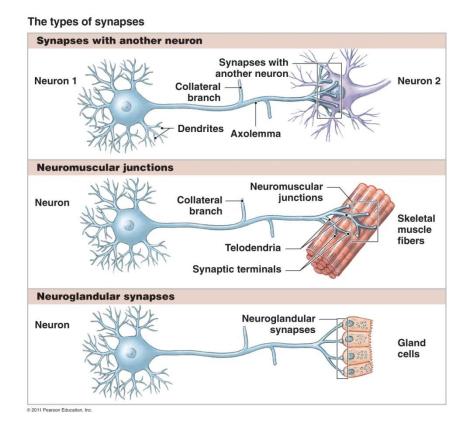
Simge Aykan, PhD

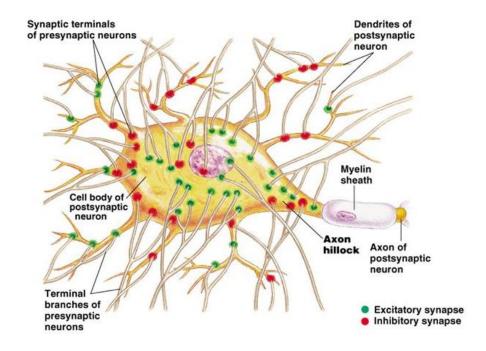
Department of Physiology

February 2021

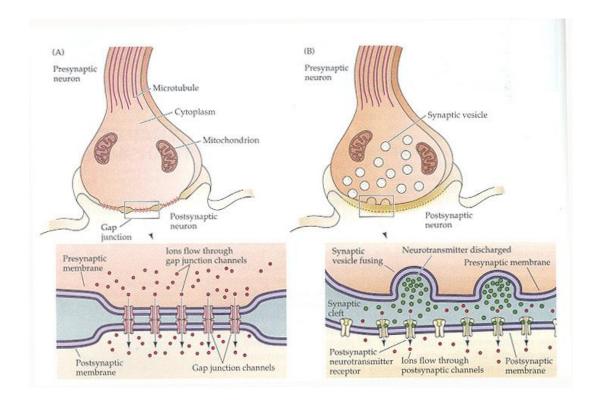
- Biological process by which a neuron communicates with a target cell across a synapse
- *Synapse* is an anatomically specialized junction between two neurons, at which the electrical activity in a presynaptic neuron influences the electrical activity of a postsynaptic neuron
- Synapse can be between a neuron and a
 - Neuron
 - Muscle
 - Gland cell



- The average neuron forms several thousand synaptic connections and receives a similar number
 - The Purkinje cell of the cerebellum receives up to 100,000 synaptic inputs
- 10¹¹ neurons, 10¹⁴ (100 trillion!) synapses

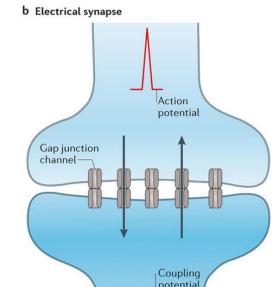


- Electrical synapse transmission: transfer of electrical signals through gap junctions
- Chemical synaptic transmission: release of a neurotransmitter from the pre-synaptic neuron, and neurotransmitter binding to specific post-synaptic receptors



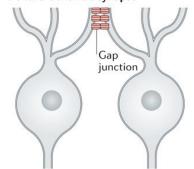
Connection through gap junctions

- Narrow gap between membranes (3 nm)
- Connexin → connexon → gap junction
- Direct ion passage from one neuron to another
- Big enough for many small organic molecules to pass through (1-2 nm)
- Mostly between dendrites

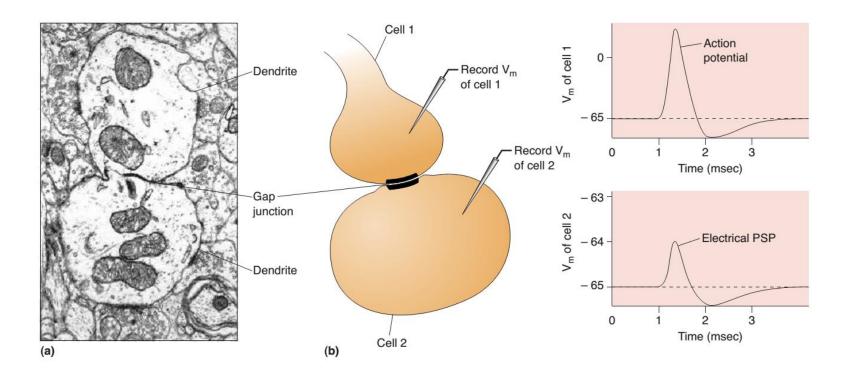


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a Dendro-dendritic synapse

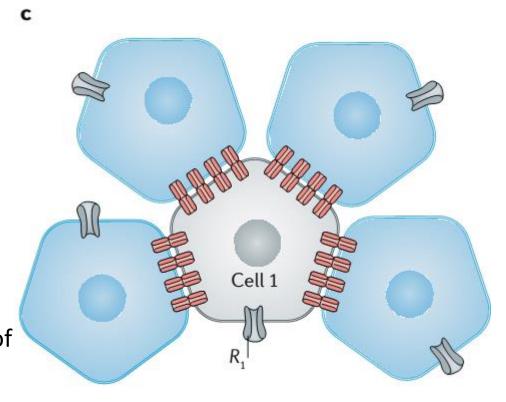


• Electrical postsynaptic potential (PSP) induced by ionic current flow (1 mV or less)



- Advantages
 - Extremely rapid
 - Orchestrating the actions of large groups of neurons
 - Can transmit metabolic signals between cells

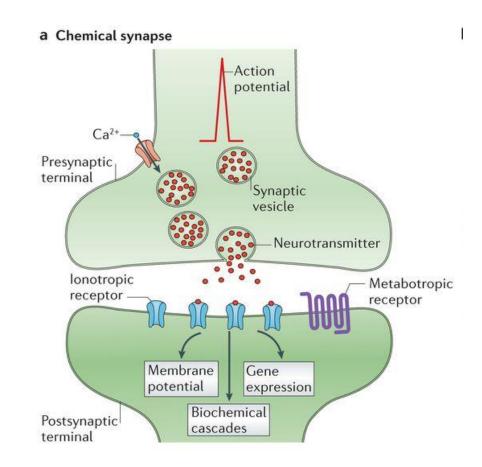
- Less common in vertebrate nervous system
 - Require a large area of contact; restricting number of synaptic inputs
 - Cannot be inhibitory



- Found where normal function requires that the activity of neighbouring neurons be highly syncronized
 - During prenatal and postnatal brain development, neighbouring cells share both electrical and chemical signals to coordinate their growth and maturation
 - Hormone-secreting neurons within the hypothalamus to facilitate a burst of hormone secretion into the circulation

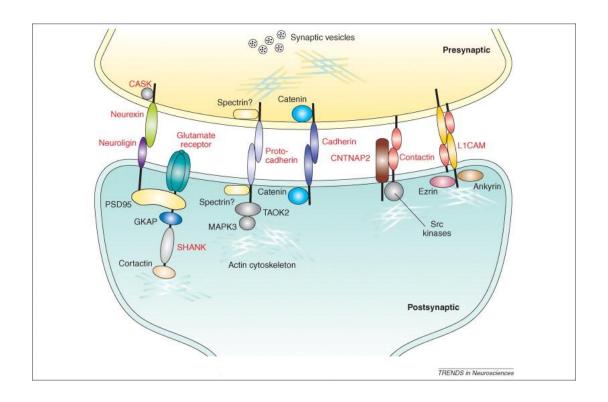
Chemical Synapses

- No structural continuity
 - Synaptic cleft (20-40 nm)
 - Diffusion of neurotransmitters
- Presynaptic terminals contain 100 to 200 synaptic vesicles, each filled with several thousand molecules of the neurotransmitter
- The synaptic vesicles are clustered at active zones



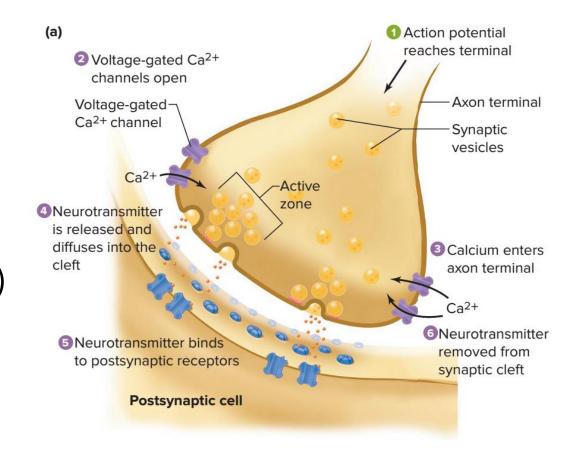
Chemical Synapses

- Cell Adhesion Molecules (CAMs)
 - proteins in the pre- and postsynaptic membranes that project from these membranes into the synaptic cleft, where they bond to each other
- Ensures that the pre- and postsynaptic membranes stay in close proximity for rapid chemical transmission



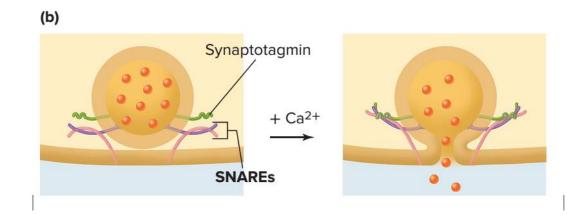
Presynaptic Terminal

- Terminal boutons
- Voltage-gated Ca²⁺ channels
- Ca²⁺ influx
- Fusion of vesicles
 - Synaptic vesicles (neurotransmitter)
 - Secretory granules (neuropeptides)
- Exocytosis



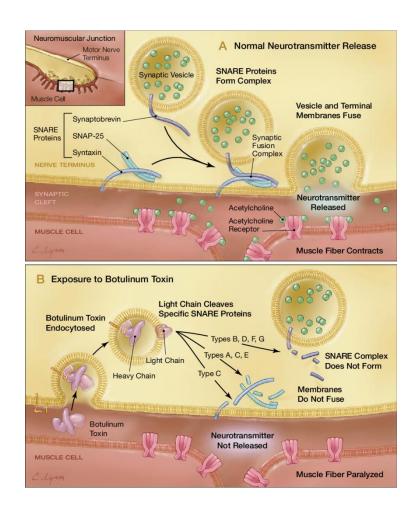
Presynaptic Terminal

- Vesicles are docked in the active zones by the interaction of proteins
 - SNAREs
- Ca²⁺ interaction with synaptotagmin
- Conformation change in the SNARE complex
- Membrane fusion



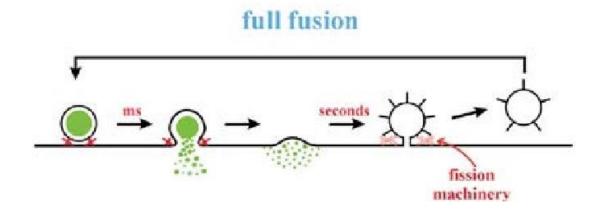
Botulinum toxins targets
 excitatory synapses that release
 ACh as a neurotransmitter and
 digests one of the SNAREs

 Muscles are unable to contract (flaccid paralysis)

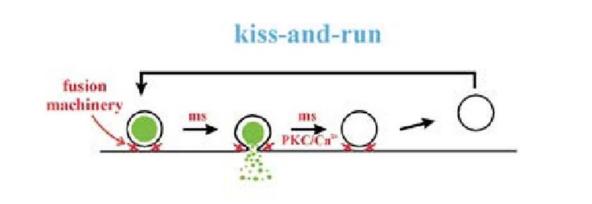


Presynaptic Terminal

 Vesicles completely fuse with the membrane and are later recycled by endocytosis from the membrane at sites outside the active zone



 At synapses with high action potential firing frequencies, vesicles fuse briefly then reseal the pore and withdraw back into the axon terminal ("kiss-and-run fusion")

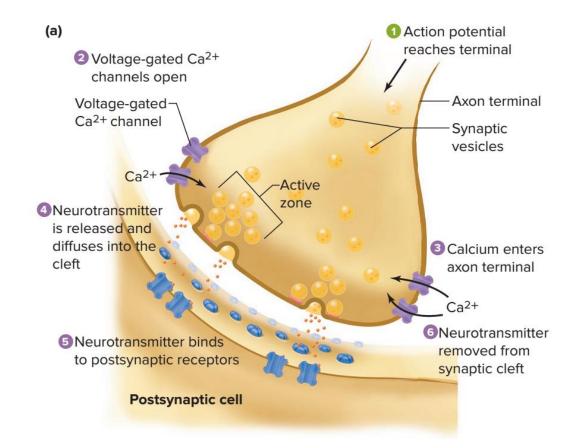


Synaptic Cleft

Neurotransmitter diffusion

• 20-40 nm

- Neurotransmitters rapidly and reversibly bind to receptors on the plasma membrane
 - Bound ligand is in equilibrium with the unbound form



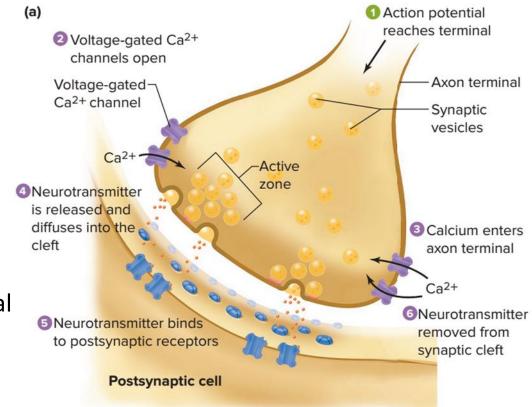
Synaptic Cleft

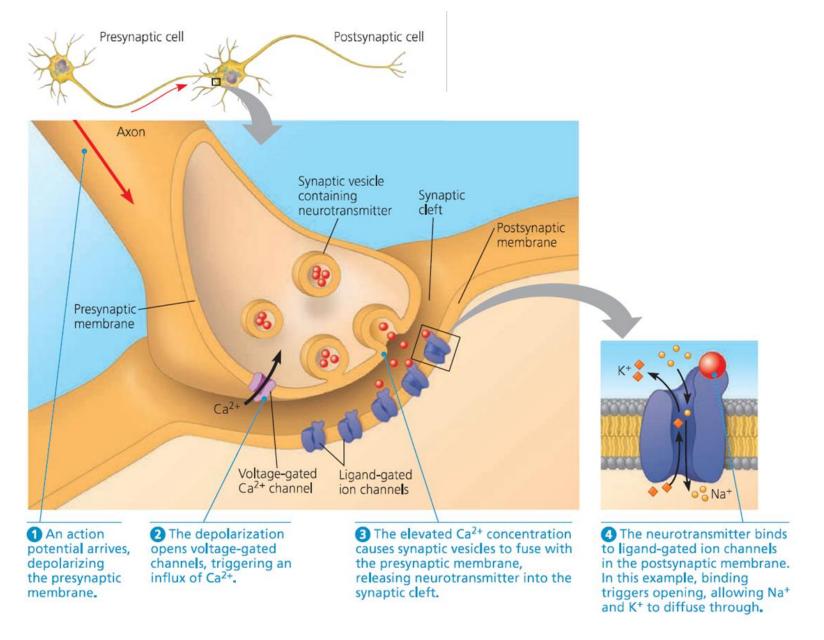
- Unbound neurotransmitters are removed from the synaptic cleft
 - 1. actively transported back into the presynaptic axon terminal for reuse (reuptake)
 - 2. transported into nearby glial cells where they are degraded (astrocytes)
 - 3. diffuse away from the receptor site
 - 4. enzymatically transformed into inactive substances

Postsynaptic Terminal

 Postsynaptic density: area with high protein accumulation under the postsynaptic membrane (receptors)

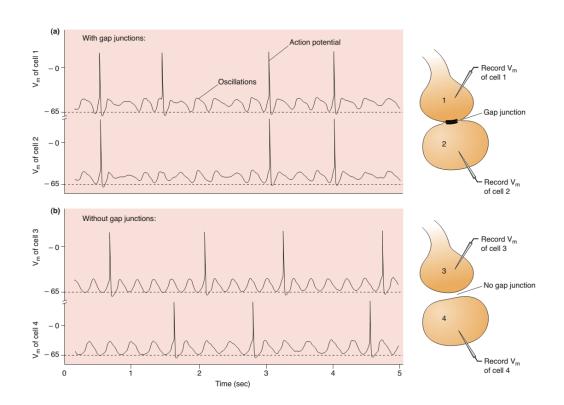
 Neurotransmitter receptors: convert intercellular chemical signal (i.e., neurotransmitter) into an intracellular signal (i.e., a change in membrane potential or a chemical change)





Postsynaptic Neuron

• Synaptic delay (at least 0.3 msec) between the arrival of an action potential at a presynaptic terminal and the membrane potential changes in the postsynaptic cell



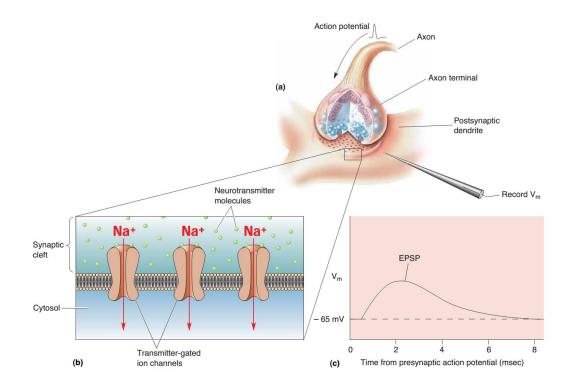
Electrical vs Chemical Synapses

Type of synapse	Distance between pre- and postsynaptic cell membranes	Cytoplasmic continuity between pre- and postsynaptic cells	Ultrastructural components	Agent of transmission	Synaptic delay	Direction of transmission
Electrical	4 nm	Yes	Gap-junction channels	Ion current	Virtually absent	Usually bidirectional
Chemical	20–40 nm	No	Presynaptic vesicles and active zones; postsynaptic receptors	Chemical transmitter	Significant: at least 0.3 ms, usually 1–5 ms or longer	Unidirectional

Postsynaptic Potentials

 Excitatory postsynaptic potential (EPSP) a transient postsynaptic membrane depolarization

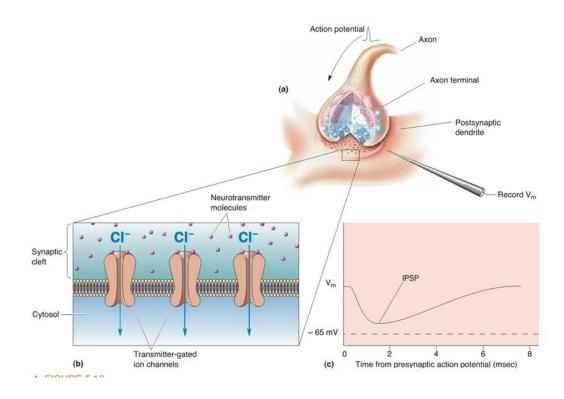
 EPSP is a depolarizing graded potential that decreases in magnitude as it spreads away from the synapse by local current



Postsynaptic Potentials

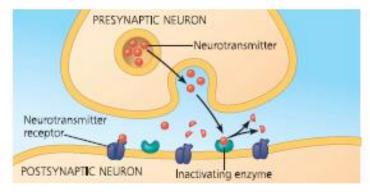
 Inhibitory postsynaptic potential (IPSP) a transient postsynaptic membrane hyperpolarization

 Activated receptors on the postsynaptic membrane open Cl⁻ or K⁺ channels

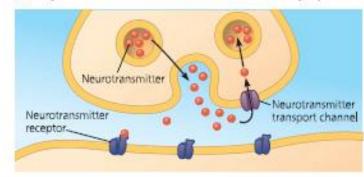


Termination of Neurotransmitter Signaling

- After a response is triggered, the chemical synapse returns to its resting state
- The neurotransmitter molecules are cleared from the synaptic cleft
 - Enzymatic clearence
 - Diffuse away from the cleft
 - Active transport back to the presynaptic terminal



(a) Enzymatic breakdown of neurotransmitter in the synaptic deft



(b) Reuptake of neurotransmitter by presynaptic neuron

