Neurotransmission and Postsynaptic Potential (PSP)

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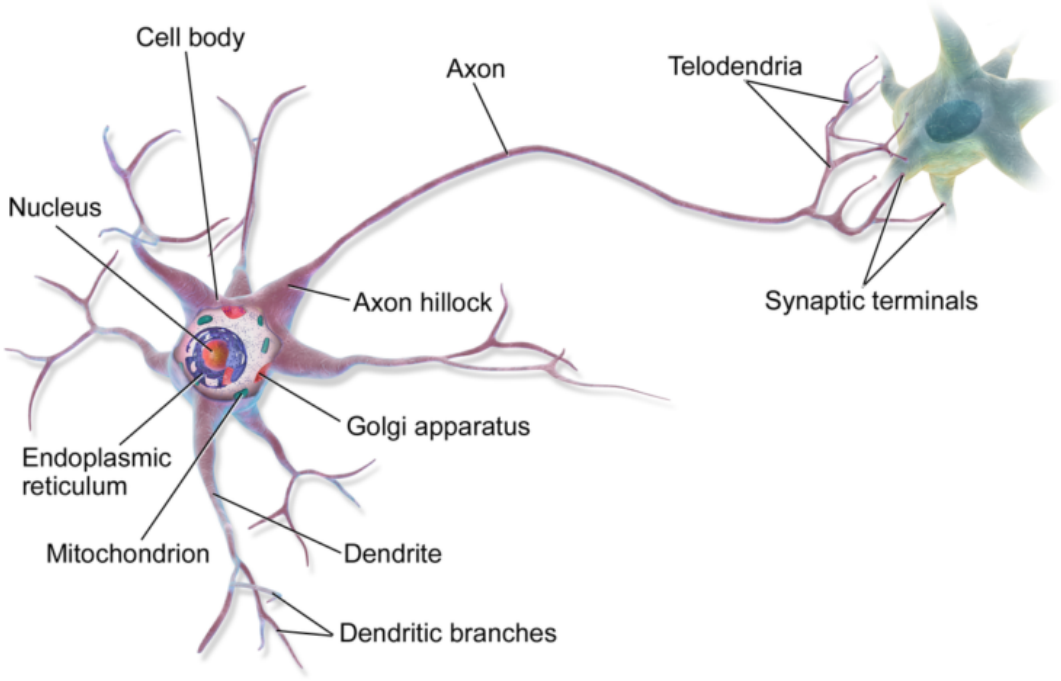
A nerve is made up of countless neurons which are responsible for carrying signals from different parts of the body to the nervous system and vice versa. Neurons which carry the signals from the sense organ to the nervous system are called sensory neurons and form the sensory nerve fibers. Similarly, neurons which carry signals from the nervous system to the effector organs, muscles or glands are called the motor neurons. These motor neurons form the motor nerve fibers. Relay neurons carry the signals across the nervous system. The signal transmission from the sense organs to the nervous system and then to the effectors is essential in the maintenance of homeostasis. Any disruption in this pathway leads to the loss of a specific sensation or response.



Structure of a Neuron

A neuron consists of a central **cell body** which constitutes the nucleus, mitochondria, endoplasmic reticulum, and golgi apparatus. Cell processes which carry the signals towards the nucleus are called the **dendrites,** while the one which carries the signals away from the cell body is termed as the **axon**. Axon forms telodendria and synaptic terminals.

Synapse

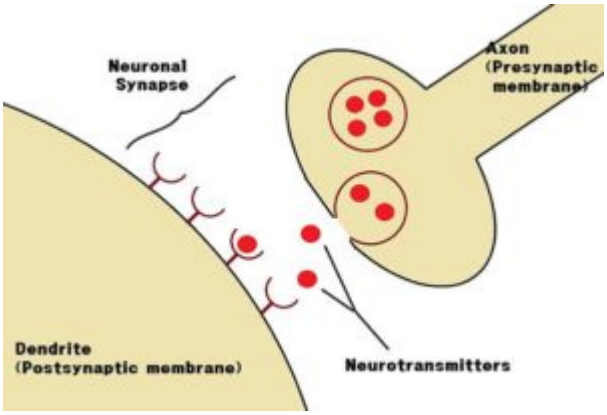


Image: "Depiction of a Neuronal Synapse." by Edk006 – Own Work. License: CC BY-SA 3.0

A neuron may terminate into:

- A muscle, causing it to contract
- A gland, resulting in the production of secretions
- Another neuron, to pass along the nerve signals.

The junction between the two neurons is called synapse. The neuron that carries the signal to the other neuron is called pre-synaptic neuron, while the other neuron is called the postsynaptic neuron. The space between the two neurons is called the synaptic cleft.

Types of synapses

A synapse is a structure that allows a neuron to pass a chemical or electrical signal to another neuron. Thus, it can be classified as either electrical or chemical.

In an **electrical synapse**, the two neurons are connected through **charge-carrying ions**, which flow between them in the **gap junctions**. Although it is an unbroken way of transmission of signals, it is essentially either 'on' or 'off.' These synapses are **unregulated**. If one neuron is activated via an action potential, the second neuron will definitely be activated. Such synapses are rare in the human nervous system, however, found in specialized locations such as **pulp of the tooth** and **retina of the eye**.

The chemical synapse consists of the release of specific chemical substances into the synaptic cleft after an action potential reaches the end of the pre-synaptic neuron. These chemical substances are called **neurotransmitters** and are contained in **vesicles** of the **synaptic knob**, swelling at the end of the pre-synaptic neuron. Chemical synapses are abundantly present in the human nervous system and therefore described in detail below.

Signal transmission across a synapse

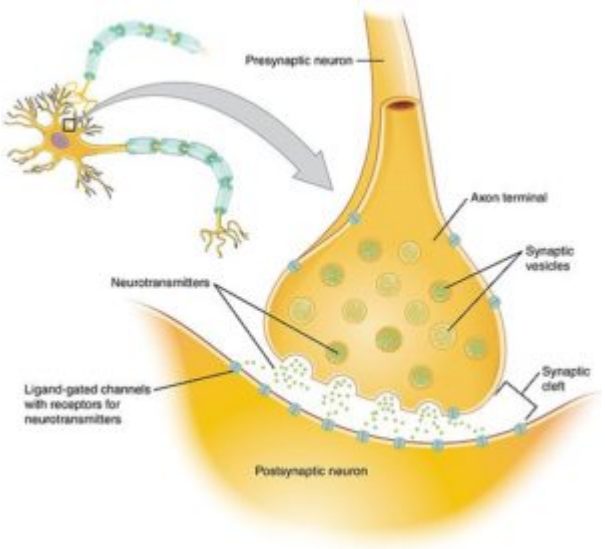


Image: “Signal Transmission across a Synapse.” by OpenStax – https://cnx.org/contents/FPtK1zmh@8.25:fEI3C8Ot@10/Preface. License: CC BY 4.0

When an **action potential** reaches the end of the pre-synaptic neuron, it causes specific changes in the cell membrane, which leads to the opening of **voltage-gated calcium channels** in the synaptic knob.

Calcium ions being in excess amount in the extracellular fluid move down the concentration gradient into the synaptic knob.

The calcium ions cause a **release of neurotransmitters** in the synaptic cleft. The vesicles containing neurotransmitters move towards the cell membrane, fuse with it and are released by the process of **exocytosis.**

The neurotransmitters bind to their specific **receptors** on the sub-synaptic membrane, which is the portion of the post-synaptic membrane lying immediately below the synaptic knob.

The receptors are an integral part of specific **ion channels** on the post-synaptic membrane. Binding of the neurotransmitters to their receptors open up these channels. This changes the ion permeability of the cell membrane.

The synapse is **unidirectional** i.e. from pre-synaptic neuron to the postsynaptic neuron as the former releases the neurotransmitters and the later has receptors on its cell surface membrane. The pre-synaptic neuron releases only one type of neurotransmitter.

The conversion of this chemical signal back to an electrical signal requires time, often referred to as the **synaptic delay**. It is usually about 0.5 – 1msec. As the pathway becomes more and more complex, the total synaptic delay also increases which causes a **longer reaction time**. The figure illustrates the signal transmission across a synapse.

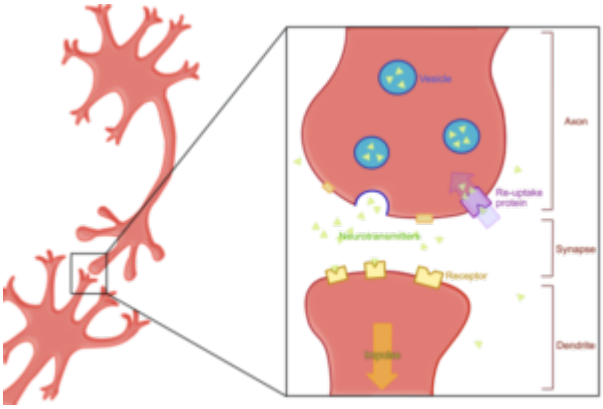


Image: “Reuptake of Neurotransmitters.” by Sabar – Self-Made, Created with Corel Painter and Adobe Photoshop. License: Public Domain

If the neurotransmitters remain bound to the receptors, the potential change produced in the post-synaptic membrane continues. However, in order to receive a new synapse, the **neurotransmitters must first be removed from the receptor site and the synaptic cleft.**

These neurotransmitters are either taken up by the pre-synaptic neuron, to be stored and released for another signal transmission (see figure), or they are inactivated by the enzymes present in the synaptic cleft. The response therefore produced by the neurotransmitters is terminated.

Neurotransmitter classes

Class	**Name**	**Class**	Name
Small molecule		**Peptides**	
Amino acid	• Glutamate • y-Aminobutyric acid • Glycine	Opioid	• Dynorphins • Endorphins • Enkephalins
Cholinergic	Acetylcholine	Tachykinin	• Neurokinins • Substance P
Catecholamine	• Dopamine • Norepinephrine • Epinephrine	Enteric	Gastrin-releasing peptide
Monoamine	• Serotonin • Histamine		

Types of synapse depending upon the permeability changes in the post-synaptic neuron

There are two types of synapse depending upon the permeability changes in the post-synaptic membrane. It could either be an **excitatory synapse** or an **inhibitory synapse**.

In an **excitatory synapse**, the **sodium** and **potassium ions** are opened up in the post-synaptic membrane. The permeability of these ions increases, however, their net movement depends upon their electrochemical gradient across the cell membrane.

At **resting membrane potential**, the concentration of sodium ions is abundantly higher in the extracellular fluid, therefore, **sodium ions diffuse into the postsynaptic neuron**. Potassium ions, on the other hand, are already in excess inside the cell; therefore, only a few of them leak out of the cell as the movement of sodium ions changes their permeability across the membrane.

The net movement of positive ions inside the cell changes the membrane potential to

a **less negative value**. A single excitatory synapse only produces a small depolarization in the post-synaptic neuron and does not reach the **threshold value**. The action potential in the post-synaptic neuron is only generated if the threshold value is reached when many excitatory inputs are given.

In an **inhibitory synapse**, the neurotransmitters released to cause the opening of **potassium and chloride ion channels. Potassium ions** being more abundant **diffuse out** of the post-synaptic neuron. **Chloride ions** are abundant in the extracellular fluid, therefore, **diffuse into** the post-synaptic neuron. This increases the negativity inside the cell and the cell membrane is said to be **hyper-polarized**.

The hyper-polarization of the cell membrane moves it further away from the threshold potential, thereby minimizing the generation of an action potential in this neuron.

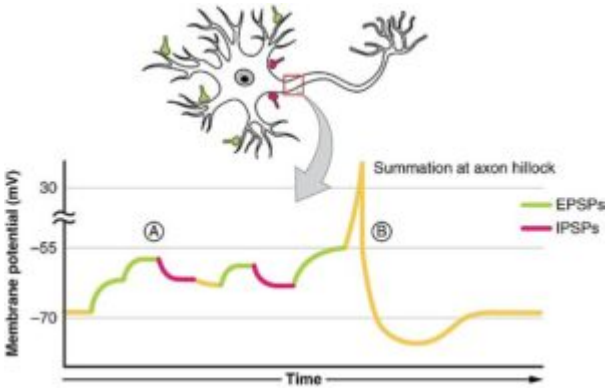


Image: “Excitatory and inhibitory synapses. EPSPs: Excitatory post-synaptic potentials, IPSPs: Inhibitory postsynaptic potentials.” by OpenStax – https://cnx.org/contents/FPtK1zmh@8.25:fEI3C8Ot@10/Preface. License: CC BY 4.0

The net charge across the cell membrane of the post-synaptic neuron is a composite of all the excitatory and the inhibitory synapses, as shown in the figure. It is known as **the grand post-synaptic potential (GPSP)**. The action potential in the post-synaptic neuron is generated at the **axon hillock** as it has the lowest threshold potential, due to the presence of abundant **sodium channels**.

Some neurotransmitters, such as **glutamate,** produce excitatory post-synaptic potential while others, such as **gamma-aminobutyric acid (GABA),** produce inhibitory post-synaptic potential.

Summation

As mentioned earlier, a single excitatory synapse is not enough to produce excitatory post-synaptic potentials. **The summation** is a process by which several pre-synaptic signals are **summed up** to produce an **action potential** in the post-synaptic neuron. Depending upon the number of signals, the magnitude of the response varies. There are two types of summation: temporal summation and spatial summation.

Temporal summation is the process in which the presynaptic neuron generates action potentials in very **close succession**. The post-synaptic membrane becomes **depolarized** due to the first action potential of the pre-synaptic neuron.

As the second action potential generated in the pre-synaptic membrane causes further **depolarization** in the postsynaptic membrane, the later reaches the threshold potential;

thus, an action potential is generated in the postsynaptic neuron.

Sometimes, up to 50 excitatory postsynaptic potentials are required to generate an action potential. The **frequency** of action potentials generated in the pre-synaptic neuron is decisive of the **number of neurotransmitters released** and the **magnitude of depolarization** in the postsynaptic membrane.

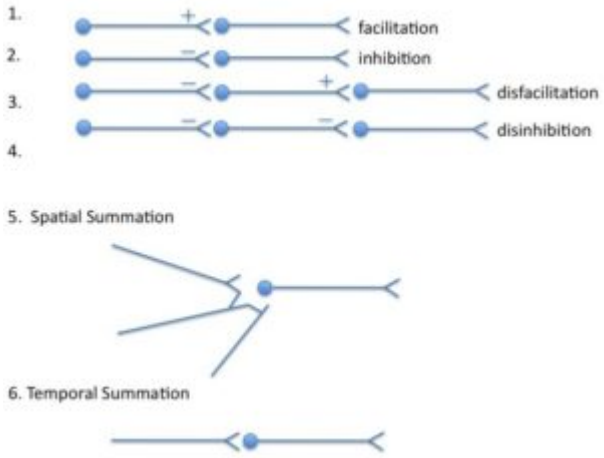


Image: “Interneuronal Relations. Diagram of the basic ways that neurons can interact with each other when converting input to output.” by Bbelai – Own work. License: CC0 1.0

Spatial summation is the process in which **simultaneous action potential** in several presynaptic neurons releases a large number of neurotransmitters into the synaptic cleft. The magnitude of depolarization generated in the post-synaptic neuron reaches the threshold potential and an action potential is generated. The figure beside gives an outline of the process of summation.

Convergence and divergence

Convergence is the property of neuron in which a **single neuron receives** input signals from a **number of neurons**, due to the presence of several dendritic branches.

Divergence is when a **single neuron sends** input signals to **many other neurons**. The branching of axon facilitates divergence.

Applied Clinical Physiology

Selective serotonin reuptake inhibitors (SSRIs) are a group of anti-depressant drugs which block the **reuptake** of **serotonin** neurotransmitter by the pre-synaptic neuron. Serotonin, therefore, remains in the **synaptic cleft** for a longer duration of time. This prolongs its effect on the post-synaptic neuron, thereby minimizing **anxiety symptoms**.

Cocaine, a common substance of abuse, exerts it effects by blocking the **reuptake** of neurotransmitter **dopamine**. It **competitively** binds to the dopamine reuptake transporter, which prolongs the duration of dopamine in the synaptic cleft. The abuser gets a continuous pleasure sensation.

The postsynaptic neurons become **desensitized** to the level of dopamine and eventually require a greater amount for the generation of an action potential. This explains the strong **addiction** to cocaine. With prolonged use of cocaine, the **number of dopamine receptors is also reduced** on the post-synaptic membrane.

Myasthenia gravis is an **autoimmune disease** in which there is a production of **auto-antibodies** against **acetylcholine receptors** on the post-synaptic membrane. These receptors are blocked, causing the failure of muscle contraction.

Patients complain of **exhaustion** and **fatigue** as the day ends. The classical symptom is the **drooping of the eyelids** as the night time approaches. The symptoms are treated with **acetylcholine-esterase inhibitors.**

Acetylcholine-esterase is an enzyme present in a normal individual which breaks down the **acetylcholine** neurotransmitter in the synaptic cleft. Blocking this enzyme will **increase** the level of acetylcholine in the synaptic cleft which will compete with the auto-antibodies.

Parkinson's disease is a neurodegenerative disorder in which the production of **dopamine** is **decreased** due to the destruction of the cells producing it. This results in symptoms such as **hypokinesia**, **rigidity**, **dementia**, **hallucinations,** and **depression**. The disease is treated with **levodopa**, **dopamine agonists** and **monoamine oxidase B (MA0-B) inhibitors.** MAO-B is an enzyme that causes the destruction of dopamine in the synaptic cleft.

Tetanus toxin prevents the release of GABA, an inhibitory neurotransmitter. This results in unchecked excitatory signals to the **skeletal muscles** which go into **spasm**. The **jaw muscles** are specifically affected giving the classical sign of 'lockjaw.' As the disease progresses, the **respiratory muscles** also get involved causing death.

Strychnine poison binds to the glycine receptors on the post-synaptic neuron. Glycine is an inhibitory neurotransmitter. When it does not bind to its receptors on the post-synaptic membrane, the post-synaptic **inhibition is abolished** resulting in unchecked **excitatory pathways**. The patient dies of **convulsions** and **muscular spasm**.

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Notes