Bioelectricity
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Lecture - 14

Welcome back to the lecture series on NP-TEL on Bioelectricity. So, today we are into the fourteenth lecture. So, in the last lecture, we initiated with the simple circuits, the primitive circuits of the system. So, we started talking about the stretch reflex arc and I explain you the three major component of the stretch reflex arc in the muscle, the motor neuron, the sensory neuron. Sensory neuron is the one, which is carrying the message from the muscle about the change in length; and motor neuron is bringing back the message telling the muscle to come back to its original position.

So, there are within this domain, there are few other small elements. So, the sensory neuron which goes into the spinal cord and conveys the message to the motor neuron, it may do it either by directly synapsing on the motor neuron or it may synapse via a inter neuron. These are series of small neurons, which perform a wide range of function in terms of computation at the central nervous system. Now at the level of muscle, there are two components; the one component is the component, which senses the change in length or the sensor elements; the other one is the actual muscle, which is getting stretched and coming back to its original position.

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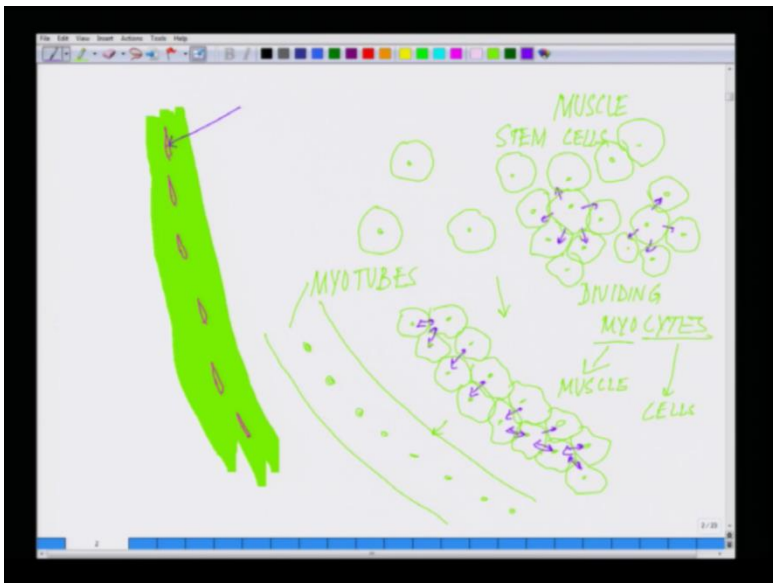

So, last time when I showed you the circuit I did not introduce all those integrity details. So, today I will introduce all those integrity details. So, coming back to the slides, so this is lecture fourteen and let us draw the circuit now. So, this is the muscle - drawing in green now. So, there is a change in the length of this muscle which matters and within that muscle you have certain elements like this, these elements are essentially the elements which could sense the change in length. So, they have a special name, those are called muscle spindle.

So, now talking about muscle, I have to tell you little bit about the muscle before I could explain what is muscle spindle and what is a regular muscle. So, muscles generally if you go through any physiology or developmental aspect of muscle, you will realize muscle development is a very interesting process. What initially happens, when the embryo is developing and all the muscle all our musculatures are being formed, it kind of a starts like this. So, you have certain specific cells which are destined to become muscle. Those, which are destined to become muscle, initially divides; after division, they align themselves kind of in a line, and then those individual cells loses their part of their cell membrane and becomes a continuous structure which is called a myotube.

So, say for example, just what I am trying to tell you, it starts like this. Say for example, these are individual muscle cells or say for example, these are the muscle, these are the initial cells which are destined to become muscle like this. So, these cells initially starts dividing. So, the division process starts, they are dividing now. You will see clustering of them, they are dividing out parent cell to daughter cells likewise, same here, same here. So, once they divide and next thing they do, they align themselves something like this. They are aligning themselves as if they are standing in a line, as if you are in a morning assembly in a school and you are standing in a line, they align themselves like this.

Once they align themselves, the next thing what will happens is that these contact boundaries what I am drawing now, these contact boundaries are now merged. So, there is no individual boundary left between these muscles and this is exclusively I am talking about the skeletal muscle. So, essentially what you obtain is a structure like this, a continuous structure with all the nuclei of the individual. So, these structures are called these are the smallest functional unit of muscle these are called myotubes, and these are called the muscle stem cells you can call them, they are sometimes also called satellite cell, because these are the cell which are destined to become muscle, and these are

dividing myocytes; myo means muscle, cytes means cells. So, this is how the myotubes are formed.

Now then how come this next element which I was trying to tell you these spindles are formed. So, that is something a different story. So, they are two existing theories. So, let me explain the theory then I will tell you diagrammatically exactly what happens. One theory says then when we talk about muscle stem cells, there are cells which destined to become a different kind of muscle - this is one theory.

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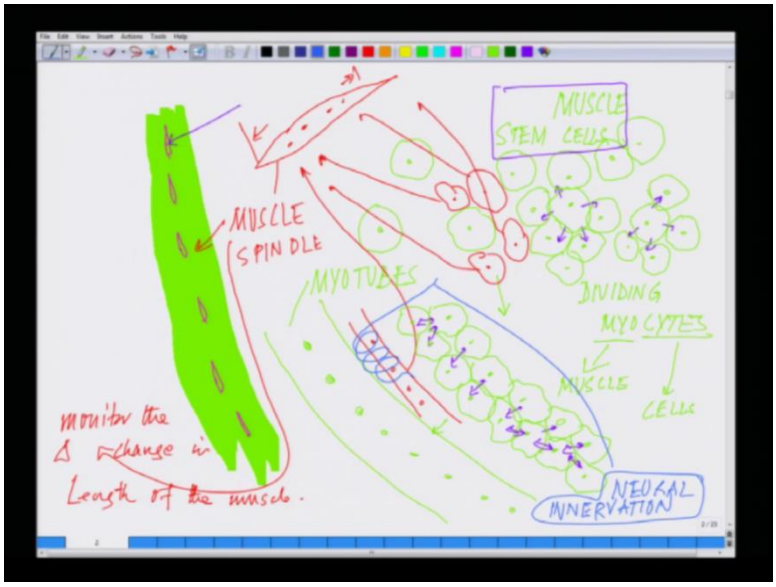

So, in other word, coming back to the drawing if I come back to the drawing out in this slide, so whenever we talk about this muscle stem cells, so there may be other kind of muscle cells which are different from the existing ones like this. And they attain a different path way instead of making a myotube like this, they form a very specialized structure like something like this, a spindle shaped structure. And these spindle shaped structure has the ability to they are called muscle spindle, which is essentially this kind of structures, and these muscle spindles have the ability to monitor the change or change in length of the muscle - this is what existing theory, it is not really clear.

There is another theory; the other theory is even more interesting. It says that the muscle starts developing from the common route there is a pool of cells, the stem cells which destine to become muscle, they become myotubes, but at the myotube level some of the myotubes, so at this stage now coming back to the slides again. At this stage some of the

myotubes go for a different fate and those myotubes eventually becomes muscle spindle, but how exactly this development is going on. And of course, there is another catch to this game, they say that this formation of the muscle spindle is also a function of the neuronal innervations. The kind of neuron, the blue what you see is the neuronal innervations I am drawing, say that this formation of muscle spindle is a function of a kind of neuron which is synapsing on them decides what will be the fate of that particular myotube.

So, whatever be the story we really do not know how they originates, and how they are formed, but what we know is the first drawing which I drew for you people coming back to the slides, if you look at it like this. So, basically if I now redraw, it will be something like this. So, these are the myotubes all over the place, and within the myotubes there are another series of different kind of myotubes, different kinds of structures which are these ones, they are embedded. The proportion of these muscle spindle is far less as compared to the gross the muscle.

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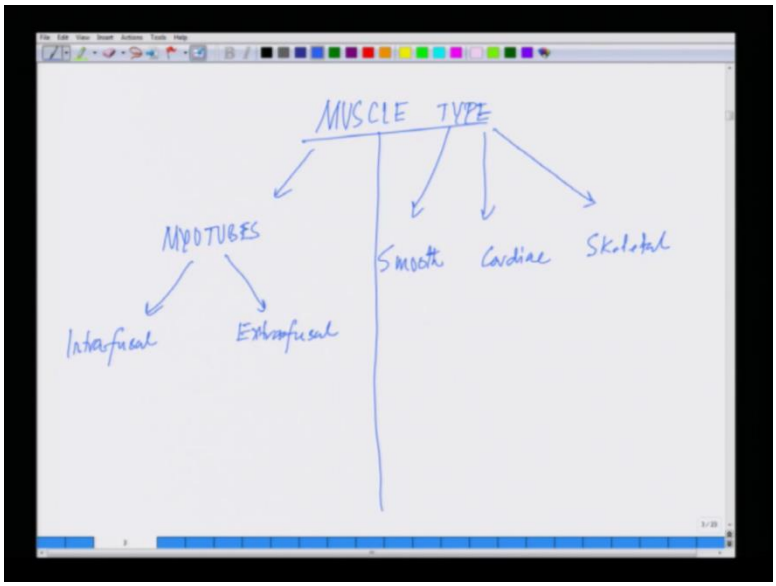

So, there is another classification on this that classification is essentially called muscle type, if you have to say or myotube type muscle type. So, irrespective of this is so there are multiple ways you can classify the muscle one classification is of course, most traditional classification, which is the smooth muscle, cardiac muscle and skeletal muscle, this is a kind of, but there is at the level of myotubes, there is another set of

classifications which is called interfusal muscle and extrafusal muscle. So, extrafusal is that bulk structure of the muscle what is present, and interfusal are those muscle spindle like structure which proportionately are very less as compared to the extrafusal muscle. So, now these are the two elements which are the contribution or the muscle component of the stretch reflex arc circuit.

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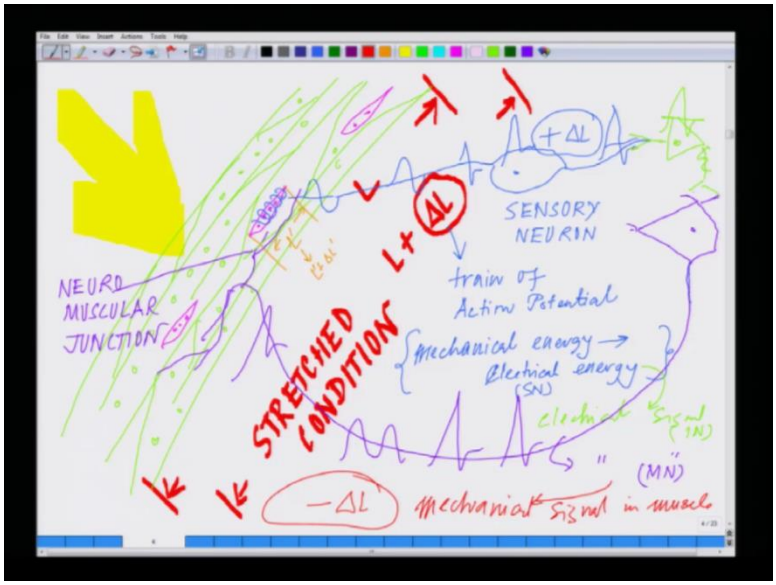

So, what I am now slowly slowly opening up the circuit. So, now if this is the case and now if this is a extrafusalfibre likewise, and just for your interest to realize these extrafusal fibers or the bulk fibers, these individual myotubes form super coil structure among each other and they form fibers - myofibers. So, we started with myocytes, we formed myotubes; from myotubes, we formed myofibers, and these individual myofibers that those spiral like those intertwined structure then interact with other intertwined structure of fibers, and they form what you see is your muscle - the whole muscle fiber. So, it is a very interesting three dimensional structure of coiling and super coiling which constitute gives you all the strength of all the work you do all your life.

So, coming back, now we are now dissecting out the individual component. So, among this, so this is your extrafusal fiber all over the place; and within this extrafusal fiber, you have these interesting component of muscle spindle which are sitting like this. And they are actually spindle shaped kind of structure, and these are the nuclei and out here there are multiple nuclei likewise. Now this circuit first of all here so as I told you that it is the

muscle spindle which has the ability to sense the change in length. So, now impact falling on this that is I am showing in yellow; once the impact falls on it, what happens is this, this muscle length gets changed. So, say for example, if it is a finite length, let us assume it is a finite length of L, L you can put any unit centimeter, millimeter whatsoever.

So, now when the stretch falls, this length changes to become L plus delta L. So, delta is the deformation which has taken place in the muscle, muscle is stretched now - in a stretched condition. Now at this stage what will happen, now let us add one more component to this circuit that component is the sensory element component. So, where is the sensory element component sitting, the sensory element component, so one more thing, the muscle has changed simultaneously, this stretch has also change the length of the muscle spindle. So, if this was initially L, it becomes L plus, if it is L prime then this becomes L prime delta L prime, this is individual smaller part of it. So, there is a change in this. So, this muscle spindle is innovated by the sensory neurons like this, and the sensory neuron is like this. It is the cell body out here, and it is going all the way to the spinal cord.

So, now, whenever there is a change in signal, this muscle spindle senses this change and sends a electrical stimuli like this in the form of train of action potential to a sensory neuron. So, this is your sensory neuron. Sensory neuron enters inside the spinal cord. Once it enters inside the spinal cord, I told you there are two options. This change in length it has already decoded. So, the message there is a change in length, there is a specific train of action potential, this change is communicated by a train of action potential. In other word, what happen now a mechanical energy is translated into electrical energy, first translation, first change in the energy formatting.

Now this reaches the spinal cord and as I told you there are two options at spinal cord; it may either directly convey this signal to the motor neuron or it can convey this signal through a small interneuron present, there are multiple interneuron present in the spinal cord. So, we put both the situation or actually most of the time it is through a interneuron. So, let us put a interneuron out here which is awaiting which is picking up the signal and this it is conveying. This signal now conveyed to the motor neuron out here, it is the motor neuron component. So, here in violet, you have motor neuron component. So, here this electrical signal which came from this train of electrical signal

which came from sensory neuron is now transmitted to the interneuron. So, this mechanical to electrical signal now moves to another set of electrical competition.

From this interneuron, this train which is now modified the information has been decoded is transmitted to in the form of electrical current to the motor neuron. So, another level of competition taken. So, look at it in such a simple circuit, another set of electrical signal, and this electrical signal is the motor neuron, the previous one was in the interneuron and the first one was in the sensory neuron -SN, SN is sensory neuron. IN is the interneuron and last one is the motor neuron. Now motor neuron out here, which is the largest neuron carries the message back to the muscle, and this junction is called neuro muscular junction.

So, now the electrical signal of the motor neuron is translated again back to a mechanical signal in muscle. And this essentially the train of electrical impulse send by the motor neuron is essentially telling, if this signal which was conveyed by the sensory neuron was the signal of plus delta L - change in length, and this mechanical signal which is send by the motor neuron through the muscle essentially tries to tell it minus delta L. So, first set of electrical simulate which from the muscle after the stretch and after the increase in a delta L length is convey through the spinal cord motor neuron via interneuron.

Now, the motor neuron compute the signal and send back a message in the form of a electrical impulse to the muscle, and tell the muscle the change in length what you had at few in decimal t time before this should be retracted back, it should be minus delta L now. So this electrical signal what out here is originating on the motor neuron is diametrically opposite if you have to understand it from this signal which was convey in terms of plus delta L and this one keeps stays minus delta L.

So, come back to its original position. So, after this change it will tell you come back, so that it should be again becomes L. So, this is essentially if you look at it for such a primitive for such a simple circuit, this is most primitive circuit which is evolve, millions of year. Even this circuit also has first mechanical signal to a electrical signal then that electrical signal gets a modified at two different level and then again the electrical signal after all the modification come back and telling convey its getting converted into

electrical to mechanical signal. So, this is the beauty of biological computation, and how you can study we already talked.

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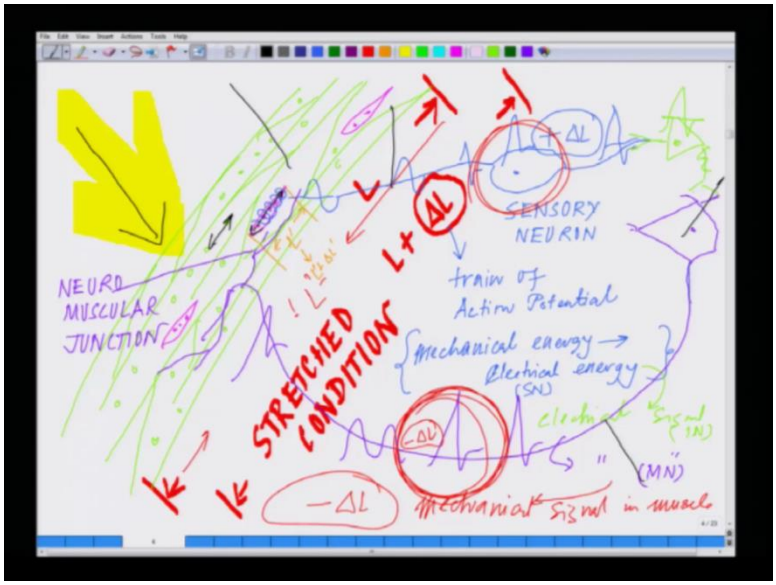

We can poke a electrode out here, you can poke an electrode here, if you can rarely rebuild the circuit on a chip or you can do it in animal proportions very tricky though. You can pick an electrode here you can poke an electrode here, several ways you can really measure all the signals, you can stimulate this circuit and you can do the measure. But yet there are several things which on this circuit what we have in touched, first thing you have to touch let me tell you is how when there is stretch on the muscle, how this change is been sensed or in other word this change in length, I told that there is change in length on the muscle spindle. Change in the length change in the muscle spindle how that information on muscle spindle is transmitted to spinal cord, because I will tell you why I am asking this question.

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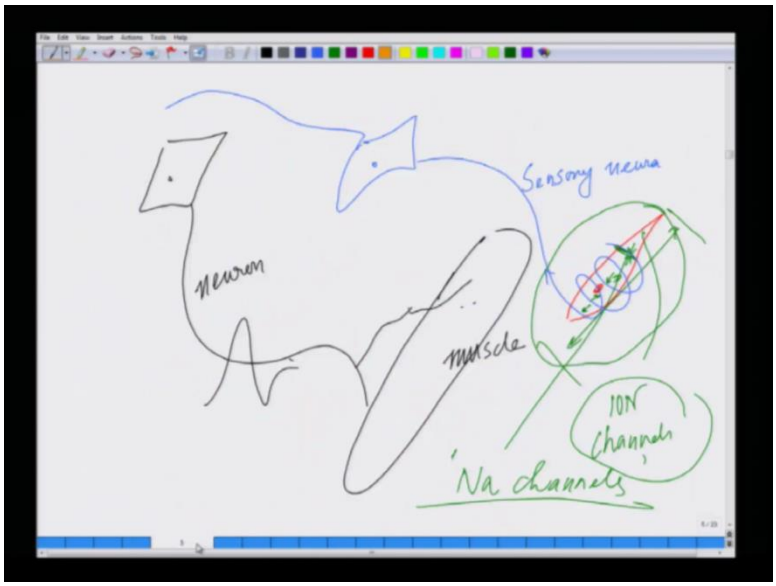

Because as of now in the last class, I was trying to explain the synapse everything I told you something like this, it is working like this. If this is muscle and this is neuron then the signal which comes from here the train, which comes from here is conveyed here. But think of it there is reverse situation happening, if this is muscle spindle this signal is been picked up by if this is the sensory neuron and blue this signal is been picked up out here. So, this transaction out here I am showing it you in green, this transaction how this signal how this change in the length is been conveyed is not clear. It is really really tricky to understand, how this information from muscle spindle is transmitted through sensory neuron. It is not yet know, there is lot of research is going on to understand what kind of ion channel are detecting phenomena and where exactly the signal is it just a physical change or the stretch or push and pull. Or is it because of this is stretch these two structure these integrated structure between muscle spindle and the sensory neuron so integrated.

So say for example, imagine this is your muscle spindle, and these are processor of the sensory neuron and the pressure following on this something like this, is it so integrated that how that electrical signal is transmitted it still mystery, it is not really clear. It is suspected though there are some very specialized kind of sodium channel which are involved, but what are the nature, and how they are functioning is a matter of speculation at this stage. There is no clear cut prove to tell how this transaction is taking place. This is one area which is unknown in this circuit, because as of now building muscle spindle,

full fledge in muscle spindle outside the system is kind of very challenging. There are very few labs who has manage little bit in that area, but the significant work is yet to be accomplished before we really understand what muscle spindles are.

If you look back while I was to trying to tell you the origin of this, so this is thing we really do not know the original muscle spindle, but they are those element which are kind of biology if you heard this word MEMS - microelectronic mechanic system. So, these are biologist (( )) of micro electro-mechanical devices. There is small yet they could translate mechanical information into electrical information and likewise and at the micron level. So, we really do not know coming back we really do not know how this information of change in length is being conveyed from the muscle spindle to the sensory neuron.

Next thing is what we know of course, there are two sets of motor neuron. So, when I showed you the circuit out here I told this set of motor neuron is coming all the way and you know taking care of your muscle, but I told you that there is change in the length of this muscle spindle too. So, muscle spindle has to come back to its original position how that is been taking care. So, at this stage, I will introduce one more complexity to this circuit, there is another set of motor neuron, those are called gamma motor neuron, and these are called alpha motor neurons. These gamma motor neurons simultaneously convey a message, which in a weight on the muscle spindle and ask it to reduce its length. So, now, I am introducing one more complexity to this circuit. So, this signal which went through the inter neuron is conveyed to the gamma motor neuron.

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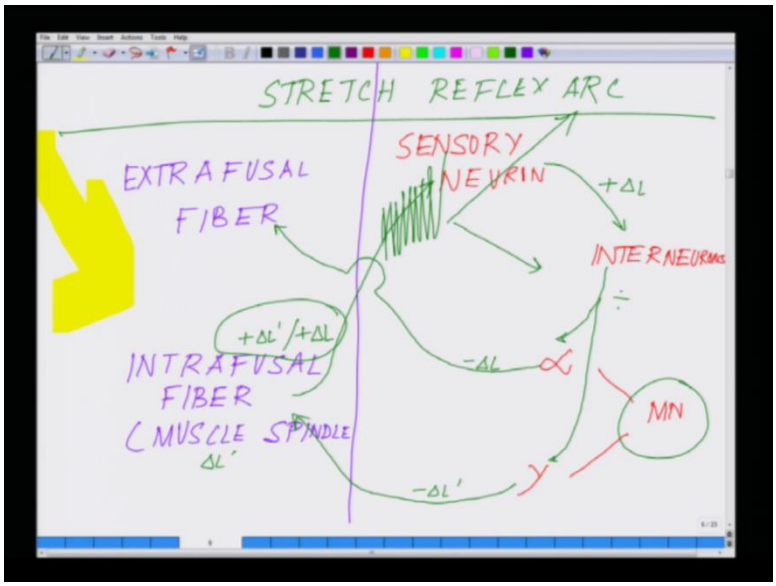

So, now, just to make slide more cleaner. So component wise, let me put all the component one by one. You have extrafusal fiber, you have intrafusal fiber or which is also called muscle spindle. You have this side you have sensory neuron, you have inter neurons one or multiple neuron, then you have motor neuron same m n alpha and gamma. So, for the same stretch reflect circuit what I started in the beginning of this class and previous class stretch reflex arc now if you look at it, there are at least six components. You have the stretch sensor the form of muscle spindle, you have the muscle which is executing the job in the form of extra fusal fiber. You have the sensory neuron which is rap on the muscle spindle, which carries the information, translate the information to the inter neurons. Inter neurons divides information into two components; and one component goes to the alpha motor neurons, and other goes to the gamma motor neurons.

The gamma motor neurons brings which innovates the muscle spindle brings backs the message that this is the change in the muscle spindle, we should come back to its original shape, because you have to send the next system ally; whereas, the alpha motor neuron tells the extrafusal fiber to come back its original position. So, let us start connecting all this what I have just told you.

So, here is the deal. So, first is the here is the impact following in yellow now back. So, this is where the first set of the signal goes from here the signal moving to inter neuron;

form the inter neuron, signal is getting divided into two parts alpha and to gamma. From here gamma is telling this to come back to its original shape, and whereas the alpha is telling the extrafusal fiber to come back to its original position shape. So, what happen here is, delta l plus this delta l information, this plus delta l information in the form electrical stimulate is being conveyed to inter neuron.

Motor neuron does series of computation and need sends a signal minus delta l change in the length of muscle spindle and minus delta l, which is change in the length of extrafusal fiber. And brings it backs, so essentially plus delta l or plus delta l prime. These are two set of the information which is coded and sent to the sensory neuron. If we really succeed in next hundred years, there will be time when these electrical signals in the form of action potential could be de-convoluted into the different component L, delta L likewise all those things.

So, when you talk about neural code it is that neuron signature or actual potential signature, which travels in the form of action potential from like translating a mechanical stimuli as (( )) stimuli, hearing off course that is also translating as a mechanical stimuli or a visual stimuli into a electrical signal, and what are those unique unique electrical feature is matter of tremendous contention that. What are those features, what makes realize you know this smell of say some specific some rose perfume or some you know jasmine perfume or this particular thing taste like that particular wine or likewise, you know these electrical signatures are all...

So, basically what essential I am trying to tell you all these information the coded within the action potential with some mechanical signal, whether it is visual signal, whether it is a taste signal, how these are coded is the area which next twenty years of mankind of understanding something called neural code. And if you look through this circuit what I have drawn for you people I mean look at the level of the complexity which are involved here.

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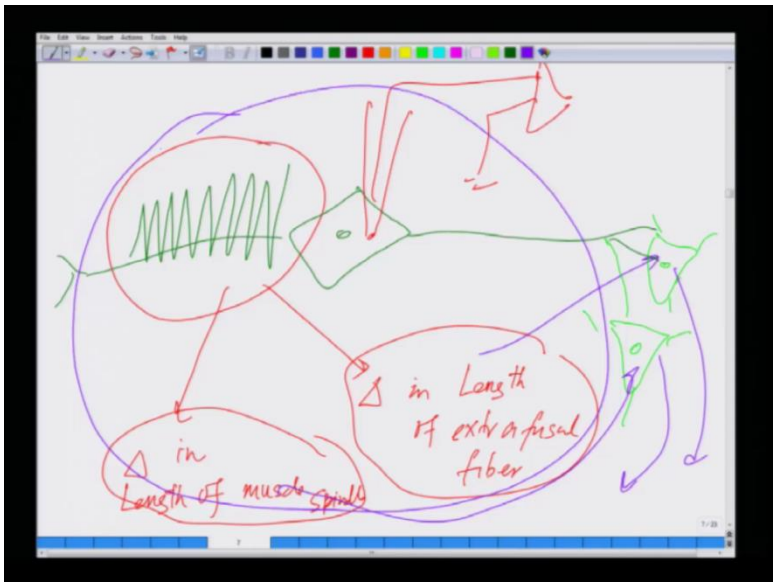

So, even at this stage, if you look at what sensory neuron doing they are so simple basically what you will see in a patch clamp. If this is a sensory neuron, what will you seeing is same like this that is it. Now how form this you can de-convoluted back and tell this component is saying the change in length of muscle spindle, and change in length of extrafusal fiber. How and these are the questions, because that was it will tell, if you put an electrode out here, a patch electrode or any extra cellular and inter cellular respect that is trainee are going to get. What kind of mathematical tools you will be needing to decipher these signal that how this process is been actually coded by neuron which could mathematics, I mean, basically what you are doing is that integrating all signal in one packet. And then within the packet which component is for whom, and then you are kind of it is just like lot of letters, and there is van and they have to distributed; and the postman is exactly knows and this will goes to this house, this is will goes to this house, this will goes to this house.

How a neuron does that how even think of it, I mean how beauty it, at this level if you come to the circuit on slide you will see this level also when it is conveying to partly conveying to to the two kind of. Say for example, it a neuron it knows which signal like which one has to conveyed to which one. At form here, again, they are following the separate part and not only that one more thing, which I have been discussed of course will going to come back on this. When this signal is coming at neuron muscular junction from the motor neuron, there is a transaction process which off course dealing will

progressing how this electrical signal is again translated into a mechanical signal in the muscle and leads to the contraction of the muscle; we have not discussed that we will be have discussing it.

So, what I wanted to kind of gate in front of you is thinking process what you guys need to cultivate to understand this whole area of bioelectricity the way things evolved the way electric signals are changing their features and way so such information is encoded in those action potential. This is something you just have to not only you read, you have to think over it because there is lot of thinking involved here, because it is on all those ways lies, very core of our existence very core who we are lies in those ways. And this needs immense amount of thinking and speculation, and imagination to figure this out and that is why I am kind of putting them instead of really bogging down with the information I am trying to tell you that see how such a simple circuit, you can get the recordings not a big deal. There are whole range of but to appreciate the bioelectrical signal you need to have your imagination in place.

You think that wow this is not something such a easy this must have taken a million years of revolution to reach to that point, where you can code the signal, and think of the application in some day somebody decode these kind of things for see for the example like this, if somebody could decode mankind do so. How easy will our next generation computers, how much information how whole communication concepts are going to change, because biology is to weigh more information; and if our average life is for eighty years, it kept on storing the information the way it wish to ok.

So, I will closing here. In the next class, we will resume further from this circuit, there are aspect of the circuit in which we have not dealt especially with the how electrical energy has translated in to mechanical energy on the muscle, we will talk about it. We will talk about the molecular structure of the muscle, the proteins how they are arranged and how they are movement brings about the contraction and how the neuronal signal is conveyed to them.

Thanks a lot.