Bioelectricity
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Lecture – 15

So, welcome back to the NP-TEL lecture series on Bioelectricity. So, let us do a bit of recap, so what we did we started with a stretch reflex arc circuit, and we talked about muscle spindle and we talked about how the muscle spindle can anticipate the change in length of a muscle. It is innervated by the sensory neuron and sensory neuron takes the message to the spinal cord; and in the spinal cord, this message is transmitted to the motor neuron through an interneuron, and then motor neuron brings back the message telling the muscle to come back to its original positions, regaining its original length. And simultaneously there is another set of motor neuron which are the gamma motor neuron, which tells the muscle spindle to come back to its original shape.

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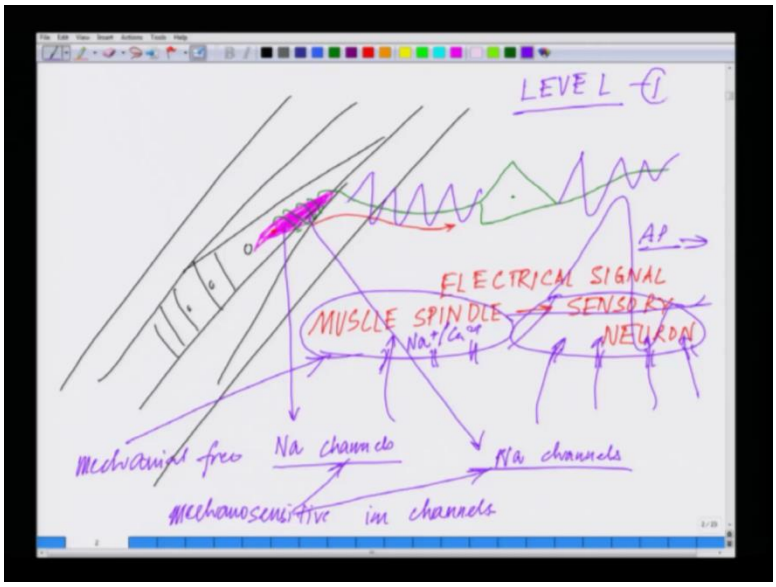

So, in this process, today we will be briefly discussing, how the signal from the muscle spindle is transmitted to the sensory neuron, and how that could be measured. So, coming back to the slides, so it is lecture fifteen. So, essentially this is the situation, here you have the muscle with all the myotubes and everything likewise, tritons, and all those things if you see. And in between you having these muscle spindle sitting there, these

muscle spindles are innervated by let me use a contrasting color something like this, there innervated by the sensory neuron ending. So, our pertinent question is, how this signal from here is being transmitted from this muscle spindle to sensory neuron, and what we know about it in terms of its electrical signatures to sensory neuron, how this electrical transfer is taking place.

So, it is believed that there may be a series of sodium channels which are either present in the muscle spindle or they are present in the sensory neuron. These channels are again this is all currently under speculation, these are believed to be mechanosensitive ion channels. So, these kind of sodium channels are considered as mechanosensitive ion channels. What do you meant by mechanosensitive ion channels as the name itself indicates because of mechanical stimulus the ion gates open up. So, it has a very unique way of opening up.

So, this is a classic case of mechano transduction or in other word mechanical energy leading to the generation of an electrical energy or mechanical energy is converting into electrical energy which so ever you want to put it. So, essentially this is the first level of energy transduction which is taking place and. So, essentially what is happening is that this muscle spindle is getting a mechanical force or this is not yet clear opens up a series of sodium or cationic channels, it may be even calcium, it is not really known and this leads to a generation of an action potential.

This is how far we know about how the interfusal fibers are communicating the signals to the sensory neurons. Things are under intense study, but still we have a long way to go before we really understand how this first level of information transfer is being executed. So, this is the first level. What is the second level? Second level, this is the train of action potential, which is traveling through likewise. Now at the level, so let us put it at level one.

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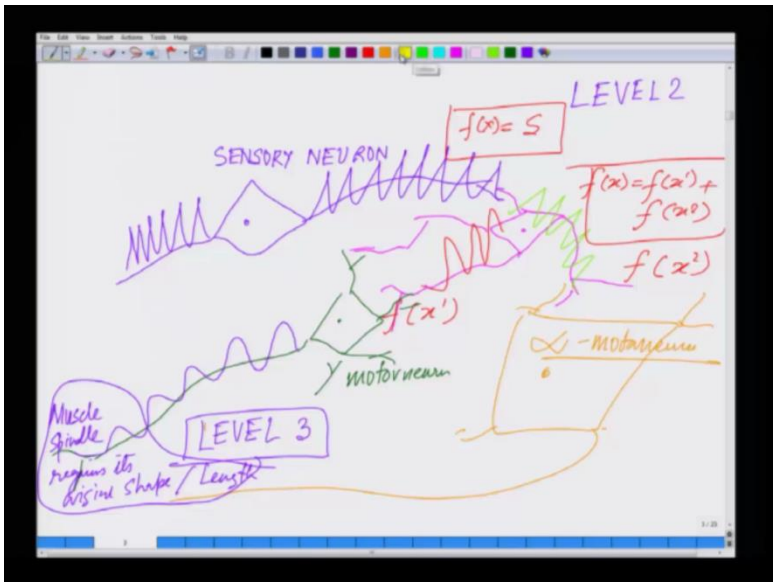

What is happening in level two coming back to level two. So, signal has arrive from the sensory neuron, this is sensory neuron, and through the interneuron this signal is being getting split up into two different components. So, one component is going for, so this is the train of action potential which is traveling, now here this signal is getting split up into two component; one component say I am representing by green, the other component I am representing by red. So, one component of this signal, if this signal I represent by some say function say f x is equal to s then here will have two signal f x 1 and f x 2 or you can represent it by any way.

And essentially signal s, so f x is equal to f x 1 plus f x 2, this is how the mathematically this could be defined. Now from here, this signal is transmitted to two different kind of neurons, one is a smaller one, which is called a gamma motor neuron; and other one is a bigger one called a alpha motor neuron. Just for the standing sake and here you have all the synopsis and everything. So, this is alpha motor neuron. Now this alpha motor neuron is the one which is responsible for contraction of the extrafusal fiber or the bulk of the muscle and the gamma is the one which ensures that the muscle spindle comes back to its original place.

So this is this is level two, and at this stage there are three levels which are starting form here we are initiating level three. So, here is the train of action potential which is travelling to ensure that the muscle spindle regain its original shape or length. Again this

part of the circuit, how the gamma motor neuron is executing this function is still not very clear. We know the end result that how it does, but the real mechanistic details are still not very clear. Instead the other part of the circuit which where the alpha motor neuron is regulating the muscle length is much more clear.

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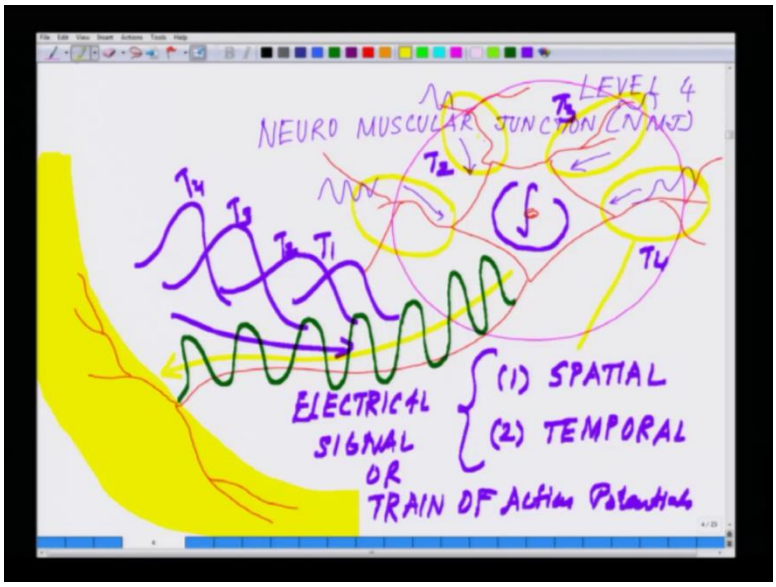

So, now what we will do we will talk in bit of a bigger detail or a greater details of this particular part of the circuit, where the alpha motor neuron is communicating its information to the extrafusal fiber, and this it does at neuromuscular junction. So, this is now where we are moving we are moving into the level four, which is of this circuit level four which is neuromuscular junction; in short it is also called NNJ. So, neuromuscular junction pretty much all over the vertebrates are regulated by a specific kind of neurotransmitter called asital cholin baring aside some of the neuromuscular junctions which are present in the drosophilam which are driven by glutamate kind of transmitters.

So, we will not take those exceptional case into account, we will only talk about the asital choline based nerve muscle junction, where your alpha motor neurons are coming and lets represent the alpha motor neuron by red. These are the huge neurons and they are the one, which are coming and innervating the muscle. Here you have the the muscle. So, and the input it is receiving from the inter neuron or directly from the sensory

neuron. So, here is the input which is arriving at its different terminals. These are the dendretic terminals where it is receiving all the inputs.

So, the direction of flow of electrical stimulus is like this. So, there is a form of spatial and temporal summation of formation; special in the sense, because if you look at this image out here. If you look at this whole image signals are coming from different location in space it is coming from here, say it is coming from here, it is coming from here, it is coming from here, it is coming from here. So, that is why it is spatial and it is also temporal, because signal may come at time T 1, time T 2, time T 3, time T 4 and one signal may over lap over another signal.

Say for example, like this and a signal coming like this another signal coming like this another signal coming like this. If this one is T 1, this is T 2, this is T 3 and this is T 4, so this is also called temporal . So, in other word, electrical signals which are arriving at the motor neuron are electrical signal or you can call it or train of action potentials or spatio temporal. They are spatial as well as temporal in nature. Then this motor neuron what is what it does it is just like a computer out here. Eight integrate all these signals and this integrated signal is now is the master signal, which starts to travel down like this, along the axon without allying any kind of back propagation of information and in this direction it is moving. So, what essentially is moving is a train of action potential which is coded with the information that how much length the muscle has to come back.

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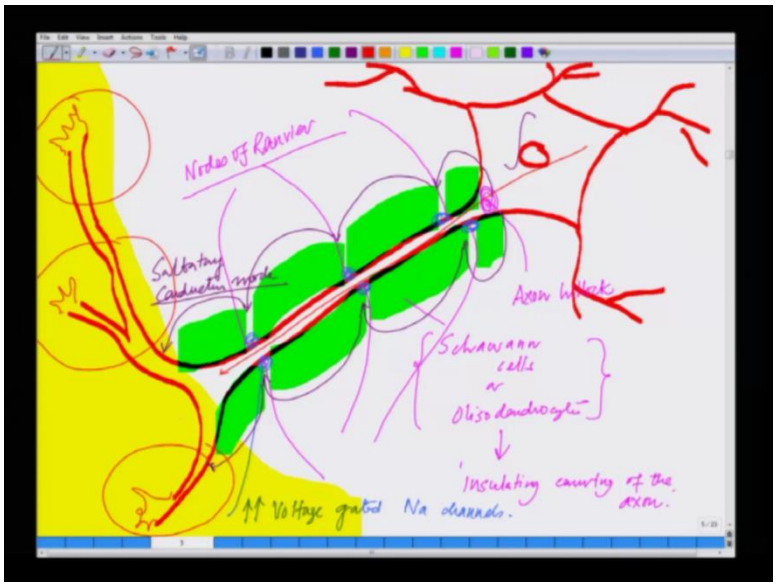

Now what happens here. So, this at this stage, there are two things which I wish to bring to your notice. First of all, these neurons are myelinated and if you look at these neurons they are, so if this is your motor neuron and this how the process is . So, now and here you have the nucleus. So, these are all myelinated structures; myelinated in the sense they are something like this. So, these are very similar to you have seen the wires on the walls. They are very similar to the wire on the walls, you cannot have a necked wire in the on the walls, because if you have a necked wire, if you touch it, you will get a shock.

So, in order to prevent that the same thing holds to for these neurons, because they are conducting electrical impulses, so the current should not be lost, when information should not be lost. So, that is why it is put inside an insulator and these insulating cells are in the case of motor neuron in the motor neuron so as long as this motor neuron is inside this spinal cord it is myelinated or the insulation is done with the specific kind of cells called oligodendrocytes. And when it is outside the central nervous system. It is insulated by another kind of neuron another kind of glial cells which are the supporting cells of the nervous system those are called schwann cells.

We will come in depth on those when will be talking about some of the diseases and how really to handle it, but at this time just remember these green covering what I have drawn, they do not allow the electrical signal to be lost from the axon to the another one there should not be any short circuit. So, these are they could be Schwann cells or any oligo dendrocytes, they ensure insulating covering of the axon. So, now, this zone where I am circling now is called the axon helok, and these small gaps what you see out here what I am labeling now are called nerves of ranviev. And at the nerves of ranviev, you have a large population of sodium channels, they are concentrated out here like this. What you see in green are high population of voltage gated sodium channels, and the current, which is now it is obtaining from all the sources; and it is doing the summation this current actually hops like this, it is called salutatory conduction mode like this salutatory conduction mode.

So, at this stage what is happening now once you are at the zone where it is in contact with that mean. So, this is the zone where this whole structure is in contact with the muscle. Now at this stage, these electrical signals had to lead translate its information to the muscle, and it does at these junctions, which are very very specialized junctions, these are the junctions where this information is being transmitted and how you will

does. So, now what we will do we have talked about the movements of the electrical impulse here, what is happening out here. So, we will magnify these images of neuromuscular junction and we will talk about them in the next slide.

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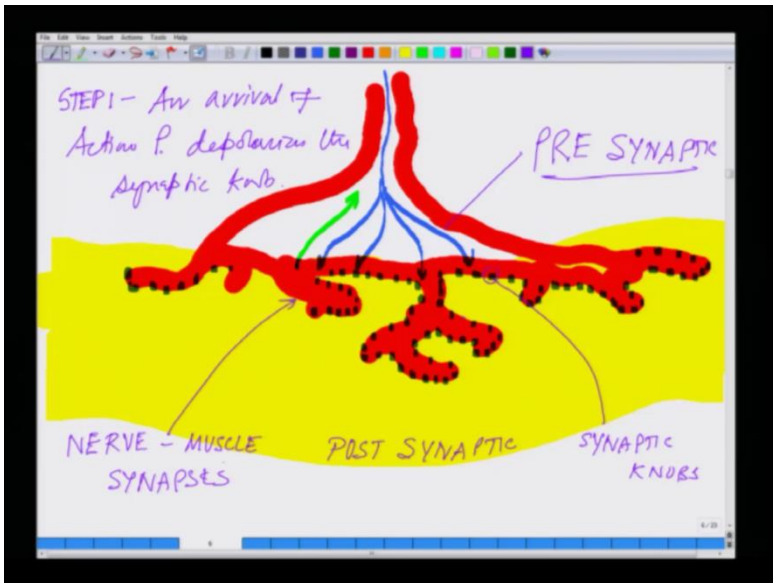

So, let us redraw the neuromuscular junction now. So, if I have to redraw the neuromuscular junction, it will be something like this, something like very similar to I am drawing it, and we will do the nomenclature very soon. So, this is the neuronal terminal and and here you have the muscle. So, at this stage, what you see here is essentially these are filled with these are filled with something like vesicles or small packets of neurotransmitters these neurotransmitters are the molecules which translate the electrical impulses into chemical impulses I will come to that.

So, these are the small vesicles, these are filled with in this situation when we are discussing about neuromuscular junction in mammals and everything they are filled with a chemical called acetyl choline like this. And these neurotransmitters actually synthesized by the neuron and they are transmitted at these different terminals and the byproduct of it is actually also carry back to the cell body and again re synthesized and brought it back. So, there are five different steps what is happening out here the first step is, so let us start numerating the steps now.

So, the step one of this game one is step one then arrival of action potential arrival of I just putting p for potential and which basically depolarizes the synoptic knobs. So, just

let me introduce two more terminologies the one which is sending the signal it is called the pre synoptic; and the one which is receiving the signal is called post synoptic. In this situation, the pre synoptic membrane is the neuron and the post synoptic membrane is the muscle. So, this is post synoptic and this is pre synoptic and these terminals these are called synoptic knobs and this small gap physical gap this is called nerve muscle synapse. So, as a step one with the arrival of action potential, it depolarizes the synoptic knobs.

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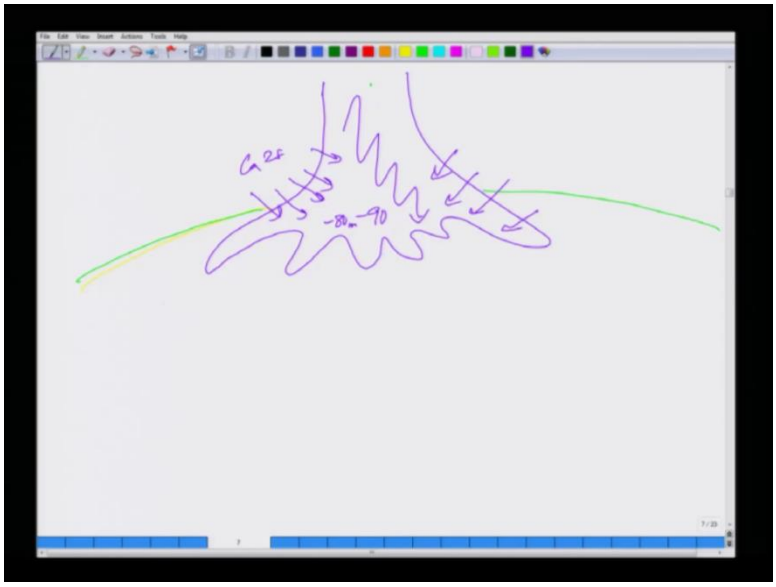

So, what essentially that mean that mean coming back to the slide that essentially mean that this step what is happening is that. So, this is the muscle. So, out here when the action potential arrives this leads to the entry of they are depolarizing in other words they are making tying to make the membrane much more positive which was that minus 90 or minus 80. So, now with the entry of the calcium what will happen there will be this membrane potential will start to depolarize from the negatively polarized state of minus 80 to minus 90 with the entry of the calcium, it will become more positive as it become more positive the next thing what will happen is this.

So, coming back to, so there is entry of calcium which is the step one this followed by this this calcium will let us coming back to this. So, with the entry of the calcium this calcium goes and binds to these synoptic vesicles and as soon as it binds to this synoptic vesicles they open up they started secreting the neurotransmitter in this zone.

So, these are the acetyl choline which are been secreted by the nerve terminal. This acetyl choline immediately goes and binds to the binds to the post synoptic membrane. It is coming back to the post synoptic on the post synoptic, there are receptors for the acetyl choline, and they bind on top of them. As soon as they bind on top of these post synoptic membranes, this opens up a series of cationic channels.

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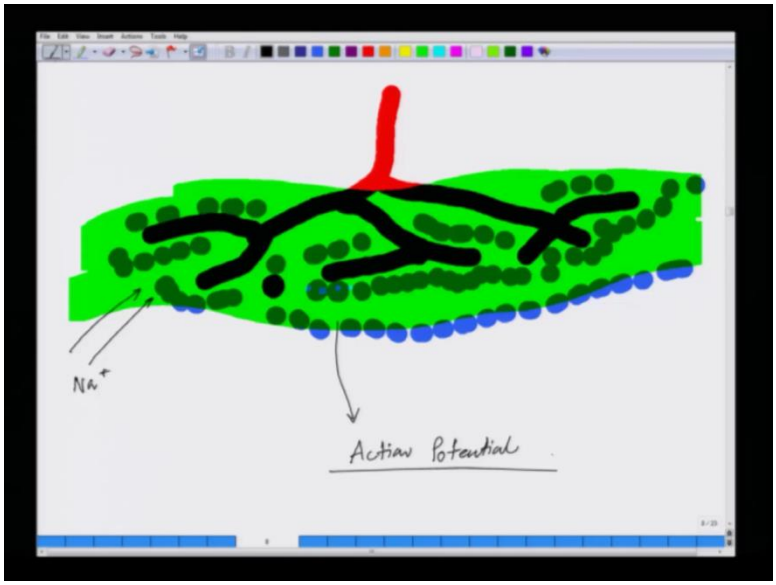

So, what is happening is like in this slide. So, these are the terminals and so this is where the synopsis are fine like this, this is the muscle. So, this muscle has a series of receptors which binds to acetyl choline. So, the green one lets represent them by lets pick up a color which is much more prominent which would be seen out here something like this let me make it thicker. So, the dots what I am drawing now are the receptors for the acetyl choline on the cosynoptic or the muscle membrane.

So, as soon as the acetyl choline is released into the synoptic clip or the space between pre synoptic and post synoptic membrane that acetyl choline goes and binds to the post synoptic membrane. Once it binds to the post synoptic membrane, it leads to the influx of sodium into the muscle and that sodium which is generated into the muscle leads to the generation of an action potential by the muscle and this leads to the generation of action potential.

So, if we have to put it in first perspective thing what happened lets go back to the first slide where where we started. So, this is how the circuit looks like from muscle spindle,

because of mechano presence of mechano-sensitive ion channels, muscle spindle kind of stretches. And this mechanical signal is translated into electrical signal then this electrical signal travels through, and through to the stage two to the inter neurons. In the inter neuron the signal is divided into two parts one goes to gamma one goes to alpha. The gamma electrical information comes to the muscle spindle and gets translated into its mechanical signal to tell the muscle spindle to come back to its original position.

Whereas on the other hand. in the case of alpha, these electrical signals travel along the alpha motor neurons as I was showing you out here without getting loss they travel out here. And after reaching here, they depolarize the membrane by allowing the entry of calcium into the cytoplasm with the entry of calcium membrane got depolarized. Once the membrane got depolarized, the calcium in the mean time goes and binds to the synoptic knobs which are filled with vessels of acetyl choline. And once the acetyl choline is released into the synoptic cleft p r in the neuromuscular junction that acetyl choline goes and binds in on the post synoptic receptors which are present on the post synoptic membrane and leads to the entry of the sodium ions into the muscle and then the muscle generates an action potential.

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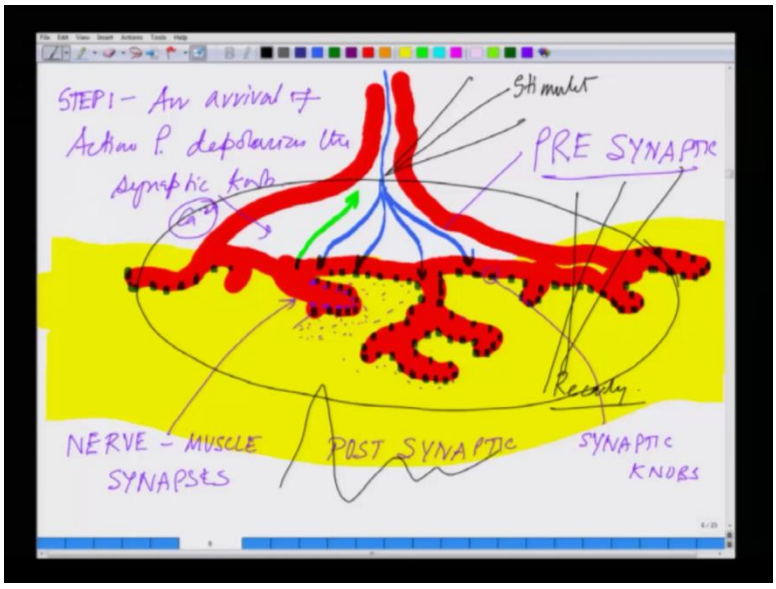

So, electrical chemical again electrical and then what we have not discussed how this action potential within the muscle leads to a generation of a muscle contraction we will come to that, but before we come to that now the way these are being studied its known.

So, if you could put an electrode here and if you could put an electrode here and if you stimulate it if you stimulate the pre synoptic membrane and then you could make the recording from the post synoptic membrane.

So, you can put an electrode like this and you can put an electrode like this. This is how all these studies over last seventy eighty years has been characterized, all the muscle contraction, all the in viewed studies there are in vintro preparation where outside the body, you have neuromuscular junctions, you have live animal preparation, there are whole series of there are slide preparations. Where all these electrical measurements are being done, all how the all the quanta's are being released as a matter of fact studying the electrical properties of neuromuscular junction has opened up wide window of understanding the synapse itself.

Because this is one of the very well accessible synapse, where you really can see how the ultra structure of synapse looks like, because all the synopsis are not that big. This is huge you really can see in an any muscle of your body, you really can see a neuromuscular junction. If you have a cross section from an experimental animal actually can do a electron microphotograph and everything you can really figure out what is happening and this whole slide what you see here is one of the hot site for pharmacological prevention there are several diseases which are related to it. So, one of the thing what happens when acetyl choline is being secreted.

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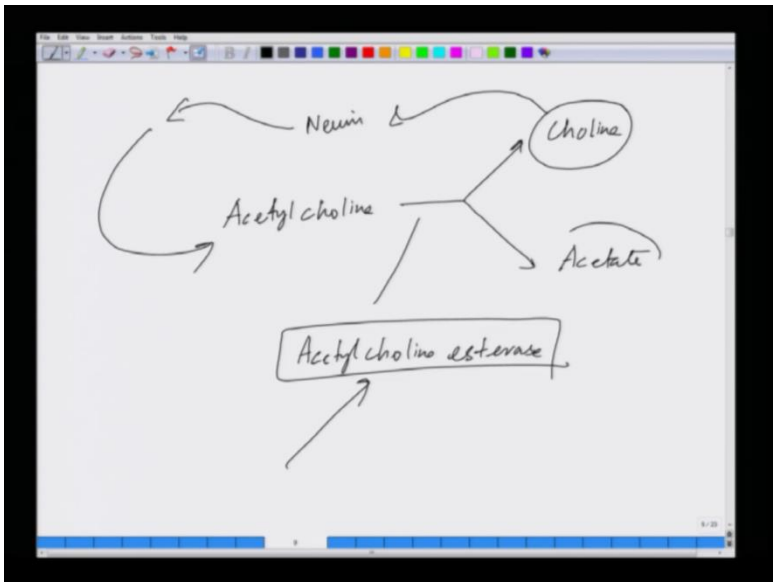

So, acetyl choline binds, but very soon very immediately at pretty much at the same time the acetyl choline has to be degraded out. So, what has to be done essentially is go to the. So, the acetyl choline which is secreted is being degraded out as choline and acetate choline and acetate and these choline is again taken up by the by the neuron in order to make new acetyl choline and acetate is again degraded this is being done by an enzyme called acetyl choline esterase. So, if you have a blocker for acetyl choline esterase then the synoptic transmission will be de balanced.

There would not be any controlled rout because then they will keep the channels open and the individual muscle will start shaking and there are several poisons which actually does that they ensure that acetyl choline esterase is not break down or or something very similar to esteryl choline or something blocks acetyl choline esterase or something of that kind. So, this is another feedback mechanism by which it is being showed at the the neurotransmitter which is translating the electrical signal or transferring the electrical signal from the neuron or the pre synoptic terminal to the post synoptic terminal. In this situation, the muscle that neurotransmitter should have a very very limited time; if it is not so then there will be problem, we will have serious issue, if this bi chemical path way is not being regulated the way it is.

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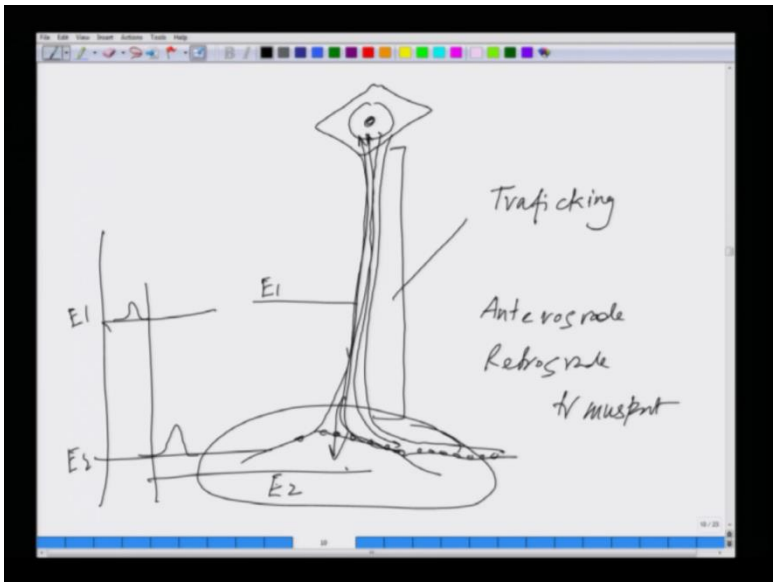

Another thing what is mentioning here as I was trying to tell you though this is not part of it just for your understanding sake and the way it works is. So, all the if I have to show

you in three dimension like this that will be easy to understand. So, all these neurotransmitters are actually synthesized in the nucleus and they are transported out into the nerve terminals and their bi products like choline or something transported back out here and this whole transport mechanism is very very essential because at times in several disease several neuro degeneratory diseases, it has been observed that this transport phenomenon is obstructed.

So, this is called a trafficking those who are not from a very well biology background then. So, this is what the trafficking process when neurotransmitters are bring put in vesicle come back, and they adhere and form the synoptic knobs out here the neuromuscular junction and there are being again taken by after they are being used. So, this is a continuous traffic trafficking process, and this is called antero graded and retro grade transport and retro grade transport of vesicle. As I have already told you that in study them by putting an electrode out here and putting electrode at the other terminals if if see a if you give a stimulus at E 1.

If this is E 1 and this is E 2, just with the slight gap, you will see a signal at electrode at E 2 that gap is the time what it takes from here to travel to the post synoptic membrane. And if you do not see such signal, it means they may be physically in close to each other, but there is no functional connection. These are acid test of figuring out whether your motor neuron is sending a signal or not, but this takes us to another level of complexity which I am going to dealt in the next class that is…