PROPERTIES OF SYNAPTIC TRANSMISSION

Transmission of signals across the synapses is characterized by:

1. **FORWARD DIRECTION**
   Transmission in synapses is unidirectional, i.e. from the presynaptic to the postsynaptic neuron, not the reverse. This is because the postsynaptic neuron cannot release a chemical transmitter at the synapse. So, the synapse acts as a unidirectional "valve" to keep the flow of signals between neurons always in the right direction.

2. **SYNAPTIC DELAY**
   When an impulse reaches a nerve terminal, it takes a delay time of 0.5-1.0 ms to pass across the synapse to the postsynaptic neuron. This time is taken for the release of the chemical transmitter, its diffusion in the synaptic extracellular fluid and then synaptic cleft, activation of receptors, induction and summation of postsynaptic potentials.

3. **SYNAPTIC AFTERDISCHARGE**
   After discharge is the persistence of output signals after stoppage of the input signals. Synaptic afterdischarge occurs at some synapses because of the delay of inactivation of the chemical transmitter. So, an impulse conducted by a presynaptic neuron may produce more than one impulse in the postsynaptic neuron. The duration of the synaptic afterdischarge is longer if the chemical transmitter released by the
presynaptic neuron is a long acting one (substance P).

4. **FATIGUE**

Fatigue is the decline in response caused by prolonged activity. For a synapse, fatigue is the decline in the response of the postsynaptic neuron after a long period of high frequency stimulation of the synapse (> 60 Hz). It is manifested by prolongation of the synaptic delay, then failure to transmit some or all of the impulses across the synapse.

The synapse is an early site of fatigue in the reflex arc and the fatigue of the neural synapses is caused by:

i. **Exhaustion** of the chemical transmitter in the presynaptic terminals which is the main cause.

ii. **Inactivation** of some postsynaptic receptors due to accumulation of metabolites.

iii. **Marked increase** of the intracellular Ca$^{2+}$ in the postsynaptic neuron. This high Ca$^{2+}$ level opens K$^+$ channels so K$^+$ efflux and hyperpolarization of the postsynaptic membrane decreasing the excitability of postsynaptic neuron.

**Fatigue is a protective mechanism against excess neuronal activity**

Fatigue is the most important means by which the excess excitability of an epileptic circuit is cut off and stopped. This leads to spontaneous ending of the epileptic fit (normal protective mechanism).
5. SYNAPTIC POTENTIATION (FACILITATION)
This is an increase in the postsynaptic response caused by previous presynaptic stimulation. It may be a short-term or a long-term potentiation.

i. SHORT TERM (POST TETANIC) POTENTIATION
This occurs after a short period of low frequency stimulation of the synapse (<60 Hz). It is caused by an increase in the intracellular Ca^{2+} level in the presynaptic neuron, which increases the release of the transmitter. Short-term potentiation lasts for few seconds up to few minutes.

ii. LONG TERM POTENTIATION (LTP)
This occurs after a short period of high frequency stimulation (>60 Hz). Long term potentiation is caused by the release of arachidonic acid from the postsynaptic neuron which acts on the presynaptic neuron to release more of the transmitter (Glutamate). Long-term potentiation occurs in several parts of the CNS, particularly in the hippocampus and it plays an important role in memory and learning.

6. SYNAPTIC DEPRESSION (HABITUATION)
Habituation is the gradual decrease in the postsynaptic response when stimulation of the presynaptic neuron is frequently repeated. With complete habituation, the postsynaptic response may disappear altogether.

Habituation is due to inactivation of Ca^{2+} channels in the presynaptic neuron which decrease in intracellular Ca^{2+} so release of smaller amount of transmitter from the presynaptic terminals.
Habituation could be short-term or long-term depending on how many times the stimulus is applied. It is an important mechanism of learning, as it enables the subject to ignore insignificant stimuli. Habituation of synapses is different from adaptation which occurs in excitable tissues. Adaptation is the decline in response to a constant maintained stimulus.

7. SENSITIZATION

Sensitization of a synapse is the potentiation of the postsynaptic response to a certain stimulus by coupling the stimulus to another intense (usually painful) stimulus (fig.2-1).

The terminal which conducts the intense or painful stimulus is called a facilitator terminal which relays on the presynaptic sensory terminal. The facilitator terminal stimulates the presynaptic sensory terminal lead to prolonged action potential in the sensory terminal and more Ca\(^{2+}\) influx into the sensory terminal so release of more transmitter and potentiated postsynaptic response result.

Sensitization is an important mechanism in memory and learning.

![Figure 2-1: The mechanism of synaptic sensitization.](image)
8. EFFECT OF pH
Alkalosis enhances synaptic transmission. A rise of arterial blood pH from 7.4 to 7.8 leads to increased cerebral excitability and convulsions.

Acidosis depresses synaptic transmission. Breathing of air with high Co2 level will lead to hypercapnea and acidosis and then depression of synaptic transmission in the brain resulting in drowsiness and sleep or even anesthesia. A drop of arterial pH down to 7.0 produces coma because of failure of synaptic transmission between various neurons in the brain.

9. EFFECT OF HYPOXIA
Hypoxia depresses synaptic transmission and prolongs reflex time due to accumulation of acidic metabolites.

10. EFFECT OF DRUGS
Caffeine, theophylline and theobromine which are found in coffee, tea enhance synaptic transmission. They increase neuronal excitability by lowering the threshold of excitation.

Strychnine enhances synaptic transmission by blocking the action of central inhibitory transmitters (e.g. glycine).

Hypnotics and anesthetics depress synaptic transmission by decreasing neuronal excitability. They stabilize the cell membrane by increasing the resting membrane potential (hyperpolarization).
PROCESSING OF SIGNALS IN THE CNS

Nerve signals (impulses) enter the CNS to be directed to various neuronal pools (collection of neurons). In the neuronal pools, input signals are processed, and output signals emerge out to proceed to specific destinations.

THE DISCHARGE ZONE AND THE FACILITATED FRINGE
(THE LIMINAL ZONE AND THE SUBLIMINAL FRINGE)

When an impulse in an excitatory input neuron reaches the neuronal pool, it stimulates a group of neurons which form the "stimulatory field" of this neuron (fig.2-3).

![The stimulatory field of an input neuron.](image)

At the middle of the field, stimulation reaches a liminal level (threshold) and the neurons in this zone discharge impulse. The zone where neurons discharge impulse is called the discharge zone or the
**liminal zone** of the input neuron.
Around the discharge zone, there is a circular zone (a fringe) in which
the neurons are only facilitated without reaching the liminal firing
level. This zone is called "the facilitated fringe" or "the subliminal
fringe" of the input neuron.
An impulse in an inhibitory input neuron produces an "inhibitory
field" with maximum inhibition at its center.

**FORMS OF SIGNAL PROCESSING IN THE NEURONAL POOLS**
Signal processing in the neuronal pools takes one of the following
forms:

[I] Convergence.

[II] Divergence.

[III] Prolongation.

[IV] Shortening.

[V] Sharpening.

[I] CONVERGENCE OF SIGNALS
Convergence is the direction of signals from several input neurons to
excite a single output neuron. There are two main types of
convergence in the neuronal pools.

**1. CONVERGENCE FROM A SINGLE SOURCE**
This is important because no neuron can be excited by a single input
terminal. So, convergence must occur on neurons to excite those
neurons (fig.2-4). The spatial and the temporal summation of
postsynaptic potentials from the multiple input terminals build up a threshold membrane potential to excite the neuron.

Figure 2-4: convergence from single source

2. CONVERGENCE FROM MULTIPLE SOURCES
This is important because it enables neurons of the neuronal pool to receive signals from different sources (fig. 2-5).
The effect produced will be the resultant of all the inputs whether excitatory or inhibitory; e.g. motor neurons of the ventral horn of the spinal gray matter receive inputs from the pyramidal and extra pyramidal tracts and from the afferent fibers of the stretch reflex and several intermediate neurons. All these input neurons influence the contraction and relaxation of the skeletal muscles.

Figure 2-5: Convergence from multiple sources.
[II] DIVERGENCE OF SIGNALS

Divergence is the spread of a signal from one input neuron into more than one output neuron. There are two main types of divergence in the neuronal pools:

1. DIVERGENCE IN THE SAME BATHWAY

This leads to spread of the signal into an increasing number of neurons as it passes from one order of neurons into another (fig. 2-6). It may be called an "amplifying divergence". It occurs, for example, in the pyramidal tract where a single pyramidal neuron in the motor cerebral cortex can excite up to 10,000 muscle fibers.

2. DIVERGENCE INTO MULTIPLE PATHWAYS

This leads to spread of the signal into two or more separate directions from the pool (fig. 2-7). It may be called a "diversifying divergence". It occurs, for example, in the paleospinothalamic tract where some signals proceed directly to the thalamus and others enter the spinoreticular tract.

Figure 2-6: Amplifying divergence.
Afterdischarge is the persistence of output signals after stoppage of the input signals. This is possible through the following mechanisms:

1. **SYNAPTIC AFTERDISCHARGE:**

2. **OPEN-CHAIN CIRCUITS**

These are circuits in which several interneuron's are arranged to form an open circuit (fig. 2-7). When interneuron (1) is excited, it sends a signal to the output neuron and collateral to excite interneuron (2). Interneuron (2) then sends a signal to the output neuron and collateral to excite interneuron (3) and so on. The result will be a barrage (train of impulses follows each other) of impulses in the output neuron. The interneurons of the open-chain circuits are called "the interneuronal barrages."
3. CLOSED {REVERBERATING} CIRCUITS
These are circuits in which the output neuron is repeatedly activated through a closed circuit of interneurons (fig.2-8). When interneuron (1) is excited, it sends an impulse to the output neuron and collateral to excite interneuron (2). Interneuron (2) then re-excites interneuron (1), and so on.

![Diagram of a closed reverberating circuit](image)

**Figure 2 - 8: A closed chain (reverberating) circuit of neurons.**

Reverberating circuits can be facilitated or inhibited by other input fibers. When facilitated the frequency and duration of discharge in output fibers increase. When inhibited, the frequency and duration decrease. The cycle of reverberation stops by either fatigue of synapses or inhibition by other input fibers. The frequency and duration of discharge from a reverberating circuit depends on the number of neurons (i.e. the number of synapses) in the circuit. The larger the number the lower is the frequency and the longer is the duration.

**RHYTHMIC SIGNAL OUTPUT**
Certain centers in the CNS produce rhythmic signals, e.g. the respiratory center in the brainstem. This rhythmic signal output is
caused by reverberating circuits involving a large number of interneurons. The large number of synapses slows down the frequency of output discharge and delays fatigue of synapses

[IV] SHORTENING OF SIGNALS
Shortening of signals means suppression of afterdischarge in the output neurons. This is done by either feedback or feed forward inhibition.

1. FEEDBACK INHIBITION
This occurs when an excitatory neuron stimulates an inhibitory neuron then the inhibitory neuron turns back to inhibit the initial excitatory neuron. In this case, stimulation of a neuron results in feedback inhibition of the same neuron to shorten the duration of discharge and prevent any afterdischarge. This occurs, for example, with the spinal motor neurons (the ventral horn cells). Each spinal motor neuron regularly gives off a collateral branch which synapses with an inhibitory interneuron called "Renshaw cell". Renshaw cell sends inhibitory signals to the cell body of the original spinal motor neuron (feedback inhibition). The inhibition of the original motor neuron suppresses any synaptic afterdischarge to prevent undesired prolonged activity of the motor nerve.

2. FEED FORWARD INHIBITION
This occurs when an input neuron stimulates an output neuron plus an inhibitory interneuron then the inhibitory interneuron inhibits the output neuron (fig. 2-9).
In this case, stimulation of an input neuron results in stimulation then rapid inhibition of the output neuron. This prevents any undesired prolonged discharge from the output neuron. Feed forward inhibition occurs in the cerebellum where a single input neuron stimulates an output neuron and a Purkinje cell. The Purkinje cell then inhibits the output neuron, cutting short any undesired afterdischarge.

Figure 2-9: Feed forward inhibition.

[V] SHARPENING OF SIGNALS
Sharpening of signals means the limitation of signals to the target neurons only. This requires the inhibition of any undesired activity in the nearby neurons. This is achieved by either lateral or reciprocal inhibition mechanisms.

1. LATERAL INHIBITION
Lateral inhibition occurs when a neuron sends collaterals to inhibit the nearby neurons through intermediate inhibitory neurons. This helps to focus the activity to the original neuron and eliminate any undesired discharge from the nearby neurons. The function of Renshaw" cell shows an example of both feedback inhibition (of the original motor neuron) and lateral inhibition (of the nearby neurons). Fig. 2-10
Lateral inhibition occurs also in sensory neurons. Sensory fibers
conducting touch (scratching) laterally inhibit itch and pain conducting fibers at the dorsal horn of the spinal gray matter. In this way scratching relieves itch and pain sensations.

Fig. 2-10 Lateral and reciprocal inhibition

2. RECIPROCAL INHIBITION

In reciprocal inhibition the activation of one output neuron is accompanied by simultaneous inhibition of another output neuron (Fig.2-10). This form of inhibition occurs, for example, during the flexor withdrawal reflex. In this reflex, contraction of the flexor muscles is accompanied by concomitant reflex relaxation of the extensor muscles. Reciprocal inhibition helps to optimize the reflex response by inhibiting any antagonistic contraction.