Bioelectricity
Prof. Mainak Das
Department of Biological Sciences and Bioengineering
Indian Institute of Technology, Kanpur

Lecture – 13

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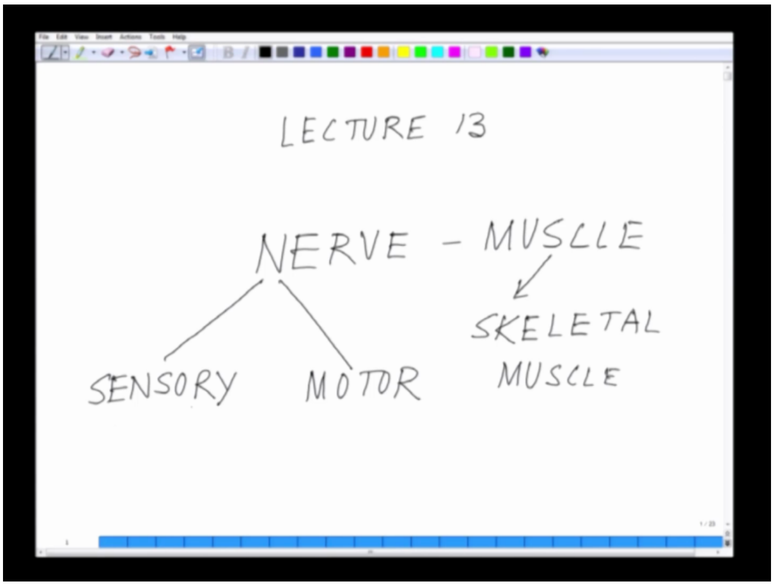

Welcome back to the lecture series in bioelectricity in NP-TEL. So as of now we have finished twelve lectures;, and in the course of these twelve lectures, I have introduced you to the whole domain of bioelectricity. Then we moved on to talk about the structures of the neurons, we talked about the simple action potentials, how they have been generated, how using Nernst equations you can calculate the balancing between the concentration gradient, and the char gradient across the membrane. And, then we talked about a series of techniques in depth we talked about patch clamp, linear patch clamp, microelectrode array, and how these are implanted, and the intercellular recording, extracellular recording, we talk about the voltage clamp, and current clamp.

So, in that whole process, I try to introduce you how the channels are been studied though I have not really talked about all the diversity of the channels, different kinds of channels, and how they have evolved. So, I am kind reserving that latter half of this lecture series where you will have a fairly good idea about the functional diversity. So, one of the thing which you will be appreciate as we will move along annual bioelectricity is this that all the functional variations, what we see in the excitable membranes of the body like cardiac, smooth muscle, skeleton muscle, neurons, and among neurons you have robs, and cons, you have the hair cells of the ear, the higher brain neurons, spinal cord motto neurons, sensory neurons, sympathetic, and parasympathetic neurons, and all these different kind of neurons or the pacemaker neurons or the pacemaker cells of the cardiac myocytes. They all have a unique signature of action potential, and this unique signature of action potential is conferred to them by the wide variation, wide diversity of ion channels. And this is extremely important as to really appreciate, because as we will move along we will see how the shape already you must have seen some of the action potential shapes are varying.

So, this is something keeping in mind, I introduce you people with the techniques, which are being used especially the patch clamp how that is been used to understand the single molecule or the single structure of ion channel. Though I plan like to introduce ion channel the detail diversity, and evolution of it, but I thought that I will delay it slightly more staggered it pretty much at the end of the animal electricity, because that will be appreciated much better. So, instead what we will do after we have talked about some of these techniques now we will move on to some of the basic circuits.

So, one of the basic circuits on which the body kind of will realize a lot are nerve muscle circuits these circuits which ensure that any sensation which takes place. Any stimuli which takes place on any kind of muscle of our body is conveyed to the processing center which could be either if it is a very rudimentary or very primitive signal. Then the processing center will be the spinal cord, but if it is a higher brain signal. Then the processing center will be the brain, and part two of it is that after the signal is being sent their it is been computed the response signal should be send back as efficiently as the way the impulse signal has been sent. So, these simple circuits.

So, the way we will study these simple circuits will first of all talk about the circuit we will talk about how the signals are been transmitted, and then we will talk about how the how these electrical signals are been major, because since now I have already introduced you to the intercellular, and extracellular recording protocols. So, we will be able to appreciate how they have been recorded how multiple patch electrodes are being used, and all these things ok.

So, let start with the nerve muscles circuits nerve muscles circuit, and here will be at this stage will be talking about the skeletal muscle, we will not talk about cardiac will take that up separate in a separate section, and among the neuron. We will talk about two kinds of neurons sensory nerve the one which is carrying the impulse, and motor nerves which are bringing back the signal.

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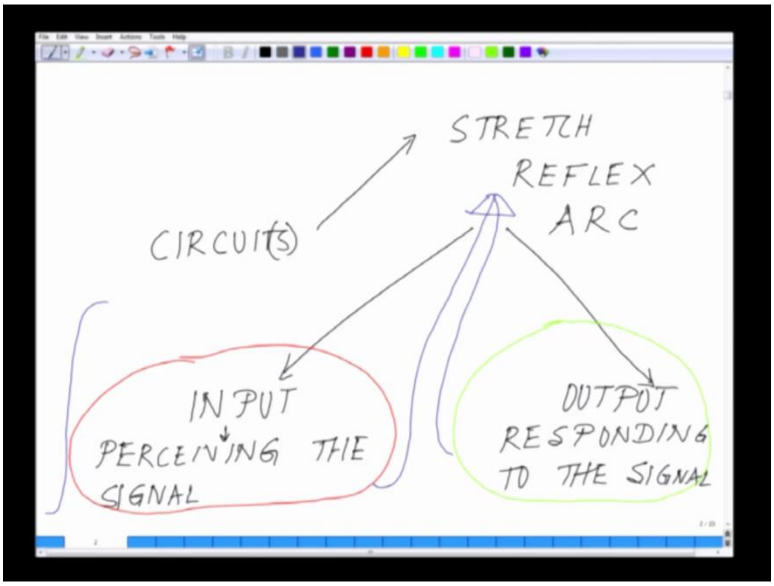

And we will be talking about two circuits, and the circuits we will be talking about are stretch reflex arc circuit, and This reflex arc circuits has two elements actually embedded with two circuits, and one of them is the input circuit, and the other one is the output circuit input circuit is the sensation sensation I should say a the right word will be how we are perceiving the signal. So, let us correct this, this should be perceiving the signal, and responding to the signal responding to the signal. So, now, what we will do after this before going before drawing it out let me give you a explanation of this circuit first.

So, all our all our surface of our body are continuously exposed to different form of a stretch they are stretching say for example, if somebody hits you there is a stretch or you are in a compressed situation they get stretched or they are some stimuli hitting there you are getting a stretch. So, these stretch essentially what it does it changes the length of the muscle. So, say for example, initially muscle is say five millimeter it becomes six millimeter fine, because of the stretch.

So, it cannot remain at six millimeter for long it has to come back to five millimeter otherwise the next stretch will come the six to seven, and the next seven will become eight, and eventually it will you know it is just like a rubber band it will eventually you cannot stretch it forever it will snap, there will be a permanent damage in the muscle that is what you do not want. So, there has to be a mechanism by which you ensure that this muscle once from five centimeter or five millimeter it becomes six millimeter it comes back to five millimeter fine how body performs that. So, the first thing it does whenever there is a stretch, and one more just kind of for your understanding I have just picked up the most primitive circuits there are enough number of such circuits which you can be dealt I am just giving an example for you which is the simplest of all which kind of has been conserved over a millions years of evolution, and a its kind of very rudimentary very primitive yet very interesting yeah coming back. So, if there is a stretch that stretch the first step is that there has to be a mechanism by which the change in length within the muscle could be quantified some way to quantify that.

So, there is this much change once it is been quantified that signal has to be sent to the spinal cord, and is essentially for these kind of reflex circuits brain does not do much of a processing, because they are is very primitive the processing takes place within the spinal cord. So, within the spinal cord the processing takes place, and a respond message is being brought back to the surrounding muscle telling them hey you know what there is a increase in muscle length you better come back to its original length essentially this is what a stretch reflex arc circuit is, and it is almost like an arc, if you look at visualize the shape.

So, there is a stretch signal goes comes back. So, that is why its stretch reflex it is a reflex circuit arc stretch reflex arc circuit. So, if you look at it if I divide the circuit into two parts one part will be the part of the sensation the stretch sensation which I was telling yo,u if you go back if you kind of see this slide. So, this is that part which is perceiving the signal, and the part two out here is the output response of the signal this is part two, and these two part essentially when get integrated. So, for integrate these two parts that what essentially makes this arc circuit that is what it is? Now what I will do I will draw the circuit for you. And I will one by one introduce the components within the circuit which will help you to understand how the circuit works.

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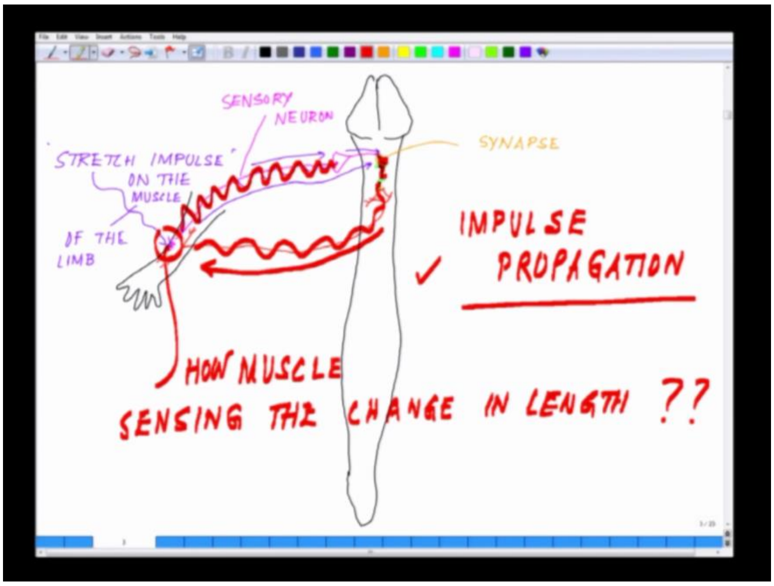

So, say for example, this is the brain of the individual, and this is the spinal cord, and say for example, sensation is coming say from hand. So, a impulse comes lets represent the impulse by a stretch impulse some form of pressure which has been put these stretched impulse is being sensed. So, this is the muscle on the muscle stretch impulse on the muscle of the limb or it could be any other part I am just since I am trying to roll limb.

So, it is on the limb these stretch impulse are being carried by a series set of neurons called sensory neurons lets represent the sensory neurons by say pink color. So, this is there, and these sensory neurons are out here having their cell body sitting just outside the spinal cord. So, these sensory neurons out here let me mark it sensory neurons these sensory neurons carries the signal the electrical impulse to the spinal cord.

So, the direction is this, in the spinal cord they convey the signal through a set of neuron called inter neurons which I am showing in light, and they convey the signal to motor neuron which are setting out here, this motor neuron brings back the signal, and tell the muscle to act accordingly. So, just show it something like this. So, what exactly has happened in this situation there are certain things which I have not discussed which I am going to discuss one by one. So, initially a impulse or a train of action potential is generated fine that action potential from here which I am showing you like this one second give me here this train of action potential travelled from the muscle all the way to the spinal cord out here.

There is a small interfacial zone zone, which is shown here the first synapse. So, we will talk about synapse synapse is where one neuron conveys it message to its target the target just its go little bit advanced to show let me verbally tell you. So, a train of action potential moving from one neuron, and this train has to be conveyed to the next neuron or to any other target it could be a muscle it could be any other tissue it could be neuro endocrine or something.

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So, there is a very narrow zone they are discontinues structure where there is a small cleft where essentially what happens say for example, now let me graphically tell you if this is the neuron which is carrying the signal, and this signal has to be conveyed to the to the muscle like this, and muscle is shown by . So, this is the muscle. So, at this at this juncture they are there is a there is a small gap here. So, physically they are there, but they are not really physically it is not. So, the way it looks like something like this if I magnify this image it will be something like this.

These are the nerve ending which I am drawing now, and these are the muscle membrane like this you see when I am drawing this I am keeping a small gap between the two see this gap I am now just I am just highlighting gap with yellow you see this gap this gap is called synaptic cleft, and this zone this narrow zone of few nanometers is called the synaptic zone.

So, this is a synapse, and since here the synapse is between nerve, and nerve, and muscle. So, this could this is also called neuro muscular junction or you can call it a nerve muscle synapse similarly I will talk come to the functionality of it just let me give you another situation where there neuron to neuron synapses is there for example, this is this is one neuron, and there is another neuron which is sitting close proximity like this processes are like this.

So if you look at this zone which I am now yellowing these are the synaptic cleft these synaptic cleft are the regions. So, put the label here synaptic cleft these synaptic clefts are the regions where electrical signal from one neuron is either transmitted to another neuron or the electrical signal from one neuron is transmitted to its target tissue it could be a muscle or a new endocrine cell or something, now what exactly happens? This is the anatomical part of it.

So, the way it transmits is this there are two level of energy trans reduction which takes place. So, electrical impulse are electrical signals which are travelling. So, when they reach a synapse these electrical signals are translated into chemical signals in the form of neurotransmitters at the nerve muscle junction or at the synapse between neuron to neuron, there are neurotransmitters which are secreted out from the sender from where the signal is coming, and those neurotransmitter are released into the synaptic zone or the synaptic cleft, and those neurotransmitter than buying to the post or the target tissue which is also called post synaptic target tissue and on the post synaptic target tissue they bind to the series of channels, and they open up the gates for the ions, and then this again the target again generates another action potential.

So, this is what I have told you verbally let me show you graphically what is happening. So, coming back here. So, here the electrical signal is travelling once this electrical signal reaches out here at the synaptic cleft say for example, here the electrical signal reaches out here this. So, in this situation this one is the presynaptic the one which is carrying the signal pre synaptic, and this one is the post synaptic presynaptic, and post synaptic. So, it is a pre synapse, and post synapse. So, at the post pre synaptic zone what is happening?

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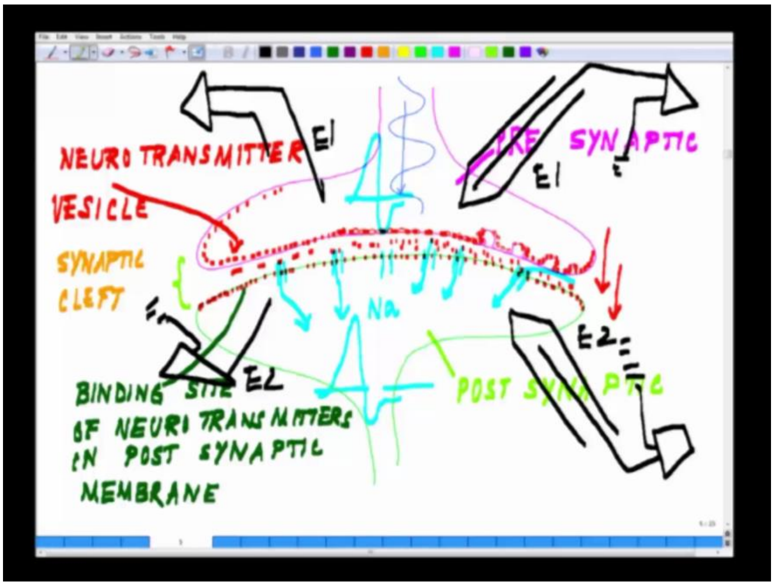

So, let us look at it see say for example, this is the presynaptic zone, and this is the post synaptic zone which I am drawing in green off course I am here showing two neurons. So, was the electrical signal reaches out here. So, here the electrical signal is reaching. So, it is travelling like this these electrical impulses leads to the secretion of neurotransmitters. So, here you have the vesicles of neurotransmitters which are setting like this. So, actually essentially they sit like this structure is more like this with series of neurotransmitters all over the place.

These red ones are neurotransmitters what I am drawing just let me all over the place now once the impulse reaches here these neurotransmitters from here are secreted out in this direction like this. So, they they are into cleft area at this cleft area the next thing happen they bind to the post synaptic neuron step two they bind to the post synaptic neuron like this once they bind to the post synaptic neurons. So, let me just mark it this is pre synaptic, and this is post synaptic, and this is the synaptic cleft, and these are neurotransmitter vesicle, and these are the binding site of neurotransmitters on post synaptic membrane, fine.

So, there are three events which are happening. So, the electrical signal reaches the synaptic zone at the synapse neurotransmitters are released by the pre synaptic membrane, those neurotransmitter defuses into the post synaptic into the synaptic cleft in the synaptic cleft they immediately bind to the post synaptic membrane after binding to the post synaptic membrane they open up. So, the next thing what happens out here they open up a series of channels out here these are the channels which leads to the flux of sodium, and off course, and then as the if it is a sufficient amount of sodium which gets in out here, and this shoots another action potential like this.

And this is how action potential impulse is propagated from one neuron to the next neuron to the third neuron likewise, and just if you try to visualize this in terms of its complexity. Now think of it, if one neuron is synapsing on ten thousand other targets how this signal is going to you know divide out in all of this at one point of time it is a very very complex network. What I am showing is the most simplistic version of a single synapse at a junction which is so clean, but really to decipher what is happening at individual synaptic level is an extremely challenging task, now how you could measure where electro physiology comes into play.

So, say for example, if you have a preparation like this, and if you have a electro setting like this. Say for example, I have a patch electrode or some kind of any electrode it could be an extra cellular, it could be intra cellular electrode, and another electrode like this. Or this is I am showing you a patch electrode or say for example, you have sharp electrodes like this sorry I have just showed you wrong now if this electrode. So, in a base line situation you are not stimulating any electrode. So, if this I call this as electrode one or pre synaptic electrode two electrode one electrode two.

So, if you are not stimulating you are just keeping the electrode intact like, you know just sitting there, you should be able to see the spontaneous responses. If at all there is if there is a spontaneous flow of impulses from the pre synaptic to the post synaptic you will be able to see the change say for example, the way it will look like. So, here basically you have to do a dual channel recording.

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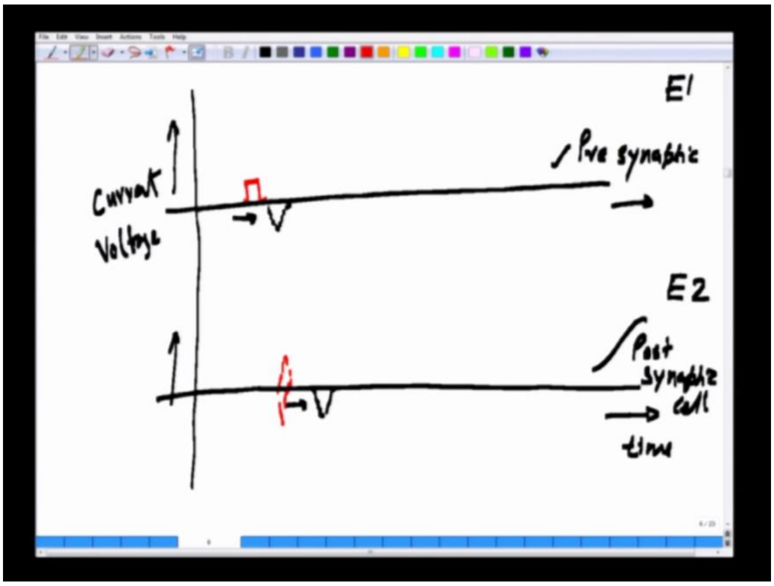

So, you have one channel. So, the way it will be say for example, if will have one scale showing like this another scale showing like this. So, this is the scale for e one, and this is the scale for e two electrode one, and electrode two.

So, both the electrodes are a kind of sitting at ease without doing anything. So, what will you see is that if there is a impulse which is there in this electrode you will see something like this a deviation out here. You could either measure the current or you can measure the voltage depending on what you want to measure, and followed by this impulse with a slight delay you will see another impulse out here if this is time why there is a delay, because look at the circuit. So, impulse comes here at t one time t one, and this impulse travels through. So, there will be a gap out here between while it is crossing the synaptic cleft all this signal there is t two.

So, with the delay you will see a change in the membrane voltage of this is the pre synaptic cell, and this is post synaptic cell with slight delay. You see a impulse get propagated or what you can do you can stimulate this cell, you can you can do it like this you can give an stimulation out here physical stimulation like this. And with a slight delay, you will see the response in this electrode something again like this. Say for example, I given stimulation say at this point I given stimulation this slight delay, I will see a a response a response could be in both direction it does not matter whether up side like whichever side.

I am showing on the on the scale you could show the impulse like this also. So, you will see a change in the membrane potential, and this is where the electrophysiology techniques the bioelectrical measurement techniques comes. So, handy were you literally can quantify the biochemical changes which are taking place out here.

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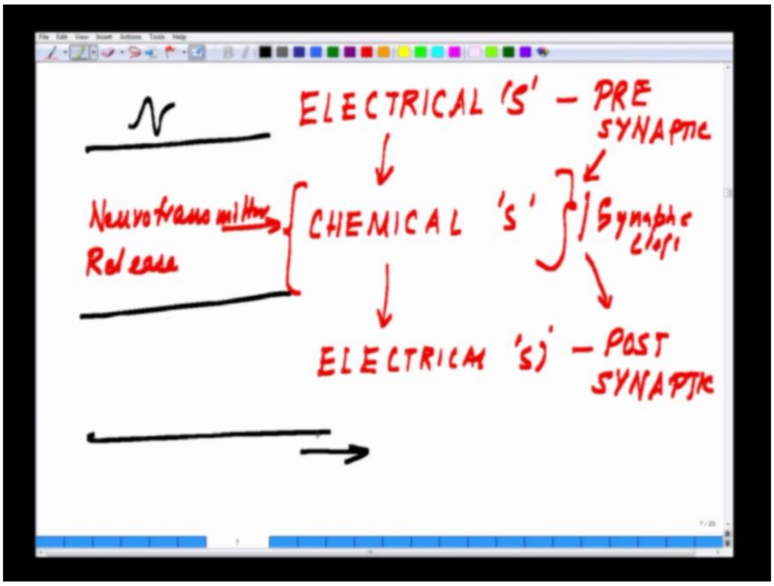

So, what essentially happened. So, if I break it down what I was trying to tell you a first an electrical signal electrical signal translated into a chemical signal s stand for signal in the form of this is in the form of neurotransmitter release followed by generation of another electrical signal, and this is in the presynaptic and.

This is in the post synaptic, and this diffusion from presynaptic via synaptic cleft to the post synaptic fine does in makes sense. So, for an example if you have one electrical signal here with a certain time delay, this is a scale I am following same scale of time slight delay. You see the signal out here, and same thing do for anything, and everything as long as you place the electrode from the sender to the receiver should be able to measure the electrical signal across the circuits. Coming back here this when you do the basically your doing in dual channel. Similarly you could have the modern electrophysiology technique may allow you to do these kind of recording on a four channels.

If you have four such electrodes you can vary channel is not problem problem is the dimension of the cell, because you are handling area within for example, in area of thirty micron diameter within thirty micron how you can it its really challenging to put four electrode like this through itself is challenging four m is more challenging some people can do it there really very good attend, but not very many can do that. So, there is physical challenge involved here you can do the similar recordings using the microelectrodes arrays for example, you have microelectrodes arrays like this ok.

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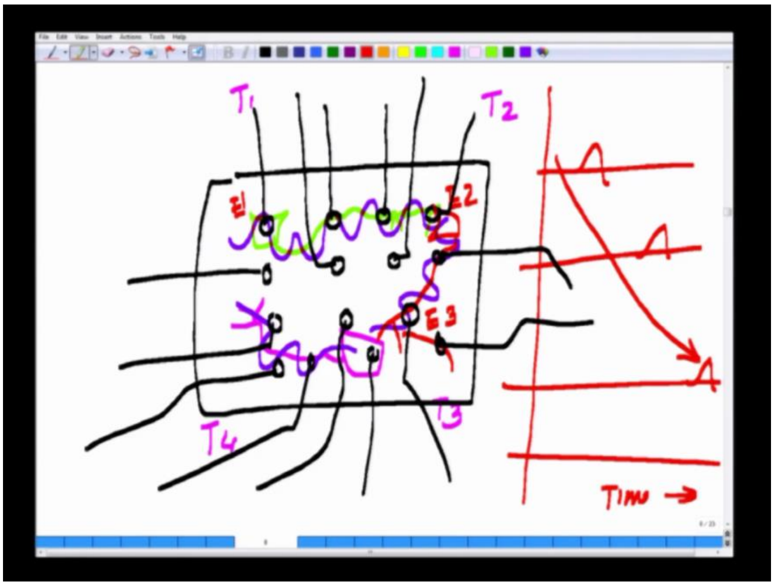

And some I mean, and something like this, and kind request please go through online into see the beautiful pictures of microelectrodary in google image it will really enhance your imagination power. So, an microelectrodes arrays for example, I have this muscles growing for example, or say series of neurons sitting like here like way, and how there making contacting another set of neurons out here another set of neurons sitting here likewise. So, any signal you will see with with the way, you will see is that t one time t two t three, and t four say for example, a signal is generated from here something like this.

So, this will travel all the way out here may be likewise. So, on a scale what will you see say for example, you have a scale like at if I name these as different electrodes say for example, e one e two say e three. So, at e one you will see a send signal, and after with a gap of sorry time you will see a signal on e two, then you will see a signal on e three likewise. So, signal is moving like this with time. So, your realizing that those techniques which I just thought you in previous classes how handy they become when you have to analyze these kind of circuits.

So, coming back. So, this is all about the impulse propagation which I really did not cover a whole lot I will talk little bit on a muscular junction as I was moving through. So, were we all started we started with talking about the circuit. So, this is from where we diverged into how the impulses getting moved from here to here. From here how the signal is transmitted through the synaptic cleft to this neuron. And by the same way, this neuron picks up the signal from here, and its coming back. Now you have understood about the impulse propagation impulse is getting propagated like this, but what we have not understood yet which we have to discuss is how the this part is taken care how the sensory neuron out here is sensing the all other the muscle lets propose the question.

How muscle sensing the change in length this part we have not discussed yet this we have to discuss. So, we will be discussing this after this. So, we will close in here, and we will initiate our discussion how the muscle senses the length, and how that is transmitted to the sensory neurons how again the electro recordings could come very helpful in understanding this. And from how that signal is being picked up by the motor neurons how again the electrophysiology will come into play. And how finally, the motor neurons transmit at the neuromuscular junction the signal to the muscle, and how within the muscle that signals get propagated. So we will close in here. So, we will resume in the next class.

Thank you.