SYNAPTIC TRANSMISSION

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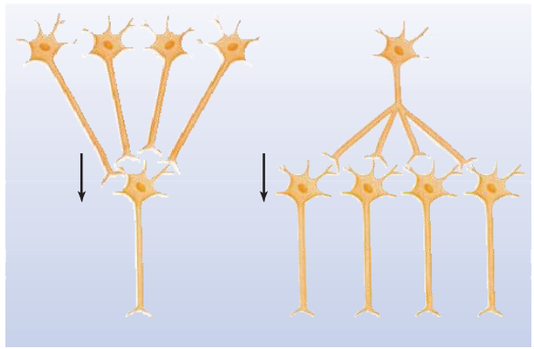
- A synapse is an anatomically specialized junction between two neurons, at which the electrical activity in one neuron, the presynaptic neuron, influences the electrical or metabolic activity in the second, postsynaptic neuron. Anatomically, synapses include parts of the presynaptic and postsynaptic neurons and the extracellular space between these two cells. According to the latest estimate, there are approximately 10^{14} (100 quadrillion) synapses in the CNS.

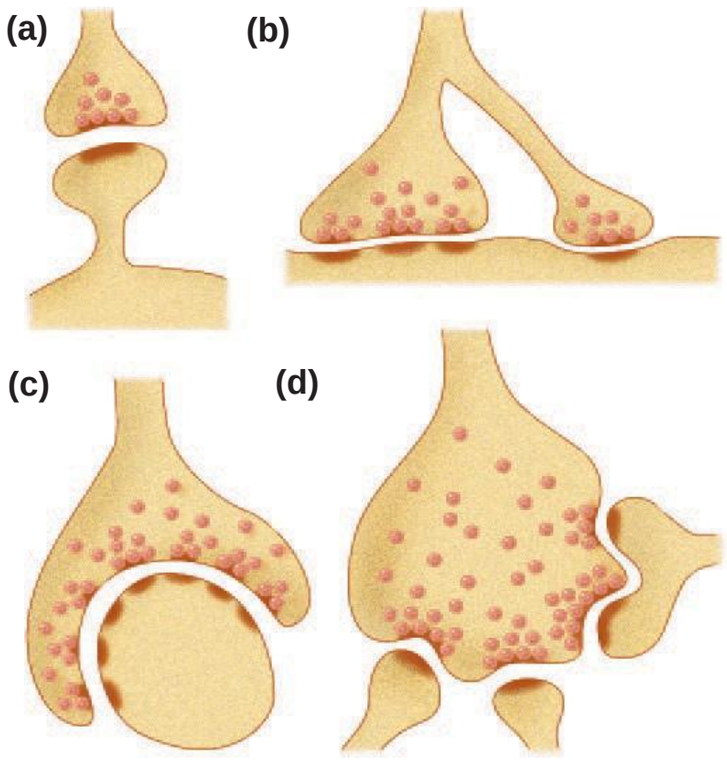
- Activity at synapses can increase or decrease the likelihood that the postsynaptic neuron will fire action potentials by producing a brief, graded potential in the postsynaptic membrane. The membrane potential of a postsynaptic neuron is brought closer to threshold (i.e., depolarized) at an **excitatory synapse,** and it is either driven farther from threshold (i.e., hyperpolarized) or stabilized at its present level at an **inhibitory synapse.**

- The level of excitability of a postsynaptic cell at any moment (that is, how close its membrane potential is to threshold) depends on the number of synapses active at any one time and the number that are excitatory or inhibitory. If the membrane of the postsynaptic neuron reaches threshold, it will generate action potentials that are propagated along its axon to the terminal branches, which influence the excitability of *other* cells by divergence.

FUNCTIONAL ANATOMY OF SYNAPSES



Convergence of neural input from many neurons onto a single neuron, and divergence of output from a single neuron onto many others. Arrows indicate the direction of transmission of neural activity.



Synapses appear in many forms as demonstrated here in views (a) to (d). The presynaptic terminal contains synaptic vesicles.

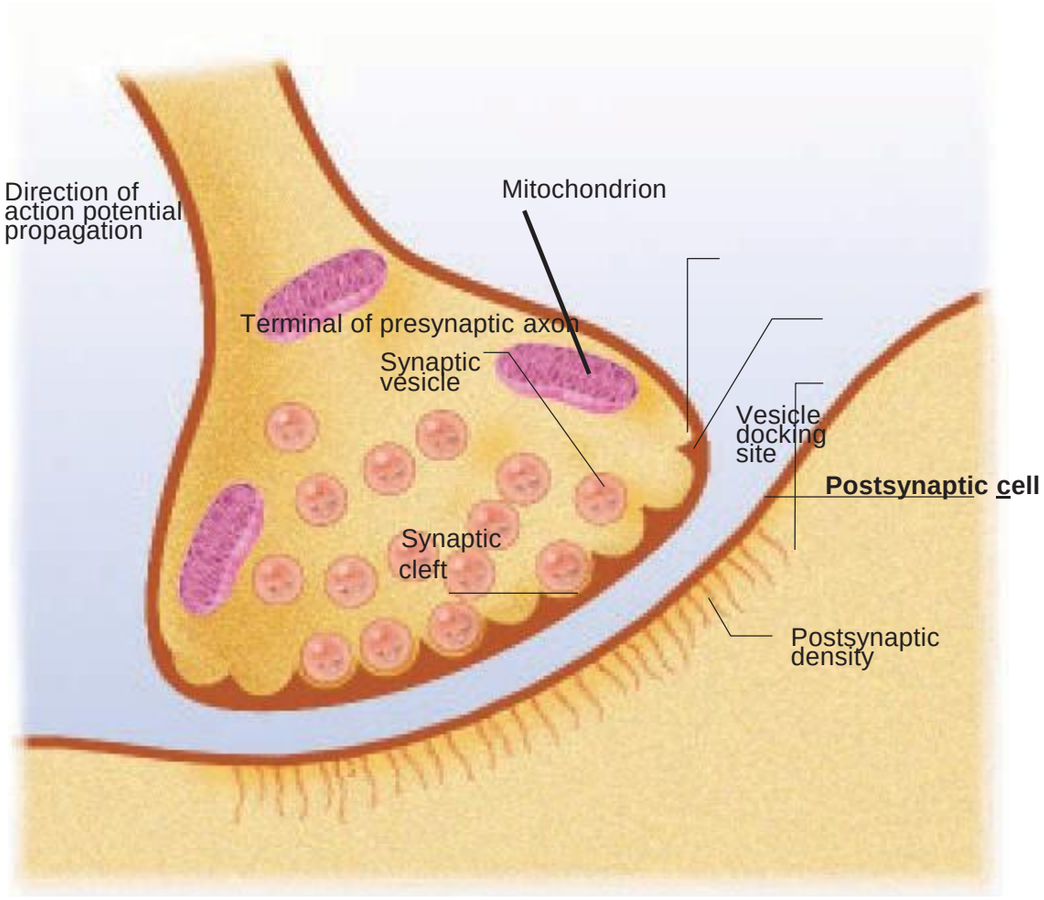
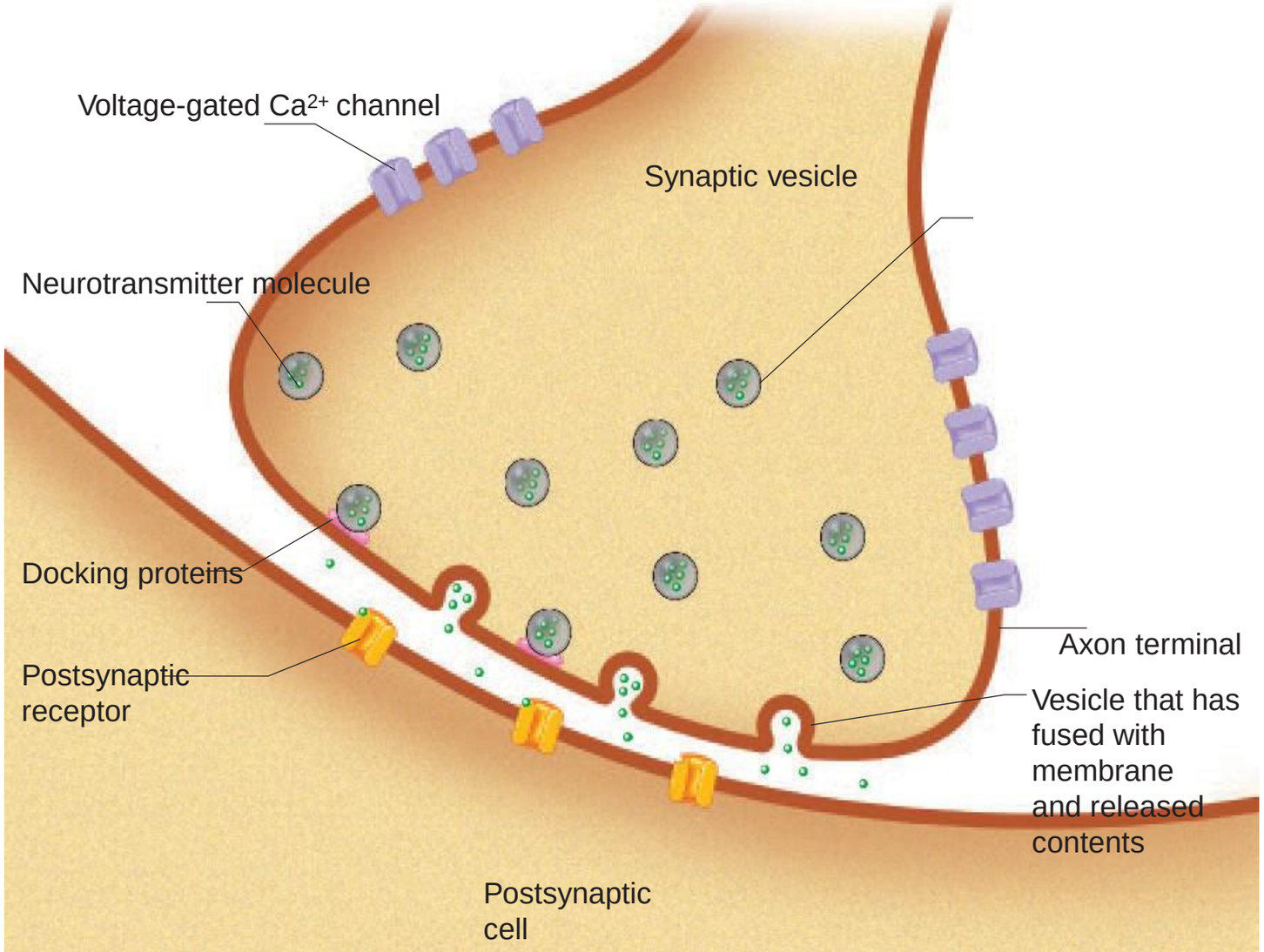


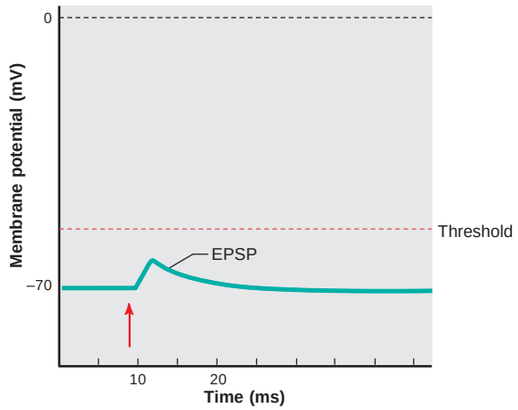
Diagram of a synapse. Some vesicles are docked at the presynaptic membrane ready for release. The postsynaptic membrane is distinguished microscopically by the postsynaptic density, which contains proteins associated with the receptors.

MECHANISMS OF NEUROTRANSMITTER RELEASE

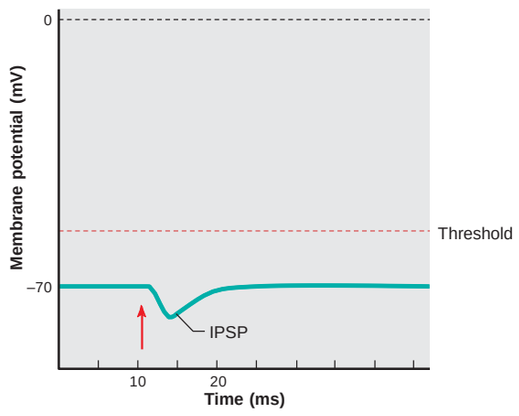


Neurotransmitter storage and release at the synapse and binding to the postsynaptic receptor. Voltage-gated calcium channels in the terminal open in response to an action potential, triggering release of neurotransmitter.

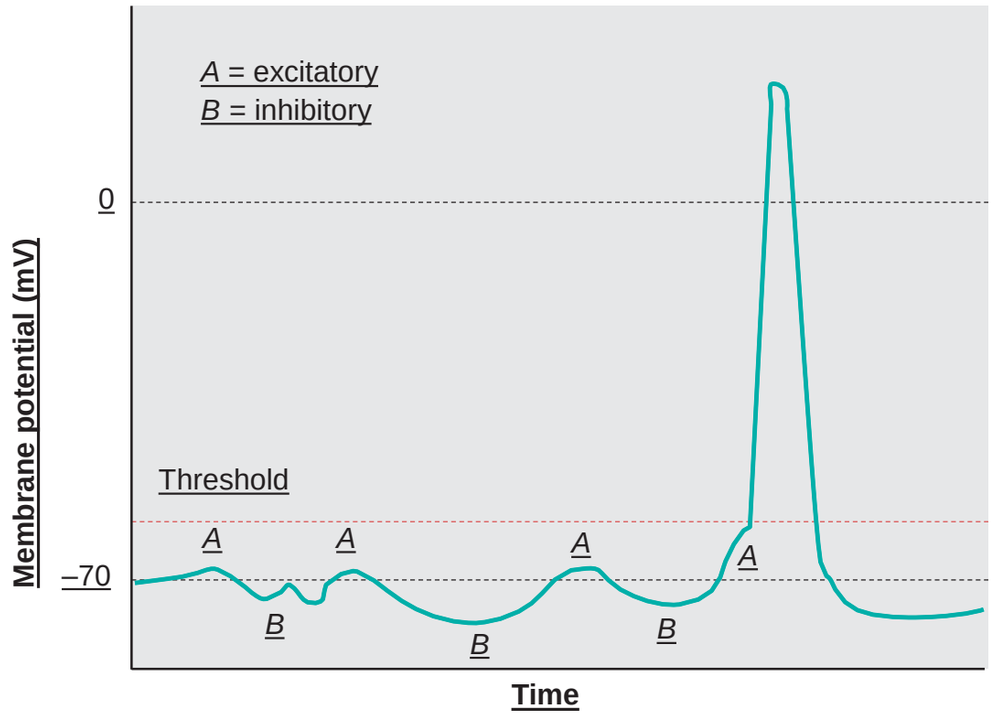
ACTIVATION OF THE POSTSYNAPTIC CELL



Excitatory postsynaptic potential (EPSP). Stimulation of the presynaptic neuron is marked by the arrow.

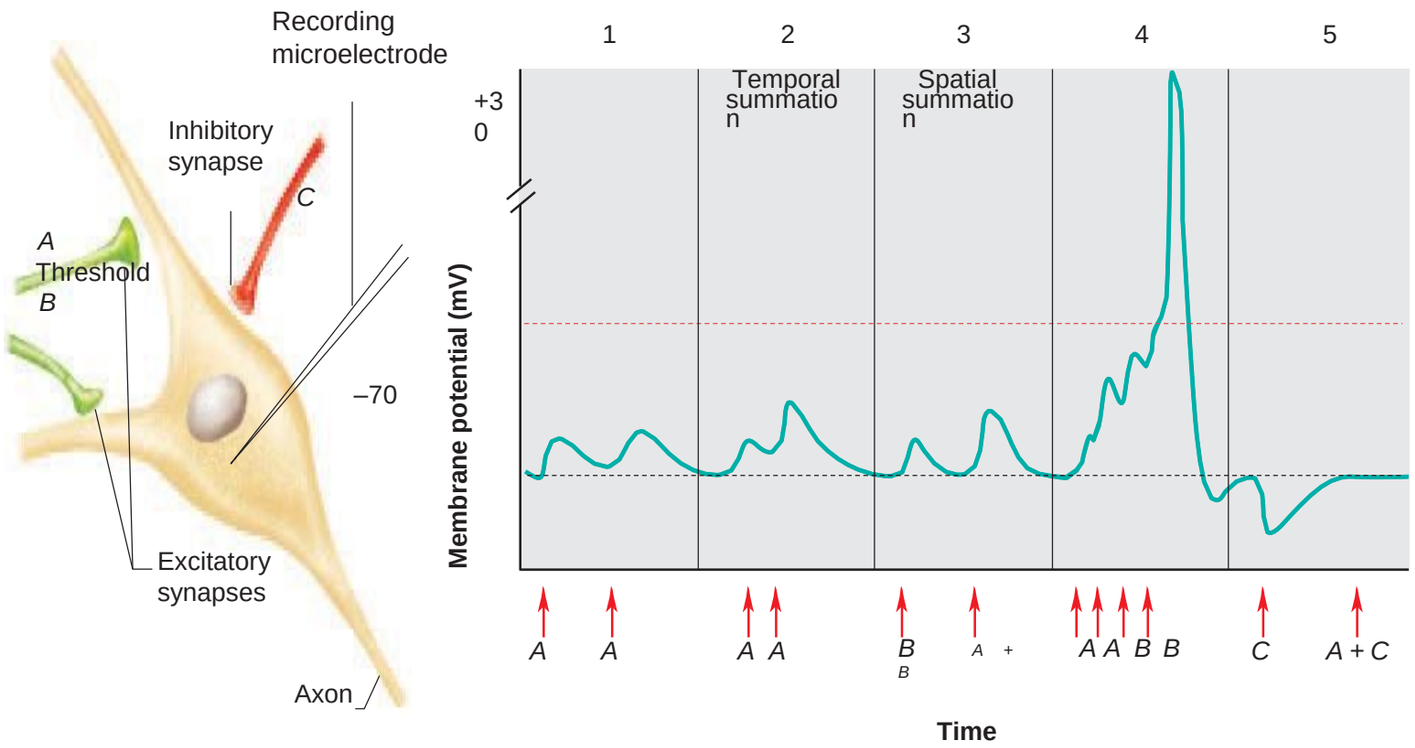


Inhibitory postsynaptic potential (IPSP). Stimulation of the presynaptic neuron is marked by the arrow.

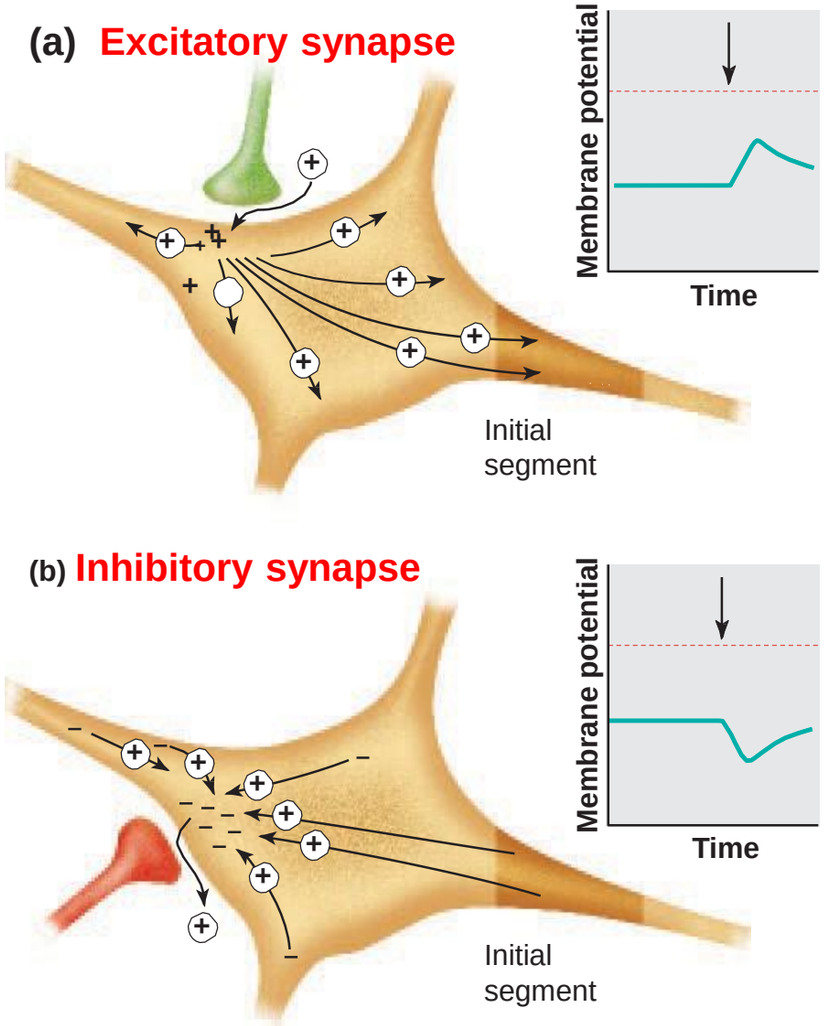


Intracellular recording from a postsynaptic cell during times of excitatory synaptic activity when the cell is facilitated (A), and inhibitory synaptic activity when the membrane hyperpolarizes (B).

INTERACTION OF EPSPS AND IPSPS AT THE POSTSYNAPTIC NEURON



Incoming neurons (A–C) were stimulated at times indicated by the arrows, and the resulting membrane potential was recorded in the postsynaptic cell by a recording microelectrode.

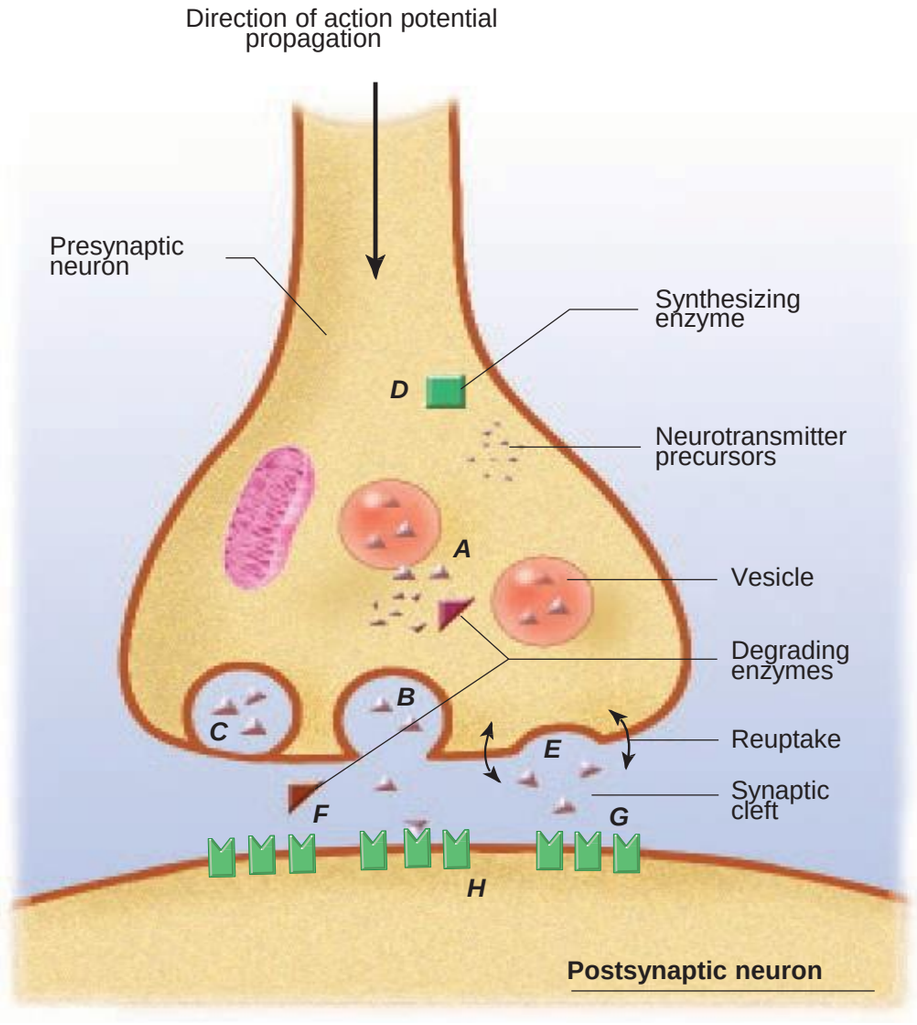


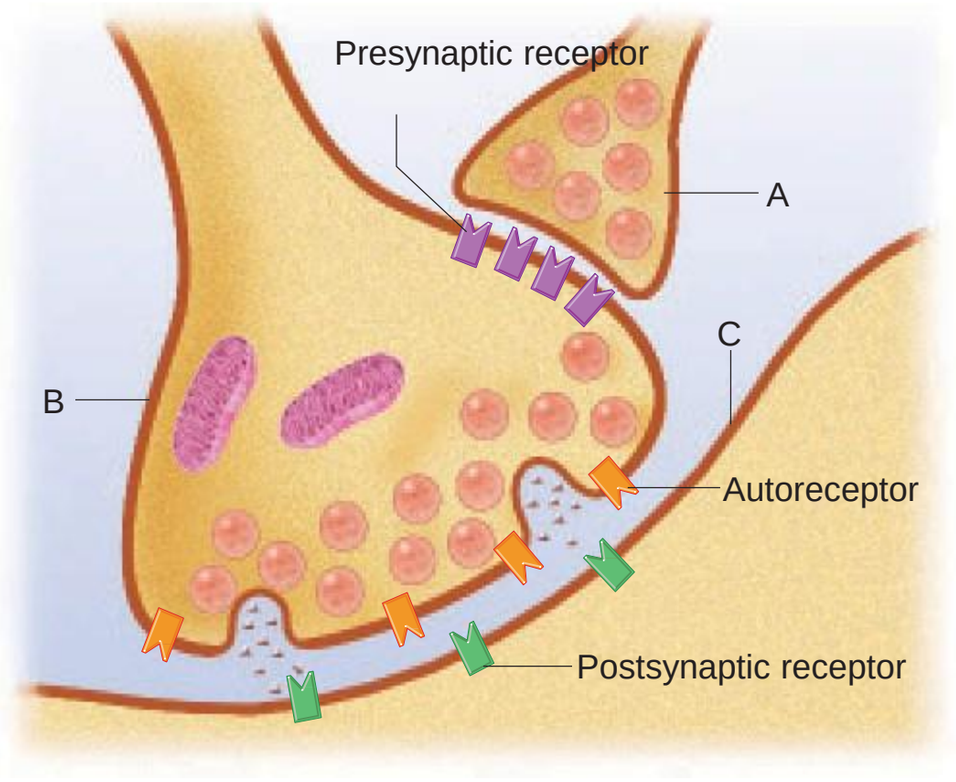
Comparison of excitatory and inhibitory synapses, showing current direction through the postsynaptic cell following synaptic activation.

(a) Current through the postsynaptic cell is away from the excitatory synapse, and may depolarize the initial segment.

(b) Current through the postsynaptic cell hyperpolarizes the membrane and may stabilize the initial segment. Arrow indicates moment of stimulus.

MODIFICATION OF SYNAPTIC TRANSMISSION BY DRUGS AND DISEASE





A presynaptic (axo-axonic) synapse between axon terminal A and axon terminal B. C is the final postsynaptic cell body.

Possible actions of drugs on a synapse: (A) Increase leakage of neurotransmitter from vesicle to cytoplasm, exposing it to enzyme breakdown, (B) increase transmitter release into cleft, (C) block transmitter release, (D) inhibit transmitter synthesis, (E) block transmitter reuptake, (F) block cleft enzymes that metabolize transmitter, (G) bind to receptor on postsynaptic membrane to block (antagonist) or mimic (agonist) transmitter action, and (H) inhibit or facilitate second-messenger activity within postsynaptic cell.

FACTORS THAT DETERMINE SYNAPTIC STRENGTH

I.Presynaptic factors

A.Availability of neurotransmitter

1.Availability of precursor molecules

2.Amount (or activity) of the rate-limiting enzyme in the pathway for neurotransmitter synthesis

B.Axon terminal membrane potential

C.Axon terminal calcium

D.Activation of membrane receptors on presynaptic terminal

1.Axo-axonic synapses

2.Autoreceptors

3.Other receptors

E.Certain drugs and diseases, which act via the above mechanisms A–D

II.Postsynaptic factors

A.Immediate past history of electrical state of postsynaptic membrane (that is, facilitation or inhibition from temporal or spatial summation)

B.Effects of other neurotransmitters or neuromodulators acting on postsynaptic neuron

C.Up- or down-regulation and desensitization of receptors

D.Certain drugs and diseases

III.General factors

A.Area of synaptic contact

B.Enzymatic destruction of neurotransmitter

C.Geometry of diffusion path

D.Neurotransmitter reuptake

NEUROTRANSMITTERS AND NEUROMODULATORS

- Certain chemical messengers elicit complex responses that cannot be simply described as EPSPs or IPSPs. The word "modulation" is used for these complex responses, and the messengers that cause them are called neuromodulators.
- Neuromodulators often modify the postsynaptic cell's response to specific neurotransmitters, amplifying or dampening the effectiveness of ongoing synaptic activity. Alternatively, they may change the presynaptic cell's synthesis, release, reuptake, or metabolism of a transmitter. In other words, they alter the effectiveness of the synapse.

1. Acetylcholine (ACh)

Acetylcholine (ACh) is a major neurotransmitter in the peripheral nervous system at the neuromuscular junction and in the brain. Fibers that release ACh are called cholinergic fibers. The cell bodies of the brain's cholinergic neurons are concentrated in relatively few areas, but their axons are widely distributed.

2. Biogenic amines

Catecholamines Dopamine (DA) Norepinephrine (NE) Epinephrine (Epi)
Serotonin (5-hydroxytryptamine, 5-HT) Histamine

3. Amino acids

Excitatory amino acids; for example, glutamate Inhibitory amino acids; for example, gamma-aminobutyric acid (GABA)

4. Neuropeptides; for example, endogenous opioids, oxytocin, tachykinins

5. Miscellaneous

Gases; for example, nitric oxide

Purines; for example, adenosine and ATP

REVIEW QUESTIONS

- Describe the direction of information flow through a neuron in response to input from another neuron. What is the relationship between the presynaptic neuron and the postsynaptic neuron?
- Contrast the postsynaptic mechanisms of excitatory and inhibitory synapses.
- Explain how synapses allow neurons to act as integrators; include the concepts of facilitation, temporal and spatial summation, and convergence in your explanation.
- List at least eight ways in which the effectiveness of synapses may be altered.
- Discuss differences between neurotransmitters and neuromodulators.
- Explain properties of EPSP and IPSP (origin, nature, differences).