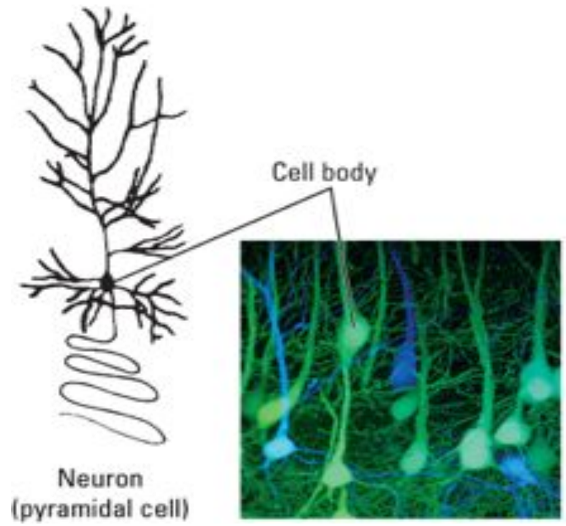
Communication in the brain

Lecture 3 ; Sept 12, 2013

Two main types of brain cells

- **Neurons**
  - The basic information processing units of the brain.
  - Approximately 80 billion in the human brain.



- **Glial cells** – *“glue (G.)”*
  - Support and modulate neurons’ activities.
  - Creates the *myelin sheath.*
  - Approximately 100 billion in the human brain.

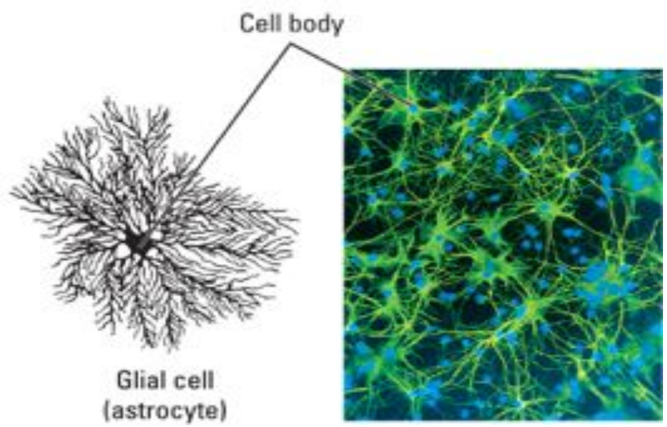
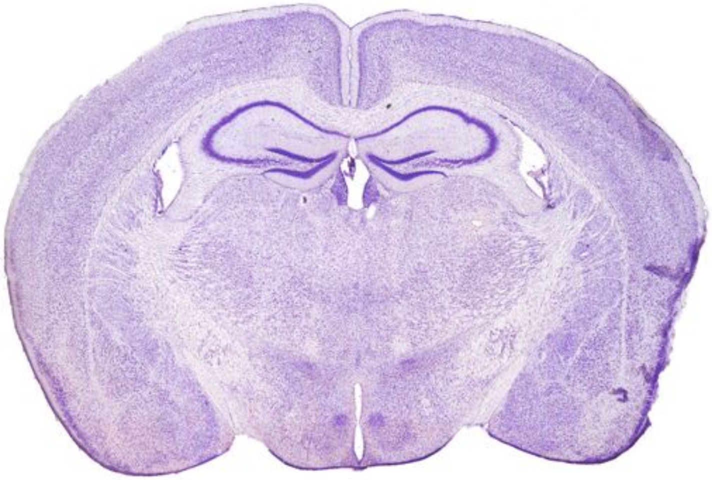


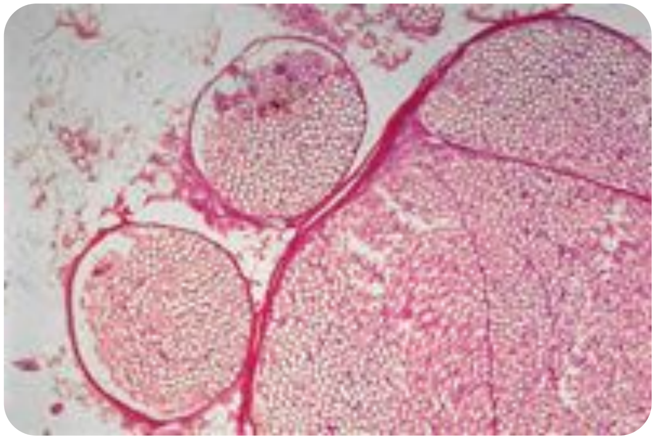
Illustration from Kolb & Wishaw, *An Introduction to Brain and Behavior*. Sinauer, 2014

Some terms

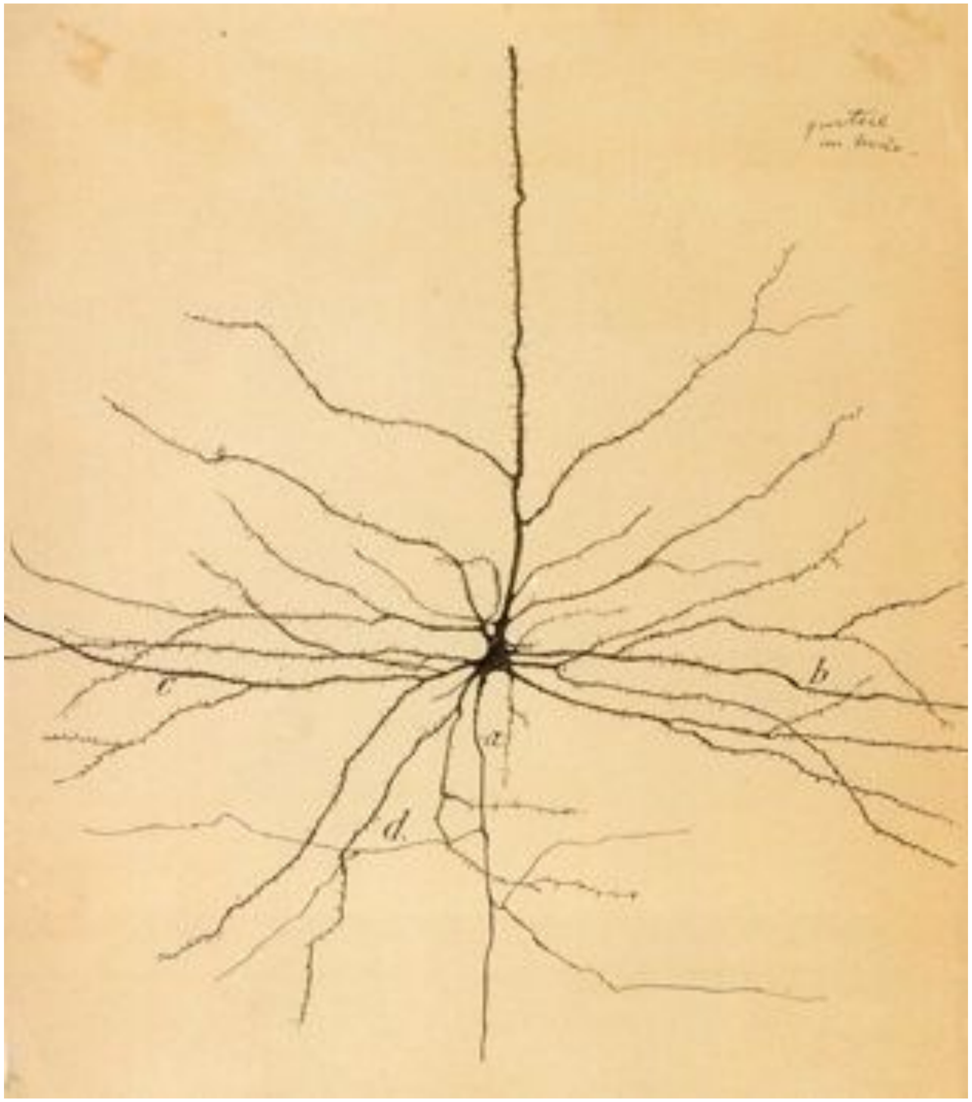
- **Nucleus** (pl. nuclei)
  - A group of neurons forming a cluster that can be identified with special stains to form a functional grouping.
    - Examples: Ventral Tegmental Area (VTA), Arcuate Nucleus (ARC) etc.,
- **Nerve**
  - A large collection of axons forming connections in the PNS.
    - Examples: Phrenic nerve (arising from C3-C5, it controls the diaphragm).
  - Large collections of axons in the CNS are called tracts.
    - Example: Corticospinal tract (connects the motor cortex to the motor neurons of the spinal cord).



Coronal section of mouse brain. Darker areas are clusters of cells (nuclei).

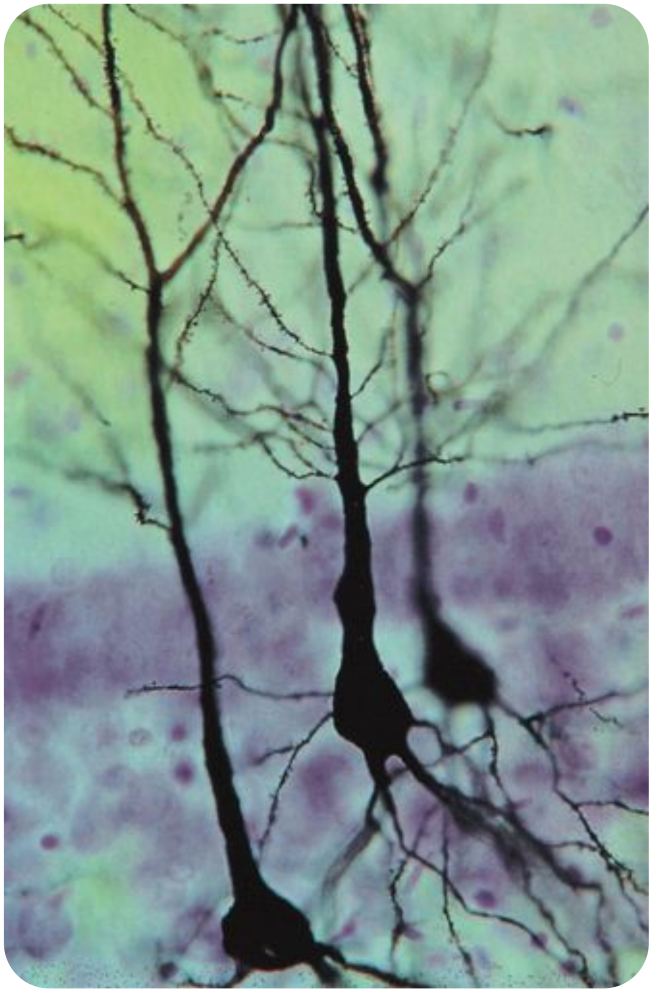


Cross section of nerves in PNS. Large bundles are nerves, small circles are cross sections of individual axons.



Pyramidal neuron.
Santiago Ramón y Cajal – 1899

Introducing the neuron



Golgi stained pyramidal **neurons** in the **cerebral cortex**.

Neurons transmit information

- **Neurons** are specialized cells that are specialized for transferring information from one place to another.

- **Neurons** have specialized structures for this purpose.
  - Dendrites – *"tree (G.)"*
    - Gather information from other neurons.
  - Cell body
    - Core region; contains the nucleus and DNA.
  - Axon hillock
    - Junction of the cell body and axon, where the *action potential* begins.
  - Axon
    - Carries information to be passed onto other cells.
  - Terminal button
    - Knob at the tip of an axon that conveys information to other neurons.
    - Connects with dendrites of other neurons.

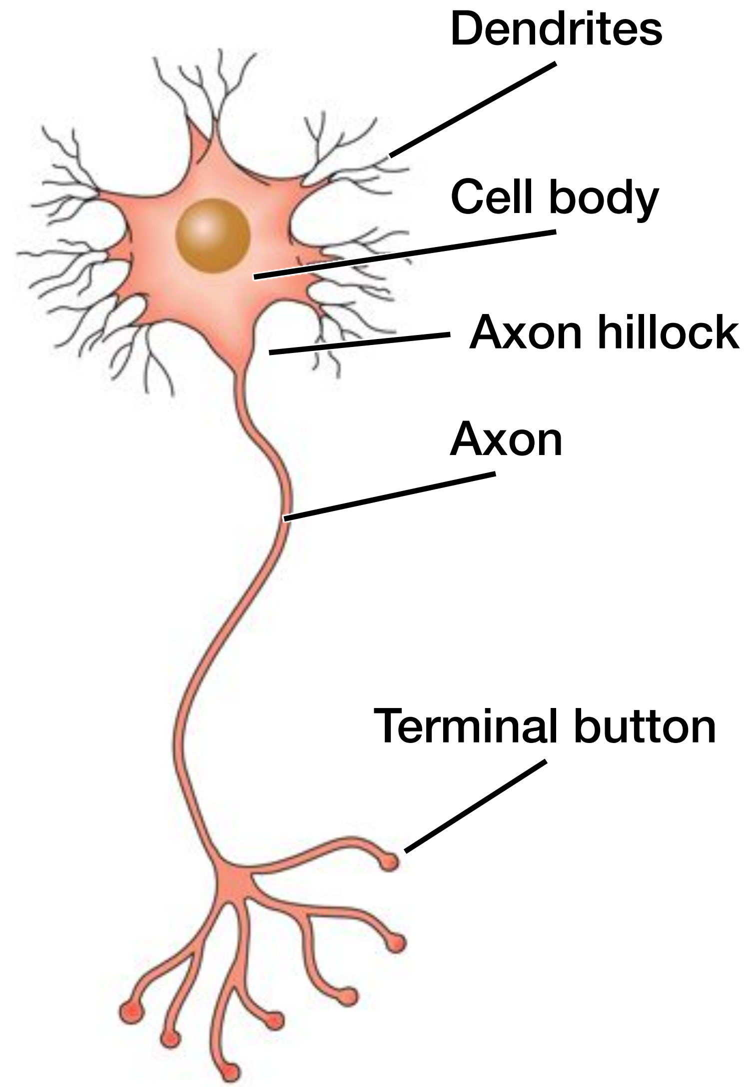


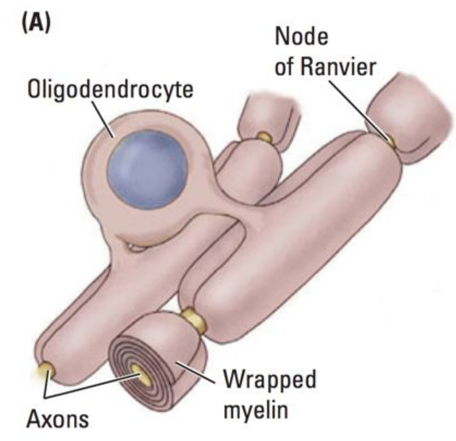
Illustration from J.P.J. Pinel, *Biopsychology*. Allyn & Bacon, 2011

Neurons transmit information

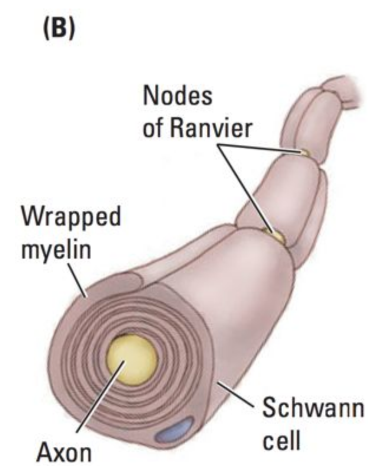
- **Axons**, especially longer ones, are usually covered with a **myelin sheath**.

- **Myelin** is a fatty substance produced by **glial cells**. **Myelin** insulates the **axon**, increasing the speed and efficiency of electrical signal conduction.

- The fatty nature of **myelin** gives **white matter** its color.



Oligodendrocytes myelinate axons in the CNS

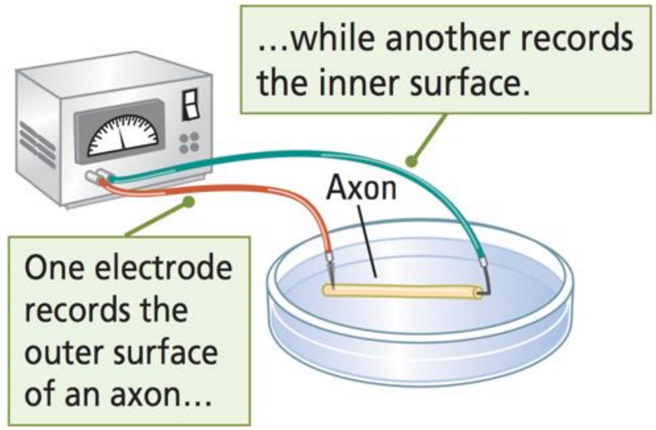


Schwann cells myelinate axons in the PNS

Illustration from J.P.J. Pinel, *Biopsychology*. Allyn & Bacon, 2011

Establishing the resting potential

- Neurons are negatively charged with respect to the extracellular fluid. The **resting membrane potential** is **-70mv**.
- This is due an an unequal distribution of ions on either side of the membrane, leading to a net negative charge.
- This state of affairs is maintained by a combination of active and passive mechanisms that govern the flow of ions across the membrane.



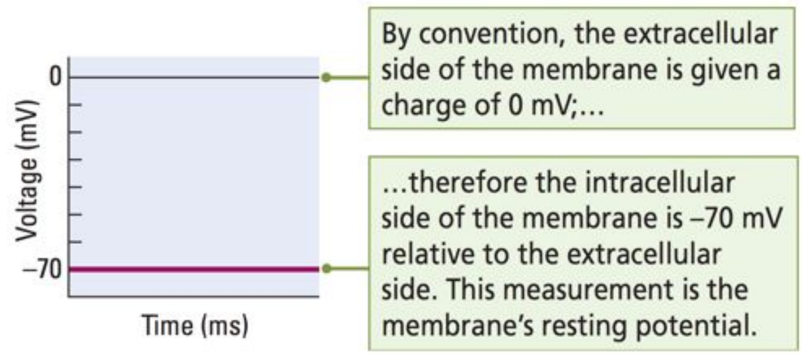


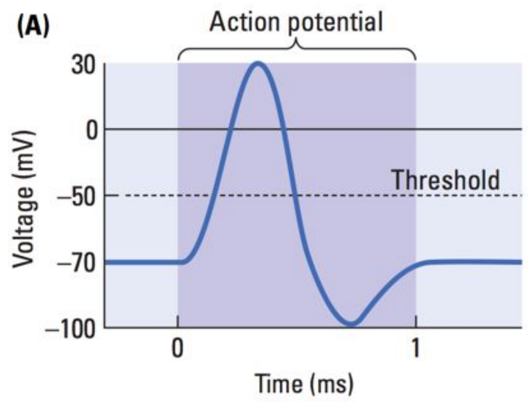
Illustration from Kolb & Wishaw, *An Introduction to Brain and Behavior*. Sinauer, 2014

Action potentials

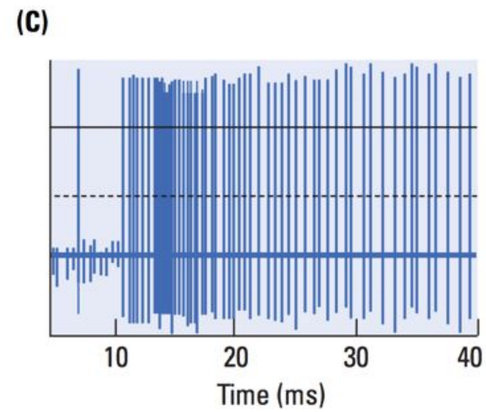
- **Action potentials** are short-lived, spreading, localized changes in membrane polarity. They are momentary disruptions to the **resting potential**.

- The neuron briefly goes from being **negatively charged** to **positively charged**, reaching around **+30mv.**

- This is caused by the movement of ions in and out of the neuron.



Action potentials take about 1ms to complete, and can be measured one at a time



Or they can be measured over larger time-scales. In this scenario, action potentials are sometimes called *spikes*.

Illustration from Kolb & Wishaw, *An Introduction to Brain and Behavior*. Sinauer, 2014

Action potentials

- Neurons transmit information by electrical signals called **action potentials.**
- Action potentials travel at a speed of 30-120m/s. **Myelinated** axons have a faster rate of conduction.
- **Action potentials** are generated at the **axon hillock.**
- Information always flows in the same direction in neurons:
  - Dendrites > Cell body > Axon > Axon terminal

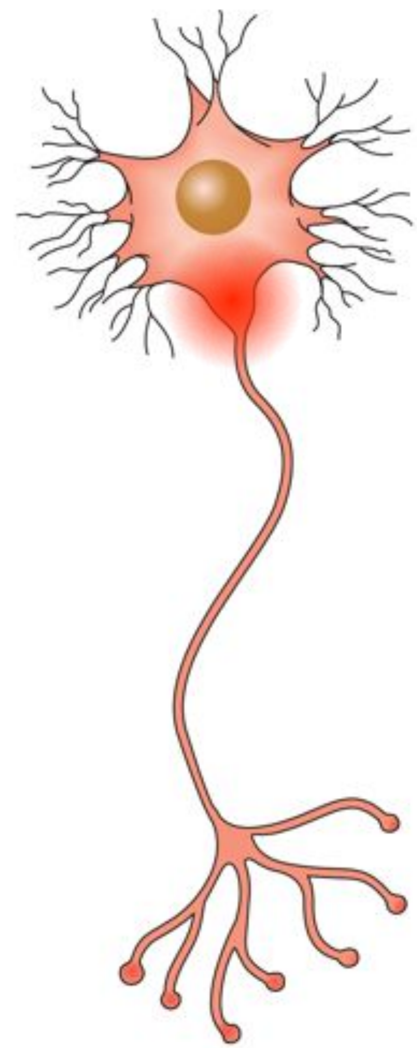


Illustration from J.P.J. Pinel, *Biopsychology*. Allyn & Bacon, 2011

The synapse

- **Synapses** – *"to clasp (G.)"* – are the points of contact between two neurons. The site of inter-neuron information transfer.

- While **action potentials** transfer signals rapidly by altering membrane electrical potential, synapses transfer signals by passing chemicals from neuron to neuron.

- Because synaptic communication relies on chemical interactions, **synapses** are frequent targets for exogenous chemical stimulation (ie. drugs).

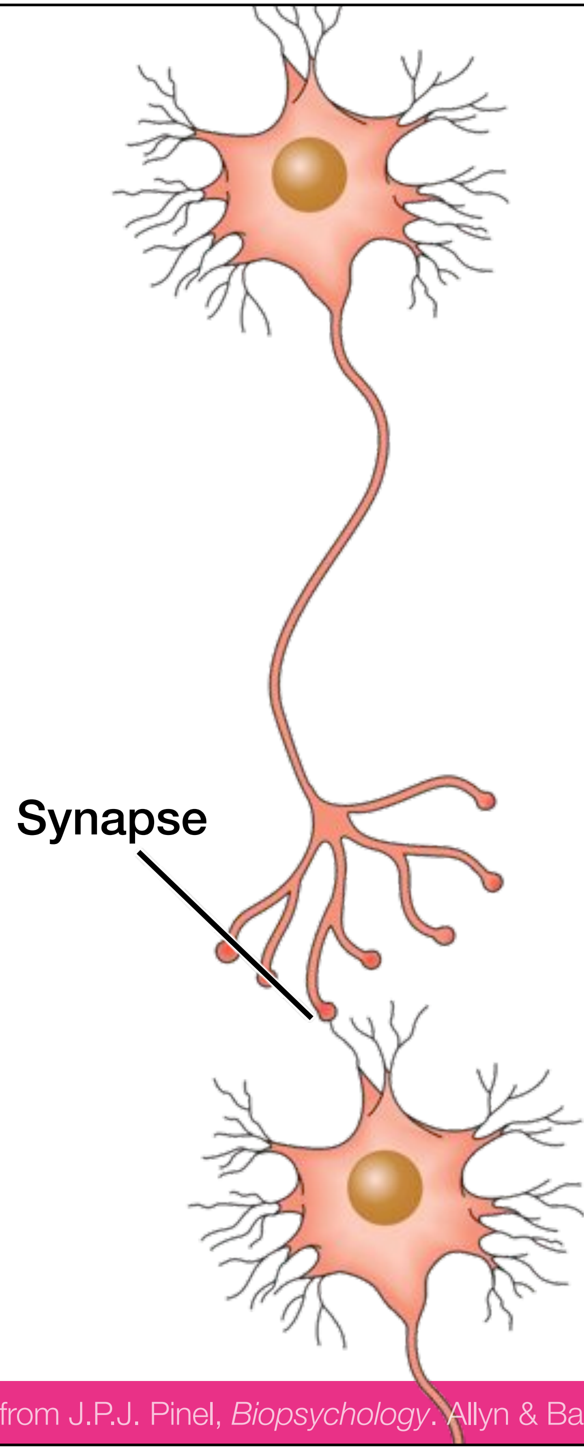
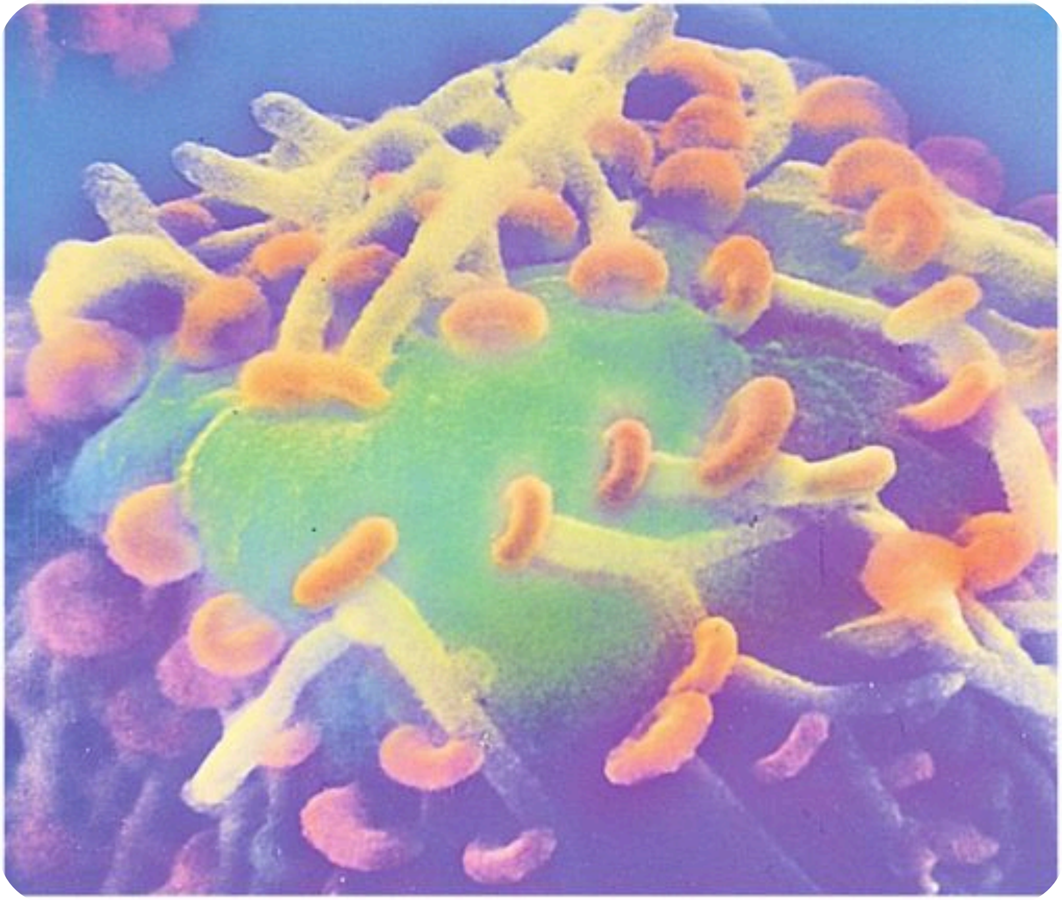


Illustration from J.P.J. Pinel, *Biopsychology*. Allyn & Bacon, 2011

The synapse



Scanning electron micrograph of **terminal buttons** making contact with a neural cell body.

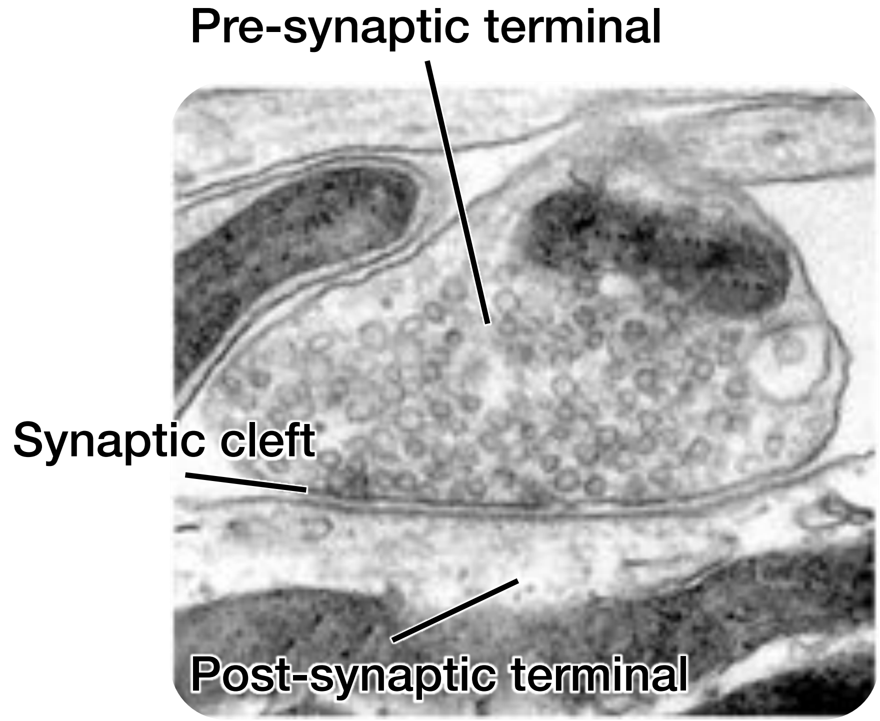
Illustration from J.P.J. Pinel, *Biopsychology*. Allyn & Bacon, 2011

The synapse

- The cell on the receiving end of the synapse is called the **post-synaptic neuron.**

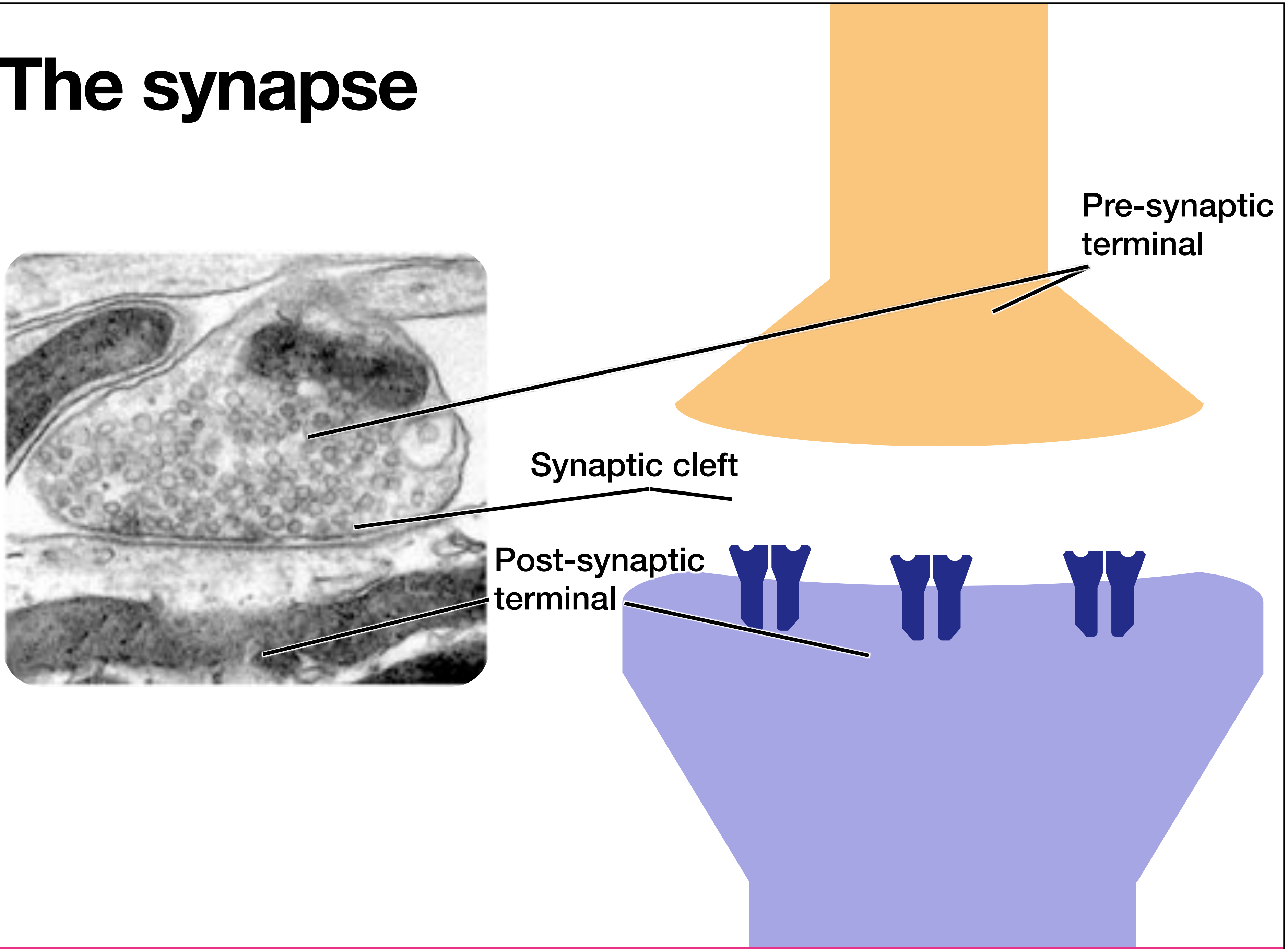
- The cell sending the signal is called the **pre-synaptic neuron.**

- The **synaptic cleft** is an empty space found between the two opposing neurons. Chemical messages are sent across this gap.



Electron micrograph of a typical synapse

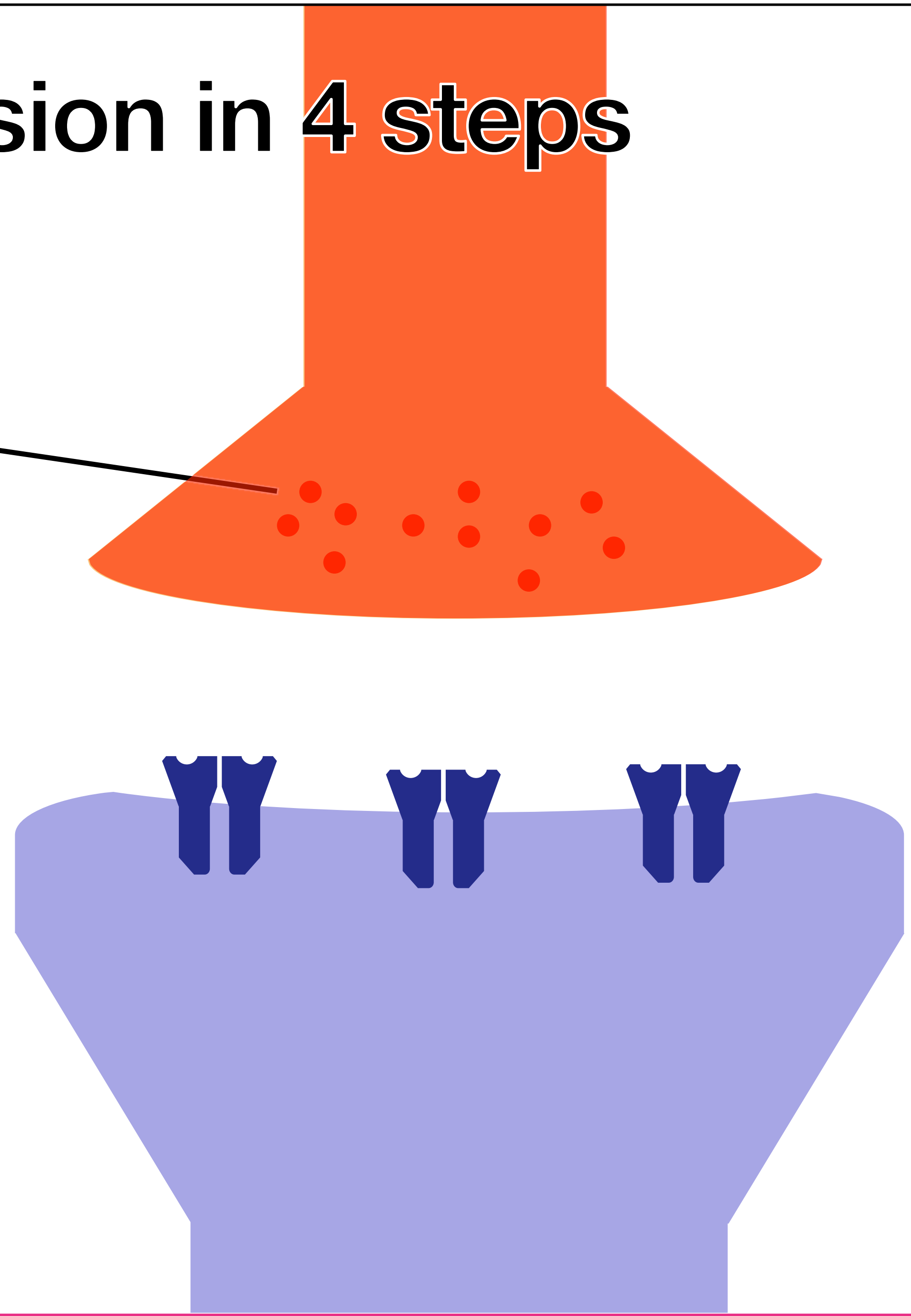
The synapse


Pre-synaptic
terminal
Synaptic cleft
Post-synaptic
terminal

Synaptic transmission in 4 steps

1. Neurotransmitters are synthesized and stored in the **presynaptic axon terminal**.

2. Action potentials stimulate the release of **neurotransmitters** into the synaptic cleft.



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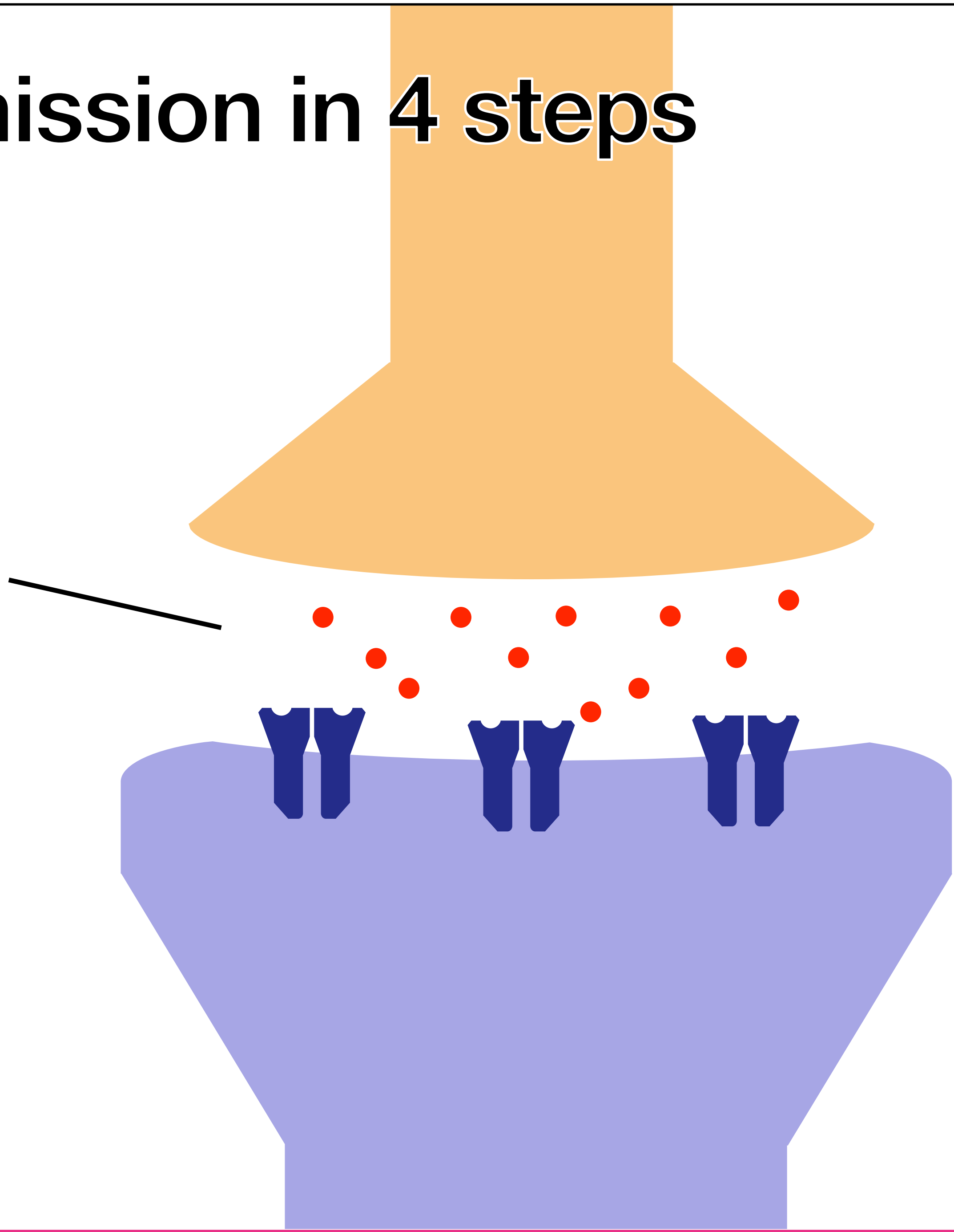

Synaptic transmission in 4 steps

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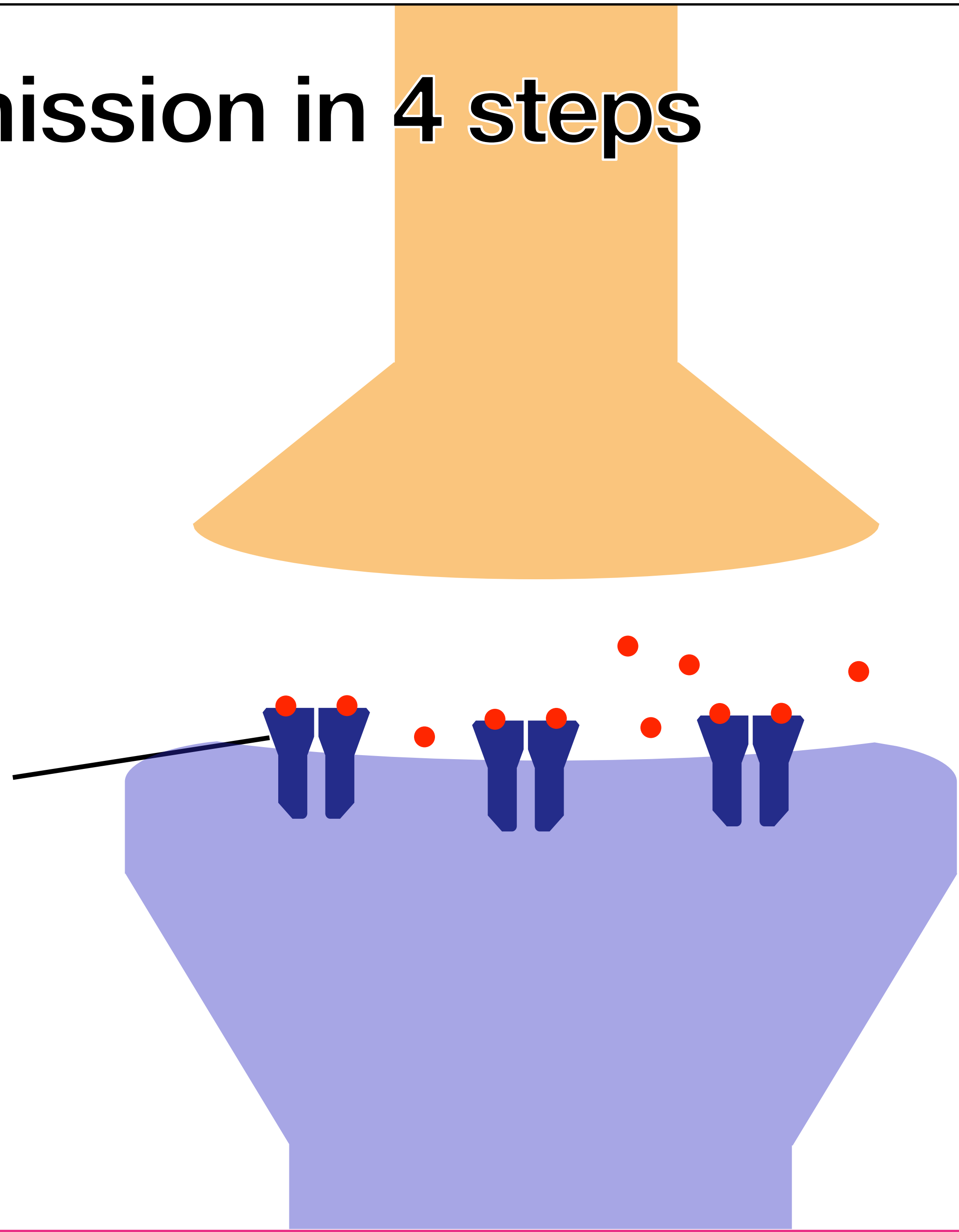
3. **Neurotransmitters** bind to **receptors** – specialized proteins embedded into the **post-synaptic membrane.**



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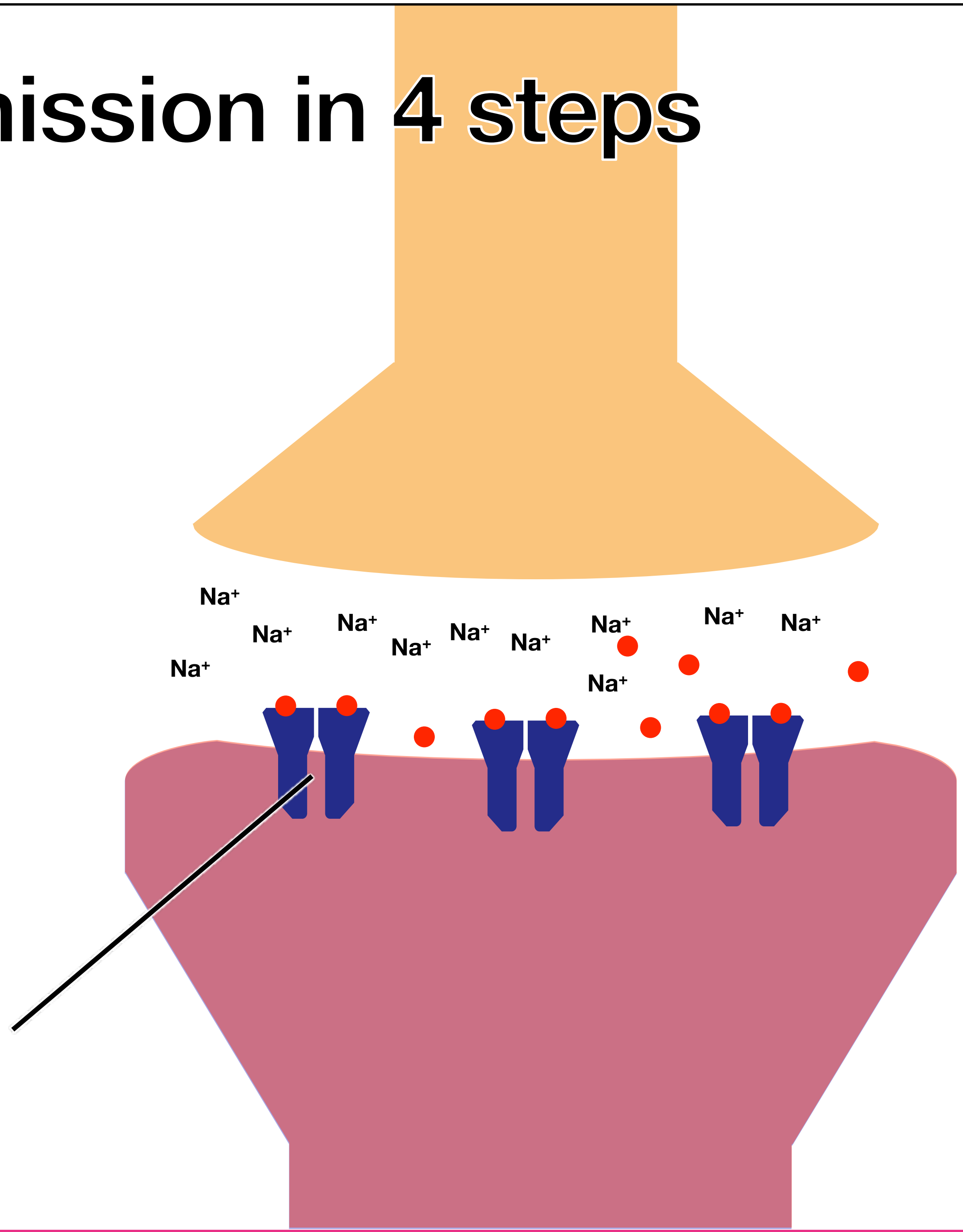
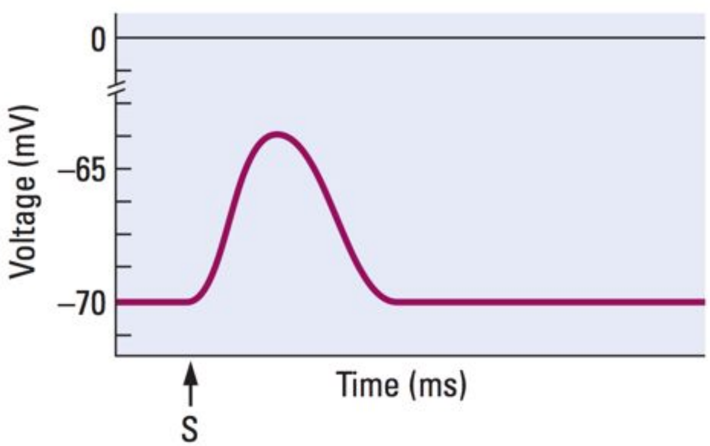
4. Receptors are often coupled to **ion channels** that open when bound to a **neurotransmitter**. The influx of ions changes the membrane potential of the **post-synaptic neuron**, causing a **post-synaptic potential (PSP).**



Excitatory and inhibitory NTs

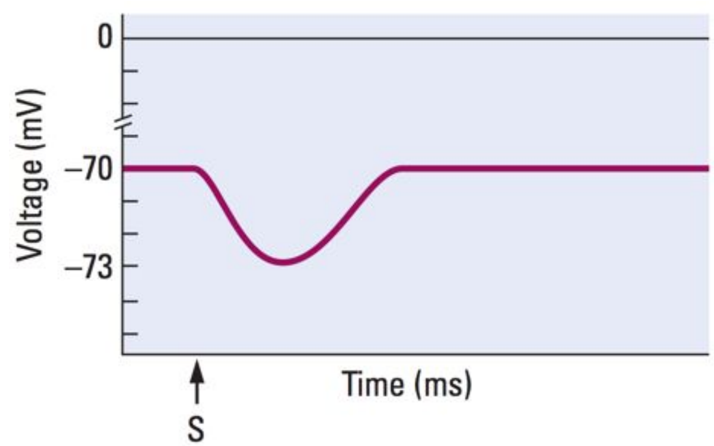
Excitatory Post-Synaptic Potentials (EPSP)



Neurotransmitters such as **glutamate** are classified as "**excitatory**" because their receptors allow the influx of **cations** (positive ions like Na^+, Ca^{++}, K^+).

Excitatory NTs **depolarize** the post-synaptic membrane, *increasing* the likelihood of another **action potential**.

Inhibitory Post-Synaptic Potentials (IPSP)



Neurotransmitters such as **GABA** and **glycine** are classified as **"inhibitory"** because their receptors allow the influx of **anions** (negative ions like Cl^-)

Inhibitory NTs **hyperpolarize** the post-synaptic membrane, *decreasing* the likelihood of another **action potential**.

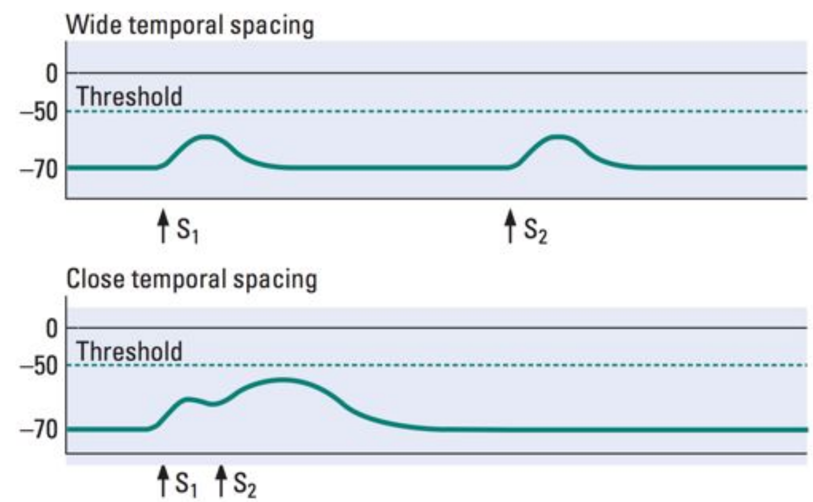
Illustration from Kolb & Wishaw, *An Introduction to Brain and Behavior*. Sinauer, 2014

Triggering an action potential

- Neurons receive hundreds of inputs. One their own, each input has a relatively small impact on the probability of an **action potential.**

- The neuron integrates the combined input from all of its synapses. If there are a sufficient number of **EPSPs** happening close together in *time* or *space*, then an **action potential** is triggered. Each **EPSP** moves the neuron a little closer to the **threshold potential** of -50mv.

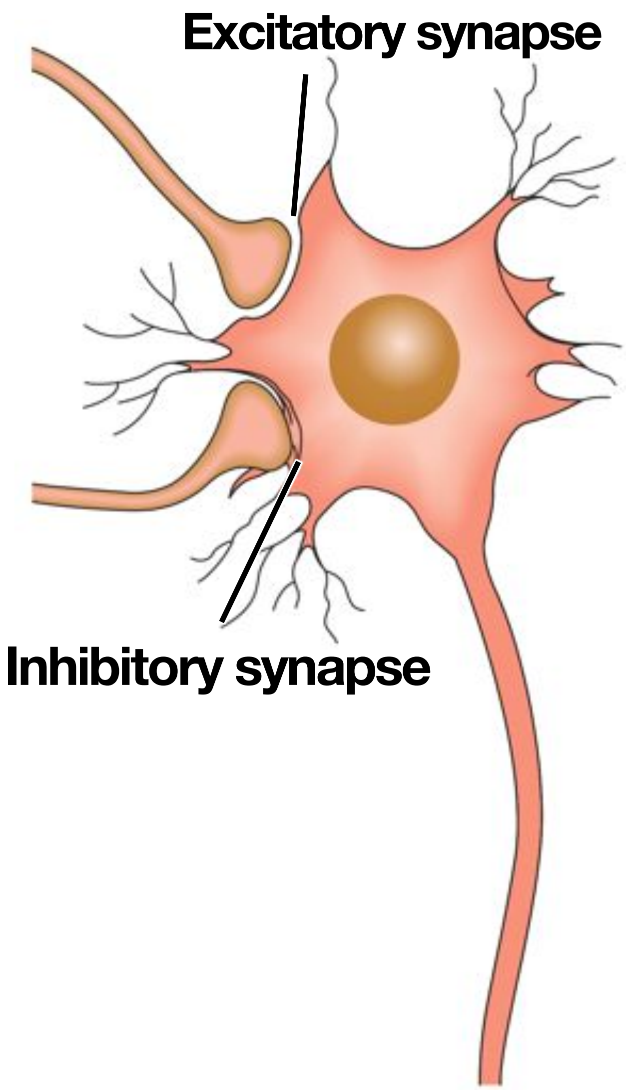
- In a sense, the hundreds of inputs "*vote*" on whether an **action potential** will take place.



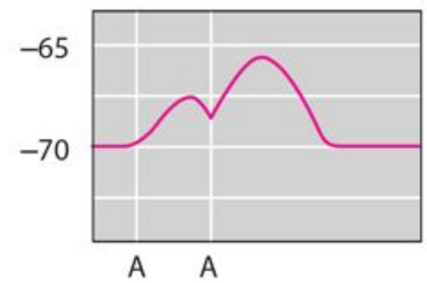
If they are too far apart, two EPSPs do not add up to anything. But if they happen close together, they add together and push the neuron closer to its *threshold potential*.

Illustration from Kolb & Wishaw, *An Introduction to Brain and Behavior*. Sinauer, 2014

Triggering an action potential



Two **EPSPs** in a row create a larger positive charge **(depolarization)**.



Two **IPSPs** in a row create a larger negative charge **(hyperpolarization)**.

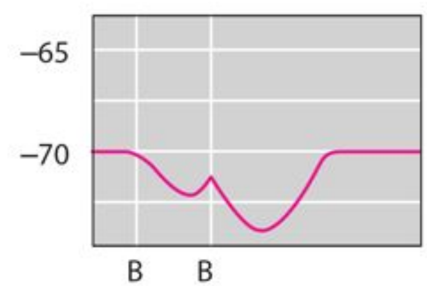


Illustration from J.P.J. Pinel, *Biopsychology*. Allyn & Bacon, 2011

Triggering action potentials

- **Action potentials** are triggered when a the neuron is sufficiently **depolarized** at the **axon hillock.**
  - The *threshold voltage* needed to trigger an action potential is -50mv.

- **All-or-none** law: unlike PSPs, **action potentials** are not graded. Once an **action potential** occurs, it invariably runs its course down the axon. In this sense, **action potentials** are "binary".

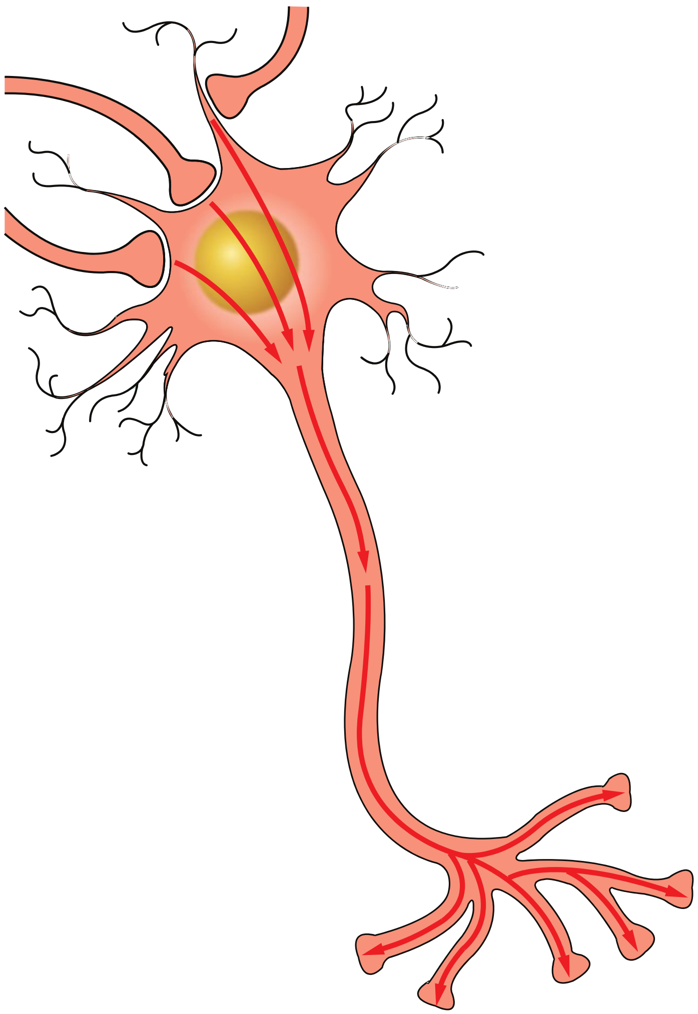
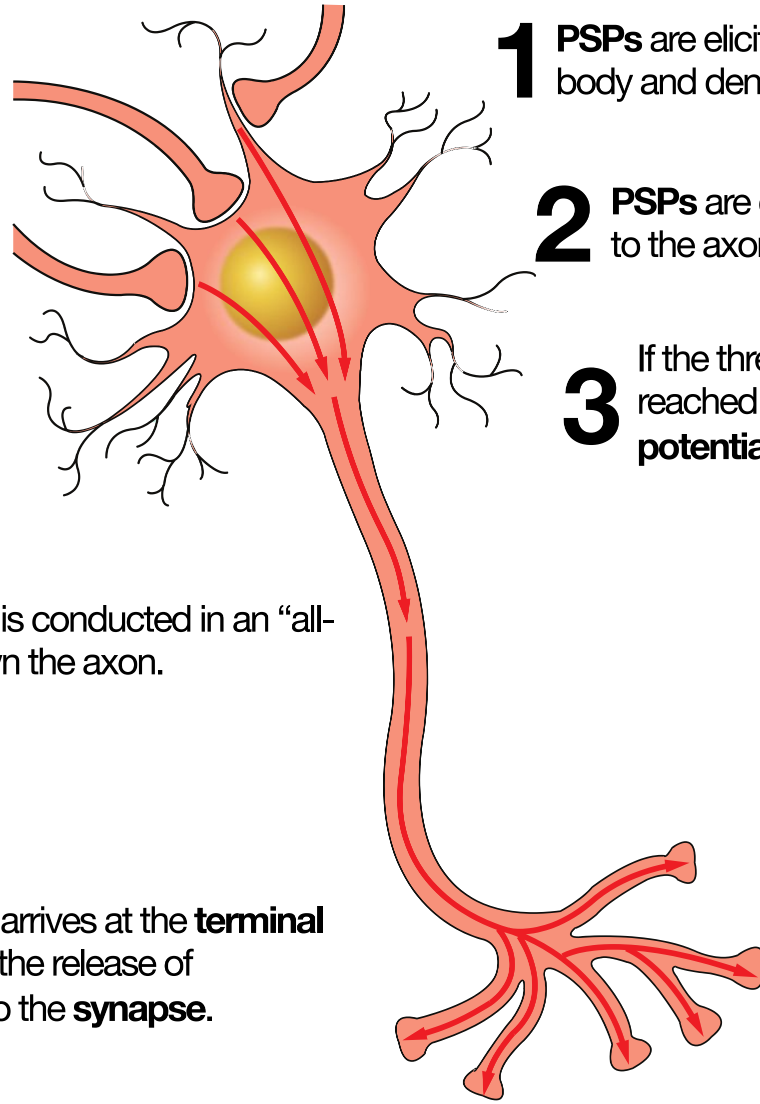


Illustration from J.P.J. Pinel, *Biopsychology*. Allyn & Bacon, 2011

Neural signaling in 5 steps



1 **PSPs** are elicited on the cell body and dendrites.

2 **PSPs** are conducted **decrementally** to the axon hillock

3 If the threshold potential (-50mv) is reached at the **axon hillock**, an **action potential** is triggered.

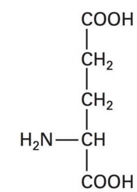
4 The **action potential** is conducted in an "all-or-none" fashion down the axon.

5 The **action potential** arrives at the **terminal buttons** and triggers the release of **neurtransmitters** into the **synapse**.

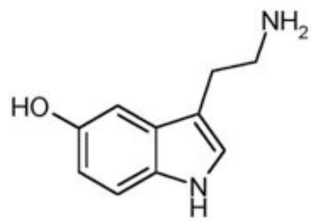
Illustration from J.P.J. Pinel, *Biopsychology*. Allyn & Bacon, 2011

Major classes of neurotransmitters

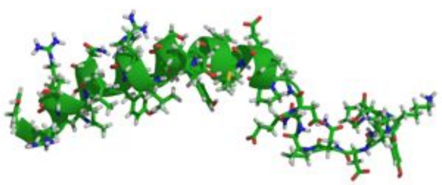
- **Amino acids:** Glutamate (Glu), Glycine (Gly) ,γ-aminobutyric acid (GABA)
- **Monoamines:** Dopamine (DA), Norepinephrine (NE), Epinephrine (EP), Serotonin (5-HT)
- **Peptides:** Vasopressin, Oxytocin, Neuropeptide Y
- **Others:** Acetylcholine (Ach), Adenosine, Anandamide, Nitric Oxide



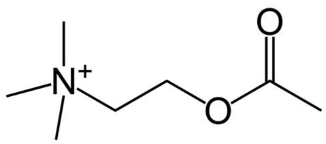
Glutamate



Serotonin



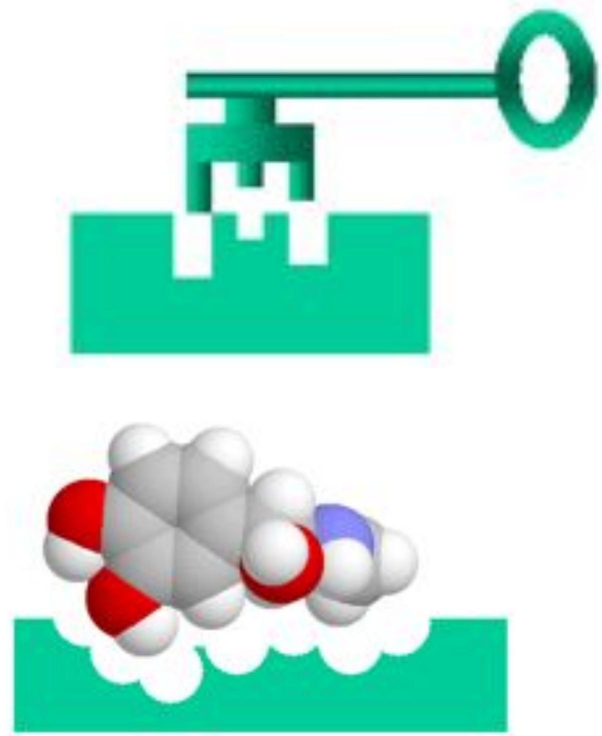
Neuropeptide Y



Acetylcholine

Receptors and ligands

- **Ligands** are molecules that bind to and activate **receptors**. **Neurotransmitters** and **hormones** are **ligands** for their **receptors**.
- The interaction between a **receptor** and its **ligand** – *"to bind/tie (L.)"* - somewhat resembles a lock and key.
- The **receptor** protein is shaped in such a way as to only accept binding from certain types of molecules. The molecular interaction between **receptor** and **ligand** is still not well understood.
- Drugs and poisons often work by interacting with **receptors** in a way that is similar to, but not identical to its natural **ligand**.
  - More on this to come in future classes.

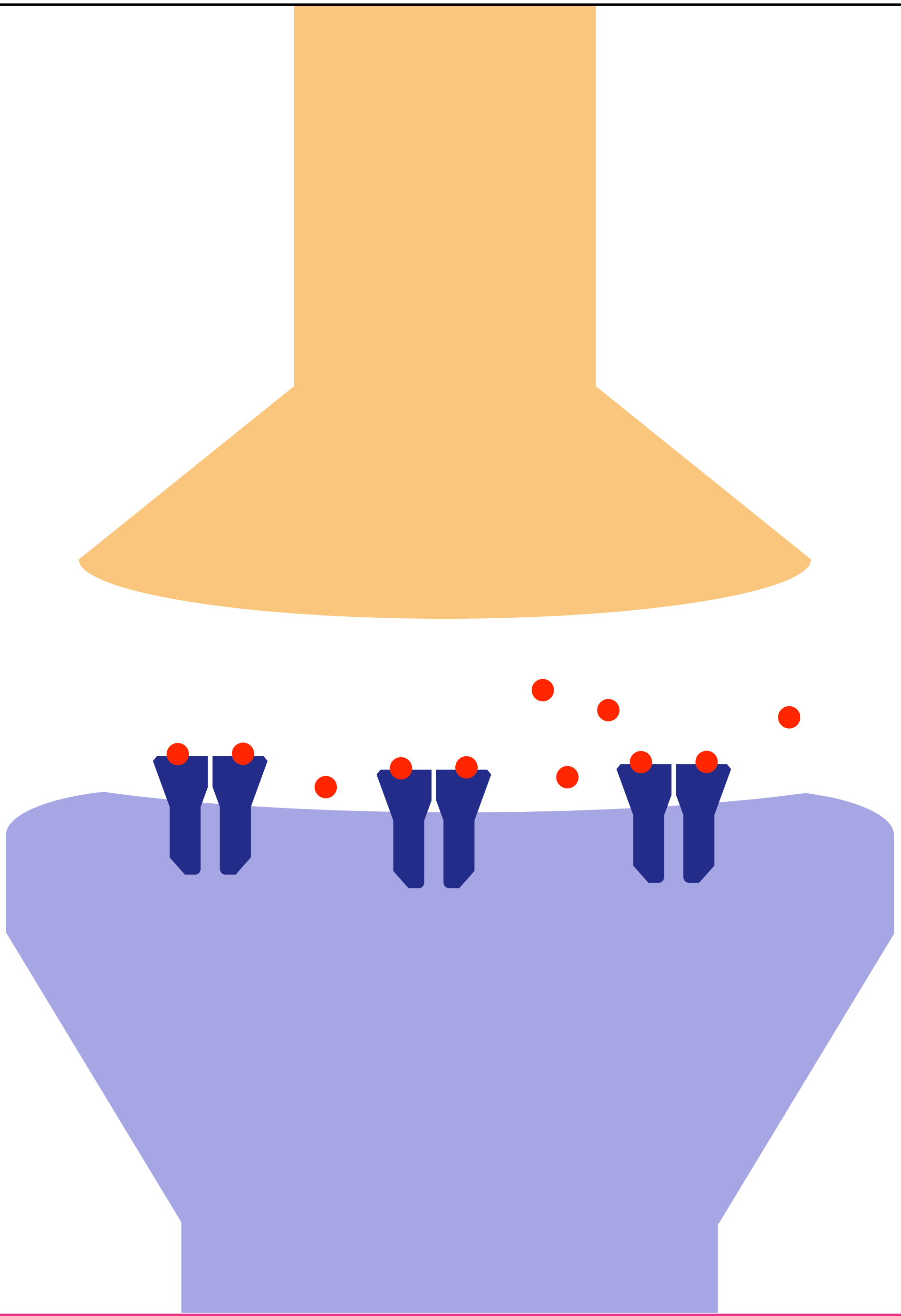


The lock and key metaphor

Deactivating NTs

Neurotransmitters do not stay in the **synaptic cleft** indefinitely. They must be removed somehow, otherwise they would continue to stimulate the **post-synaptic neuron**. This can be accomplished in *four* ways.

Diffusion: some of the neurotransmitter diffuses away from the synaptic cleft.



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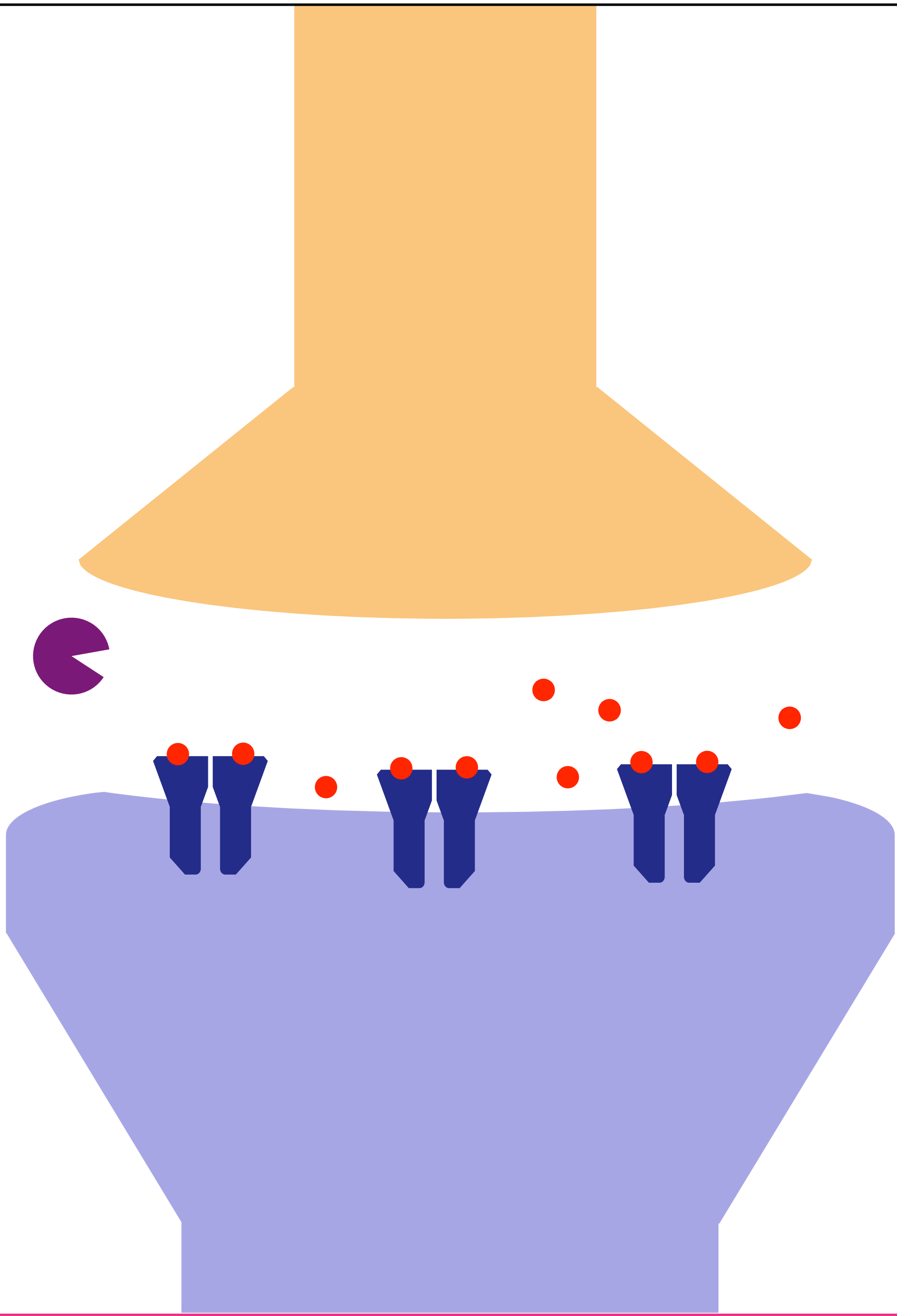

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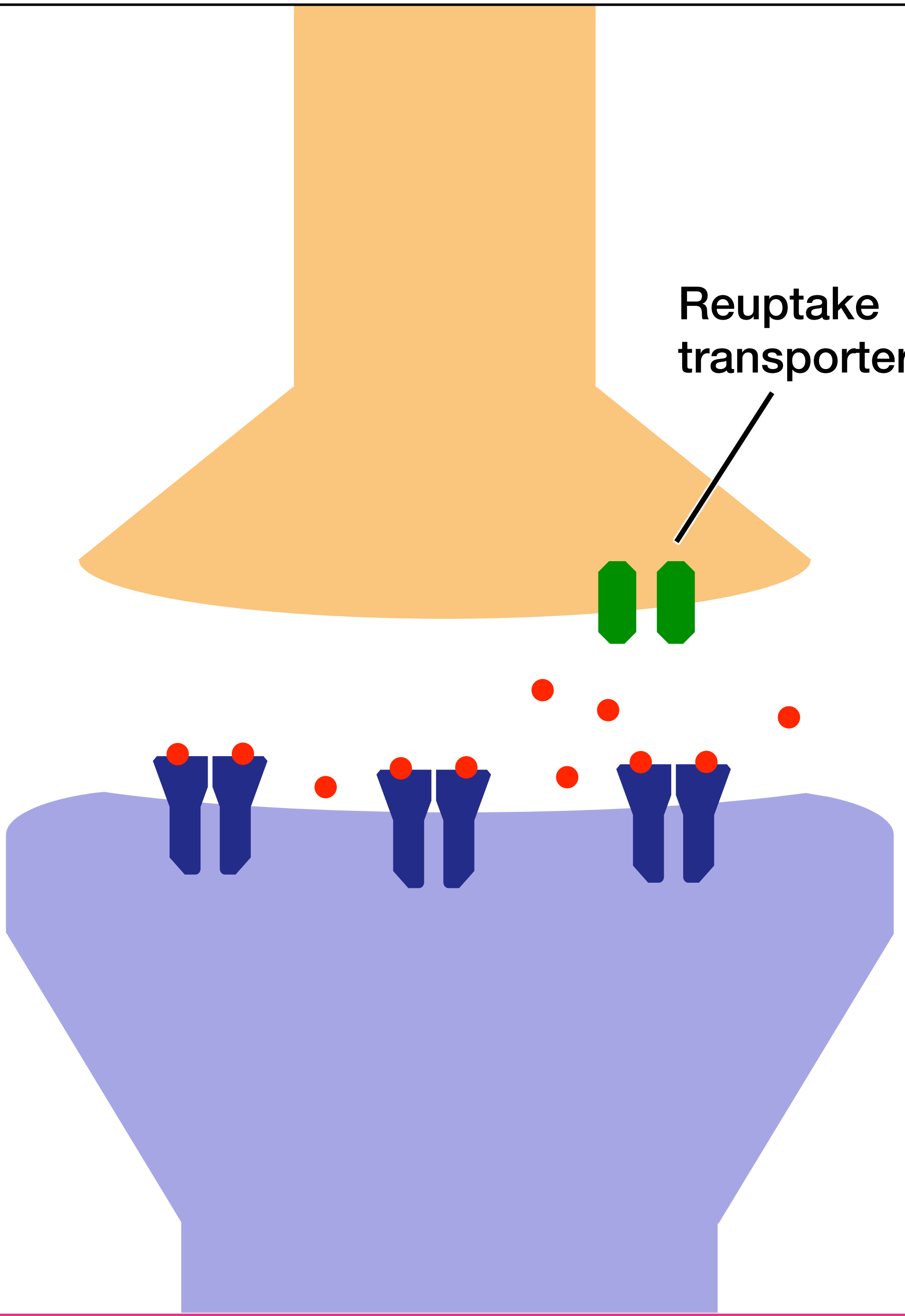
Reuptake: specialized proteins called called **reuptake transporters** re-cycle neurotransmitters back into the pre-synaptic terminal.



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Glial cells: neighboring glial cells may also take up stray neurotransmitters.