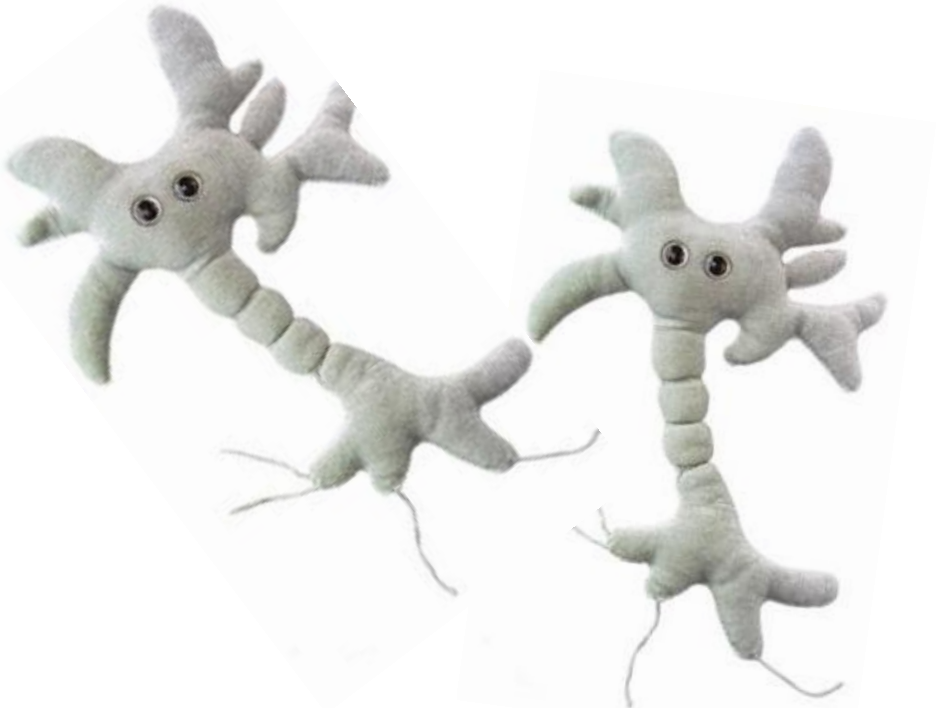
SYNAPTIC TRANSMISSION



SYNAPTIC TRANSMISSION

1897: Charles Sherrington- “synapse”
The process of information transfer at a synapse
Plays role in all the operations of the nervous system

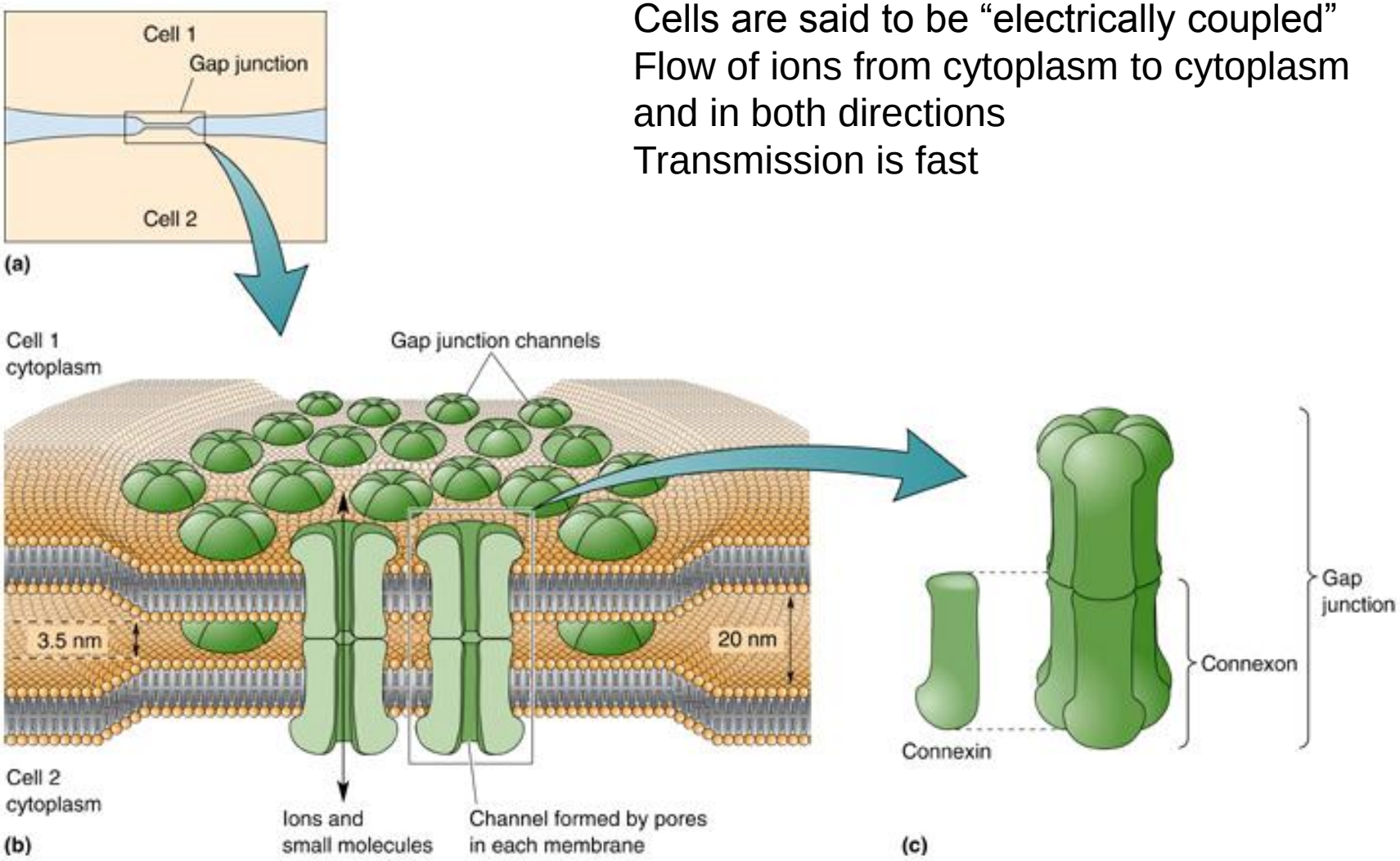
Information flows in one direction: Neuron to target cell
First neuron = Presynaptic neuron

Target cell = Postsynaptic neuron

Types of synapses:
1) Chemical (1921- Otto Loewi)
2) Electrical (1959- Furshpan and Potter)

ELECTRICAL SYNAPSES

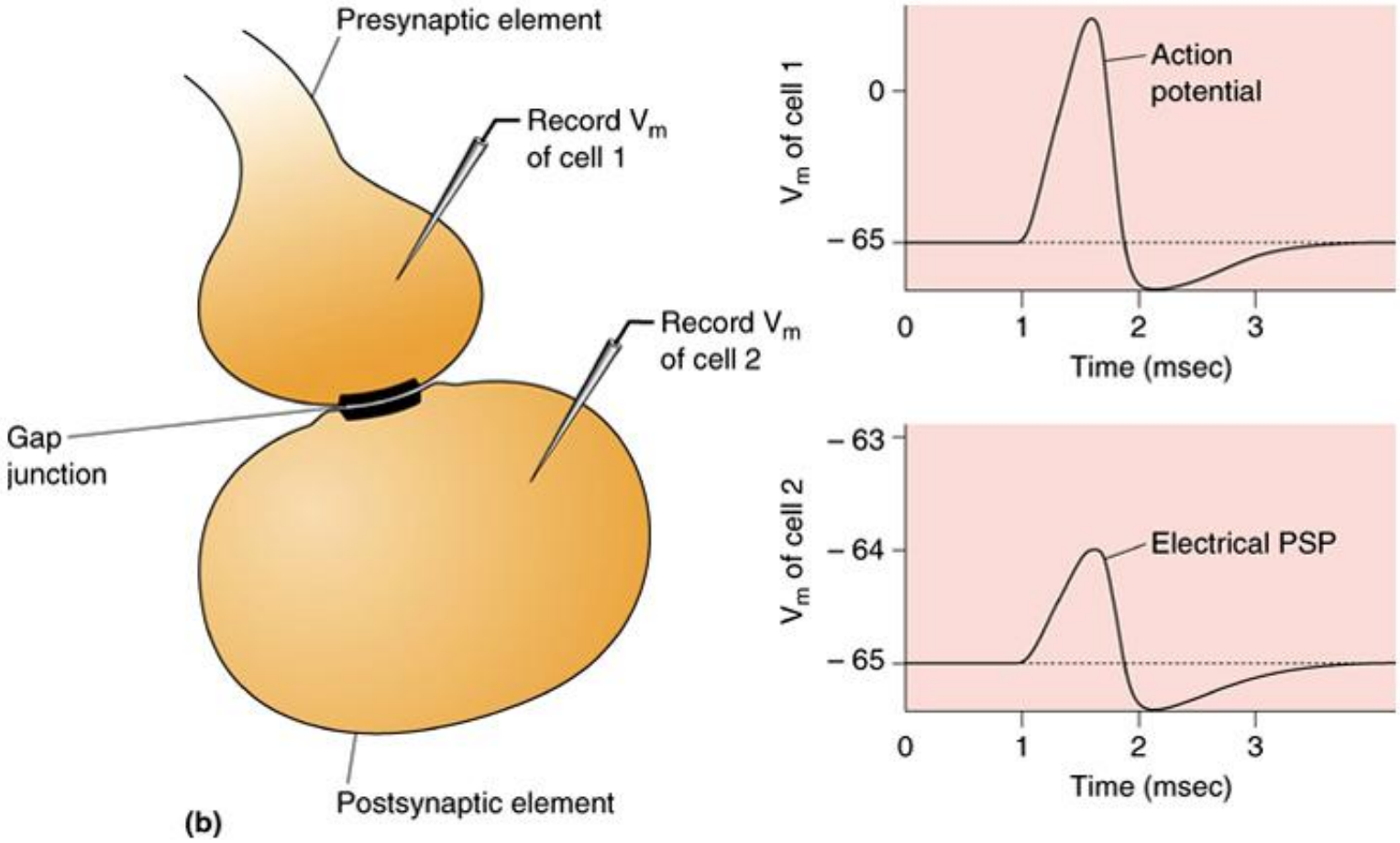
Gap junction
Cells are said to be “electrically coupled”
Flow of ions from cytoplasm to cytoplasm and in both directions
Transmission is fast



ELECTRICAL SYNAPSES

An AP in the pre synaptic cell, generate a PSP (post synaptic potential) in the post synaptic cell

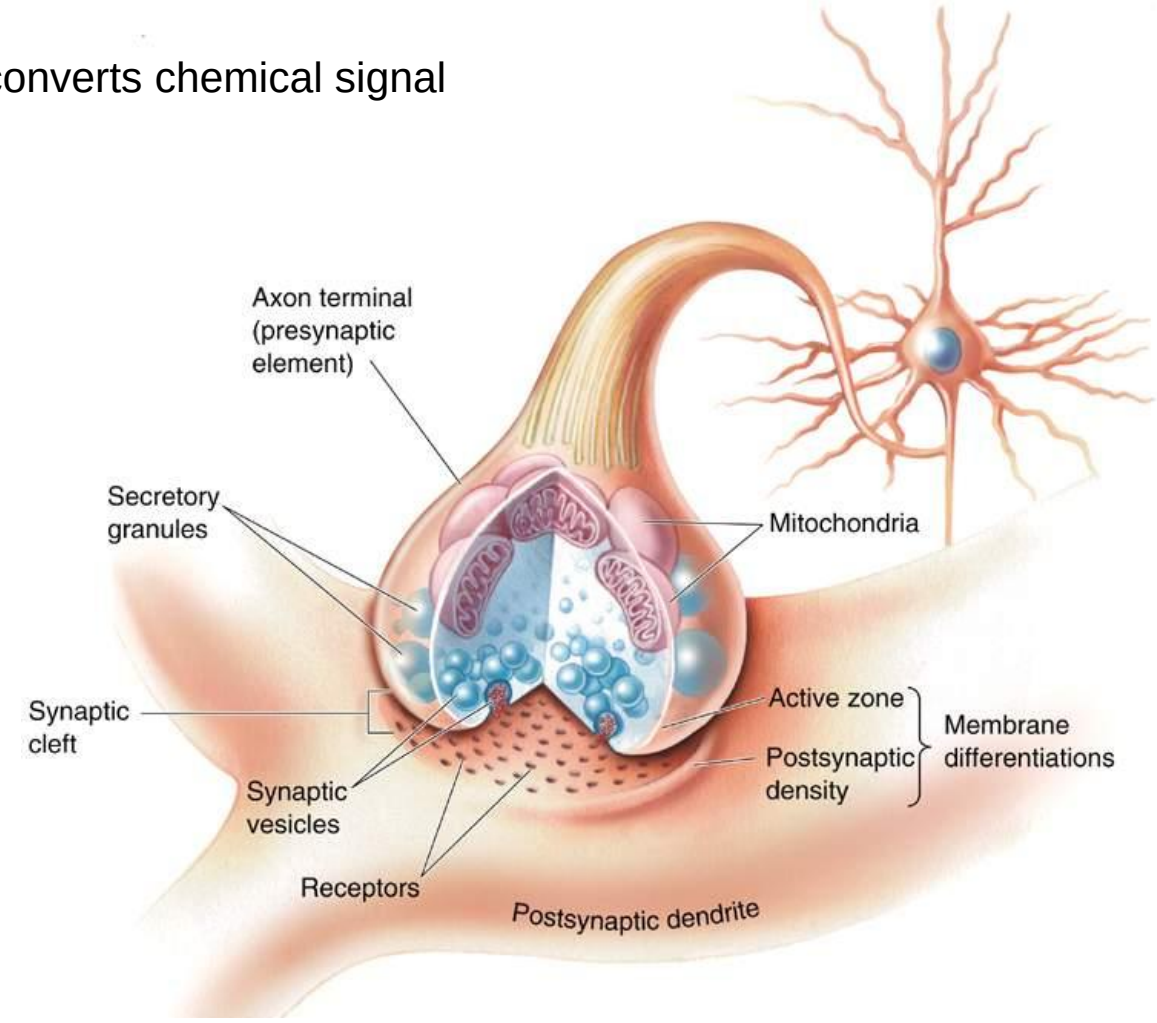
If several PSPs occur simultaneously to excite a neuron this generates an AP (Synaptic integration)



CHEMICAL SYNAPSES

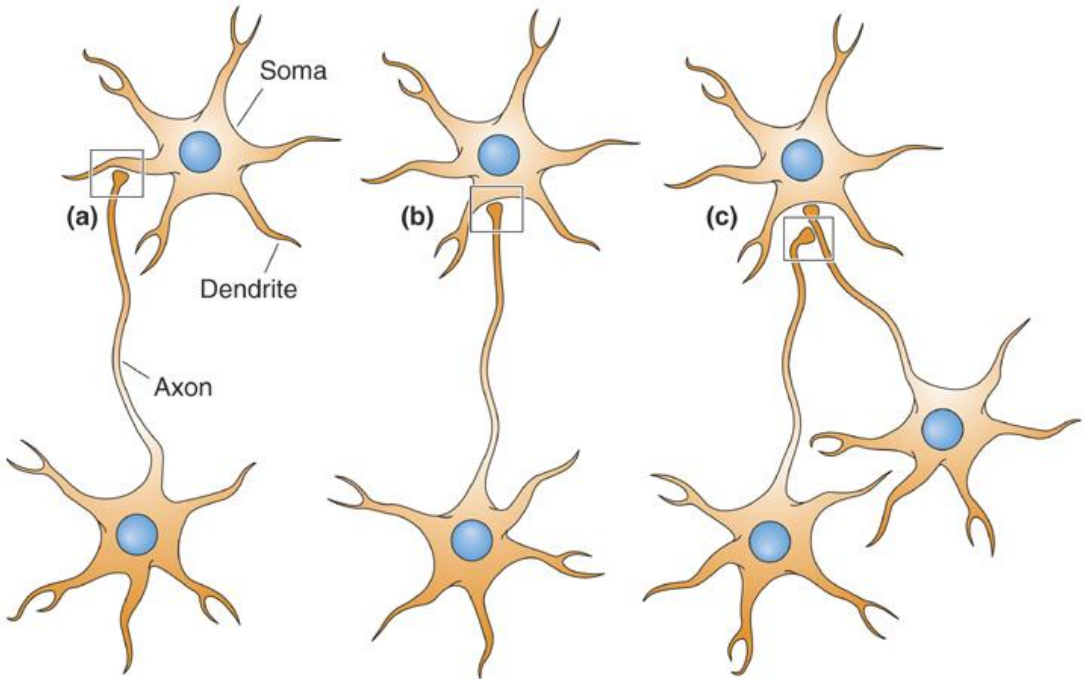
Key elements:

Synaptic cleft (wider the gap junction);
Presynaptic element (usually an axon terminal)
Synaptic vesicles (storage of neurotransmitter)
Secretory granules (bigger vesicles)
Postsynaptic density (receptor that converts chemical signal into electrical signal)
Postsynaptic cell

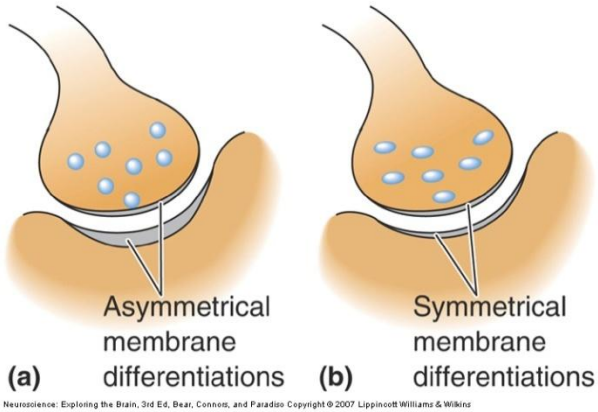


CNS SYNAPSES

Axodendritic: Axon to dendrite
Axosomatic: Axon to cell body
Axoaxonic: Axon to axon
Dendrodendritic: Dendrite to dendrite

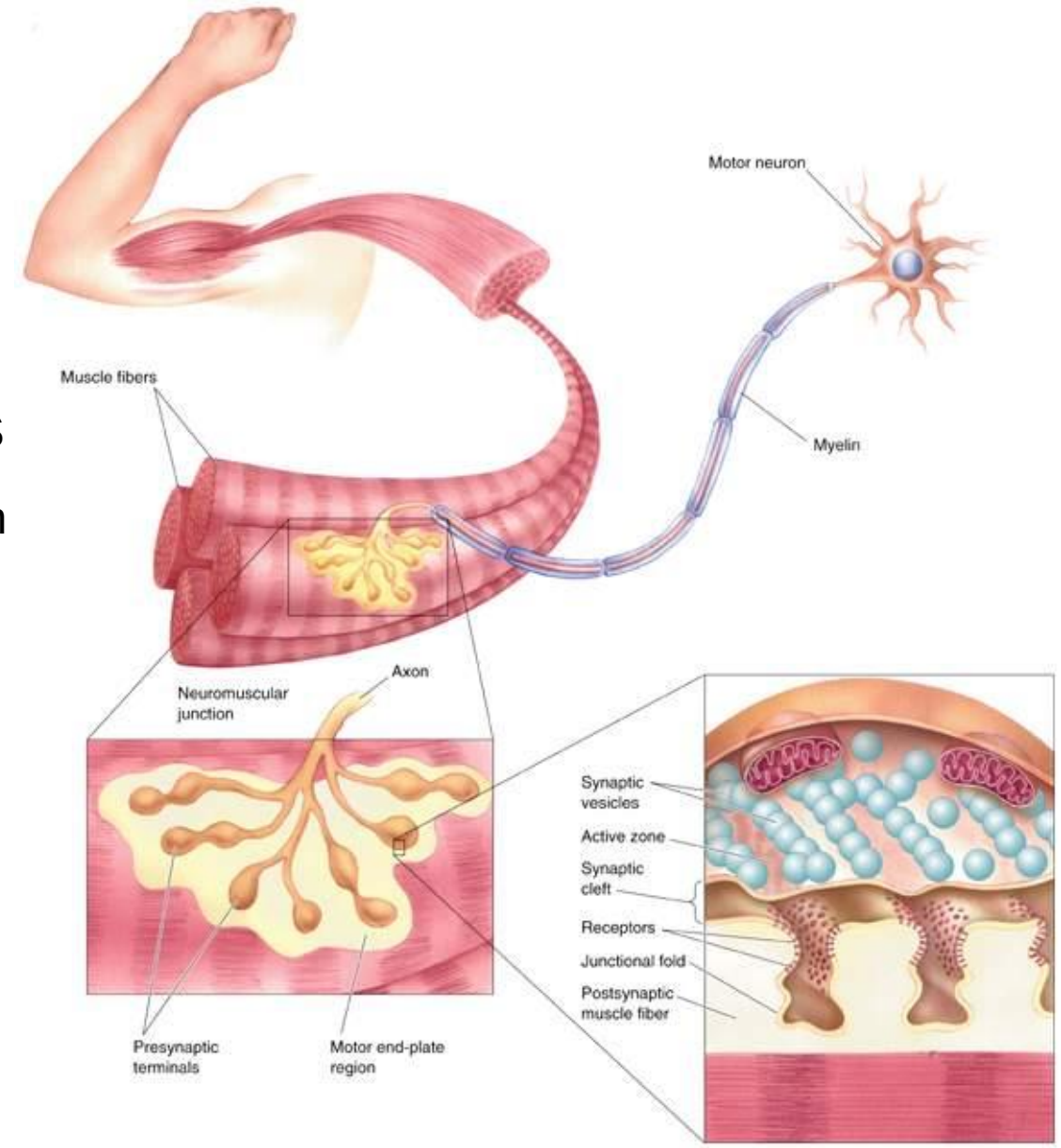


Gray's Type I: Asymmetrical, excitatory
Gray's Type II: Symmetrical, inhibitory



NEUROMUSCULAR JUNCTION

Synaptic junction outside the CNS
Studies of NMJ established principles of synaptic transmission
One of the largest and faster synapses in the body



PRINCIPLES OF CHEMICAL SYNAPTIC TRANSMISSION

Basic Steps

- Neurotransmitter synthesis
- Load neurotransmitter into synaptic vesicles
- Vesicles fuse to presynaptic terminal
- Neurotransmitter spills into synaptic cleft
- Binds to postsynaptic receptors
- Biochemical/Electrical response elicited in postsynaptic cell
- Removal of neurotransmitter from synaptic cleft

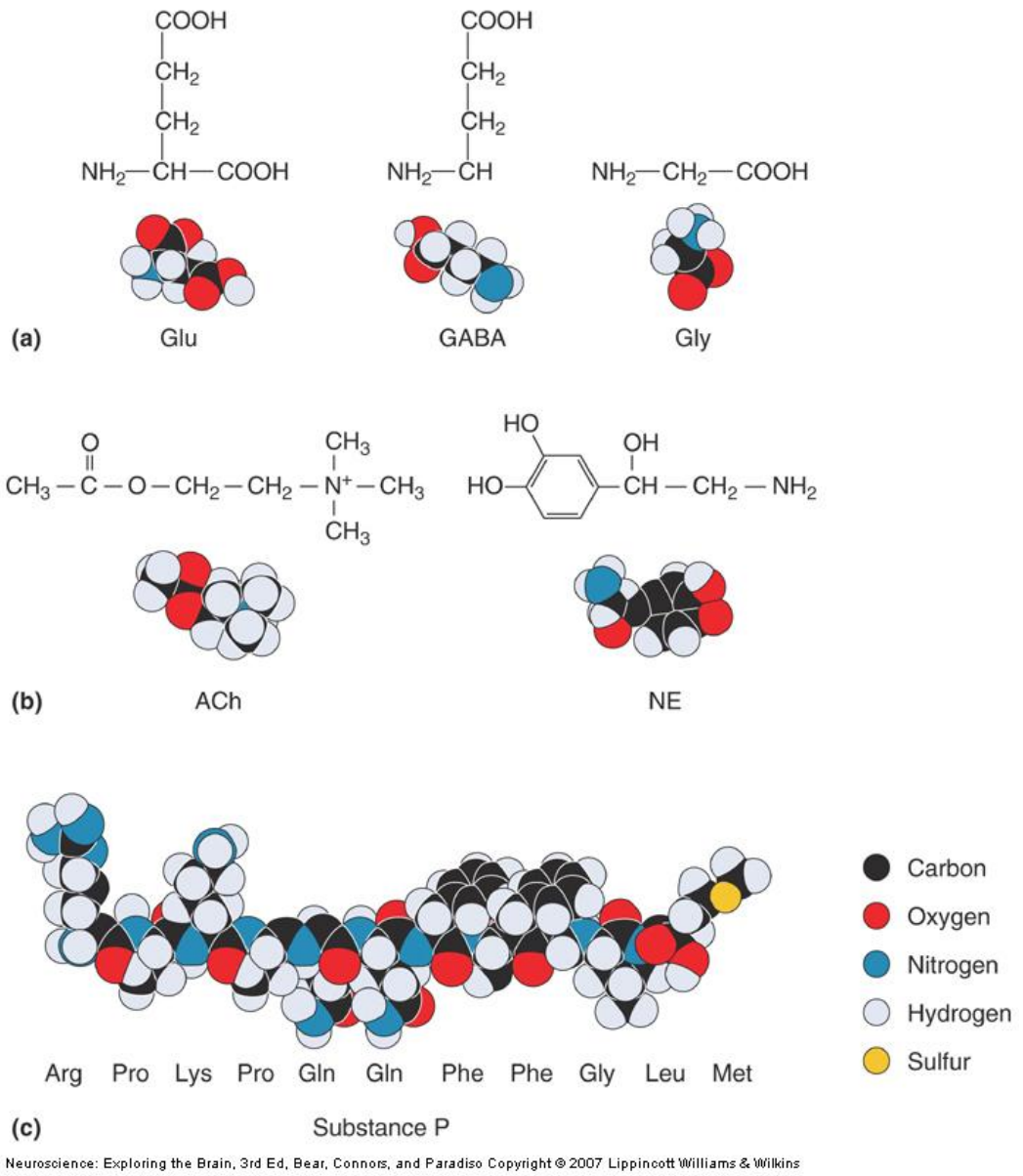
PRINCIPLES OF CHEMICAL SYNAPTIC TRANSMISSION

Neurotransmitters

Amino acids: Small organic molecules stored in and released from synaptic vesicles (Glutamate, Glycine, GABA)

Amines: Small organic molecules stored in and released from synaptic vesicles (Dopamine, Acetylcholine, Histamine)

Peptides: Short amino acid chains (i.e. proteins) stored in and released from secretory granules (Dynorphin, Enkephalins)



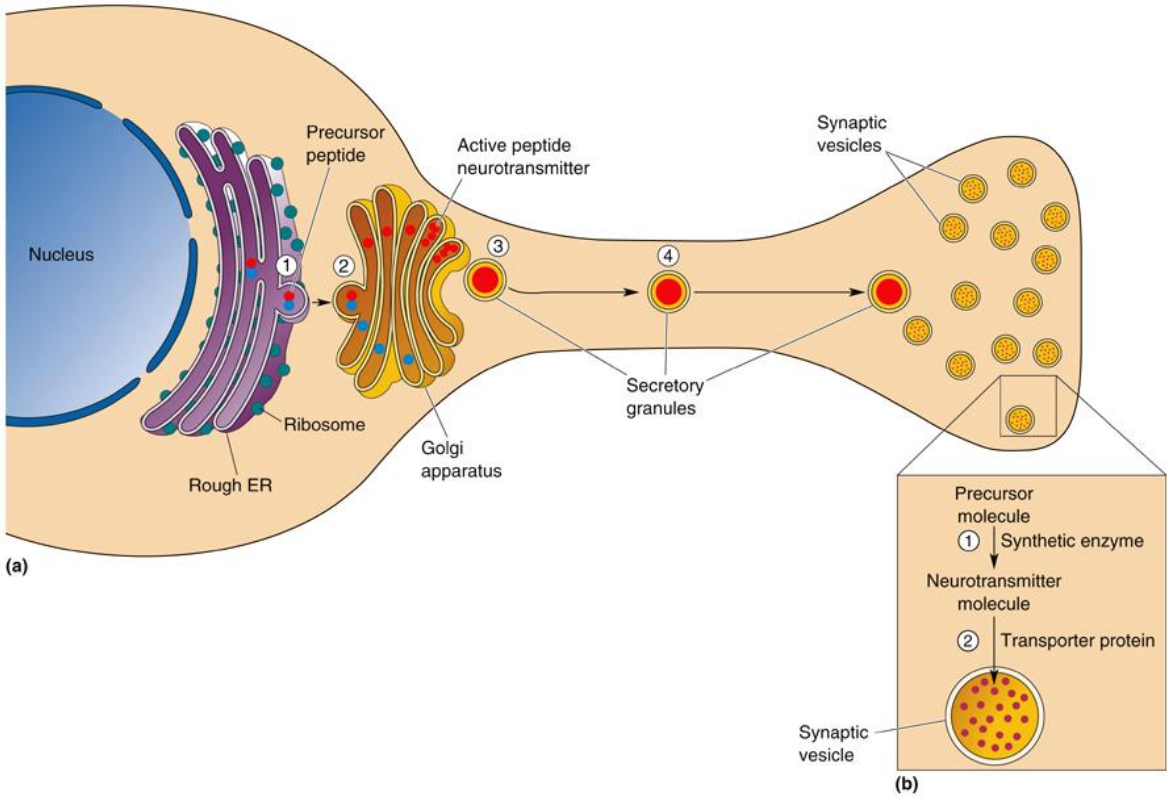
PRINCIPLES OF CHEMICAL SYNAPTIC TRANSMISSION

Neurotransmitter Synthesis and Storage

A part from amino acids, amines and peptides are synthesized from precursors only in neuron that release them.

Amine and amino acids are synthesized in the axon terminal and the take up by the vesicles with the help of the transportes .

Peptides are synthesized in the rough ER, eventually split in the Golgi apparatus and then carried to the axon terminal in the secretory granules



PRINCIPLES OF CHEMICAL SYNAPTIC TRANSMISSION

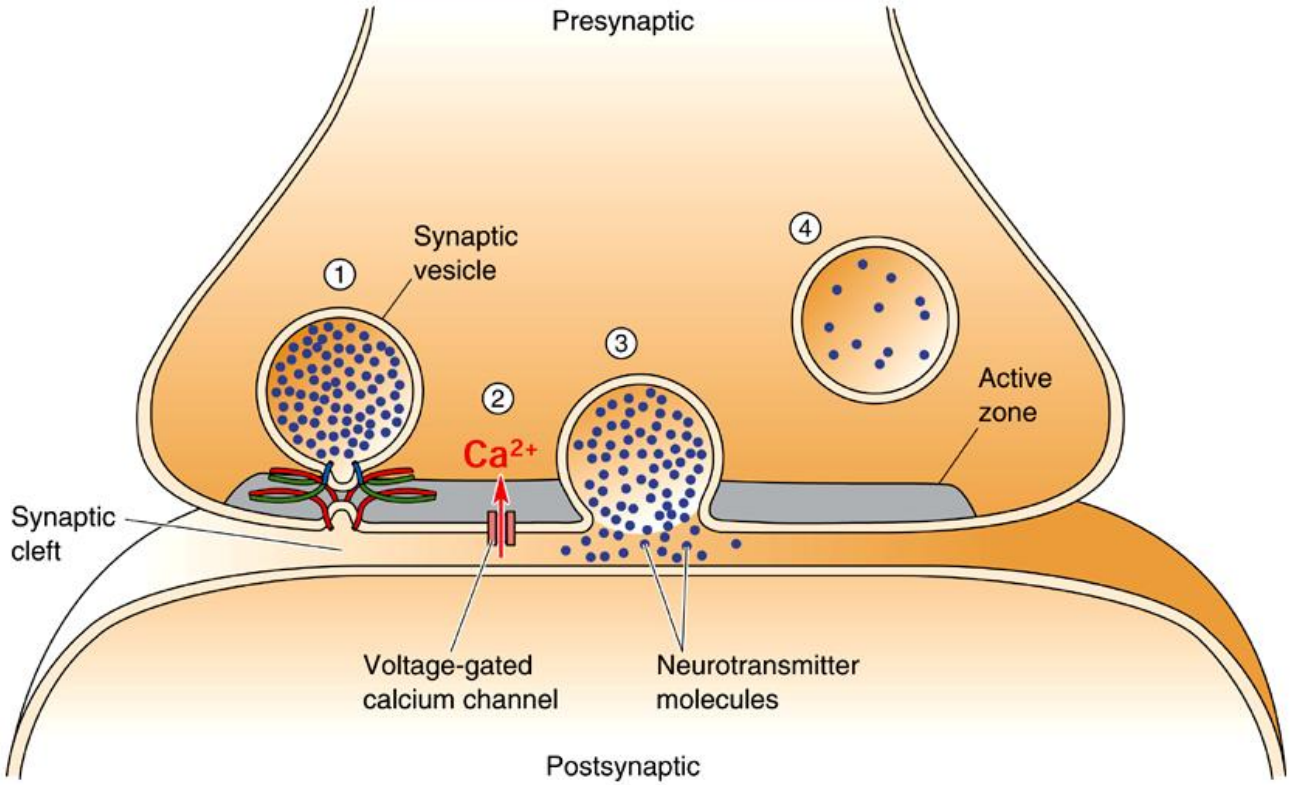
Neurotransmitter release by exocytosis

AP opens voltage gate calcium channel

Process of exocytosis stimulated by release of intracellular calcium, $[Ca^{2+}]I$, due to the AP.

Vesicle membrane fuses into presynaptic membrane with subsequent release of neurotransmitter

Vesicle membrane recovered by endocytosis and then refilled with new neurotransmitter

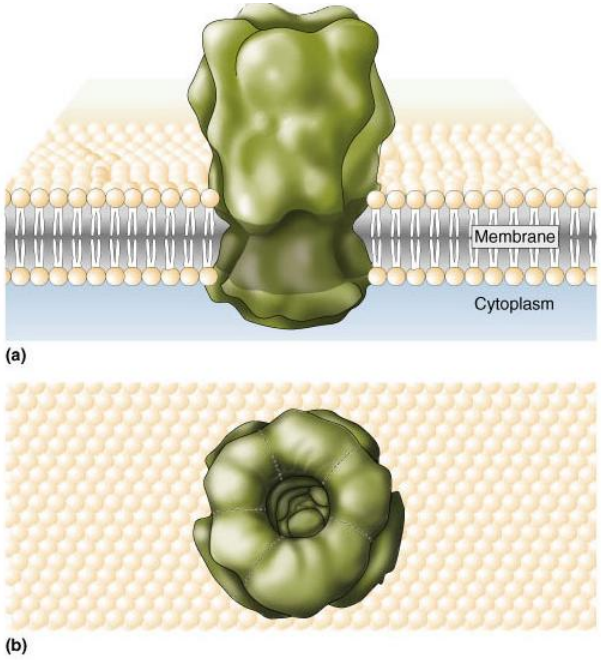


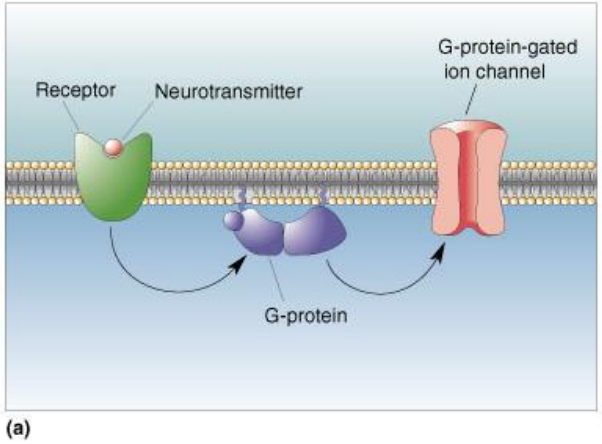
PRINCIPLES OF CHEMICAL SYNAPTIC TRANSMISSION

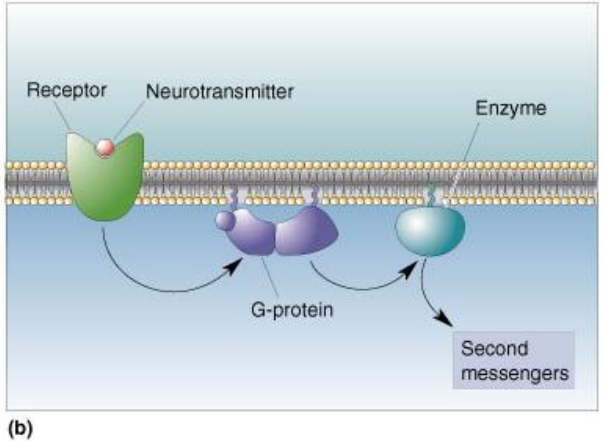
Neurotransmitter Receptors and Effectors (postsynaptic cell)

Ionotropic: Transmitter-gated ion channels

Metabotropic: G-protein-coupled receptor



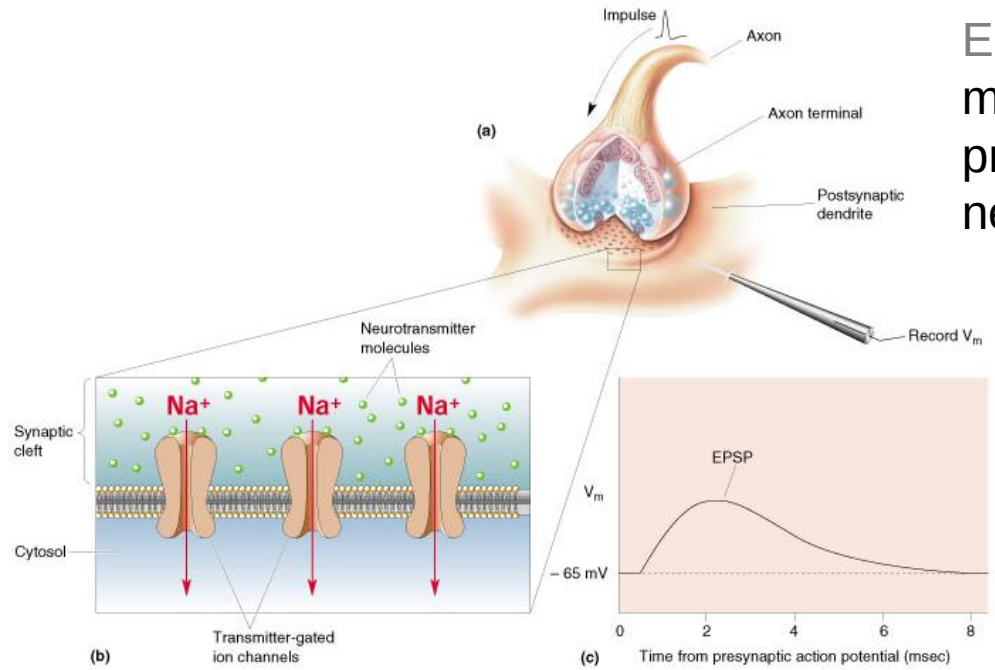




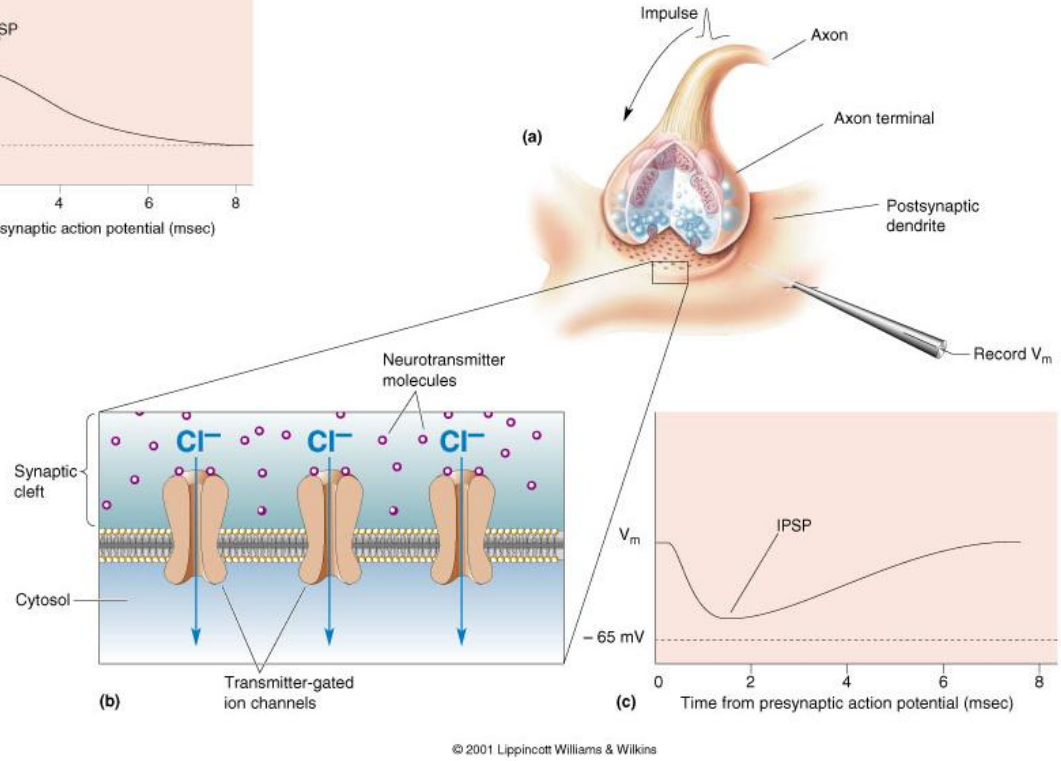
Autoreceptors: Presynaptic receptors sensitive to neurotransmitter released by presynaptic terminal. Act as safety valve to reduce release when levels are high in synaptic cleft (autoregulation)

PRINCIPLES OF CHEMICAL SYNAPTIC TRANSMISSION

EPSP: Transient postsynaptic membrane depolarization by presynaptic release of neurotransmitter



IPSP: Transient hyperpolarization of postsynaptic membrane potential caused by presynaptic release of neurotransmitter



PRINCIPLES OF CHEMICAL SYNAPTIC TRANSMISSION

Neurotransmitter Recovery and Degradation

Neurotransmitter must be cleared from the synaptic cleft. Different ways.

Diffusion: Away from the synapse

Reuptake: Neurotransmitter re-enters presynaptic axon terminal

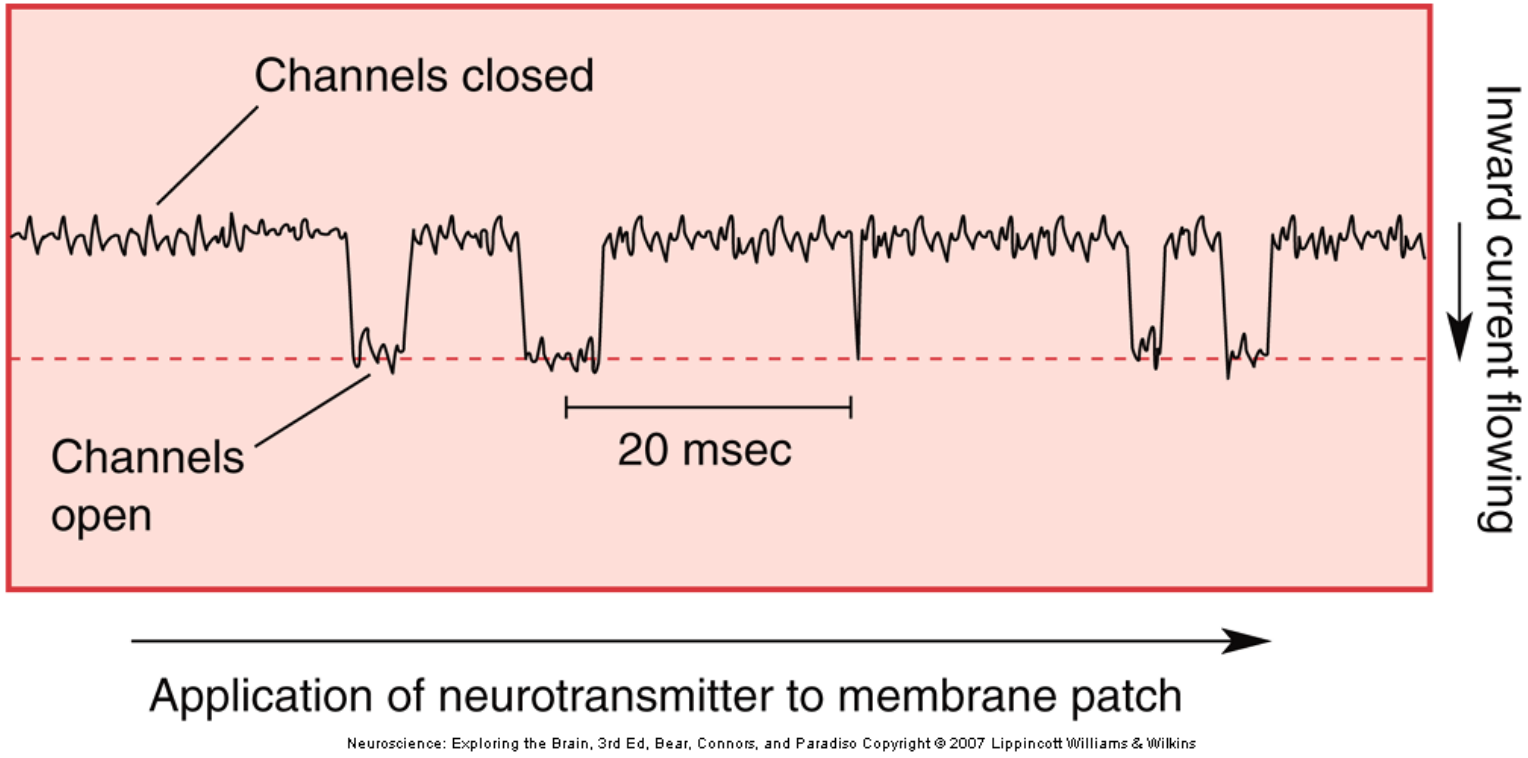
Enzymatic destruction inside terminal cytosol or synaptic cleft

Desensitization: e.g., AChE cleaves Ach to inactive state

PRINCIPLES OF SYNAPTIC INTEGRATION

Synaptic Integration

Process by which multiple synaptic potentials combine within one postsynaptic neuron



PRINCIPLES OF SYNAPTIC INTEGRATION

Quantal Analysis of EPSPs

The synaptic vesicle is the elementary units of synaptic transmission

The amplitude of an EPSP is some multiple of the response to the content of a vesicle (quantum)

Quantal analysis is used to determine number of vesicles that release during neurotransmission

Miniature postsynaptic potential ("mini") are normally generated spontaneously

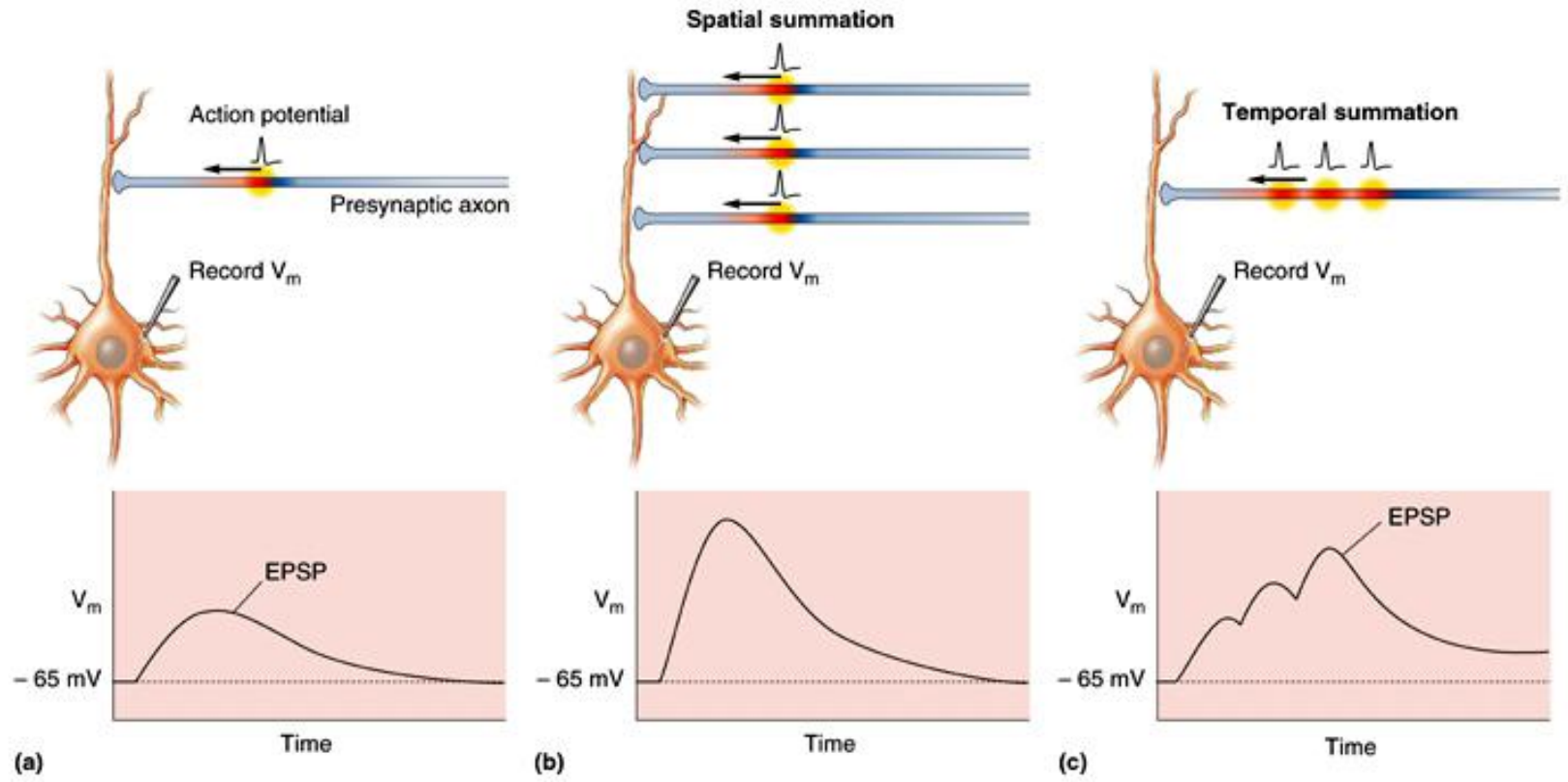
PRINCIPLES OF SYNAPTIC INTEGRATION

EPSP Summation

Allows for neurons to perform sophisticated computations. EPSPs are added together to produce significant postsynaptic depolarization. Two types:

Spatial: EPSP generated simultaneously in different spaces

Temporal: EPSP generated at same synapse in rapid succession



PRINCIPLES OF SYNAPTIC INTEGRATION

Inhibition

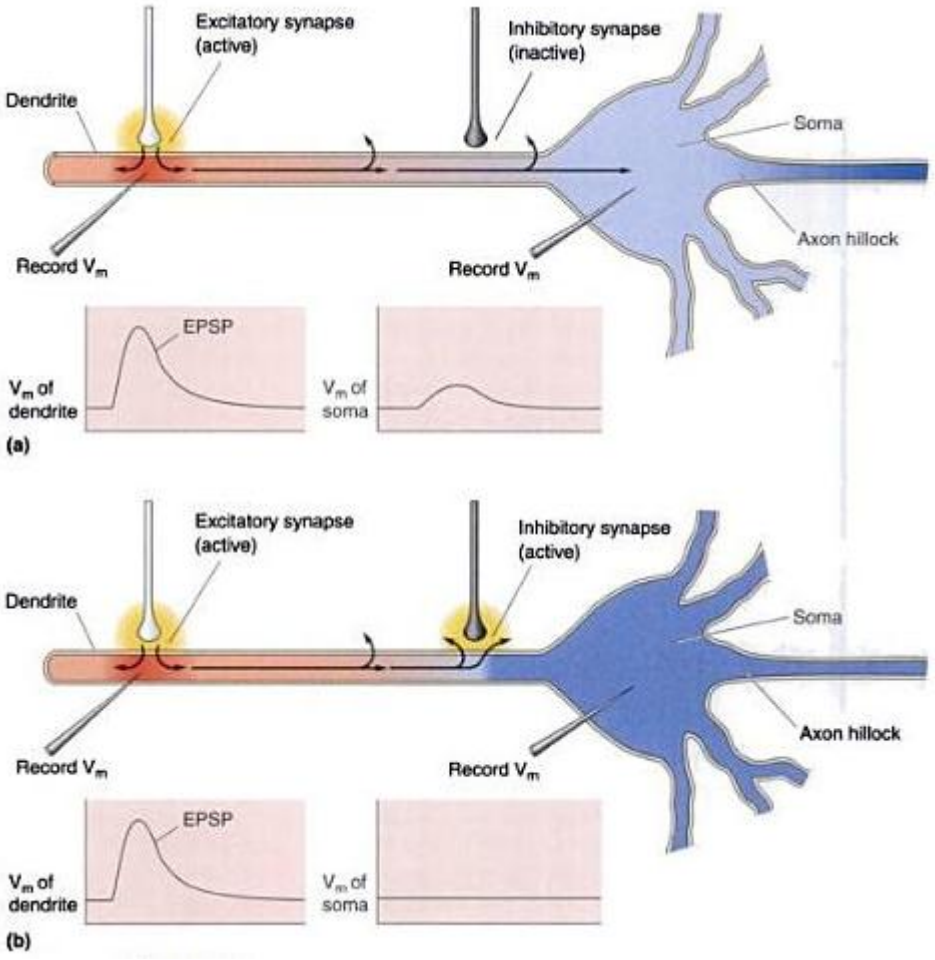
Action of synapses to take membrane potential away from action potential threshold

IPSPs and Shunting Inhibition

Excitatory vs. inhibitory synapses: Bind different neurotransmitters (GABA or Glycine), allow different ions to pass through channels (Chloride, Cl-)

Membrane potential less negative than -65mV = hyperpolarizing IPSP

Shunting Inhibition: Inhibiting current flow from soma to axon hillock



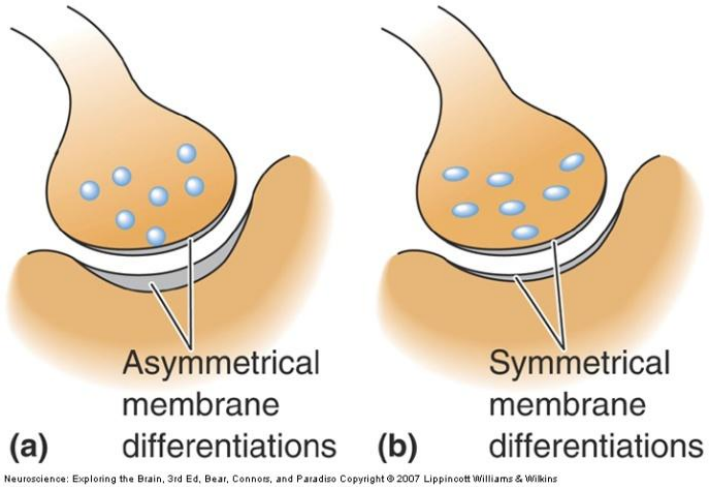
PRINCIPLES OF SYNAPTIC INTEGRATION

The Geometry of Excitatory and Inhibitory Synapses

Excitatory synapses (Glutamate) usually have Gray's type I morphology
Clustered on soma and near axon hillock

Inhibitory synapses (GABA, Glycine) have Gray's type II morphology

Gray's Type I: Asymmetrical, excitatory
Gray's Type II: Symmetrical, inhibitory



PRINCIPLES OF SYNAPTIC INTEGRATION

Modulation

Synaptic transmission that modifies effectiveness of EPSPs generated by other synapses with transmitter-gated ion channels

Example: Activating NE β receptor