How fast is the action potential?
What determines its speed?

The condution speed = $\frac{\text{1. Internal resistence of the axon (axonal diameter)}}{\text{2. Current leakage across the membrane}}$

1. Axon diameter

A neuron propagates the action potential in a way similar to how current flows along an electrical cable.
The conduction velocity depends on:

R_i – Internal resistance
Opposes the flow of current within the cytoplasm

R_m – Membrane resistance
Opposes the flow of current across the membrane

C_m – Membrane capacitance
The ability of the membrane to store charge (like a capacitor)

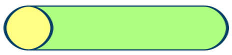
The relationship between these determines the **cable properties** of cells where:

The space constant (λ) is the distance along the membrane at which the electrical signal decreases to 37%, and it indicates how far depolarization can spread.

If λ is large → the signal **travels far** before weakening
If λ is small → the signal decays quickly

The following law is used to calculate the **conduction of electrical activity** along an axon:

$\boldsymbol{\lambda} = \sqrt{R_m/R_i}$

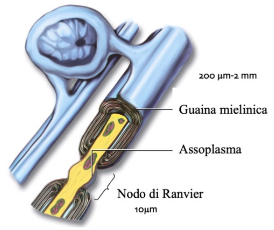


Smaller diameter
higher internal "friction" (resistance)→
slow conduction

Larger diameter
lower internal resistance →
fast conduction

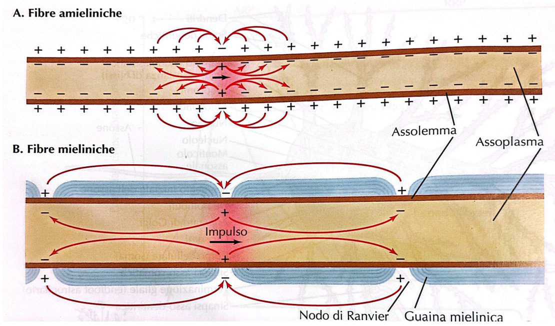
2. Current leakage across the membrane

Presence of myelin



Insulating sheath made of membrane phospholipids
Schwann cells in the PNS
oligodendrocytes in the CNS

What does it do :
⇩ Cm (**Membrane capacitance)**
⇧ Rm (**Membrane resistance)**



=

In these segments, the current flows inside the axon without crossing the membrane. In these cases, the propagation of the potential occurs only at the nodes of Ranvier
SALTATORY CONDUCTION

In the vertebrate nervous system, many neurons are myelinated, meaning they are covered by layers of an insulating sheath made of membrane phospholipids, formed by Schwann cells in the peripheral nervous system and by oligodendrocytes in the central nervous system.
Myelin:
decreases Cm
increases Rm
= the current in these segments flows inside the axon without crossing the membrane
In these cases, the propagation of the potential occurs only at points where there are interruptions in the myelin sheath, known as nodes of Ranvier (saltatory conduction).

Example:
a narrow, leaky pipe → slow water (small, unmyelinated axon)
a wide, insulated pipe → fast water (large, myelinated axon)

When is a myelinated axon needed and when an unmyelinated one?

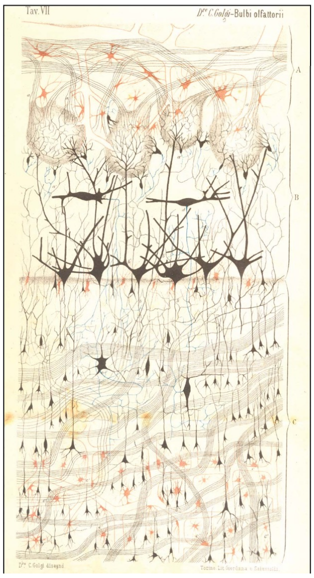
Myelinated axons → fast and precise signals

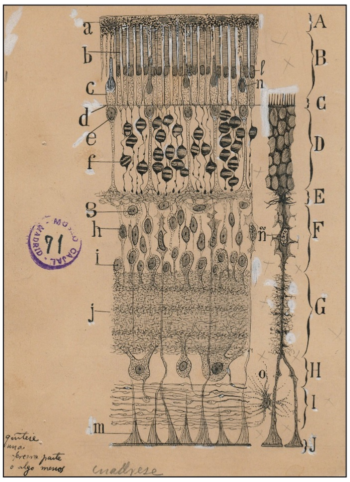
used for:
voluntary movement (muscles)
rapid reflexes
fine touch
proprioception (body position)

Myelinated axons → slow and diffuse

used for:
slow pain (dull, persistent)
temperature
visceral sensations (internal organs)

The neurons that make up a neural circuit are separate entities that communicate through specialized junctions

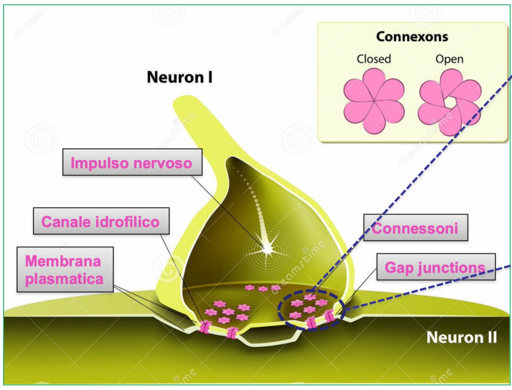


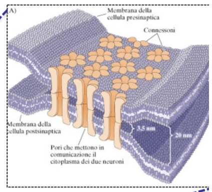


1897: Sir Charles Sherrington used the term "**synapse**" to refers to the functional junction between two neurons

- **ELECTRICAL SYNAPSES**
- **CHEMICAL SYNAPSES**

Electrical Synapsis





Electrical current passes from one cell to another through tight junctions (gap junctions)

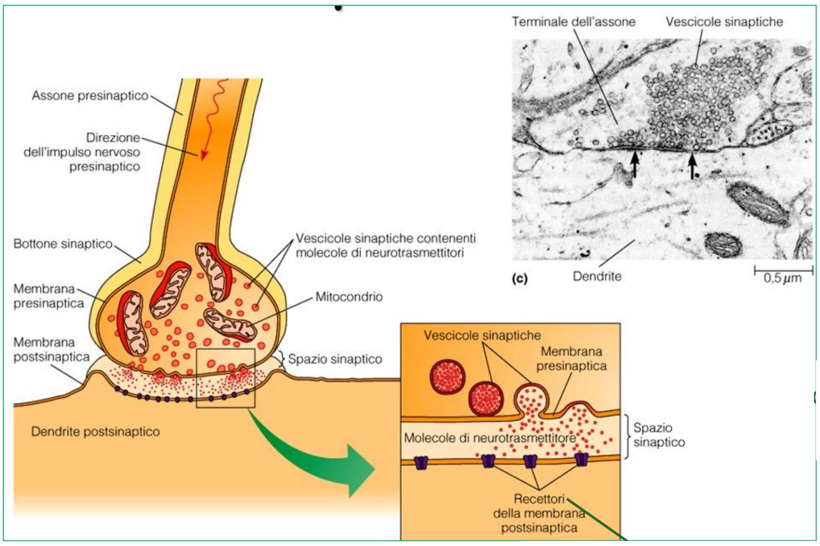
- *Used during embryonic development*
- *Cardiomyocytes*
- *Smooth muscle cells*

CONNEXONS: Intermembrane channel-forming proteins allow the passage of:
- Ions
- Water-soluble molecules with MW < 500 Da
- Cellular metabolites (e.g., second messengers)
- ATP

Electrical synapses are very common during embryonic development, where they promote the synchronization of neuronal activity; in adults they are less frequent and limited to specific circuits.

To clarify:
They do not generate new graded potentials
The current passes directly from one cell to another (so the electrical signal is already transmitted as a graded potential)
In fact, the signal is already electrical
It can generate an action potential

Chemical Synapsis



Post-synaptic reply: about 1ms

In chemical synapses, a key role is played by the neurotransmitter which, when released from the presynaptic neuron, induces a change in the membrane potential of the postsynaptic neuron through the following steps:

Depolarization, due to the action potential, propagates along the axon of the presynaptic neuron to the synaptic bouton (axon terminal), where it causes the opening of voltage-gated Ca^{2+} channels.

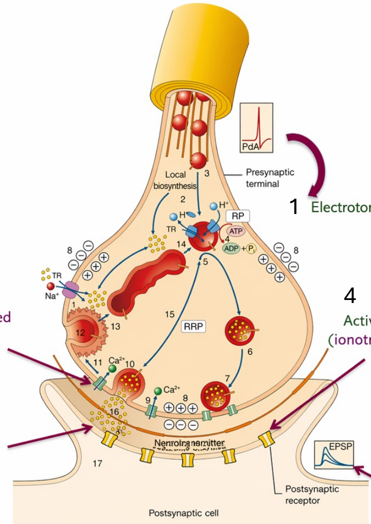
The entry of Ca^{2+} into the presynaptic terminal triggers the release of the neurotransmitter, stored in vesicles.

The neurotransmitter diffuses across the synaptic cleft and binds to specific receptors on the membrane of the postsynaptic neuron.

The receptor–neurotransmitter binding induces a change in the membrane potential of the postsynaptic neuron.

To clarify:
In chemical synapses, graded potentials are generated because:
the neurotransmitter opens channels
a postsynaptic potential is generated
= this is a graded (electrotonic) potential

Neurotransmitter release



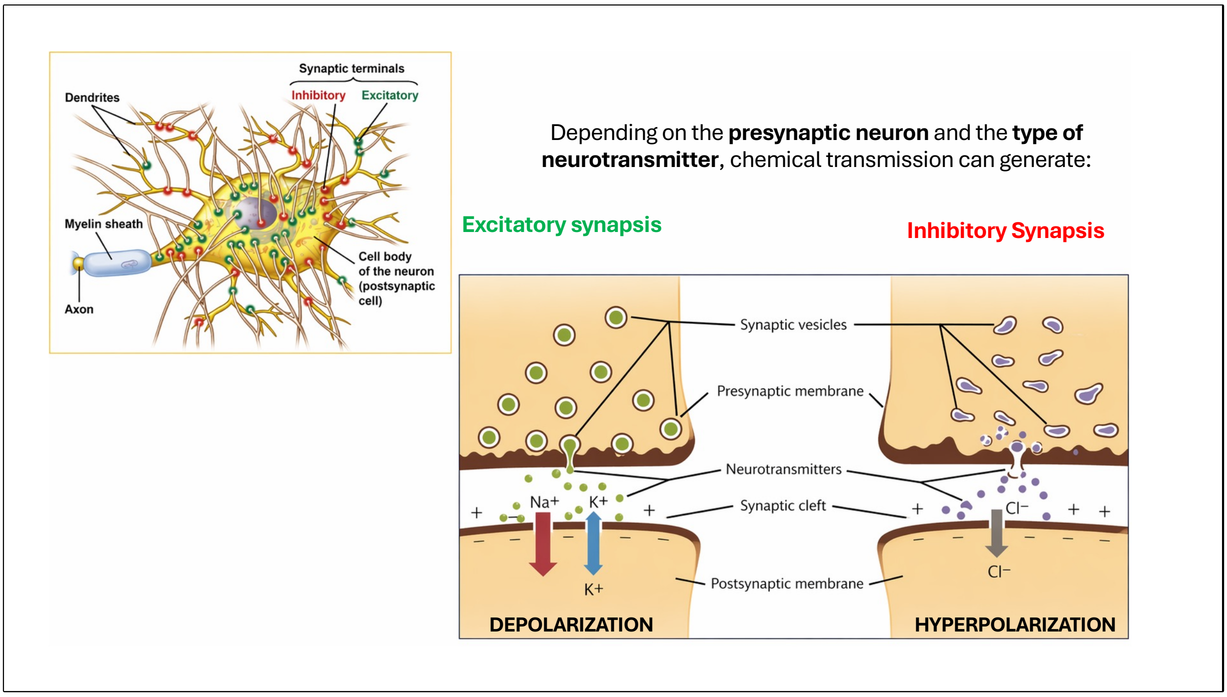
1 Electrotonic spread of the potential

2 Opening of voltage-gated Ca^{2+} channels

3 Exocytosis of the neurotransmitter

4 Activation of postsynaptic receptors (ionotropic or metabotropic): a synaptic current is generated

5 Synaptic current can be depolarizing (excitatory) or hyperpolarizing (inhibitory): a postsynaptic potential is generated

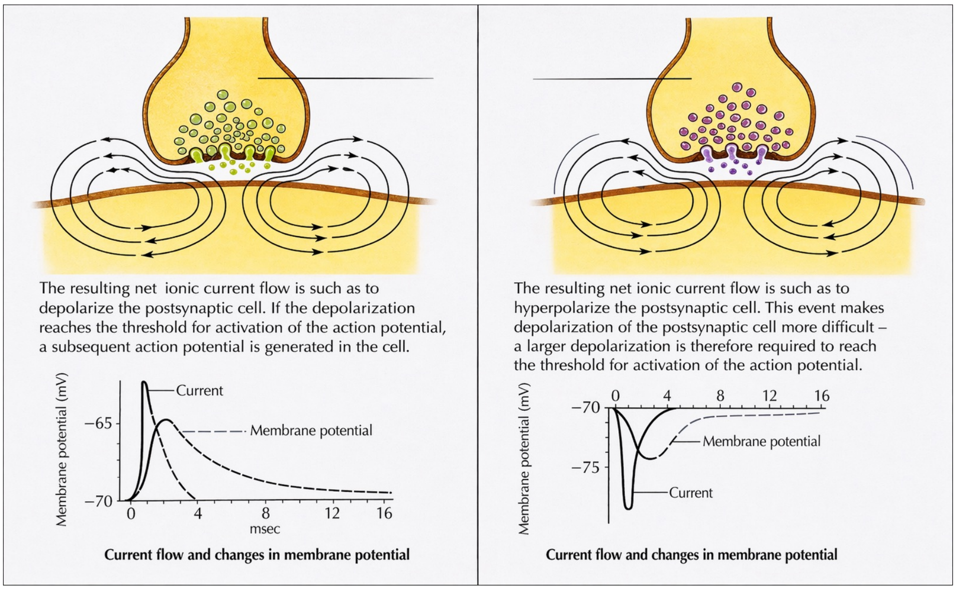


Depending on the presynaptic neuron and the type of neurotransmitter, chemical transmission can generate:

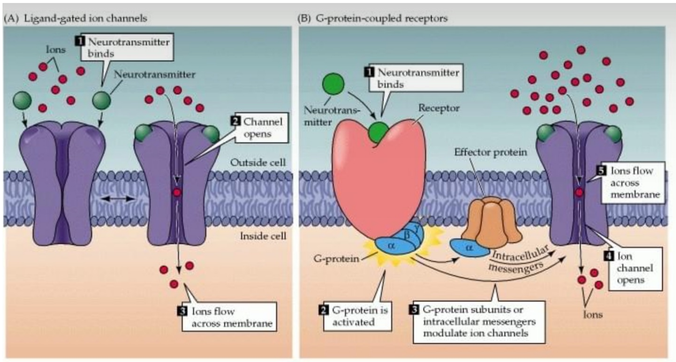
an excitatory postsynaptic potential (EPSP) – **EXCITATORY SYNAPSE**
→ promotes depolarization of the postsynaptic neuron
→ mainly associated with Na^+ influx

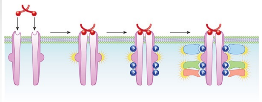
an inhibitory postsynaptic potential (IPSP) – **INHIBITORY SYNAPSE**
→ induces hyperpolarization of the postsynaptic neuron
→ mainly associated with Cl^- influx

Excitatory synapsis **Inhibitory Synapsis**



Focus on receptor activation: Ionotropic vs. Metabotropic





- Ion channels

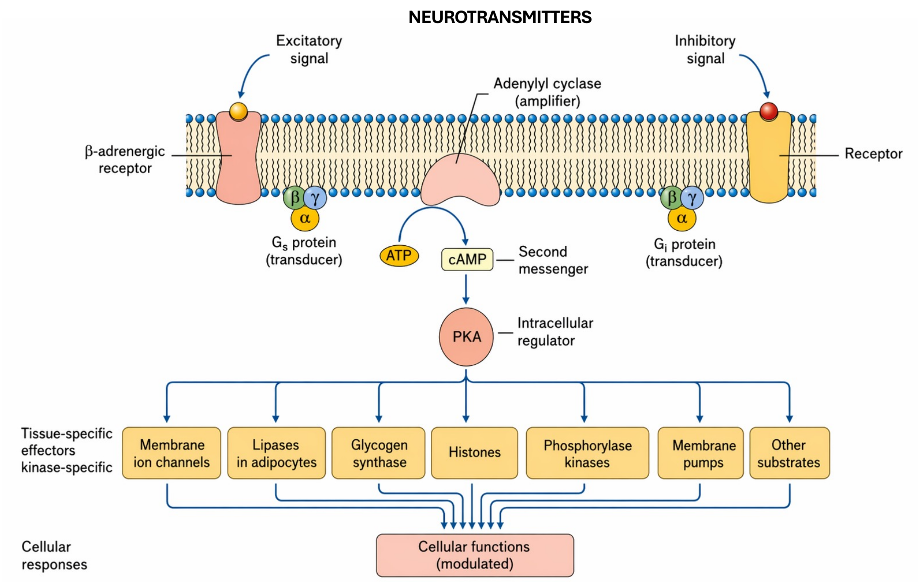
- G-coupled receptors
- Tyrosin-kinase receptors

Fast chemical transmission
milliseconds

Slow chemical transmission
seconds

Let's see what distinguishes them and what they have in common.
Both are membrane proteins that span the plasma membrane completely and have the function of transmitting a signal inside the cell.
As for the differences, ionotropic receptors are actually ion channels. When the neurotransmitter binds to the receptor, the channel opens directly and allows the passage of ions, such as sodium or chloride. This produces a very rapid response because the mechanism is direct.
Metabotropic receptors, on the other hand, are not ion channels (they can be G protein–coupled receptors or tyrosine kinase–associated receptors). When the neurotransmitter binds, the receptor activates a G protein, which in turn triggers a cascade of intracellular reactions. These reactions lead to the production of second messengers, which can modulate cellular activity, for example by opening or closing ion channels or regulating other cellular processes.
For this reason, the response of metabotropic receptors is slower, but also more modulable and longer-lasting. In some cases, it can lead to long-term effects, such as changes in gene expression and neuronal excitability.
In summary, ionotropic receptors mediate fast and direct responses, whereas metabotropic receptors play a more modulatory role and produce slower but longer-lasting effects.

Excitatory and inhibitory G proteins



G proteins can have opposite effects: some activate intracellular pathways (Gs), while others inhibit them (Gi), thereby modulating the cell's response.

On the left, we have an excitatory G protein (Gs). When a neurotransmitter binds to the receptor, it activates the G protein. The α subunit stimulates an enzyme called adenylyl cyclase, which converts ATP into cAMP (a second messenger). cAMP activates PKA, which then regulates different targets such as ion channels, enzymes, and gene-related proteins.

The final effect is an amplified, excitatory response.
On the right, we have an inhibitory G protein (Gi). When the receptor is activated, the G protein inhibits adenylyl cyclase, reducing cAMP production and PKA activity.
The result is a weaker, inhibitory cellular response.

Neurotransmitter types

Amino Acids	Amines	Peptides
Gamma-aminobutyric acid (GABA)	Acetylcholine (ACh)	Cholecystokinin (CCK)
Glutamate (Glu)	Dopamine (DA)	Dynorphin
Glycine (Gly)	Adrenaline	Enkephalins (Enk)
Histamine	N-acetylaspartylglutamate (NAAG)	
Noradrenaline (NA)	Neuropeptide Y	
Serotonin (5-HT)	Somatostatin	
	Substance P	
	Thyrotropin-releasing hormone	
	Vasoactive intestinal peptide (VIP)	
⇩	⇩	⇩
Fast	Intermediate speed	Slow
Direct transmission	Modulation	Long term modulation