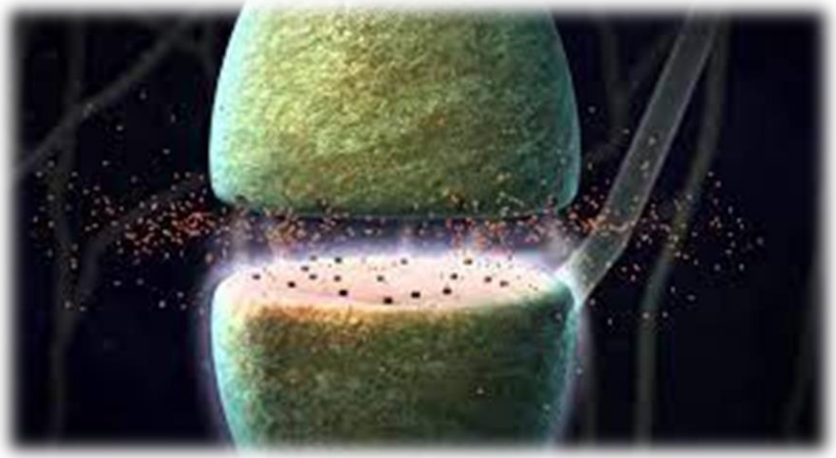


SYNAPTIC TRANSMISSION

Faculty of Dentistry

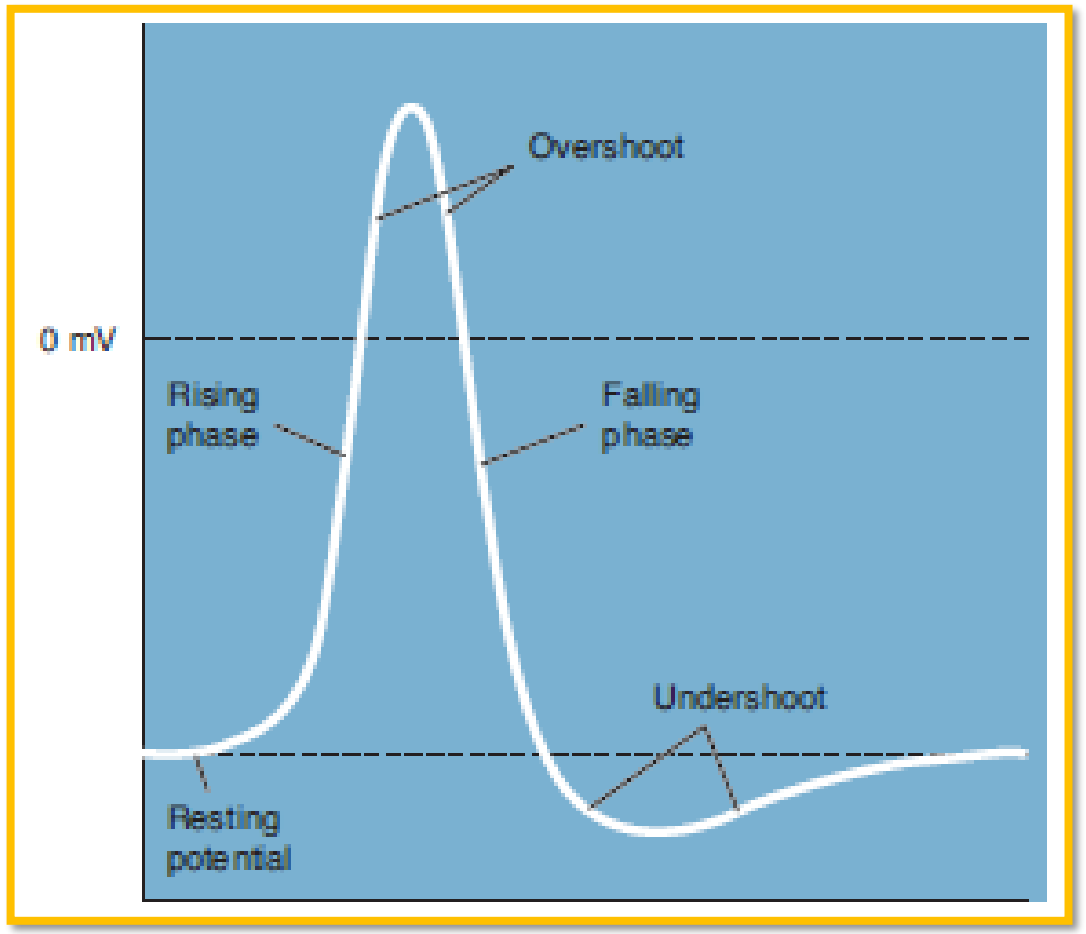
Nervous System

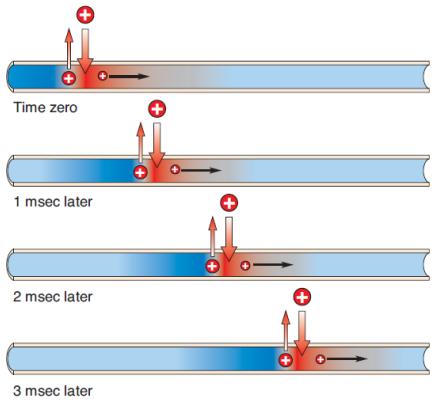
Assoc. Prof. Güvem GÜMÜŞ AKAY

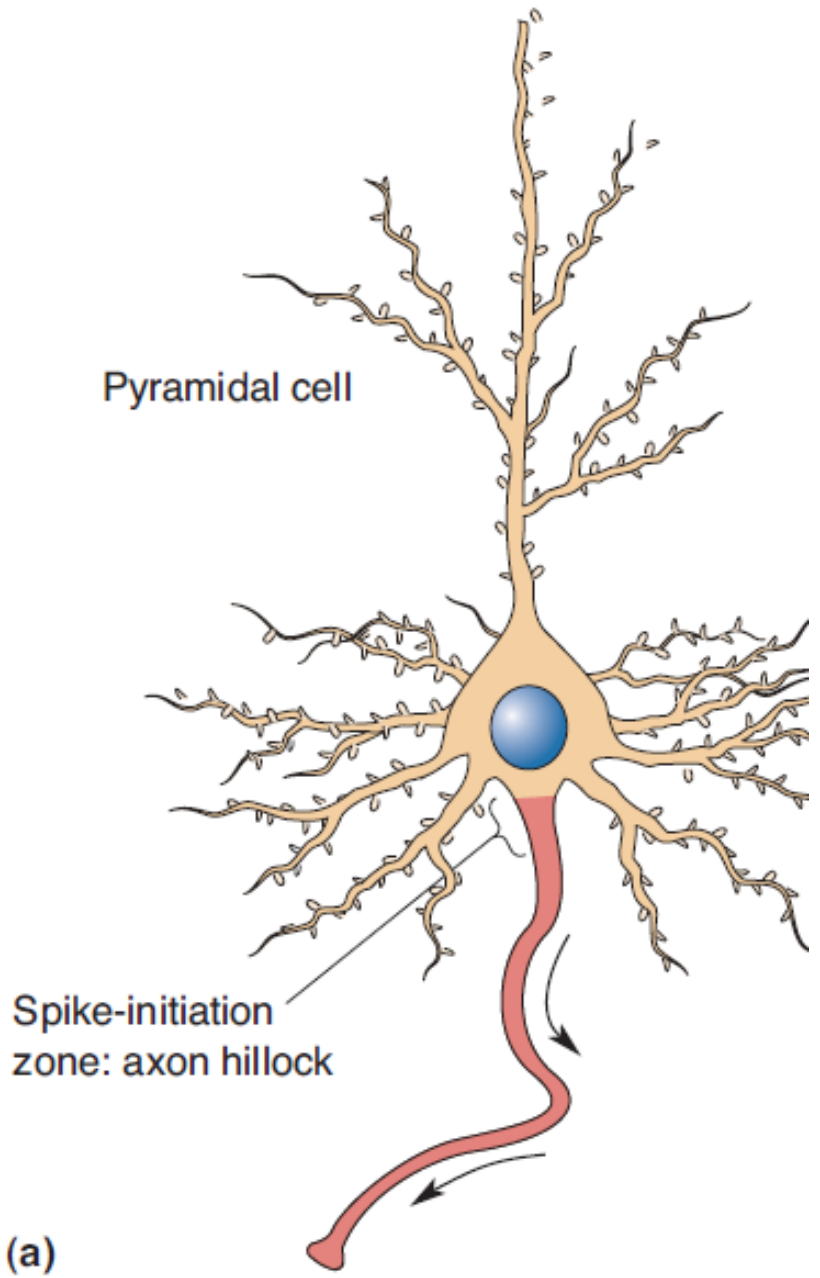
guvemakay@gmail.com

Ankara University School of Medicine

Department of Physiology


Overshoot
0 mV
Rising phase
Falling phase
Undershoot
Resting potential


Time zero
1 msec later
2 msec later
3 msec later


Pyramidal cell
Spike-initiation zone: axon hillock
(a)

Synapse

Syn (together) + (Haptein) to clasp

Anatomically specialized junction between two neurons, at which the electrical activity in a presynaptic neuron influences the electrical activity of a postsynaptic neuron

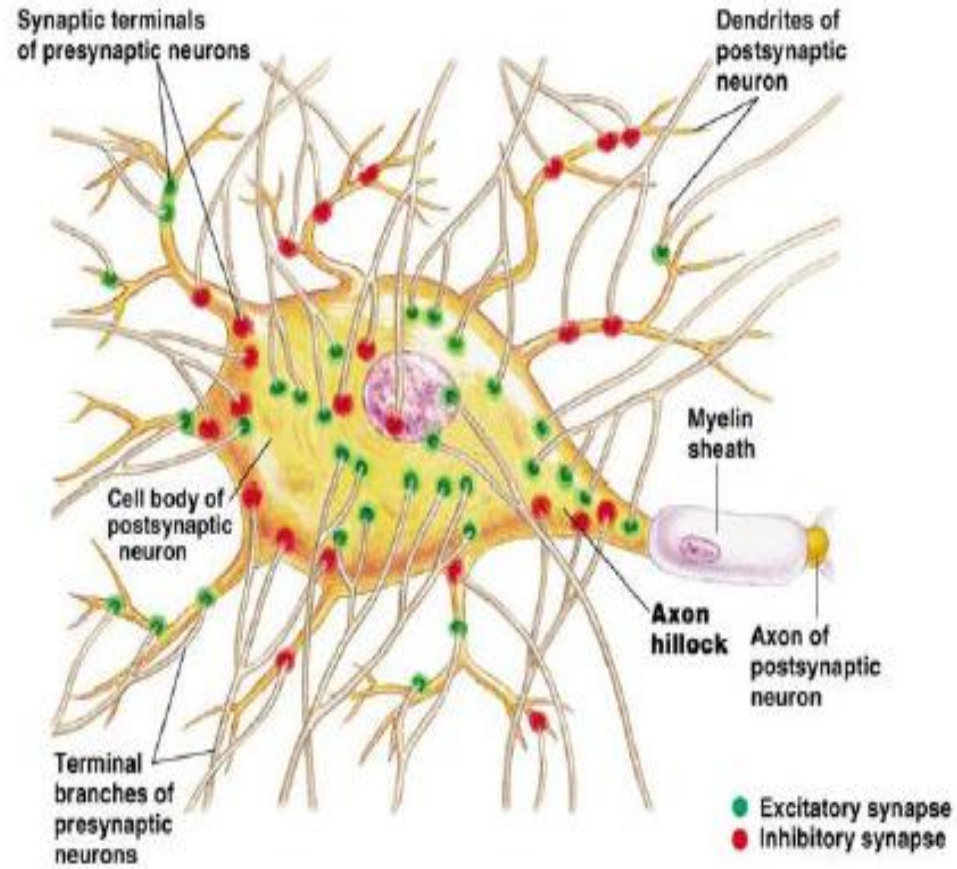
The process of information transfer at a synapse is called **synaptic transmission**

- Synapse can be between a neuron and a
  - Neuron
  - Muscle
  - Gland cell

- Information generally flows in one direction, from a neuron to its target cell.
- The first neuron is said to be ***presynaptic*** , and the target cell is said to be ***postsynaptic*** .

- 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

- 10^{11} neurons, 10^{14} (100 trillion!) synapses



Types of Synapses

Based on signal transmisson

- Electrical Synapses
- Chemical Synapses

Electrical Synapses

- Relatively simple in structure and function
- Allow the direct transfer of ionic current from one cell to the next
- Occur at specialized sites called **gap junctions**

- At a gap junction, the membranes of two cells are separated by only about 3 nm, and this narrow gap is spanned by clusters of special proteins called *connexins*
- Six connexin subunits combine to form a channel called a *connexon*
- Two connexons (one from each cell) meet and combine to form a *gap junction channel*
- The channel allows ions to pass directly from the cytoplasm of one cell to the cytoplasm of the other

- Most gap junctions allow ionic current to pass equally well in both directions; therefore, unlike the vast majority of chemical synapses, electrical synapses are **bidirectional**.
- Because electrical current (in the form of ions) can pass through these channels, cells connected by gap junctions are said to be *electrically coupled* .
- **Transmission** at electrical synapses is **very fast** and, if the synapse is large, **nearly fail-safe**.

Electrical Synapses

- Found where normal function requires that the activity of neighbouring neurons be highly syncronized
  - During prenatal and postnatal brain development, neigbouring 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

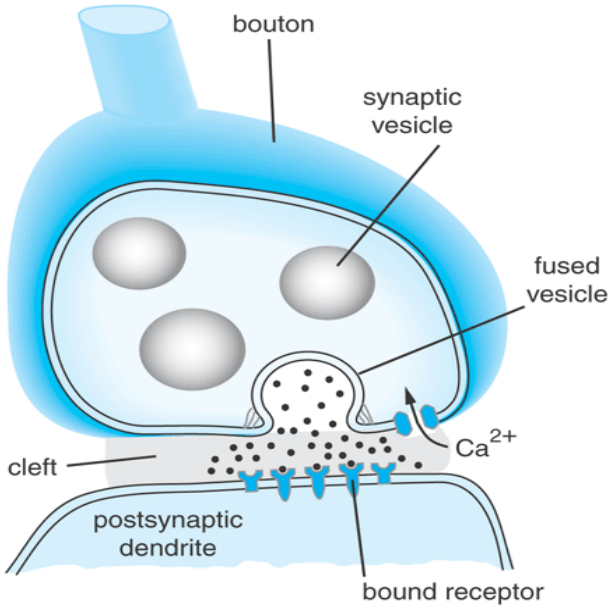
Chemical Synapses

- Most synaptic transmission in the mature human nervous system is chemical
- The presynaptic and postsynaptic membranes at chemical synapses are separated by a ***synaptic cleft*** that is 20–50 nm wide.
- The cleft is filled with a matrix of fibrous extracellular protein.
- One function of this matrix is to serve as a “glue” that binds the pre- and postsynaptic membranes together

Functionally important synaptic regions and structures of chemical synapses

Presynaptic terminal

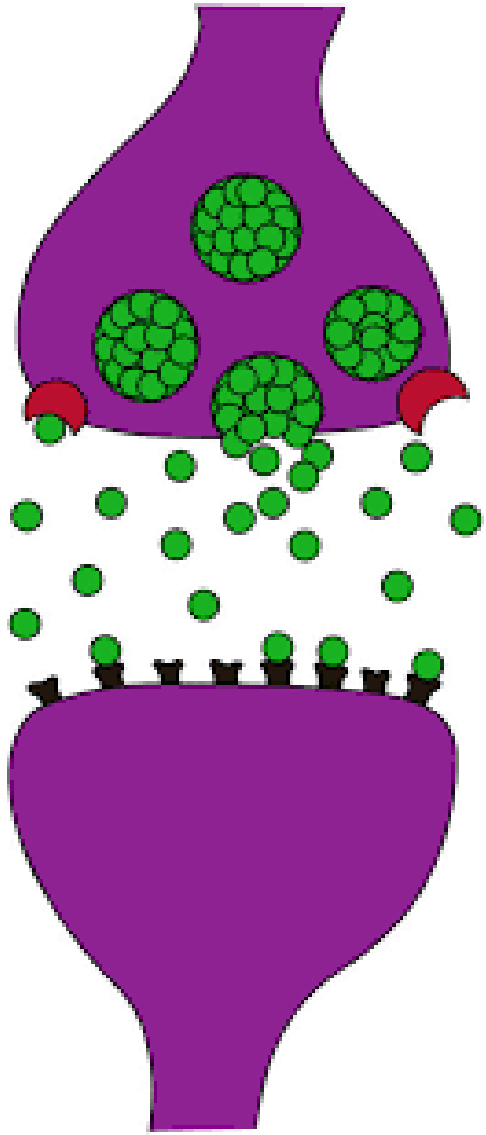
- Axon terminal/Axonal bouton
- Presynaptic vesicles / Neurotransmitter vesicles



- Synaptic vesicles are clustered in the cytoplasm adjacent to the active zones
- Voltage-gated Ca2+ channels

Synaptic cleft

- The region located between the presynaptic axon and the postsynaptic dendrite and is approximately 20 nm
- Not a «space»
- Electron dense material
  - Standard ECM proteins
  - Specialized synaptic proteins



Postsynaptic terminal

- The protein thickly accumulated in and just under the *postsynaptic* membrane is called the **postsynaptic density**
- Contains the **neurotransmitter receptors**, which convert the *intercellular* chemical signal into an *intracellular* signal in the postsynaptic cell.

Cell Adhesion molecules

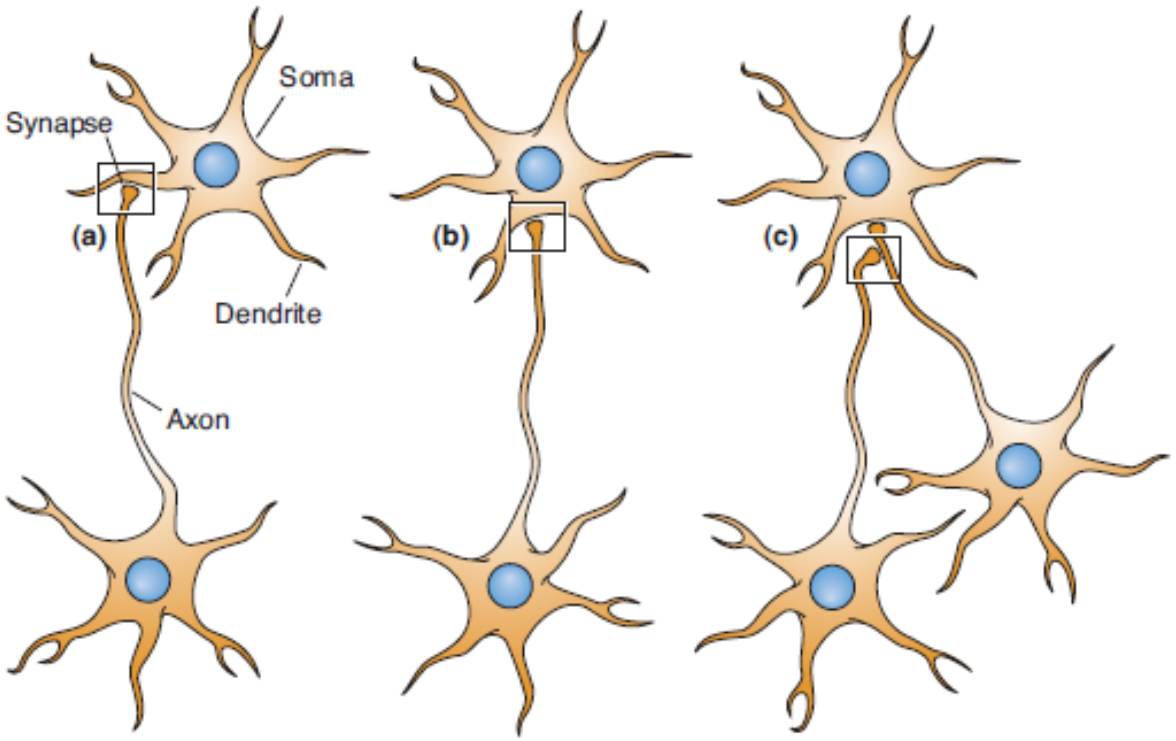
- Proteins in the pre-and postsynaptic membranes that project from these membranes into the synaptic cleft, where they bond to each other

- Ensure that the pre-and postsynaptic membranes stay in close proximity for rapid chemical transmission

Types of Chemical Synapses

Different types of synapse may be distinguished by which part of the neuron is postsynaptic to the axon terminal?

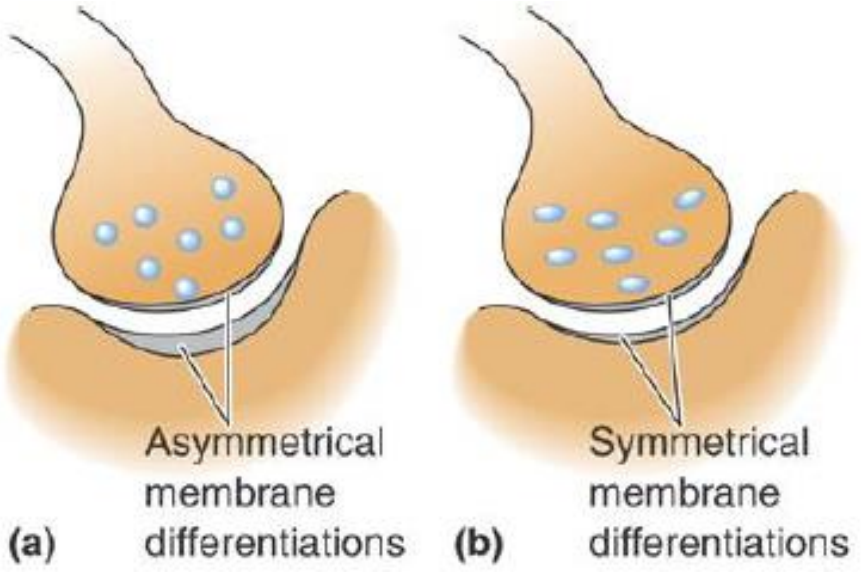
- ✓ Axodendritic: Axon to dendrite
- ✓ Axosomatic: Axon to cell body
- ✓ Axoaxonic: Axon to axon
- ✓ Dendrodendritic: Dendrite to dendrite

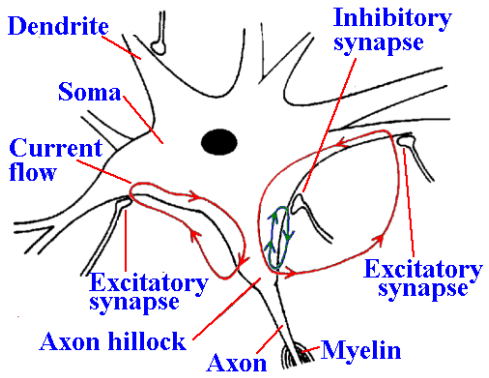


Synaptic arrangements in the CNS. (a) An axodendritic synapse. (b) An axosomatic synapse. (c) An axoaxonic synapse.

Synapses may be further classified into two general categories based on the appearance of their presynaptic and postsynaptic membrane differentiations.

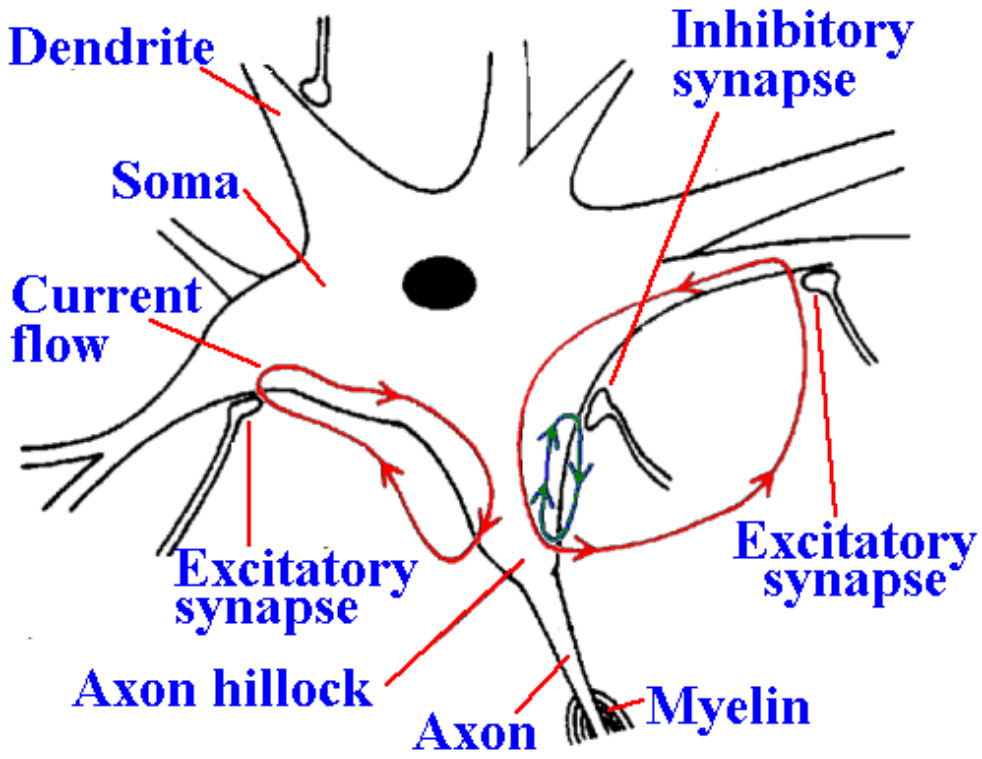
- Excitatory synapses
  - Gray's type I morphology, Asymmetrical
  - Spines: Excitatory synapses
- Inhibitory synapses
  - Gray'stype II morphology, Symmetrical
  - Clustered on soma and near axon hillock

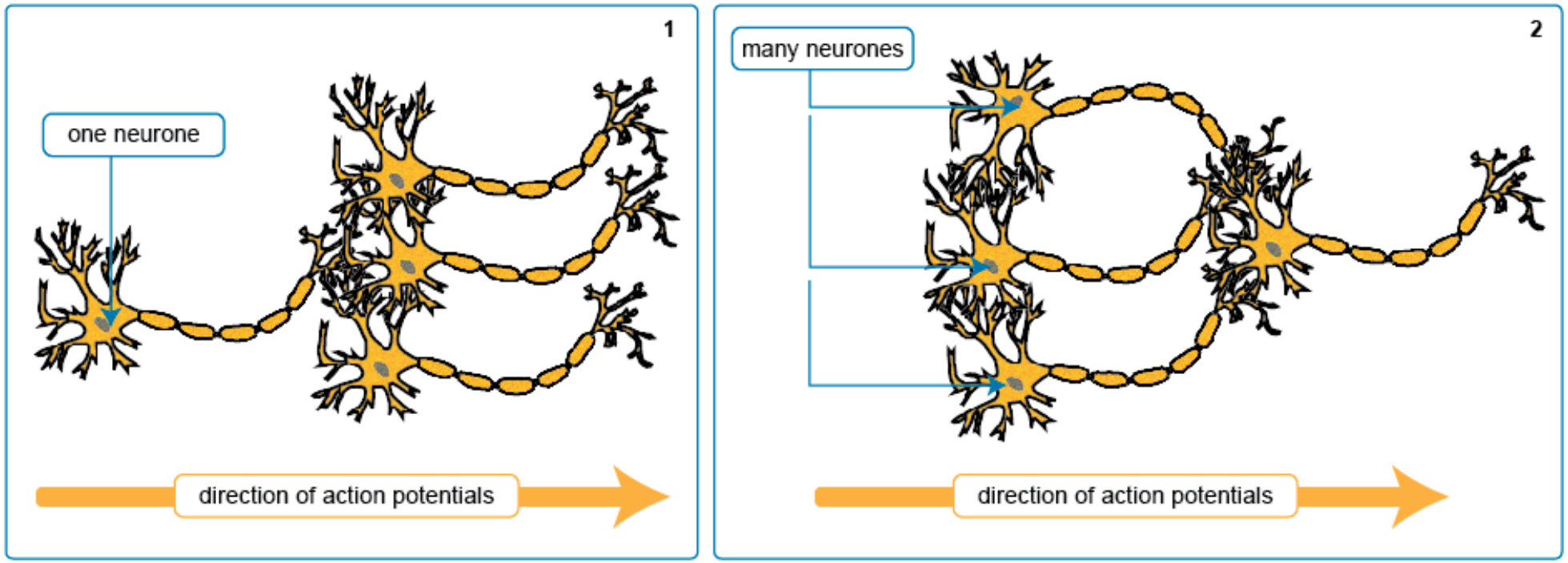




Excitatory synapses:
Dendrites and
dendritic spines

Inhibitory synapses:
Cell body (soma) and
axon initial segments





Divergent synapses: Individual neuron can make divergent connections to many different postsynaptic cells

Convergent synapses: One postsynaptic cell receives convergent input from a number of different presynaptic cells

Synapses Vary in Size and Strength

Larger synapses allow the presynaptic neuron to have a larger and more reliable effect on the postsynaptic neuron

Principles of Chemical Synaptic Transmission

- When the action potential depolarizes the presynaptic membrane, the voltage-gated Ca2+ channels open
- Ca2+ enters in to the presynaptic neuron (i.e. Ca2+ influx)
- Synaptic vesicle exocytosis, causing NTs to be released into the synaptic cleft.
- Occurs when Ca2+ binds to synaptotagmin.

- **R-SNARE:** Transport vesicle → v-SNARE
- **Q-SNAREs:** Target membrane → t-SNARE

When voltage-gated Ca^{2+} channels are opened

ion	Inside	Outside
Na^+	18 mM	145 mM
K^+	135 mM	3 mM
Cl^-	7 mM	120 mM
$Ca2^+$	100 nM	1.2 mM

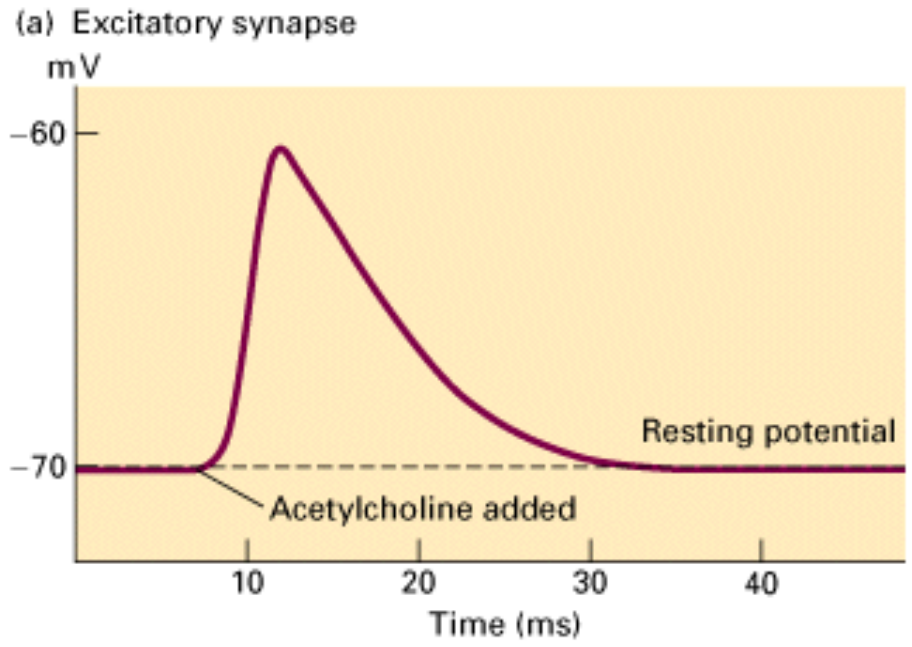
X 15.000

WHAT IS HAPPENING IN THE POSTSYNAPTIC CELL?

Exitatory Synapses

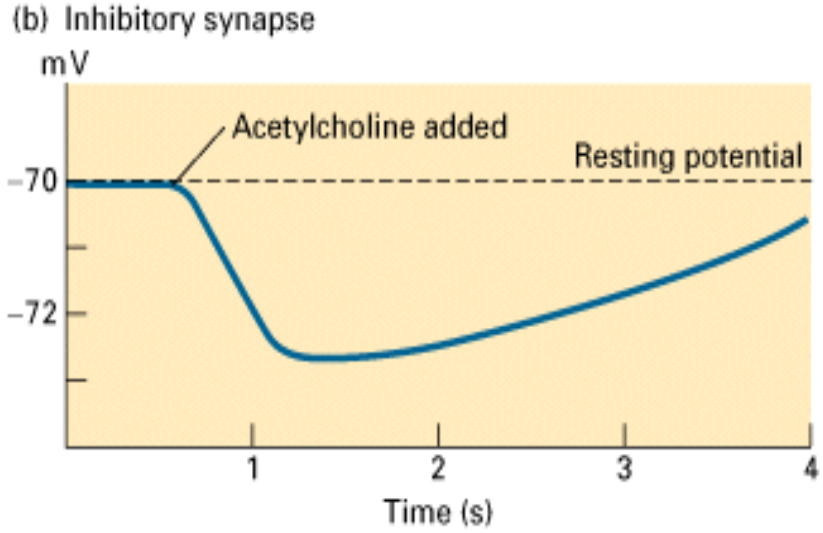
- At an excitatory synapse, the post-synaptic response to NT is a depolarization that brings the membrane potential closer to the threshold.
- The overall effect of the activated receptor on the postsynaptic membrane is the opening of ion channels that are permeable to positively charged ions.

- The net movement of positive ions into the cell causes a slight depolarization.
- These potential changes are called «Excitatory postsynaptic potentials= EPSPs».
- Synaptic activation of ACh-gated and glutamate-gated ion channels causes EPSPs.



Inhibitory synapses

- The potential change in the postsynaptic neuron is the hyperpolarizing graded potential called the «inhibitory postsynaptic potential = IPSPs».
- Activation of an inhibitory synapse reduces the likelihood of the postsynaptic cell to depolarize to the threshold and generate an action potential.



- At an inhibitory synapse, activated receptors on the postsynaptic membrane are the Cl- and K+ channels
- Cl- influx /K+ eflux take place
- The membrane becomes hyperpolarized
- Synaptic activation of glycine-gated or GABA-gated ion channels cause an IPSPs.

Neurotransmitter Recovery and Degradation

Once the released neurotransmitter has interacted with postsynaptic receptors, it must be cleared from the synaptic cleft to allow another round of synaptic transmission.

- **Simple diffusion** of the transmitter molecules through the extracellular fluid and away from the synapse
- **Reuptake** into the presynaptic axon terminal or into glial cells followed by degradation or recycling
- **Enzymatic destruction** the synaptic cleft itself.
- **Uptake** by the post synaptic neuron.

References

- Widmaier E.P., Raff H., Strang K.T. (2019) Vander's Human Physiology. Mc Graw Hill Education.
- Bear M.F., Connors B.W., Paradiso M.A. (2016) Neuroscience: Exploring the Brain. Wolters Kluwer