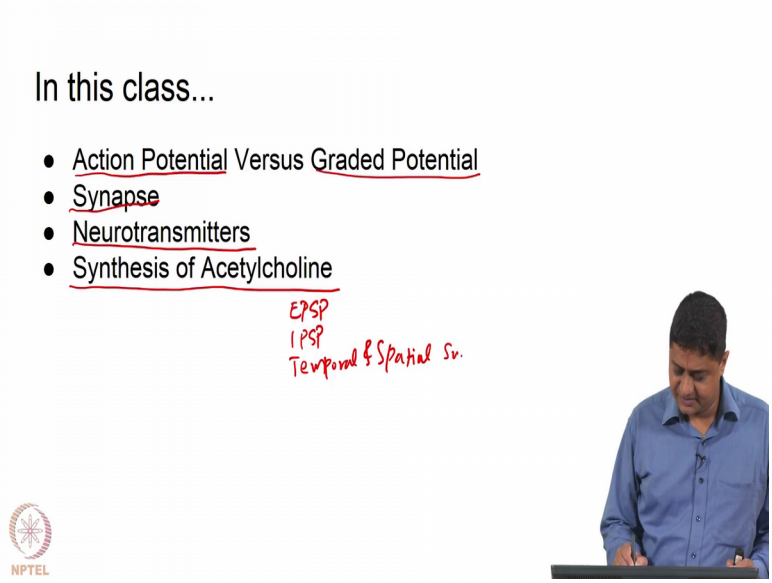
Neuroscience of Human Movement
Department of Multidisciplinary
Indian Institute of Technology, Madras

Lecture - 11
Review of Action Potential & Neurotransmitters

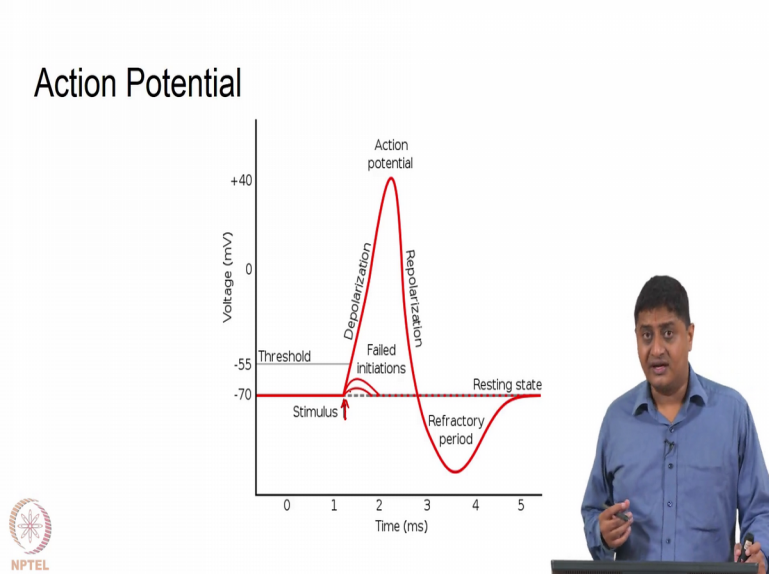
So, welcome to this class on Neuroscience of Human Movement. In this class we will be reviewing our discussion on action potential and I will be discussing a new topic which is basically neurotransmitters.

(Refer Slide Time: 00:28)



So, in this class we will discuss the differences between action potential and graded potential and we will discuss the concept of a synapse, and we will discuss neurotransmitters, we will discuss how acetylcholine synthesized. We will discuss excitatory postsynaptic potentials and inhibitory postsynaptic potentials and we will discuss temporal and spatial summation that we introduced in the previous class ok.

(Refer Slide Time: 00:59)



So, let us remember a stimulus when it is arriving it may or may not cause and action potential. If the stimulus is strong enough to take the membrane potential to threshold and action potential will be caused. Any other situation or any other stimulation that leads to sub threshold response are basically, sub threshold stimulus causes what are called as graded potentials like these. A supra threshold stimulus by definition always gives stereotypical transient change in membrane potential right which is what we called as action potentials this we have seen. What are the differences between the graded potential and action potential let us try and summarized this right.

(Refer Slide Time: 01:50)

Graded Potential	Action Potential
Depending on the stimulus, graded potentials can be depolarizing or hyperpolarizing.	Action potentials always lead to depolarization of membrane and reversal of the membrane potential.
Amplitude is proportional to the strength of the stimulus.	Amplitude is all-or-none; strength of the stimulus is coded in the frequency of all-or-none action potentials generated.
Amplitude is generally small (a few mV to tens of mV).	Large amplitude of ~100 mV.
Duration of graded potentials may be a few milliseconds to seconds.	Action potential duration is relatively short; 3-5 ms.
Ion channels responsible for graded potentials may be ligand-gated, mechanosensitive, or temperature sensitive channels, or may be channels that are gated by cytoplasmic signaling molecules.	Voltage-gated Na^+ and voltage-gated K^+ channels are responsible for the neuronal action potential.
No refractory period is associated with graded potentials.	Absolute and relative refractory periods are important aspects of action potentials.

Graded potential depending on the stimulus may or may not be depolarizing. We saw in the previous class that sometimes graded potentials can be hyperpolarizing whereas, by definition action potentials always lead to depolarization of the membrane. By definition graded potentials the response is proportional to the strength of the stimulus or in other words a larger the stimulus, the larger will be the response. But action potential are stereotypical, once the threshold is crossed the response is always the same.

So, you are going to have a stereotypical response that is all or none, either you have an action potential or you do not have an action potential. So, you do not have a situation where you have so much percentage of an action potential; either you have an action potential or you do not have an action potential right. And then the question is how is the strength of the stimulus encoded, we said that the strength of the stimulus is coded in the frequency of the action potential, how frequently it happens how the number of impulses per second that it happens right.

And in general amplitude of the action potential is relatively large, whereas, the amplitude of the greater potential is relatively small right. And the duration of action potential is relatively short for a brief amount of time it happens whereas; graded potentials can remain at a relatively low value for a long period of time sometimes the duration may be as high as some seconds right.

And the stimulus driven ion channels are responsible for graded potentials right what are these where stimuli? These stimuli are ligand gated ion channels, mechanosensitive ion channels, temperature sensitive ion channels vibration sensitive ion channels etcetera right. So, these are the stimuli that cause graded potentials whereas, action potential is almost always right always caused by voltage gated sodium and voltage gated potassium channels and it is the interplay between their conductances that cause action potential we have seen this in the previous class right.

And in action potential there is a period during which you cannot cause one more action potential right this period is called as a refractory period why is this happening? Due to the inactivation gate of the voltage gated sodium channel that is closing right there is no refractory period that is associated with graded potentials right.

(Refer Slide Time: 04:32)

Graded Potential	Action Potential
Graded potentials can be summed over time (temporal summation) and across space (spatial summation).	Summation is not possible with action potentials (due to the all-or-none nature, and the presence of refractory periods).
Graded potentials travel by passive spread (electrotonic spread) to neighboring membrane regions.	Action potential propagation to neighboring membrane regions is characterized by regeneration of a new action potential at every point along the way.
Amplitude diminishes as graded potentials travel away from the initial site (decremental).	Amplitude does not diminish as action potentials propagate along neuronal projections (non-decremental).
Graded potentials are brought about by external stimuli (in sensory neurons) or by neurotransmitters released in synapses, where they cause graded potentials in the postsynaptic cell.	Action potentials are triggered by membrane depolarization to threshold. Graded potentials are responsible for the initial membrane depolarization to threshold.
Graded potentials can occur in any region of the cell plasma membrane.	Occur in plasma membrane regions where voltage-gated Na^+ and K^+ channels are highly concentrated.

And also what you have with graded potentials is that overtime it is possible for graded potentials to be summed we called this as temporal summation, and across space graded potentials can also sum this is called as spatial summation. Whereas, as soon as one action potential is caused, you have all or none phenomenon, basically you have an action potential.

Soon after that if another stimulus is caused it cannot cause an action potential why? Because there is a refractory period because the inactivation gate of the voltage gated sodium channel is closed, the membrane is in a refractory period. So, two action potentials cannot sum.

However multiple graded potentials can sum and produce an action potential, but and action potential itself cannot sum with another action potential even if it arrives at the same time, even if there is a super threshold stimulus that is maintained, it cannot cause higher amplitude action potential right. So, action potential usually refers to a stereotypical response right so, summation is not possible. And graded potentials travel by passive spread are diffusion of ions from one point to another, action potential travels by regeneration of a new action potential we discussed this case right.

So, suppose this is the membrane and there is one voltage gated channel and there is one other voltage gated channel. Here there is an action potential here another action potential is regenerated, because threshold is crossed at that point right so, this may sum

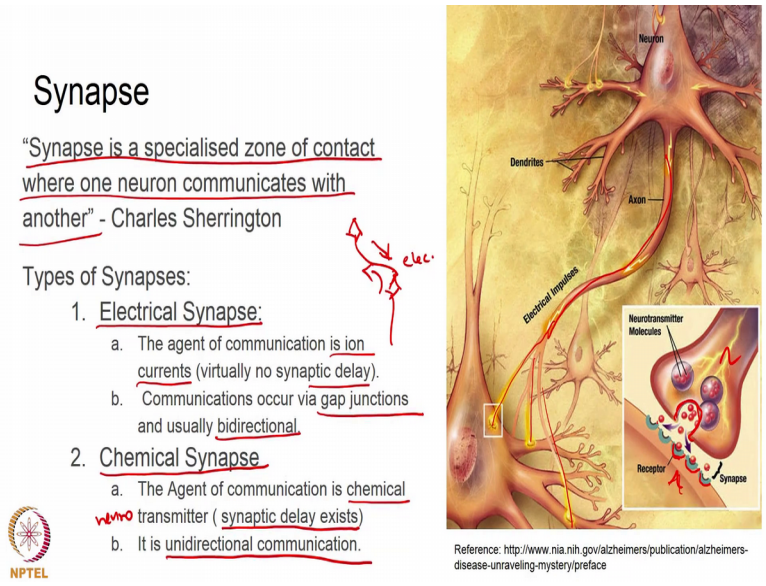
right. So, at each point in time and sorry at each point in the space are at each voltage gated sodium channel, a new action potential is regenerated right. Because there is passive spread in graded potentials, amplitude will diminish as the distance increases this is to be expected because there is a diffusion rate. So, some sodium ions will miss right. So, not all the sodium ions will travel and reach the next channel. So, amplitude diminishes as the distance increases so that is decremented.

Whereas, in action potentials amplitude does not diminish why because a new action potential is generated; actually in practice the amount of sodium that enters at one point reduces diminishes, but at the new voltage gated sodium channel, the amount of sodium that reaches the new voltage gated sodium channel is sufficient to cause an action potential there, which is where you actually have the amplitude not reducing the phenomena the situation where the amplitude is not reducing ok.

And graded potentials are usually brought about by external stimuli, this may be sensory stimulus such as touch or such as pain are by neurotransmitters released in synapses. And this cause graded potentials and let us remember these graded potentials can be either excitatory or inhibitory or they can either depolarize or hyperpolarize right whereas action potentials are triggered by the voltage gated sodium channels reaching threshold right.

So, what causes the voltage gated sodium channel to reach threshold, that may be graded potentials; graded potentials possibly cause the initial trigger of action potential after that action potential travels from one point to another or in other words new action potentials are generated along the direction of propagation right. Graded potentials can essentially happen in any place along the plasma membrane, wherever there are stimulus driven channels that are available their graded potentials can happen. Whereas, action potential happens only in regions they are there is sufficiently large number of voltage gated sodium and potassium channels, because it is these channels and their conductance's that determine the characteristic of action potentials right. So, these are the differences between action potentials and graded potential right.

(Refer Slide Time: 09:12)

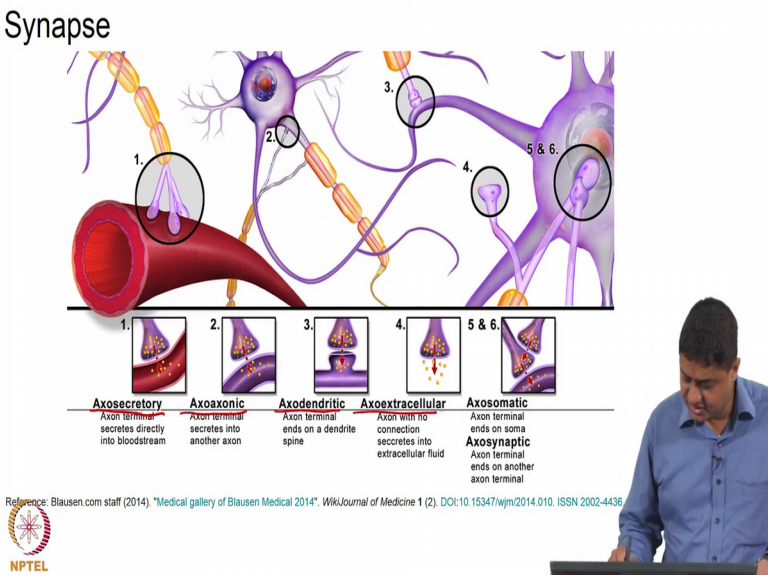


So, then the next question is how action potential causes communication with another cell right this happens in a synapse. A synapse is a specialized region where one neuron communicates with another and there are essentially two types of synapses; one is an electrical synapse here there is an opening between one cell and another cell and communication is through ions right virtually there is no synaptic delay these are called as gap junction mediated communication right, and usually this communication is bi directional. So, if there is one neuron here and that communicates with the another neuron there, through electrical synapse in that case communication can happen in this direction and also in this direction from.

So, both cells can talk with each other in in in a bi directional manner. Usually the chemical synapses are more in number. So, you usually this is not the electrical synapse is not the manner in which communication happens from one cell to another, usually the agent of communication is a chemical called as a neurotransmitter right. Because there is chemical communication from one cell to another usually it comes with the synaptic delay and one cell can talk to another cell. So, that is a speaker cell and there is a listener cell, you usually this is unidirectional communication. For example, an action potential here causes the these chemicals to be released and these chemicals are will are detected by these receptors.

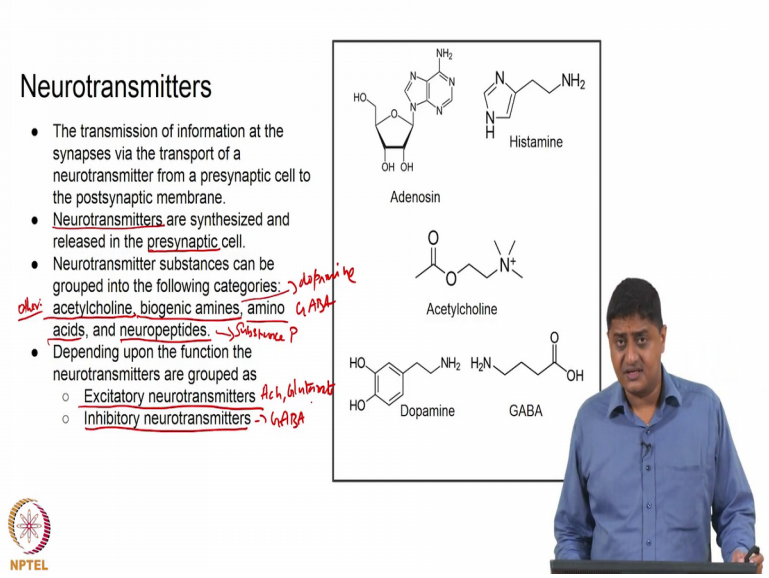
And once these receptors receive these chemicals, they cause an action potential in this region in the postsynaptic cell.

(Refer Slide Time: 11:09)



In general when we say synapse we refer to a chemical synapse and the neurotransmitter is usually in involved. In general, synapses can be classified into multiple types axosecretory, axoaxonic, axodendritic, axoextracellular, axosomatic depending on what the destination is. If the terminal is secreting into the bloodstream it is called axosecretory, if it is into another axon that is called axoaxonic, if it is into a dendrite it is called as axodendritic etcetera depending on the destination cell or the destination, the synapses are classified or the chemical synapses are classified ok.

(Refer Slide Time: 11:54)

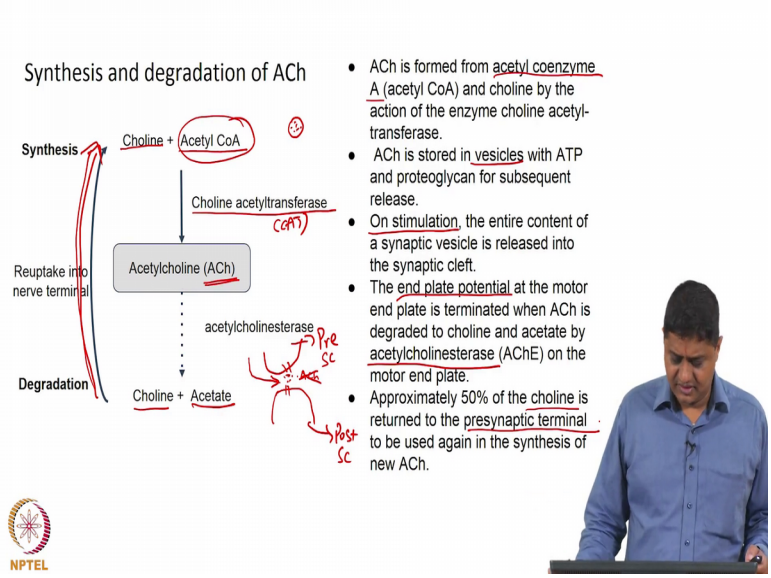


What are the neurotransmitters or what are the chemicals that we are talking about right. So, basically from a pre synaptic cell, this chemical gets transported by diffusion to the postsynaptic cell, where it is detected and the response is generated right.

And these chemicals are synthesized and released in the presynaptic cell, usually neurotransmitters are classified into various categories, these are biogenic amines example is dopamine amino acids example is GABA glutamate. Neuropeptides example is substance P are (Refer Time: 12:44) static right and then there are other neurotransmitters and important neurotransmitter is classified as other neurotransmitters, that is acetylcholine it is an important neurotransmitter that is classified as other neurotransmitters.

In general depending upon whether the neurotransmitter is causing excitation or inhibition in the postsynaptic membrane, they are classified as excitatory neurotransmitters or inhibitory neurotransmitters. Examples of excitatory neurotransmitters are acetylcholine, glutamate and the famous example for inhibitory neurotransmitters is GABA. In general acetylcholine causes an excitation of the postsynaptic membrane and in general GABA causes an inhibition of the presynaptic membrane; however, there are exceptions to this rule.

(Refer Slide Time: 13:42)



Let us discuss the case of acetylcholine how acetylcholine is synthesized. Acetylcholine is synthesized by the reaction of acetyl coenzyme A are also called as acetyl CoA and choline basically this is made by the protein choline acetyltransferase this is the protein that is responsible for generation, and it is stored into bags into small bags called a vesicles right.

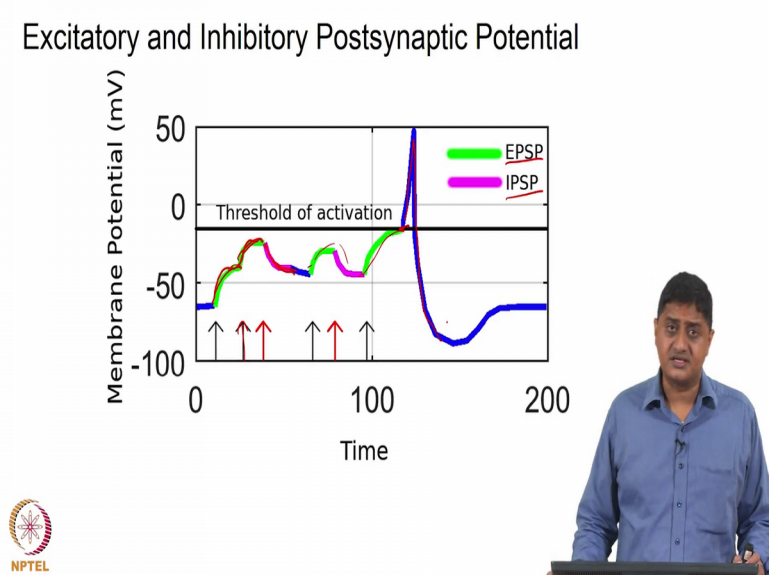
This stored acetylcholine is released on stimulation when an action potential arrives in this region right, this detail we will discuss in future classes right. So, suppose acetylcholine is released from a vesicle the end plate at the motor side or the motor endplate generates a small potential called as a endplate potential right. So, whenever acetylcholine is released into the synaptic cleft, a small amount of potential is generated on the motor endplate this is called as a motor endplate potential right.

The smallest amount of endplate potential that can be generated is due to one acetylcholine molecule is it not. This is called as a miniature in plate potentials, now if acetylcholine is present suppose now let us suppose this is the presynaptic membrane and this is the post synaptic cell it is a presynaptic right. Suppose acetylcholine is released here and it is remaining here itself, then it could spontaneously trigger new action potentials in the postsynaptic cell right. Is to avoid the possibility chemicals are generated and these chemicals can degrade acetylcholine these chemicals that can

degrade acetylcholine are called as esterase are in this case in the case of acetylcholine this is called as acetylcholine esterase.

This acetylcholine esterase basically breaks acetylcholine into choline and acetate. This choline can be reuptaken by the presynaptic cell for making more acetylcholine ok. So, choline is reuptaken or recycled then the question is where acetyl coenzyme a comes from that comes from the presynaptic cell ok. So, approximately 50 percent of choline is returned to the presynaptic terminal and the remaining choline is excreted is cleaned out.

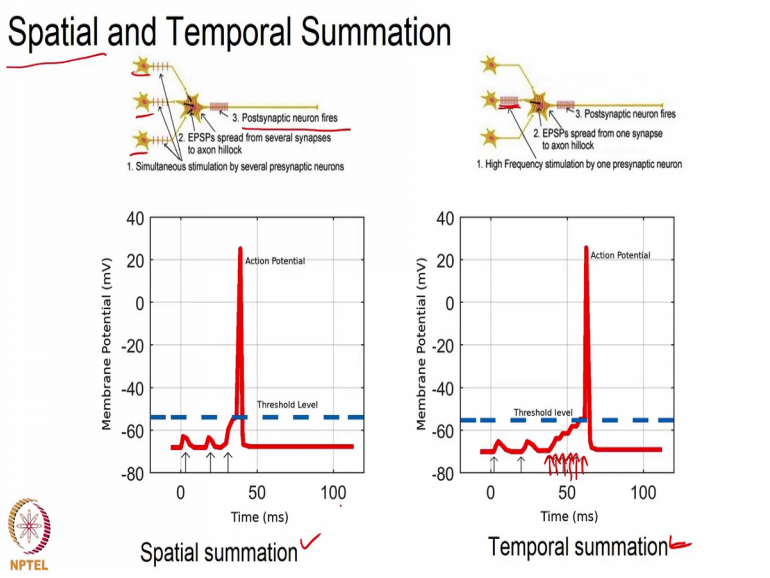
(Refer Slide Time: 16:46)



Now, what could happen at the postsynaptic cell right? If multiple excitations come one after the other in time right one after the other, this causes an excitatory postsynaptic potential and another excitatory stimulus causes another excitatory postsynaptic potential. Suppose, following that you have an inhibitory stimulus that causes an inhibitory postsynaptic potential.

So, if the postsynaptic potential causes an excitation right that is called as an excitatory postsynaptic potential, if it is inhibitory it is called as an inhibitory postsynaptic potential. It is possible for these to add in time and when the postsynaptic cell reaches threshold an action potential is generated in the postsynaptic cell until then you only have local currents are graded potentials ok.

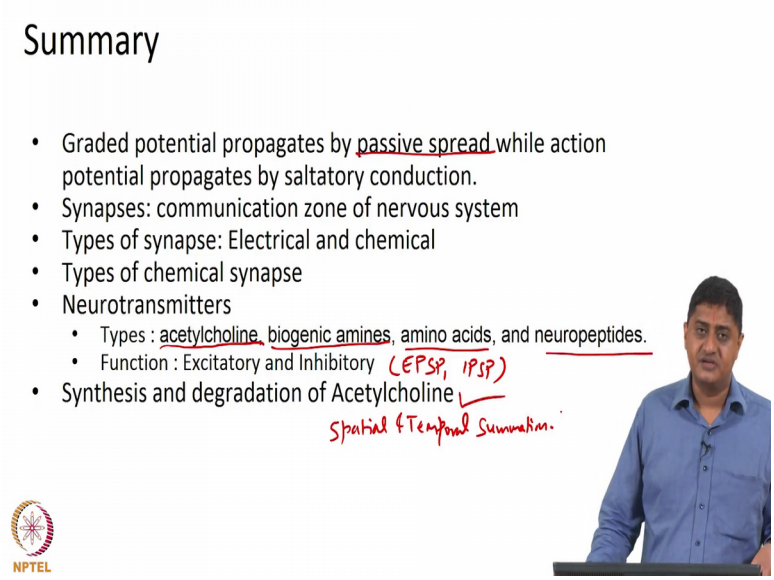
(Refer Slide Time: 17:46)



And also let us remember that multiple inputs arrive at the same point in time right that is called as spatial summation; whereas, if you have a situation where one input is happening at a relatively high frequency are one input train is followed by another input train closely in time that leads to a situation, where inputs can be added or the responses can be added in time leading to temporal summation.

Spatial summation is the situation when inputs arrive at the same time from multiple different points in space right. If inputs arrive at different points in time, but closely followed by each other from the same point in space or from the same input in front that is called as spatial summation. Actually the output that happens can be a combination of the two it need not be completely special summation or temporal summation. Usually it can be a combination of both spatial summation and temporal summation. From the viewpoint of the postsynaptic cell as long as the threshold is reached we are going to have an output you are going to have an action potential ok.

(Refer Slide Time: 19:01)



So, in summary we have discussed the differences between graded potentials and action potential graded potentials, propagates by passive spread whereas, action potential propagates by saltatory conduction or regeneration of a new action potential in the voltage gated channels. And synapses are communication zone between one neuron and another neuron and there are two types of synapses electrical synapses and chemical synapses. The most common type is the chemical synapse and there are different neurotransmitters basically biogenic amines, like dopamine amino acids like GABA neuropeptides (Refer Time: 19:42) and other neurotransmitters such as acetylcholine. And we saw that this could cause either an excitation or an inhibition in the postsynaptic cell, thereby causing an excitatory postsynaptic potential or inhibitory postsynaptic potential right. And we also discussed how acetylcholine is synthesized and how it is degraded then we also saw spatial and temporal summation. So, with this we come to the end of this lecture.

Thank you very much for your attention.