NERVOUS SYSTEM WEEK 2

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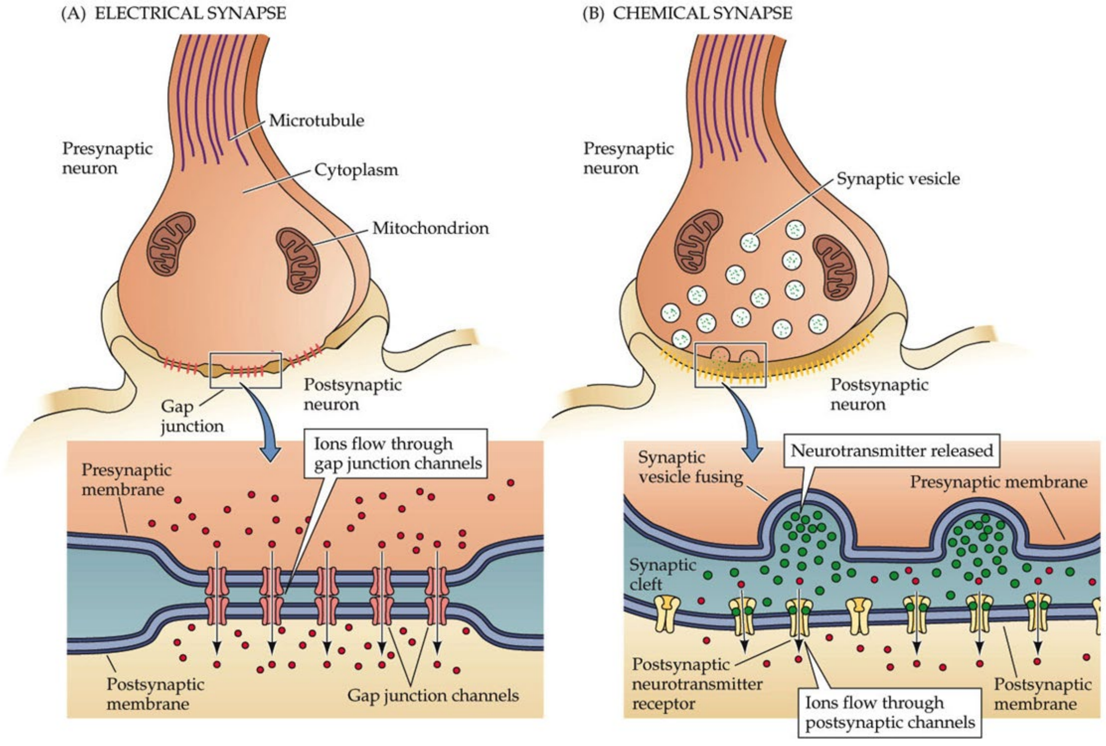
The synapse

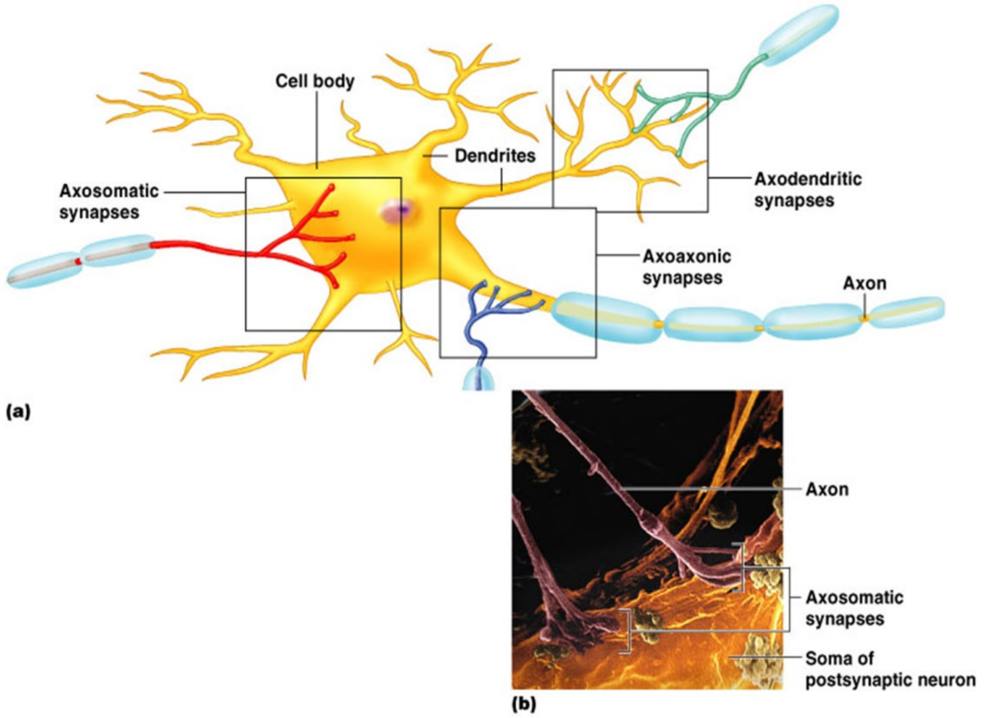
- A synapse is an anatomically specialized junction between two neurons, at which the electrical activity in one neuron, the presynaptic neuron, influences the electrical (or metabolic) activity in the second, postsynaptic neuron.
- Anatomically, synapses include parts of the presynaptic and postsynaptic neurons and the extracellular space between these two cells.



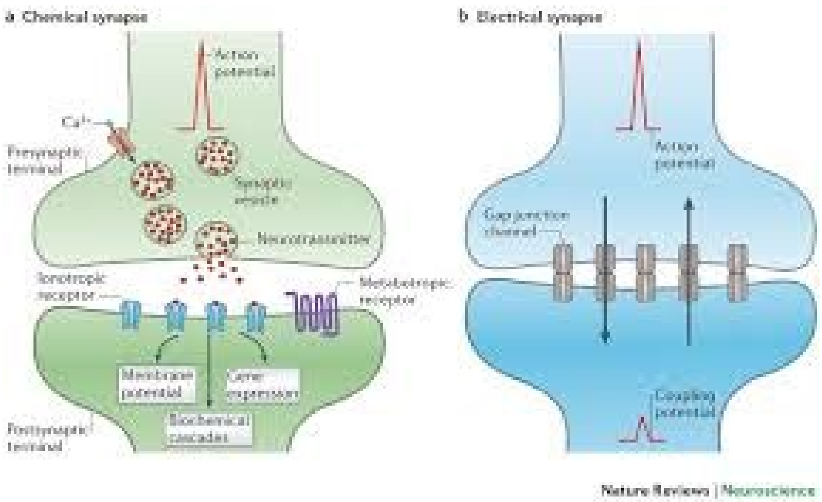
NEUROSCIENCE, *Fourth Edition*, **Figure 5.1**

Anatomical Types of Synapses

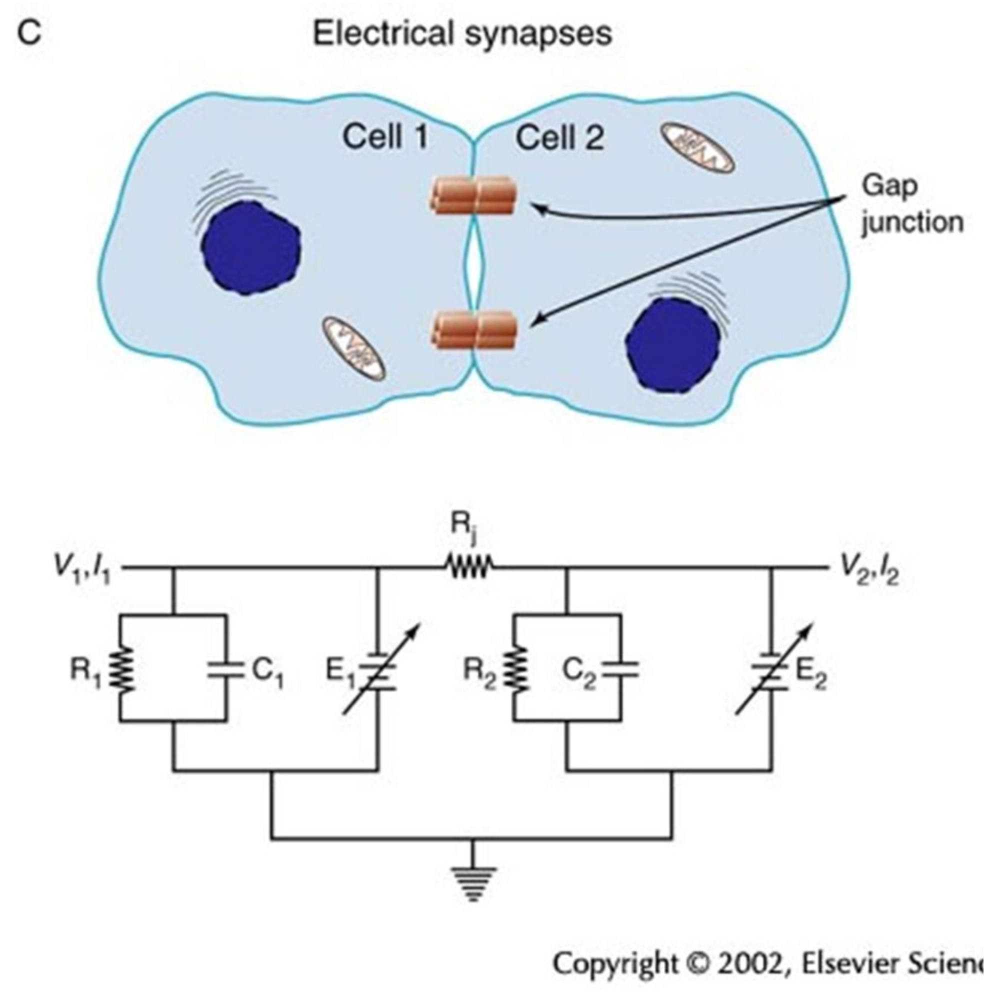
- **Axodendritic** – synapses between the axon of one neuron and the dendrite of another
- **Axosomatic** – synapses between the axon of one neuron and the soma of another
- Other types of synapses include:
  - Axoaxonic (axon to axon)
  - Dendrodendritic (dendrite to dendrite)
  - Dendrosomatic (dendrites to soma)



FUNCTIONAL ANATOMY OF SYNAPSES



- There are two types of synapses: **electrical** and **chemical.**
- At electrical synapses, the plasma membranes of the pre- and postsynaptic cells are joined by gap junctions
- These allow the local currents resulting from arriving action potentials to flow directly across the junction through the connecting channels in either direction from one neuron to the neuron on the other side of the junction, depolarizing the membrane to threshold and thus initiating an action potential in the second cell.
- Electrical synapses are relatively rare in the mammalian nervous system,

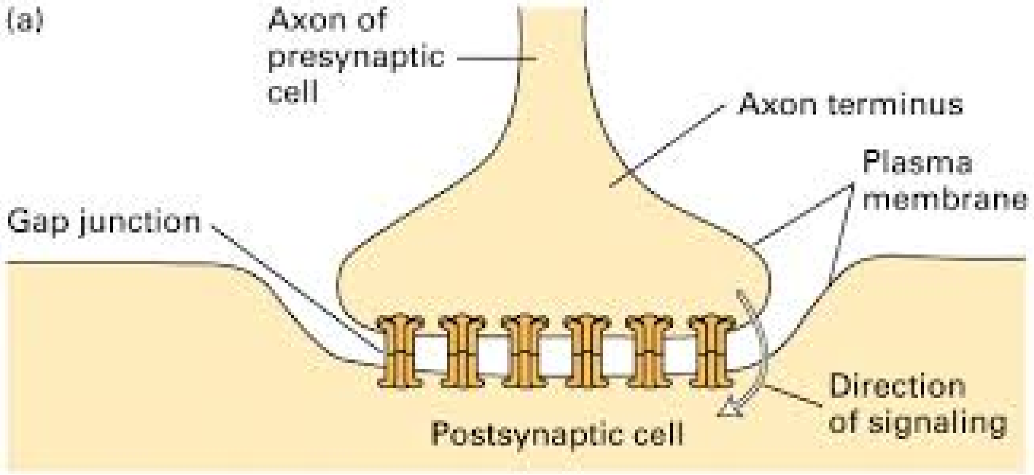


ELECTRICAL SYNAPSES

- Electrical synapses transmit signals more rapidly than chemical synapses do.
- Some synapses are both electrical and chemical. At these synapses, the electrical response occurs earlier than the chemical response.

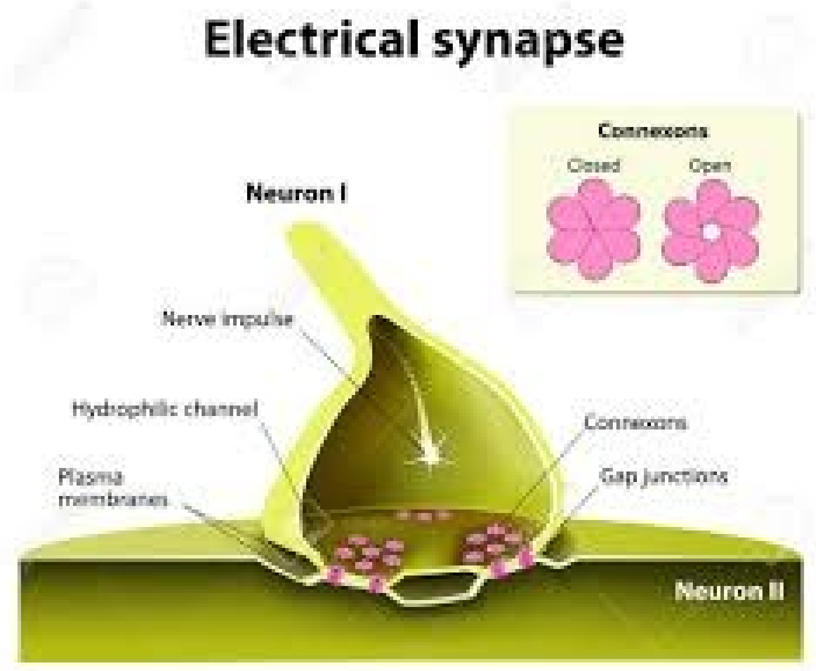
BENEFITS OF ELECTRICAL SYNAPSES

- They are fast.
- Also, electrical synapses allow for the synchronized activity of groups of cells.
- In many cases, they can carry current in both directions so that depolarization of a postsynaptic neuron will lead to depolarization of a presynaptic neuron.
- This kind of bends the definitions of presynaptic and postsynaptic!



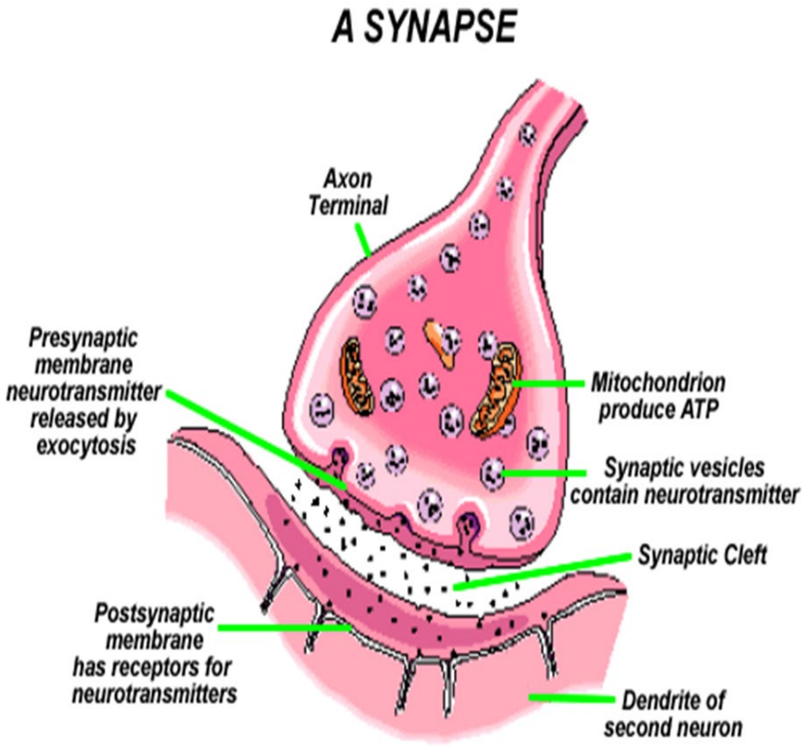
DOWNSIDES OF ELECTRICAL SYNAPSES

- Unlike chemical synapses, electrical synapses cannot turn an excitatory signal in one neuron into an inhibitory signal in another.
- More broadly, they lack the versatility, flexibility, and capacity for signal modulation that we see in chemical synapses.



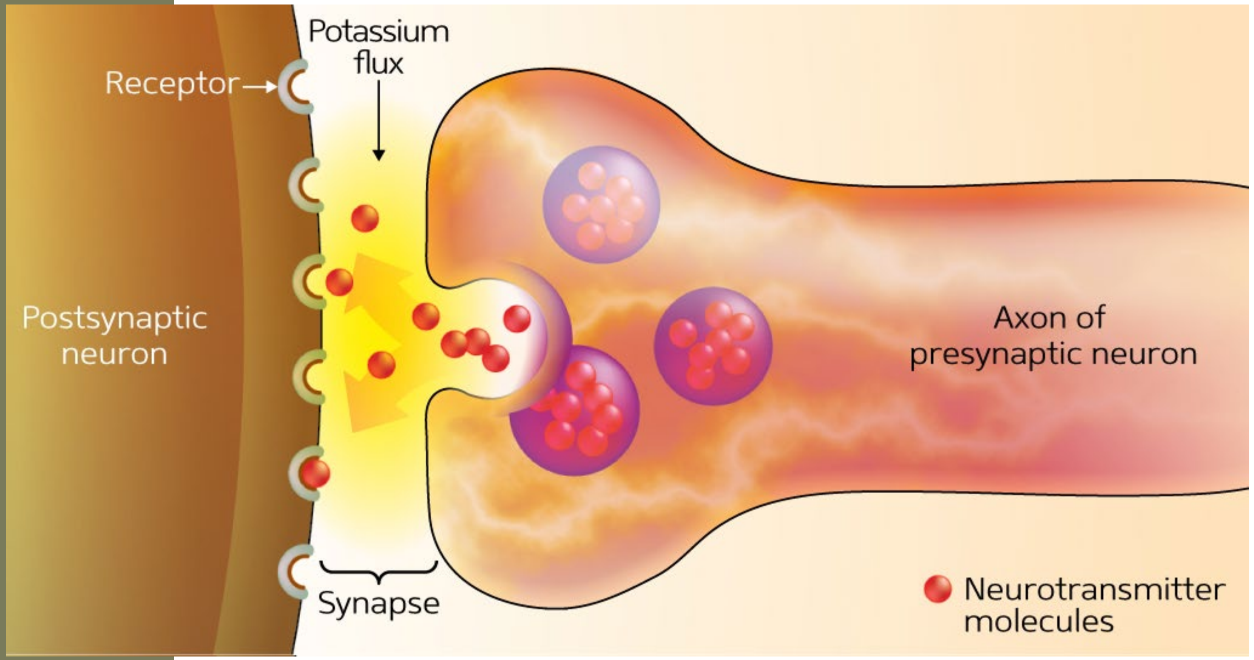
CHEMICAL SYNAPSES

- Almost all synapses used for signal transmission in the CNS of human being are chemical synapses.
- i.e. first neuron secretes a chemical substance called neurotransmitter at the synapse to act on receptor on the next neuron to excite it, inhibit or modify its sensitivity.
- The axon of the presynaptic neuron ends in a slight swelling, the axon terminal, and the postsynaptic membrane under the axon terminal appears denser.



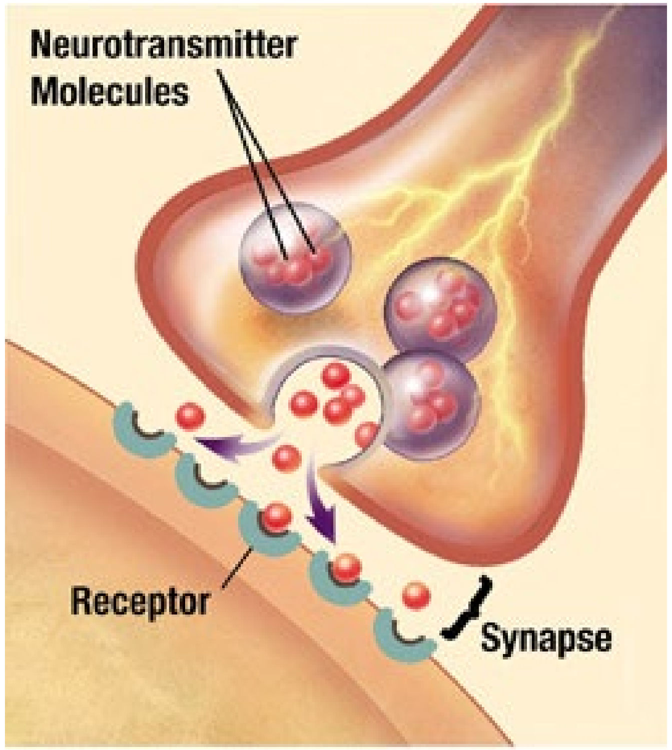
Synaptic Cleft

- separates the pre- and postsynaptic neurons and prevents direct propagation of the current from the presynaptic neuron to the postsynaptic cell.
- Instead, signals are transmitted across the synaptic cleft by means of a chemical messenger—a neurotransmitter released from the presynaptic axon terminal.



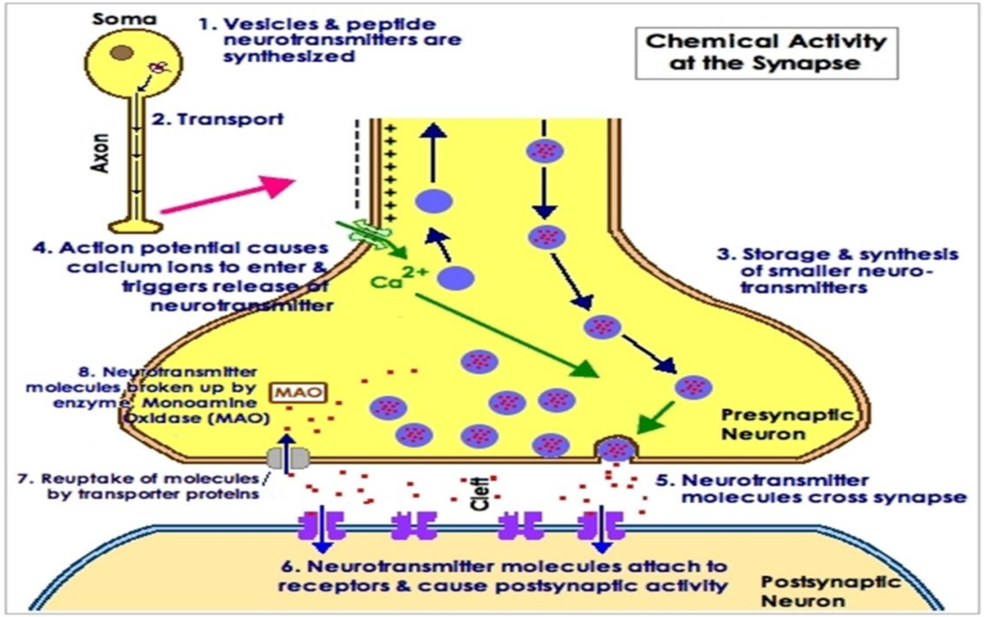
Synaptic Cleft

- Sometimes more than one neurotransmitter may be simultaneously released from an axon
- the additional neurotransmitter is called a **cotransmitter**.
- These neurotransmitters have different receptors in the postsynaptic cell.



Synaptic Transmission in Summary

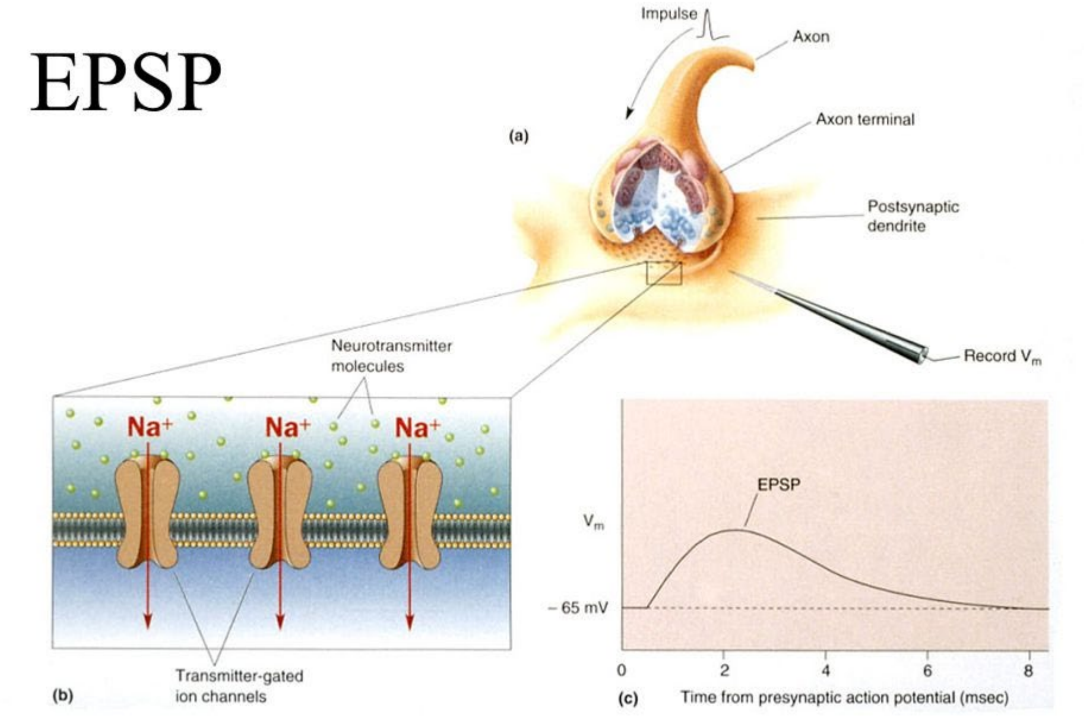
- Action potential arrives at presynaptic neuron's axon terminal and opens voltage-gated calcium channels
- Calcium enters neuron terminal and causes synaptic vesicle fusion with cell membrane
- Neurotransmitter exocytosis occurs
- Neurotransmitter diffuses across cleft and binds to receptors on postsynaptic neuron
- Ion channels in membrane of post-synaptic cell open, causing excitation or inhibition (graded potential)
- Neurotransmitter diffuses away from receptors as it is broken down in the cleft and/or taken back up by pre-synaptic neuron



Excitatory postsynaptic potential

- When a neurotransmitter binds to its receptor on a receiving cell, it causes ion channels to open or close.
- This can produce a localized change in the membrane potential—voltage across the membrane—of the receiving cell.
- In some cases, the change makes the target cell more likely to fire its own action potential.
- In this case, the shift in membrane potential is called an excitatory postsynaptic potential, or EPSP.

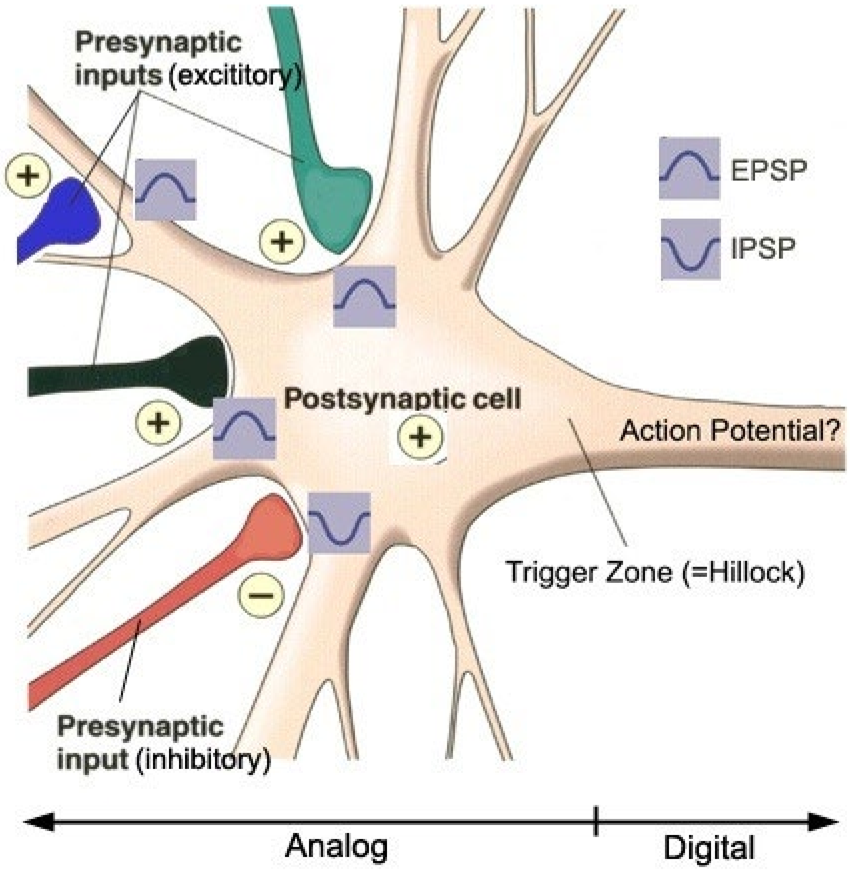
EPSP



Sodium ion flow inward is responsible for the generation of an EPSP.

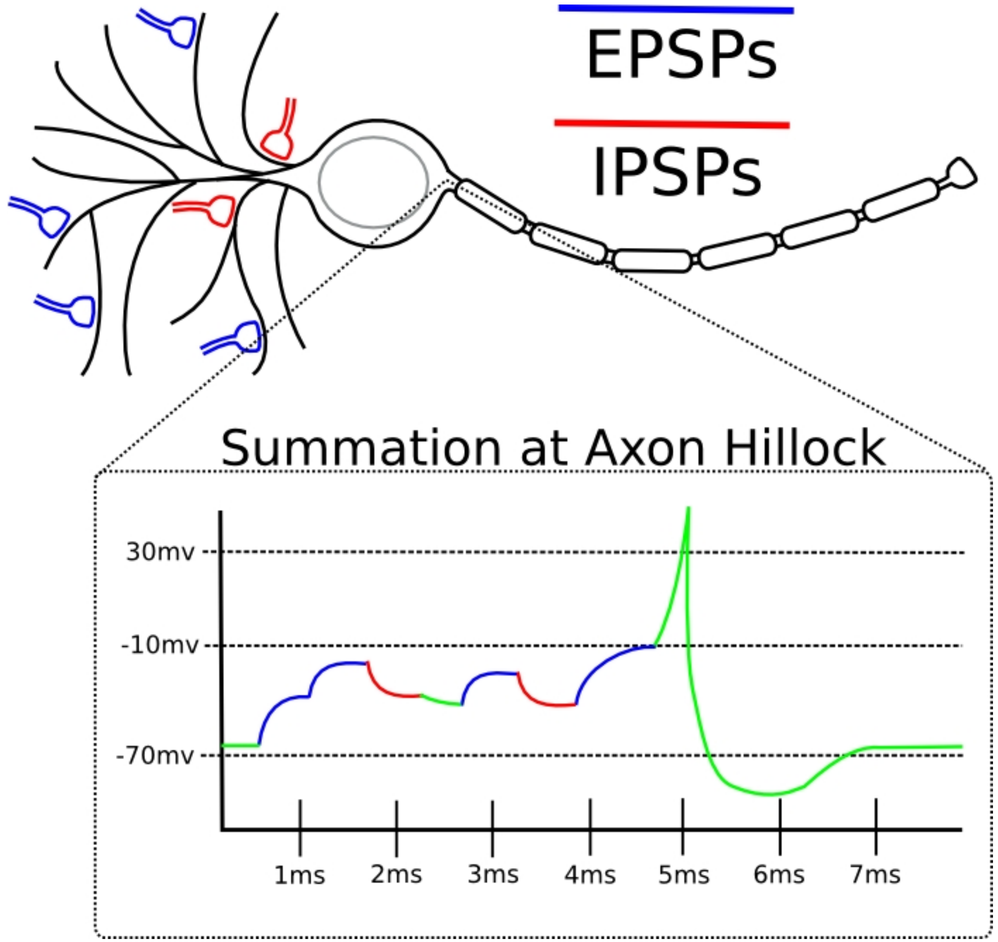
EPSP

- An EPSP is depolarizing: it makes the inside of the cell more positive, bringing the membrane potential closer to its threshold for firing an action potential.
- Sometimes, a single EPSP isn't large enough bring the neuron to threshold, but it can sum together with other EPSPs to trigger an **action potential**.
- The EPSP is a graded potential that spreads decrementally away from the synapse by local current.
- Its only function is to bring the membrane potential of the postsynaptic neuron closer to threshold.



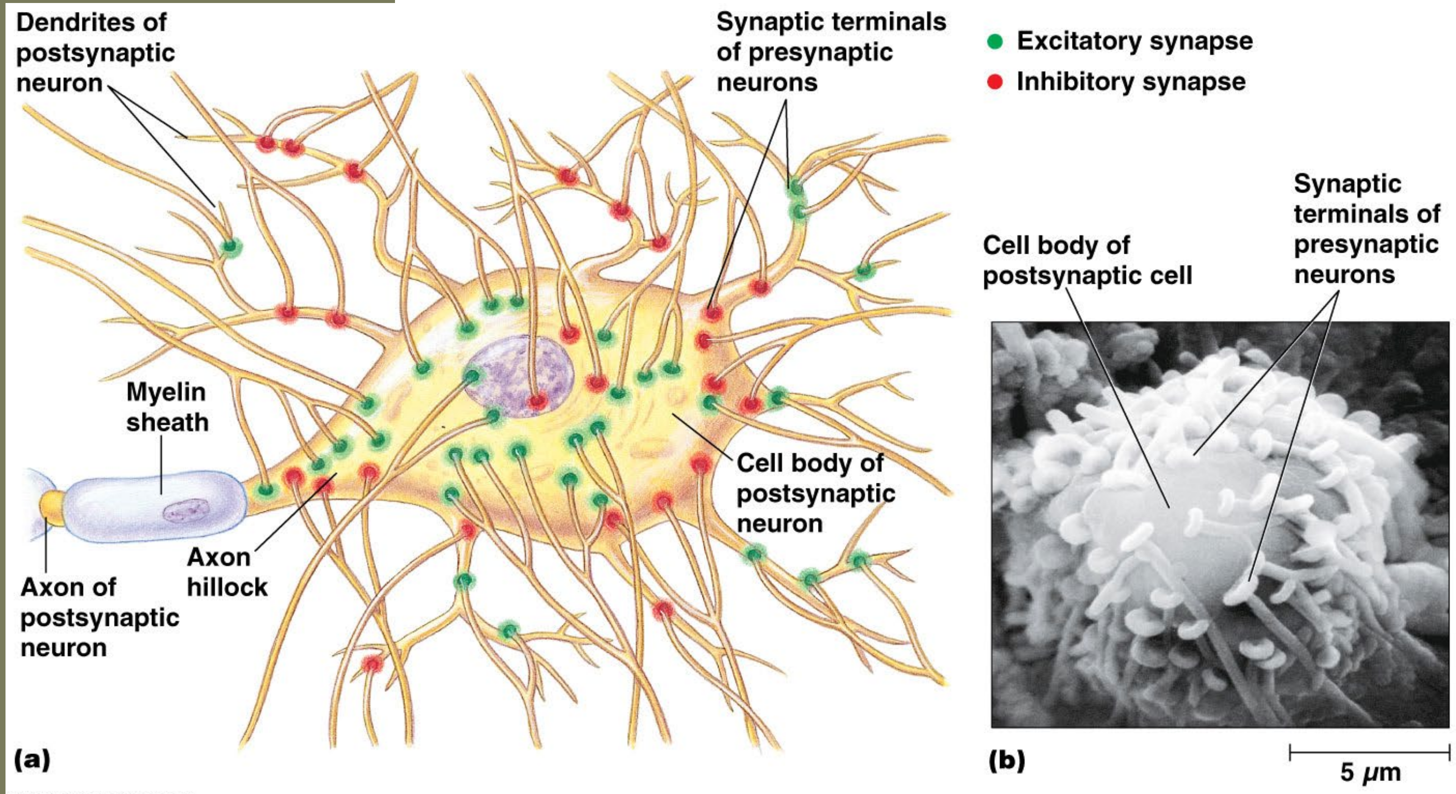
Inhibitory Synapses and IPSPs

- Neurotransmitter binds to and opens channels for K+ or Cl–
- Causes hyperpolarization (inside of cell becomes more negative)
- Reduces the postsynaptic neuron's ability to produce an action potential



Integration: Summation

- One EPSP cannot induce an action potential
- EPSPs can sum to reach threshold
- IPSPs and EPSPs can cancel each other out



SYNAPTIC TERMINATION

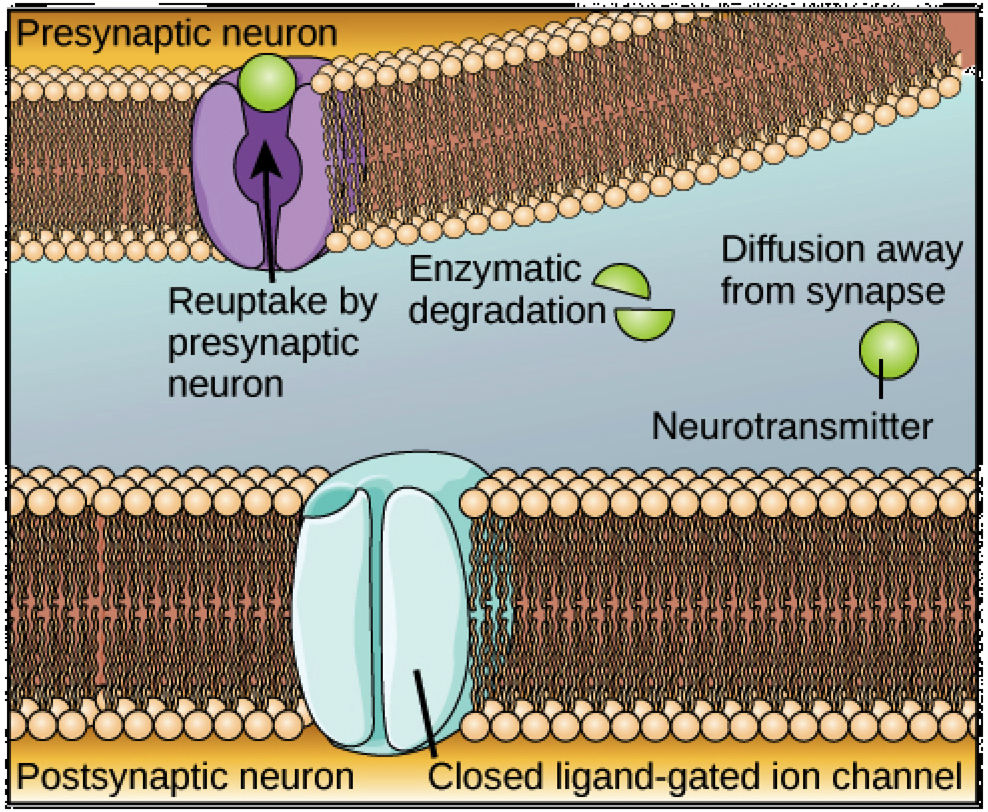
- A synapse can only function effectively if there is some way to "turn off" the signal once it's been sent.
- Termination of the signal lets the postsynaptic cell return to its normal resting potential, ready for new signals to arrive.
- For the signal to end, the synaptic cleft must be cleared of neurotransmitter.
- There are a few different ways to get this done:

✓ The neurotransmitter may be broken down by an enzyme,

✓ it may be sucked back up into the presynaptic neuron, or

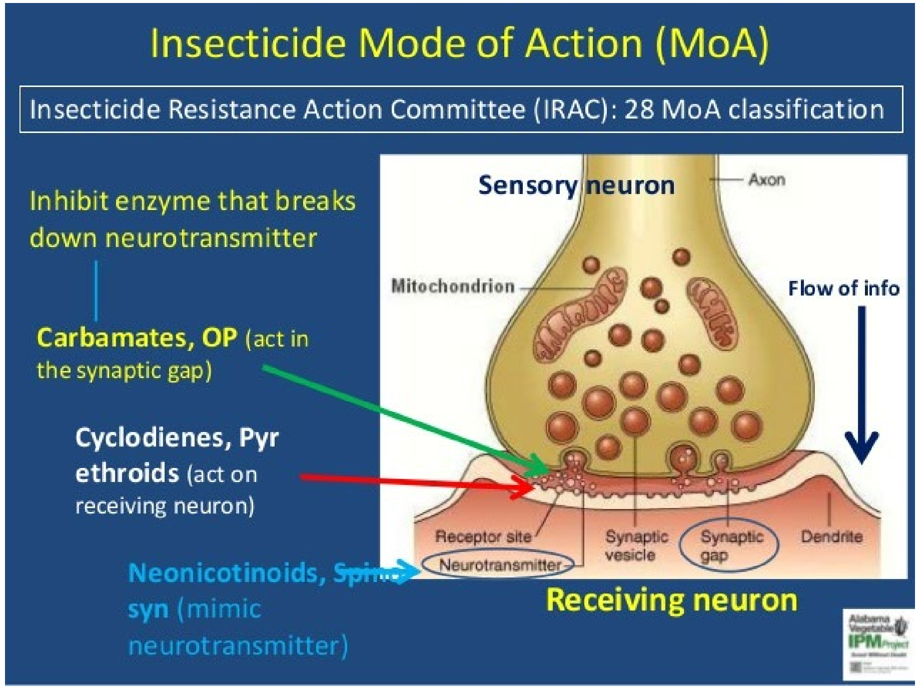
✓ it may simply diffuse away.

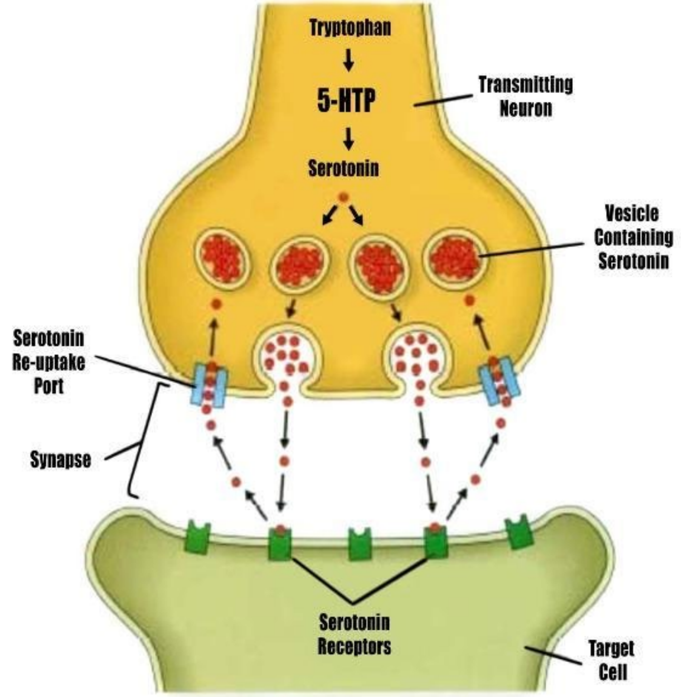
✓ In some cases, neurotransmitter can also be "mopped up" by nearby glial cells.



SYNAPTIC TERMINATION

- Anything that interferes with the processes that terminate the synaptic signal can have significant physiological effects.
- For instance, some insecticides kill insects by inhibiting an enzyme that breaks down the neurotransmitter acetylcholine.
- On a more positive note, drugs that interfere with reuptake of the neurotransmitter serotonin in the human brain are used as antidepressants.

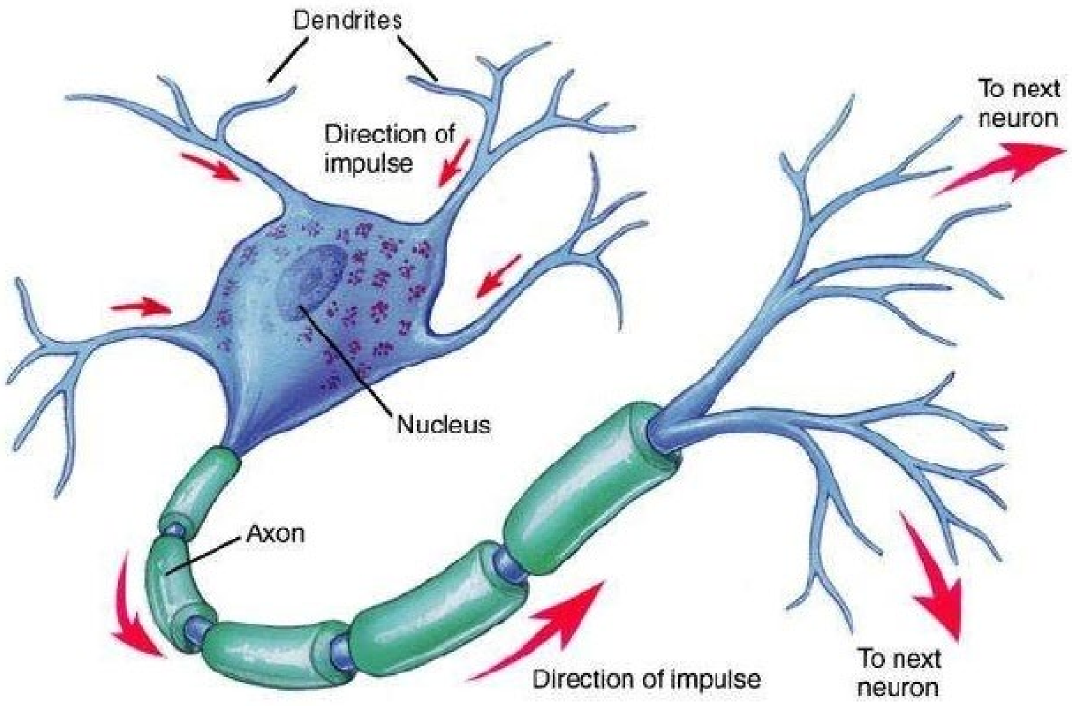




Synaptic properties

1. One-way conduction

Synapses generally permit conduction of impulses in one-way i.e. from pre-synaptic to post-synaptic neuron.

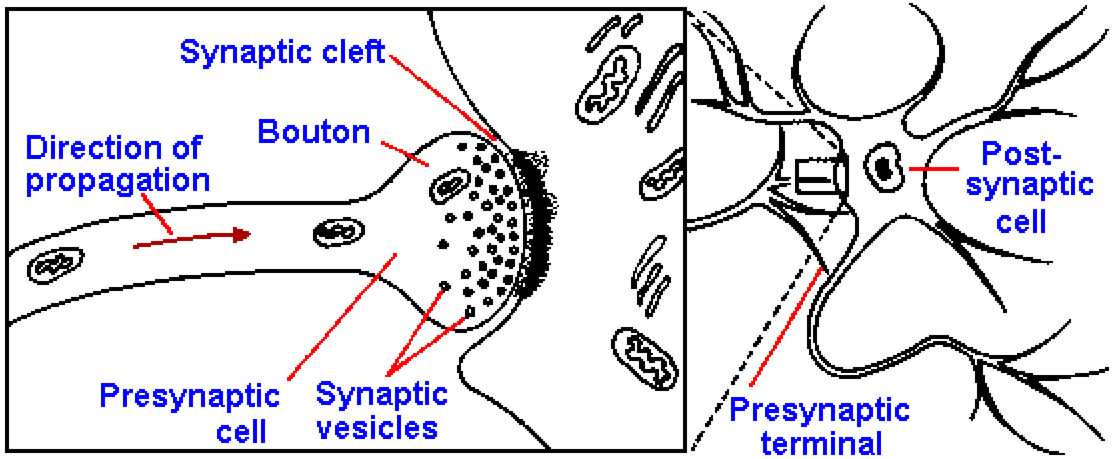


Remember, this is a specific, **ONE-WAY**, flow of messages along a neuron: impulses go from dendrite ---> cell body —> axon -—> dendrite —-> cell body ---> axon, etc.

2. Synaptic delay

Is the minimum time required for transmission across the synapse.
This time is taken by

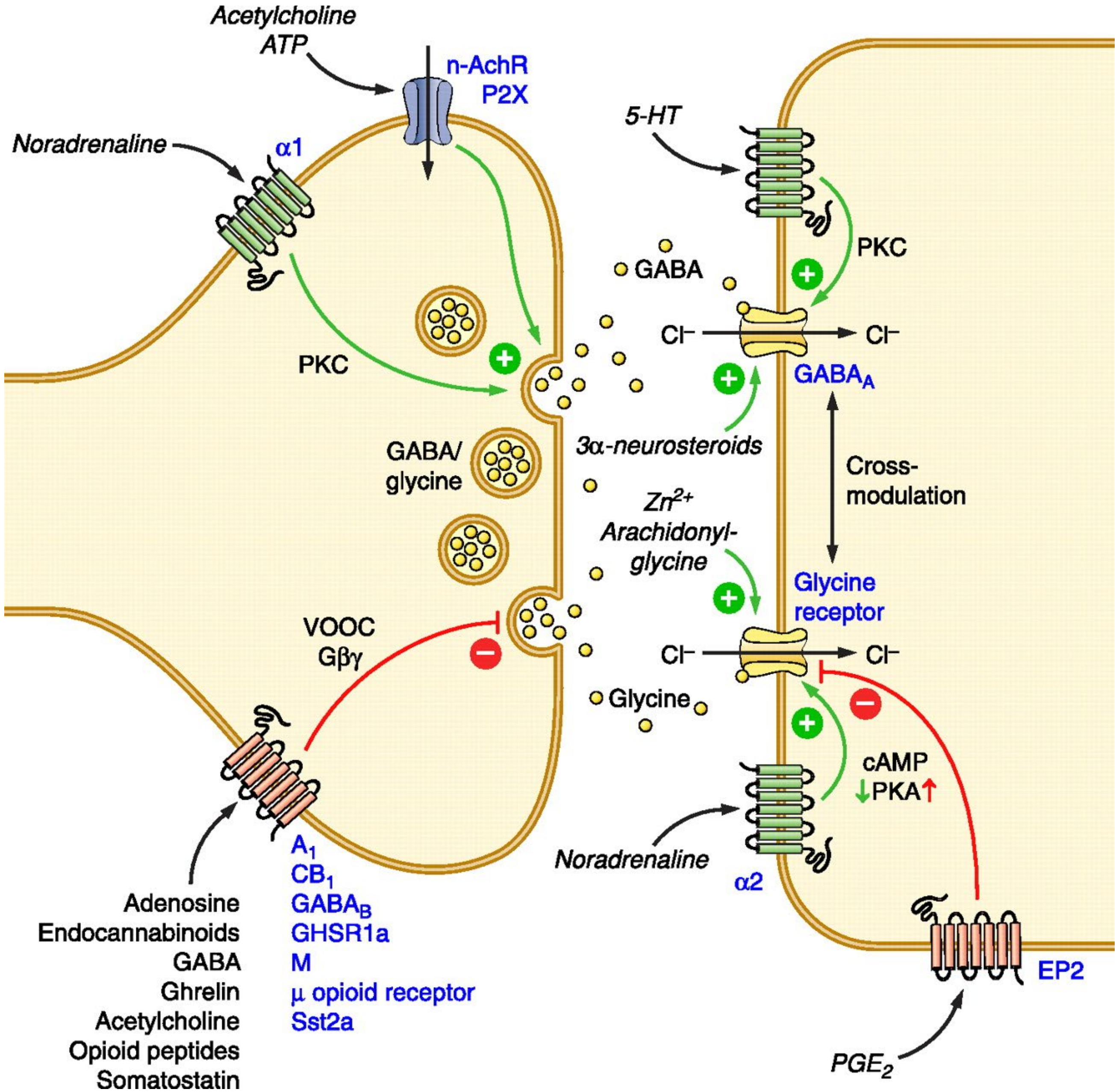
- Discharge of transmitter substance by pre-synaptic terminal
- Diffusion of transmitter to post-synaptic membrane
- Action of transmitter on its receptor
- Action of transmitter to ↑ membrane permeability
- Increased diffusion of Na+ to ↑ post-synaptic potential



3. Synaptic inhibition

Types:

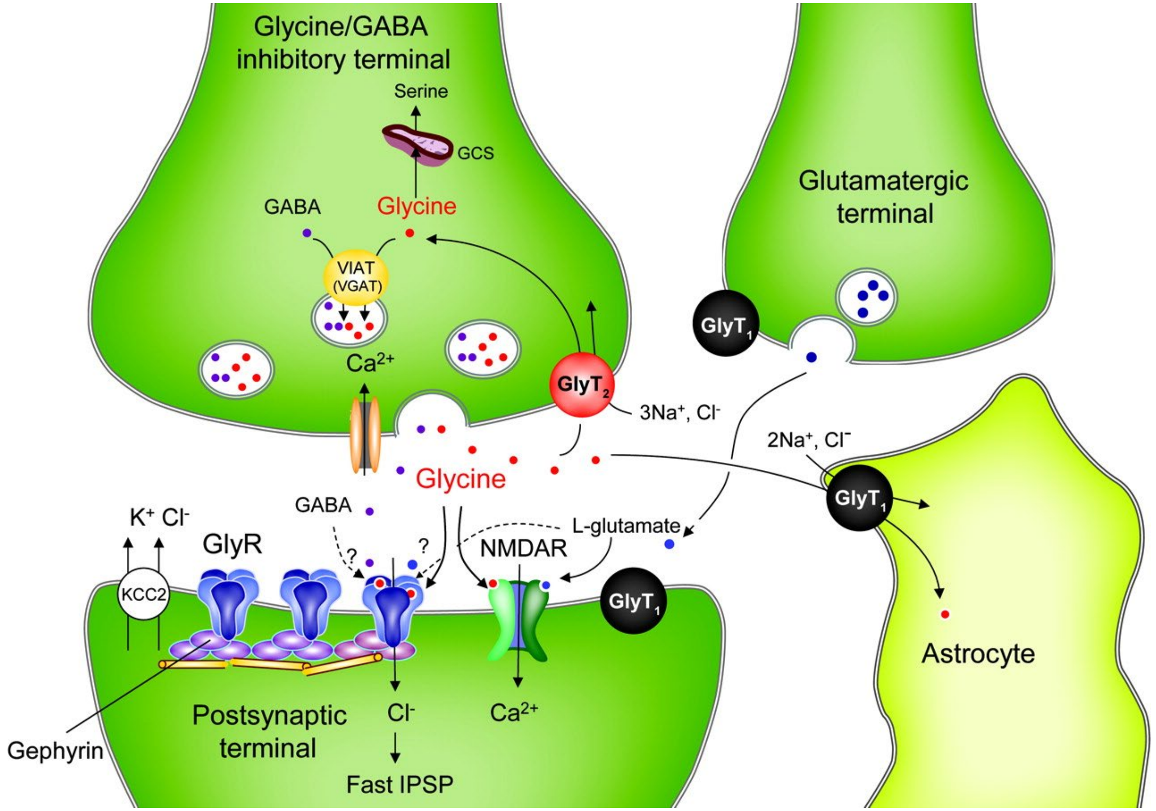
A. Direct inhibition
B. Indirect inhibition
C. Reciprocal inhibition
D. Inhibitory interneuron
E. Feed forward inhibition
F. Lateral inhibition



A. Direct inhibition

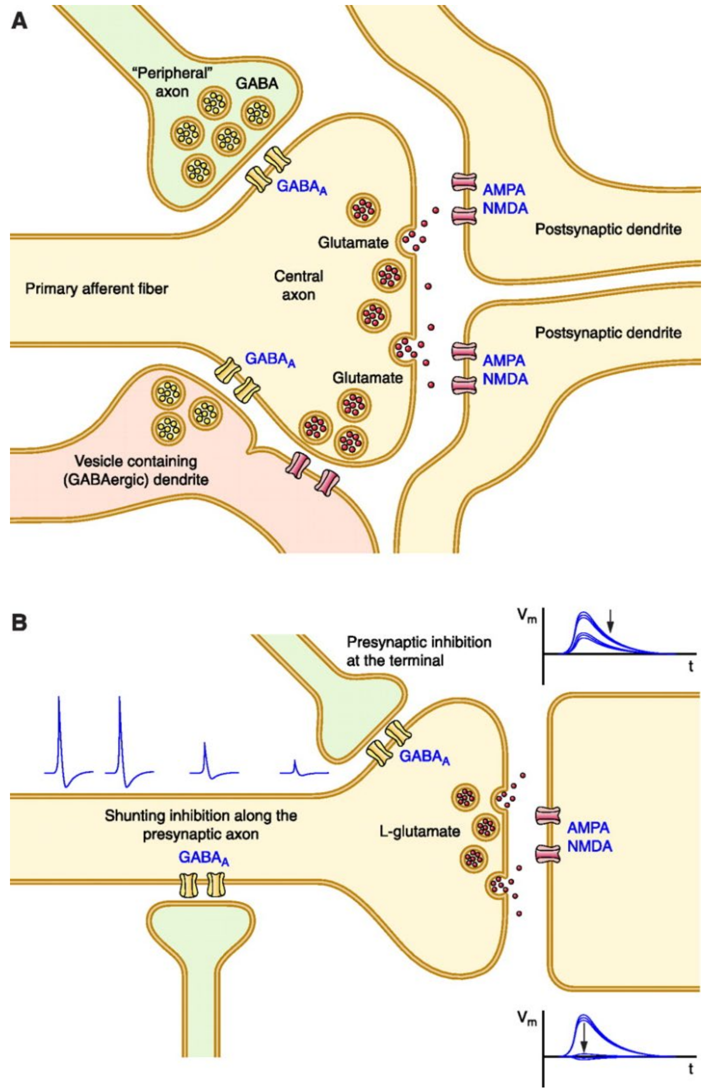
- Post-synaptic inhibition,
- e.g. some interneurones in sp. cord that inhibit antagonist muscles. Neurotransmitter secreted is Glycine.

- Occurs when an inhibitory neuron (releasing inhibitory substance) act on a post-synaptic neuron leading to → its hyperpolarization due to opening of Cl¯ [IPSPs] and/or K+ channels.



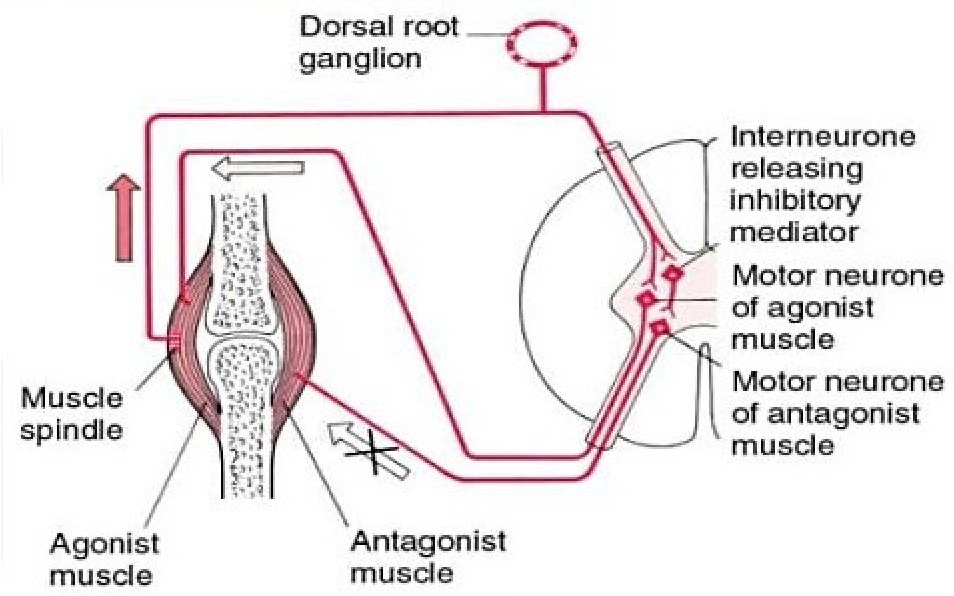
B. Indirect inhibition

- Pre-synaptic inhibition.
- Presynaptic Inhibition is a mechanism by which the amount of neurotransmitter released by an individual synapse can be reduced, resulting of less excitation of the post-synaptic neurone.
- The transmitter released at the inhibitory knob is GABA.
- The inhibition is produced by ↑ Cl^- and ↑ K+. e.g. occurs in dorsal horn → pain gating.



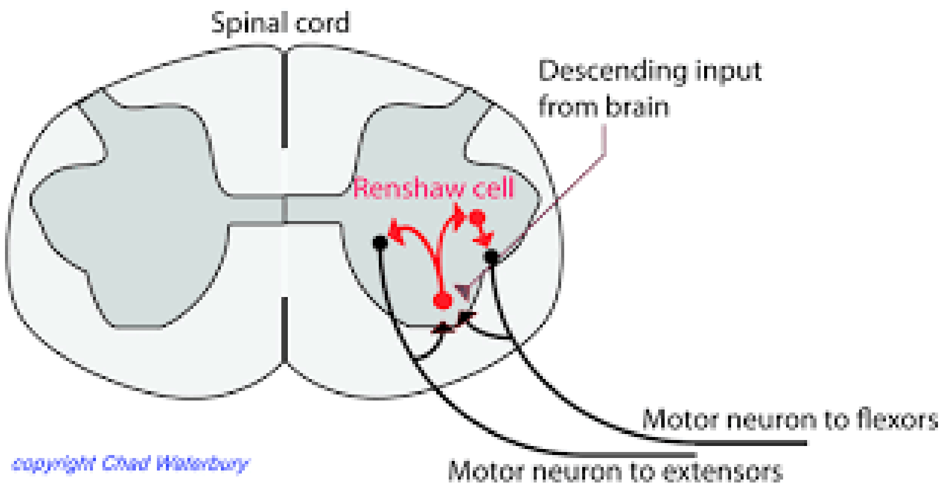
C. Reciprocal inhibition

- Inhibition of antagonist activity is initiated in the spindle in the agonist muscle.
- Impulses pass directly to the motor neurons supplying the same muscle and via branches to inhibitory interneurones that end on motor neurones of antagonist muscle.



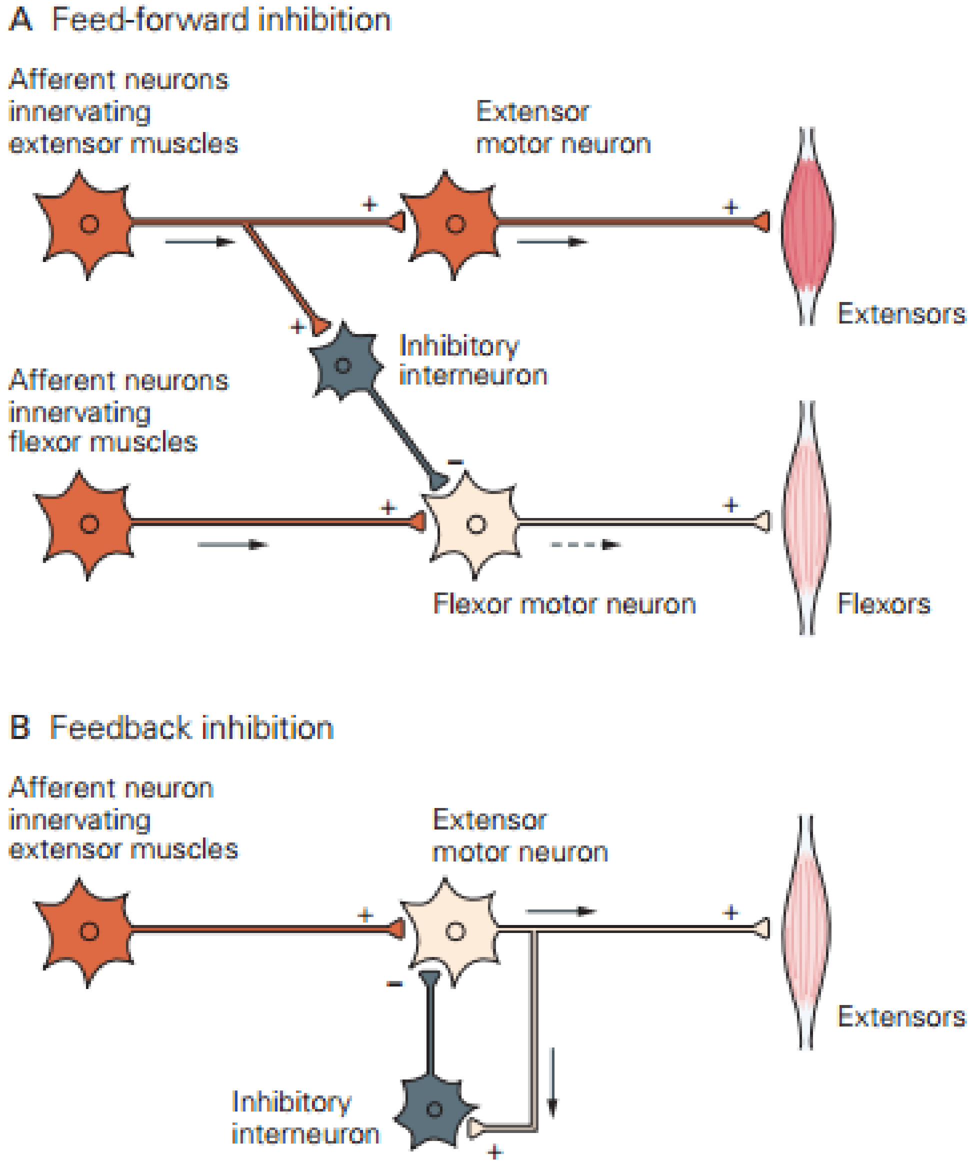
D. Inhibitory interneuron (Renshaw cells)

- The alpha motor neuron axon has a recurrent collateral in the spinal cord that synapses onto the Renshaw cell.
- The Renshaw cell directly inhibits the alpha motor neuron using glycine as the neurotransmitter.
- This is called recurrent inhibition.
- CNS actually inhibits muscle fibers of the same muscle that is contracting.
- It provides inhibitory feedback to the pool of alpha motor neurons to prevent excessive output.



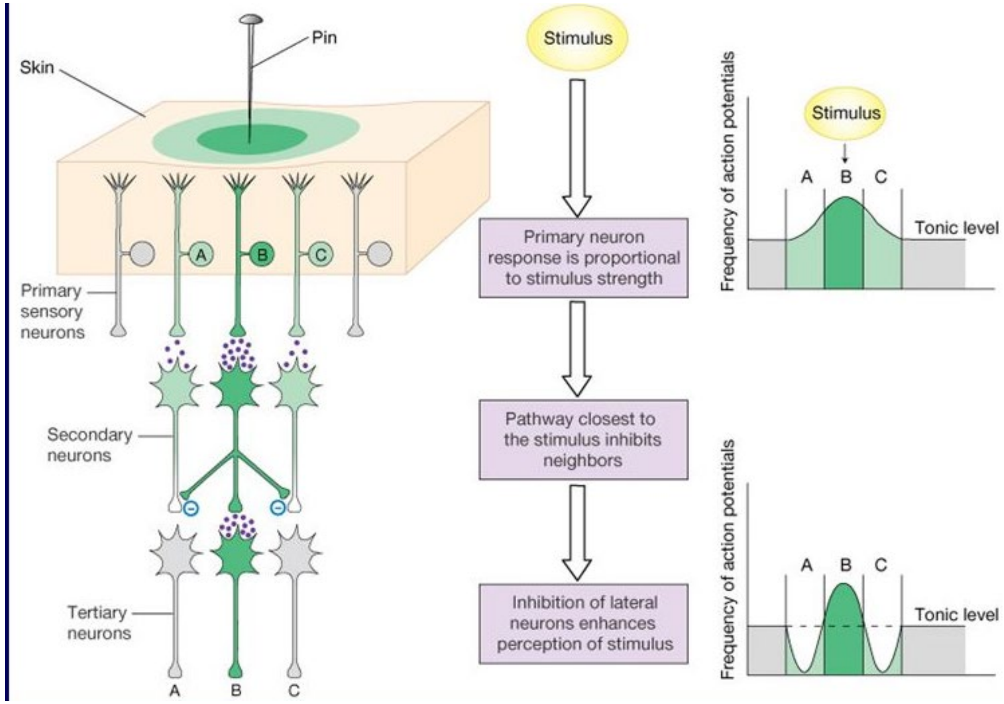
E. Feed forward inhibition

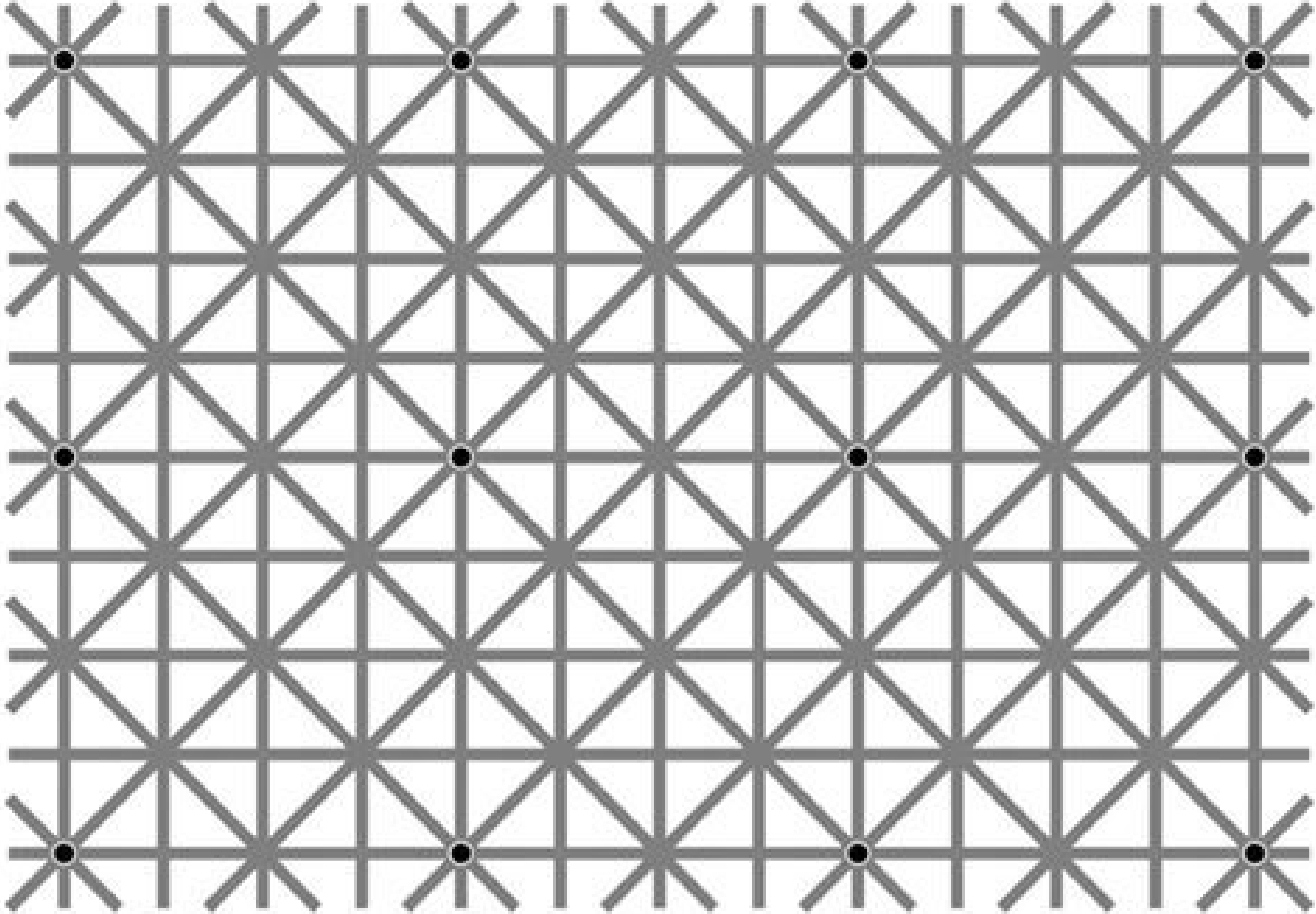
- Collateral branches of the excitatory afferent fibers excite inhibitory interneurons that inhibit neurons in the forward direction.
- Inhibitory pathways keep down the level of excitation and so suppress discharges from all weakly excited neurons. They also mold and modify the patterns of neuronal responses.
- Example: Iα afferent fibers from muscle receptors → spinal motor neurons.



F. Lateral inhibition

- Because of lateral inhibition, the lateral pathways are inhibited more strongly.
- This happens in pathways utilizing most accurate localization.

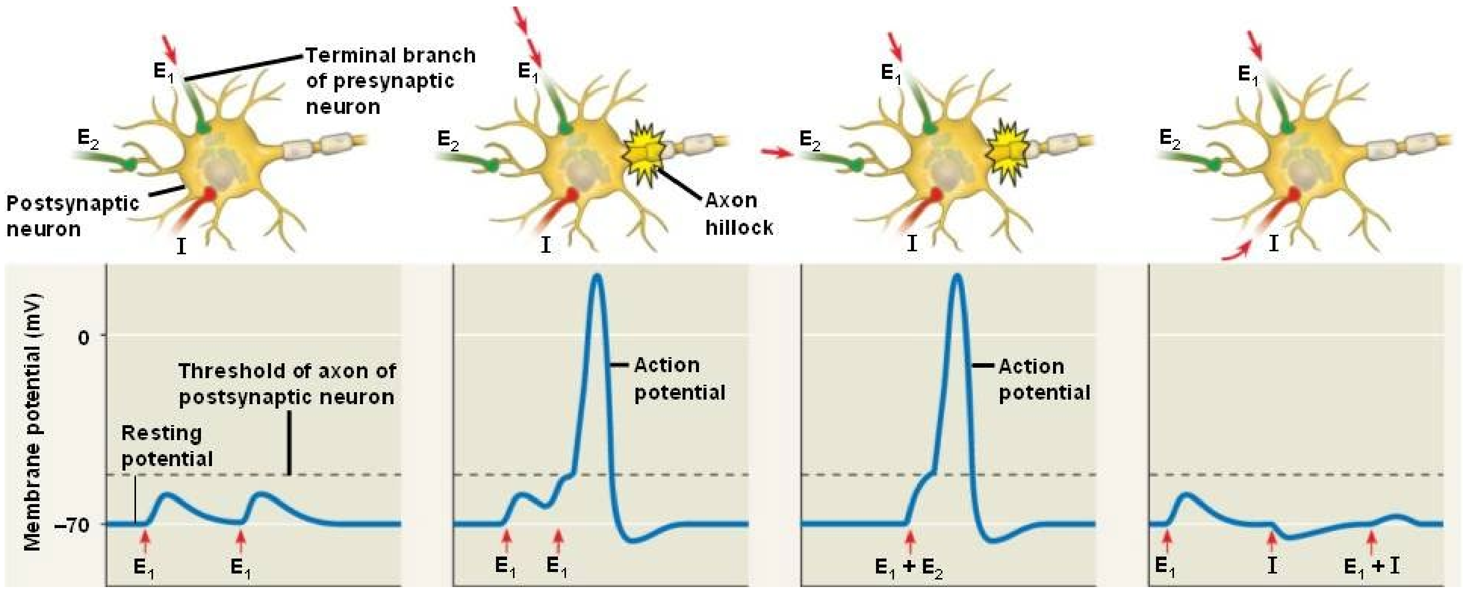




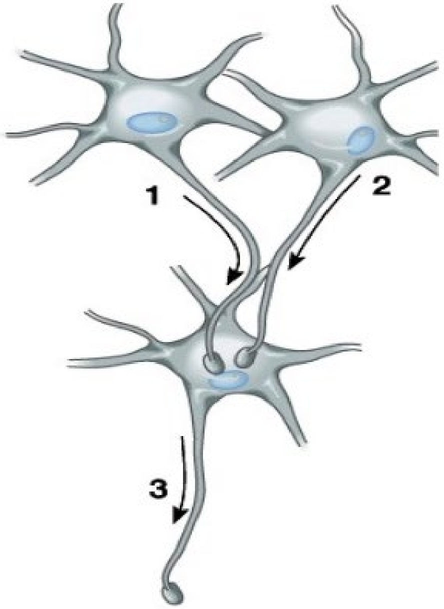
4. Summation

a) **Spatial summation.**
- When EPSP is in more than one synaptic knob at same time.

a) **Temporal summation.**
- If EPSP in pre-synaptic knob are successively repeated without significant delay so the effect of the previous stimulus is summated to the next

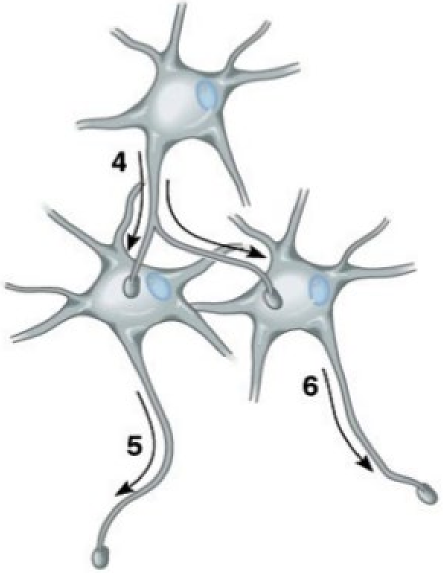


5. Convergence and divergence



Convergence

- When many pre-synaptic neurons converge on any single post-synaptic neuron.

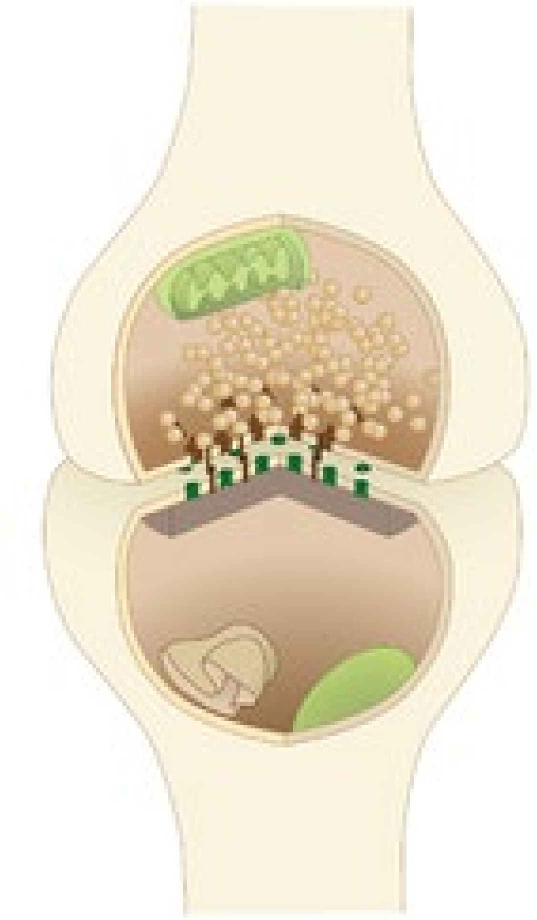


Divergence

- Axons of most pre-synaptic neurons divide into many branches that diverge to end on many post-synaptic neuron.

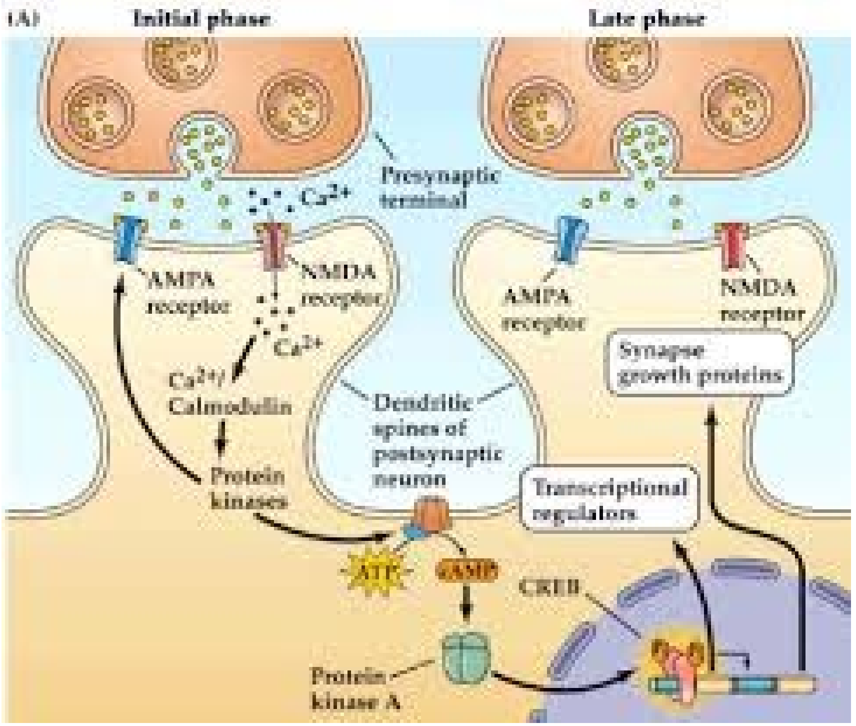
7. Fatigue

- Exhaustion of nerve transmitter.
- If the pre synaptic neurons are continuously stimulated there may be an exhaustion of the neurotransmitter. Resulting is stoppage of synaptic transmission.
- The post synaptic membrane become less sensitive to the neurotransmitter.



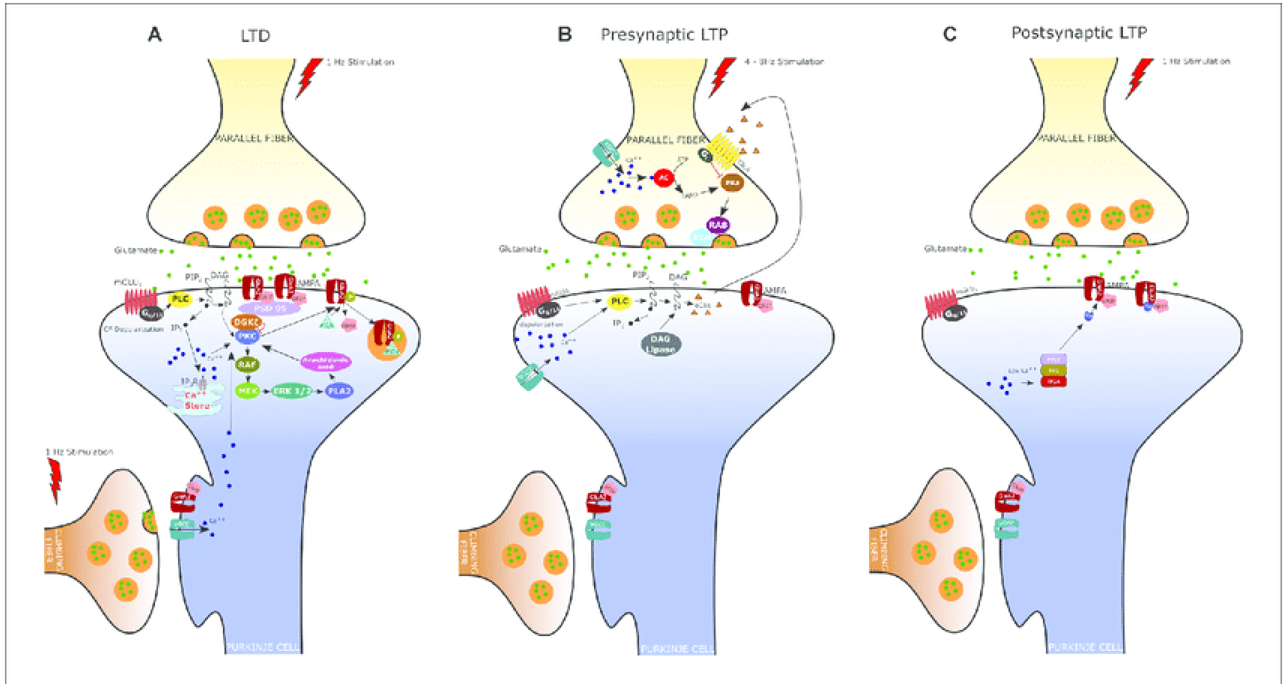
8. Long-term potentiation = LTP

- Long-term potentiation (LTP) is a persistent strengthening of synaptic connections induced by a brief period of high-frequency presynaptic activity
- ⬆Ca++ intracellular in post-synaptic membrane.
- Amygdala N-methyl-D-aspartate NMDA receptors.



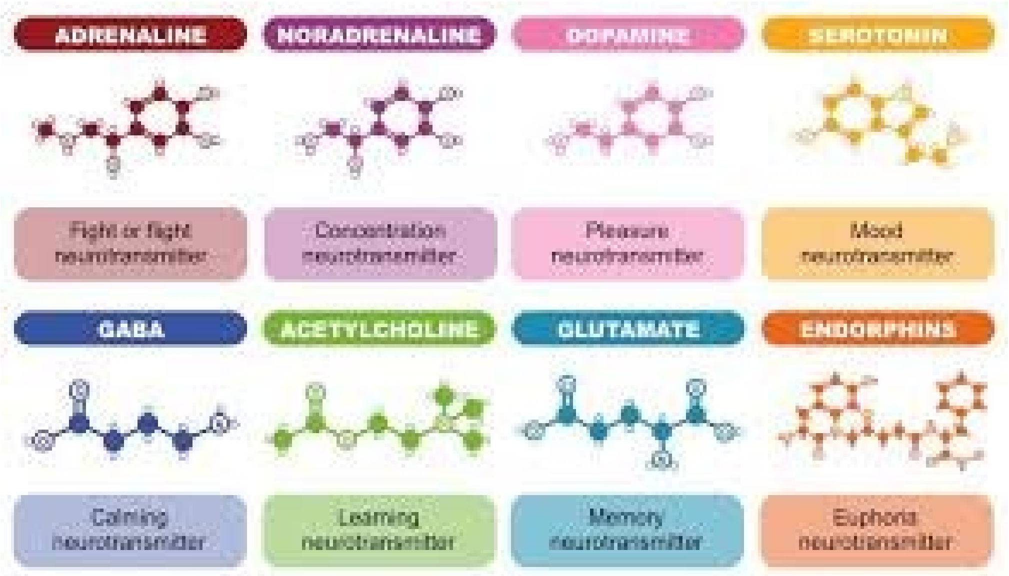
9. Long-term depression

- First noted in Hippocampus
- Later shown Through brain
- Opposite of LTP
- ↓ synaptic strength
- Caused by slower of pre-synaptic neurone
- Smaller rise of Ca++
- Occure in amino 3 hydroxy -5-methylisoxazole4-propionate AMPA receptors



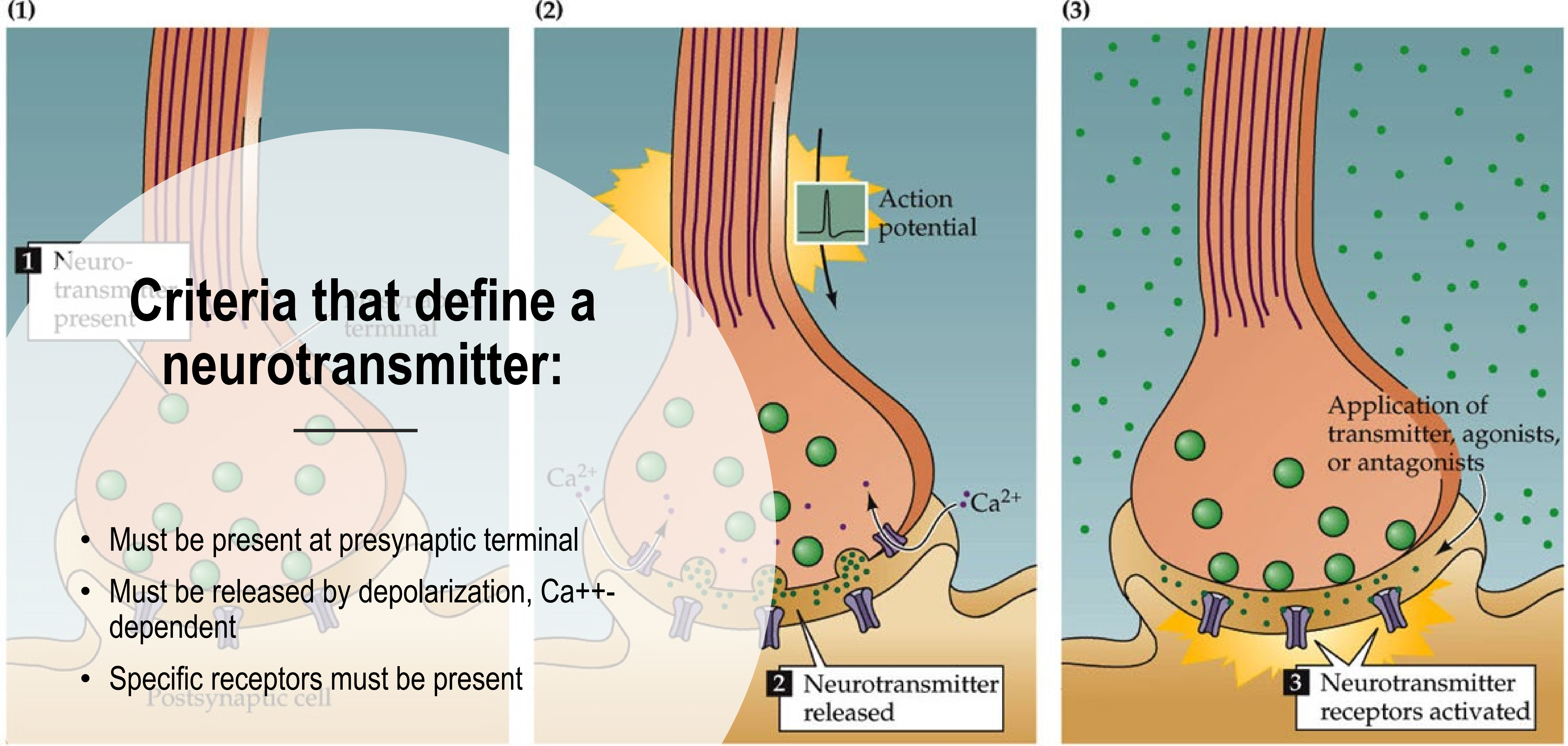
Neurotransmitters

- Most neurons make two or more neurotransmitters, which are released at different stimulation frequencies
- 50 or more neurotransmitters have been identified
- Classified by chemical structure and by function



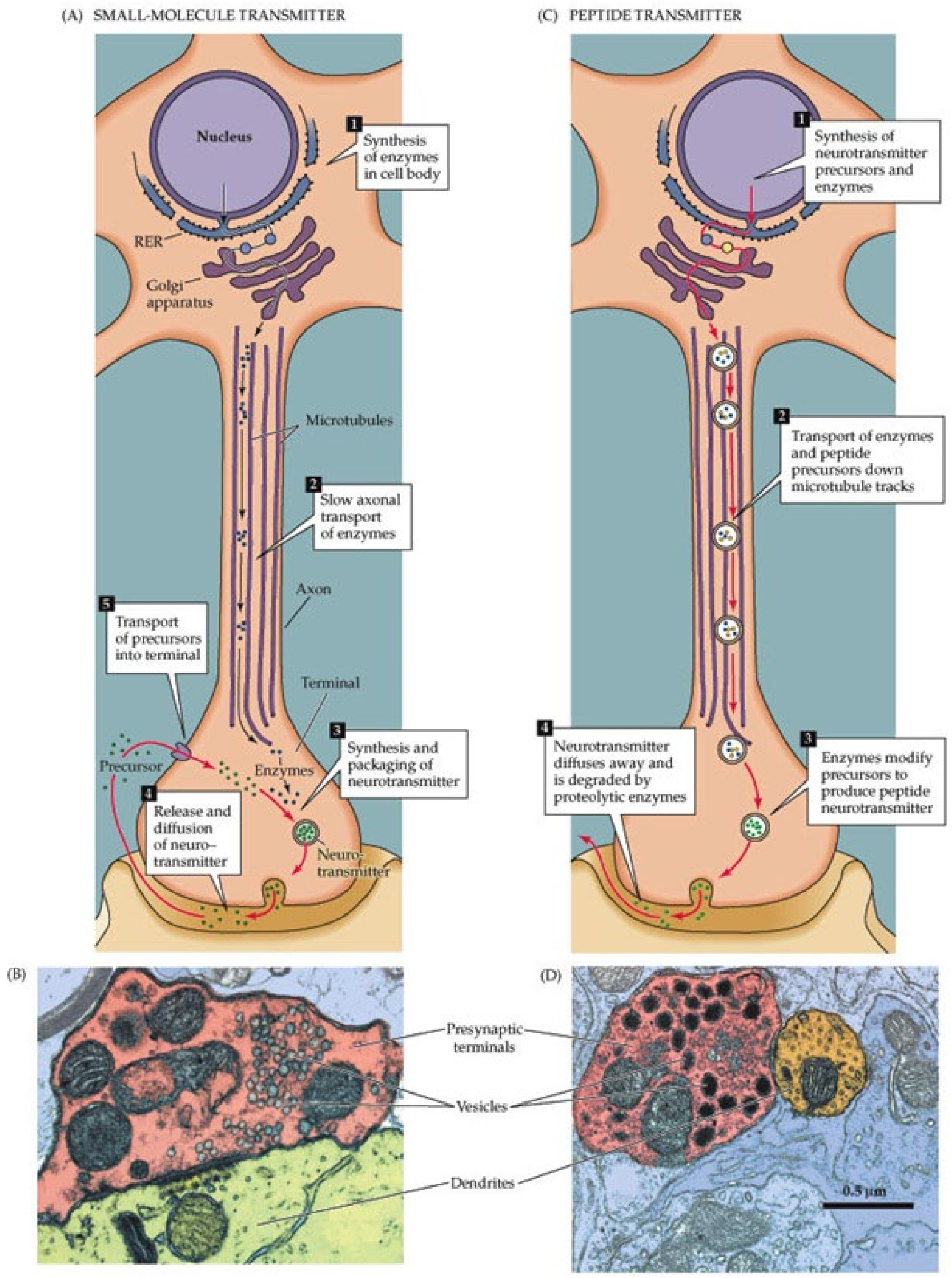
Criteria that define a neurotransmitter:

- Must be present at presynaptic terminal
- Must be released by depolarization, Ca++-dependent
- Specific receptors must be present



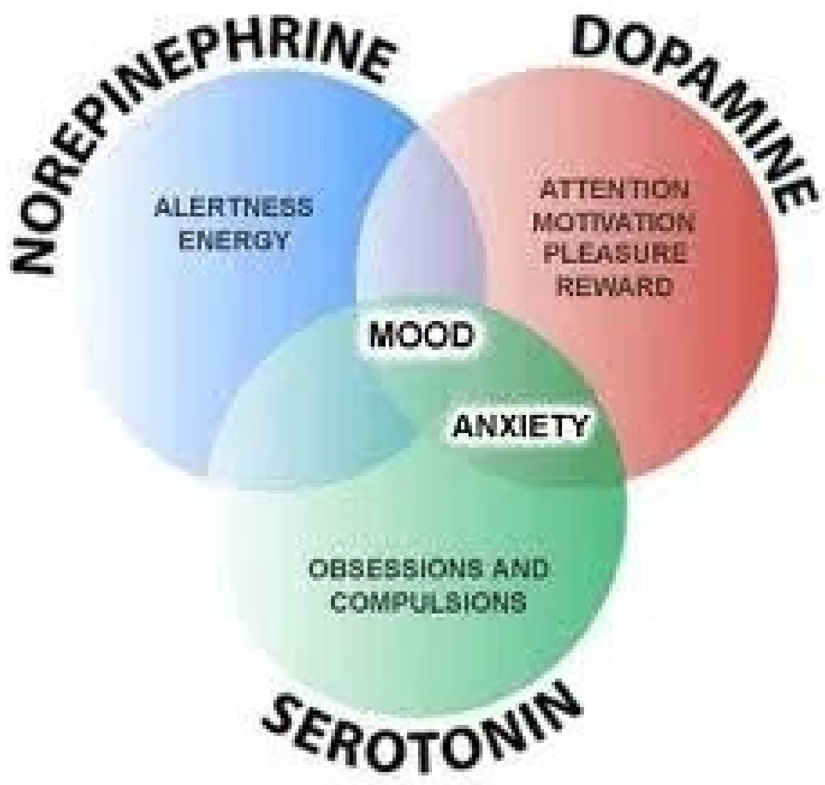
SYNTHESIS OF NTs

- Small molecule transmitters are synthesized at terminals, packaged into small clear-core vesicles (often referred to as 'synaptic vesicles'
- Peptides, or neuropeptides are synthesized in the endoplasmic reticulum and transported to the synapse, sometimes they are processed along the way. Neuropeptides are packaged in large dense-core vesicles



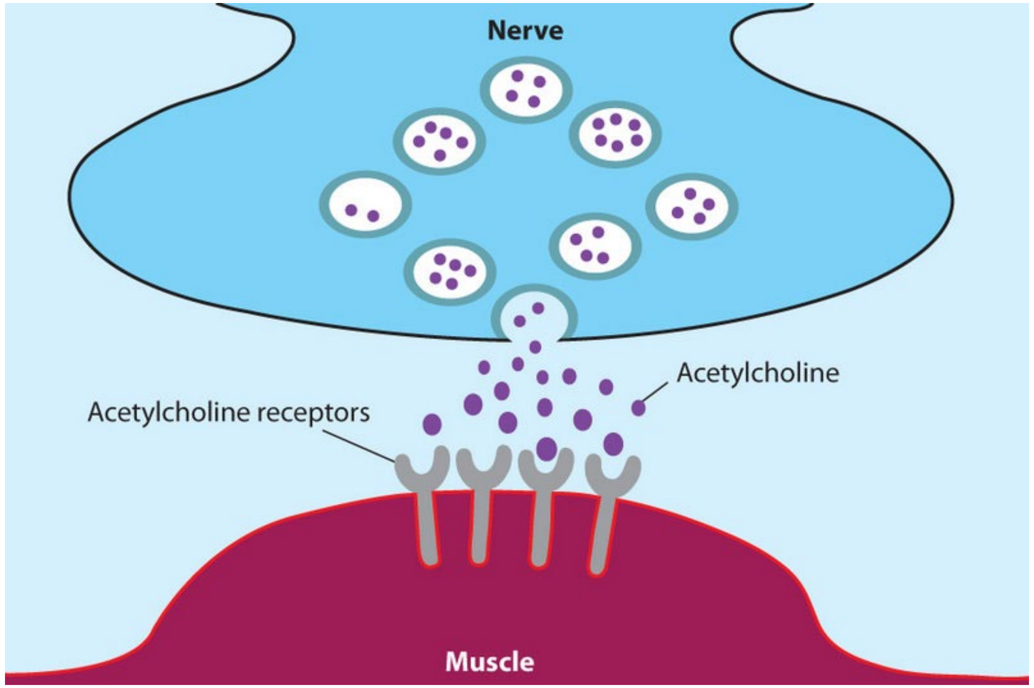
Conventional neurotransmitters

- The chemical messengers that act as conventional neurotransmitters share certain basic features.
- They are stored in synaptic vesicles, get released when Ca2+ enters the axon terminal in response to an action potential, and act by binding to receptors on the membrane of the postsynaptic cell.



Chemical Classes of Neurotransmitters

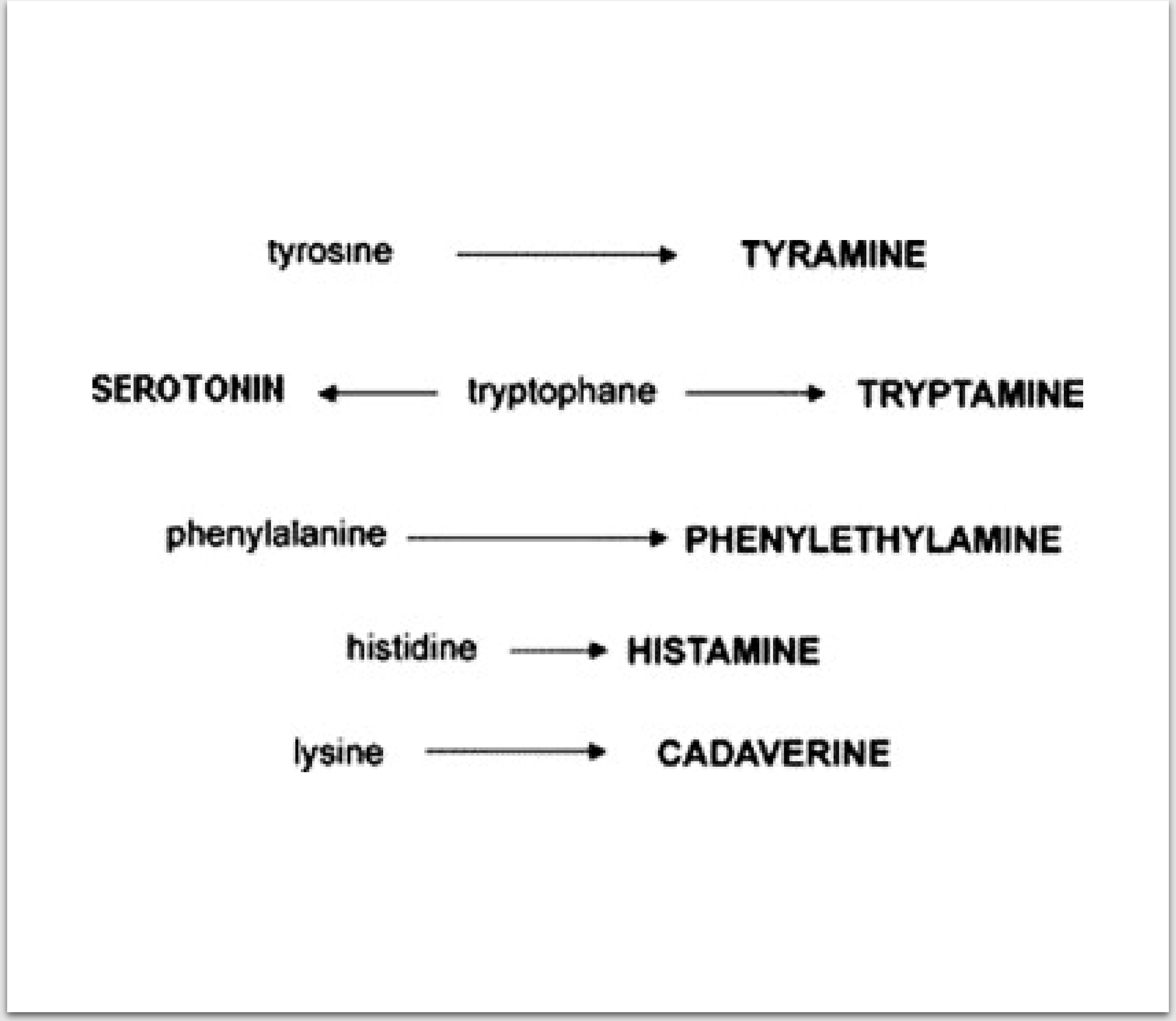
- **Acetylcholine (Ach)**
  - Released at neuromuscular junctions and some autonomic neurons
  - Synthesized in the pre-synaptic neuron
  - Degraded by acetylcholinesterase (AChE)



Biogenic amines

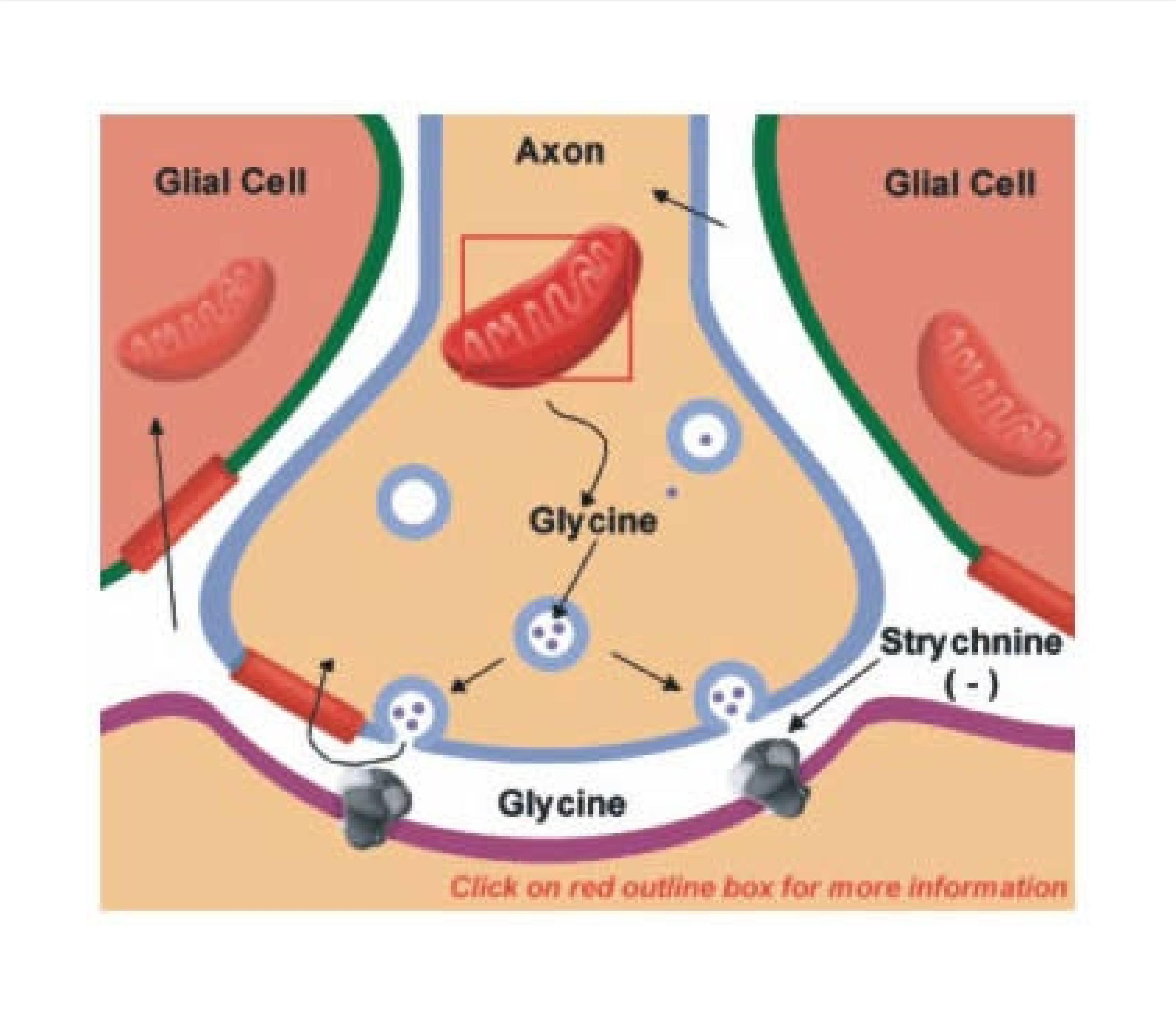
- Norepinephrine (NE)
- Epinephrine
- Serotonin
- Dopamine
- Many others

- Broadly distributed in the brain
- Play roles in emotional behaviors and the biological clock



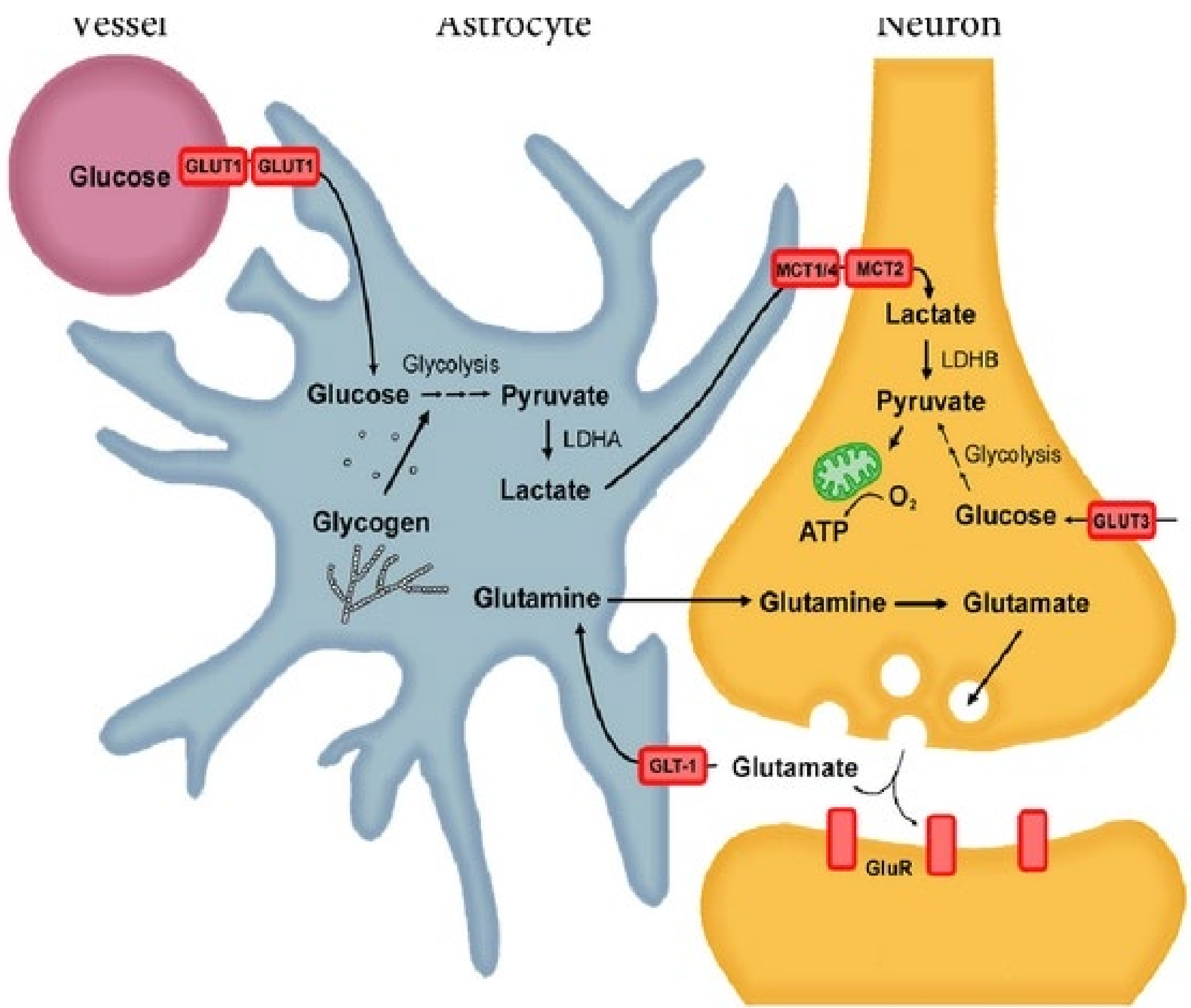
Amino acids

- GABA—Gamma (γ)-aminobutyric acid
- Glutamate
- Glycine
- Many others



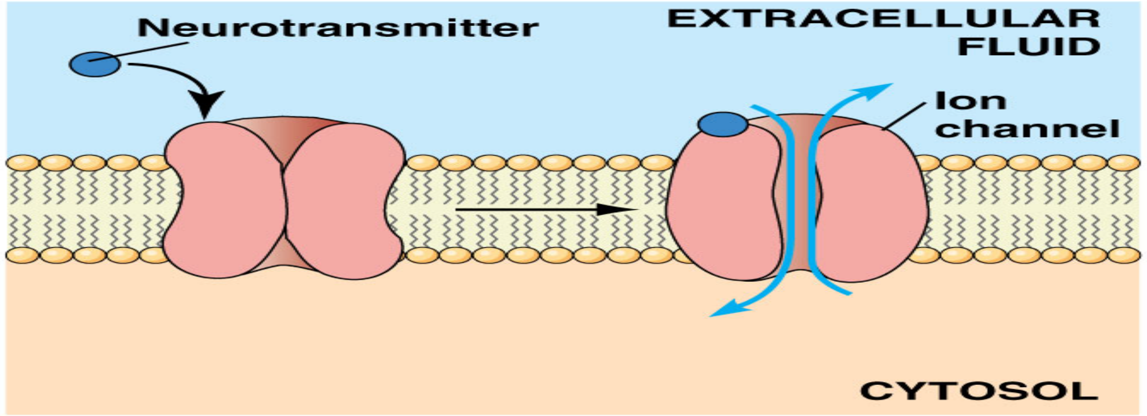
Functional Classification of Neurotransmitters

- **Excitatory** (depolarizing) and/or **inhibitory** (hyperpol.)
  - Determined by receptor type on postsynaptic neuron
  - GABA usually inhibitory
  - Glutamate, epinephrine usually excitatory
  - Acetylcholine
    - Excitatory at neuromuscular junctions in skeletal muscle
    - Inhibitory in cardiac muscle



Neurotransmitter Actions

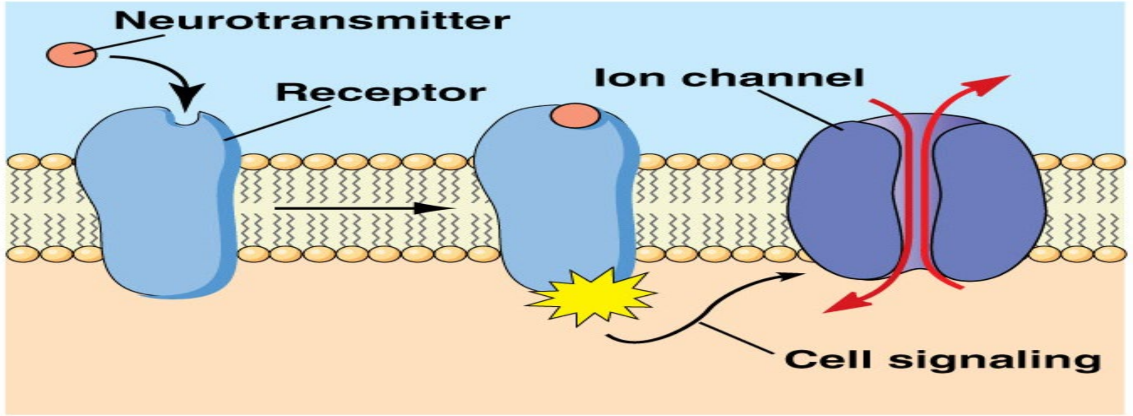
- Direct action
    - Neurotransmitter binds to channel-linked receptor and opens ion channels
    - Promotes rapid responses
    - Examples: ACh; glutamate and GABA at some of their synapses



(a) Direct neurotransmitter action (ionotropic receptor)

Neurotransmitter Actions

- Indirect action
  - Neurotransmitter binds to a G protein-linked receptor and acts through an intracellular second messenger
  - Promotes long-lasting effects
  - Examples: Norepinephrine, epinephrine, serotonin; glutamate and GABA at some of their synapses



(b) Indirect neurotransmitter action (metabotropic receptor)

Unconventional neurotransmitters

- All of the neurotransmitters we have discussed so far can be considered “conventional” neurotransmitters.
- More recently, several classes of neurotransmitters have been identified that don’t follow all of the usual rules.
- These are considered “unconventional” or “nontraditional” neurotransmitters.
- Two classes of unconventional transmitters are the endocannabinoids and the gasotransmitters (soluble gases such as NO and CO).

Unconventional neurotransmitters

- These molecules are unconventional in that they are not stored in synaptic vesicles and may carry messages from the postsynaptic neuron to the presynaptic neuron.
- Also, rather than interacting with receptors on the plasma membrane of their target cells, the gasotransmitters can cross the cell membrane and act directly on molecules inside the cell.

ANY QUESTIONS?