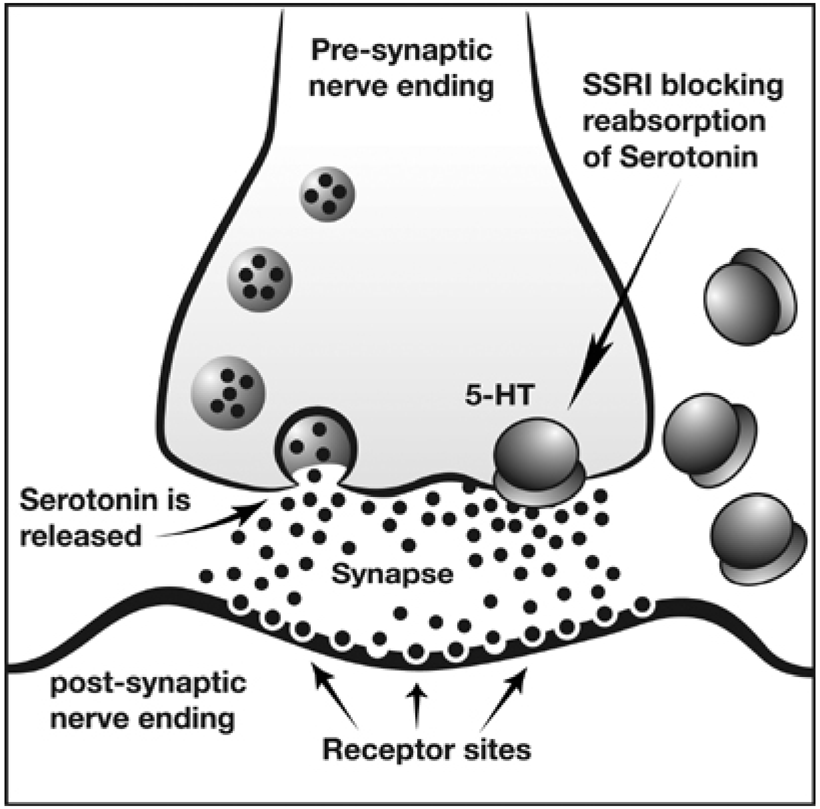
Ecstasy

Excessive release of serotonin
Hallucinogen
Euphoria
Long-term use results in depression and suicide
Death of the clump of neurons (the raphe nuclei) in the brain stem

Prozac

The link between
the known molecular/cellular change and the change in the way we actually feel

Biochemical action within hours
but therapeutic action after some ten days



Pre-synaptic
nerve ending
SSRI blocking
reabsorption
of Serotonin
5-HT
Serotonin is
released
Synapse
post-synaptic
nerve ending
Receptor sites