

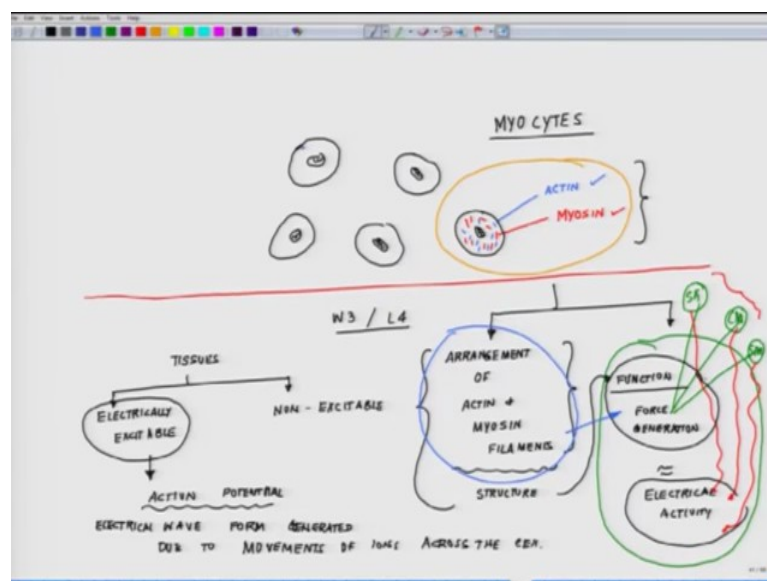
Animal Physiology
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Lecture - 14
Contraction in Muscle

So, welcome back to the 4th lecture of the third week. So, in the last class we concluded or rather we introduced the two molecular players involved in the generation of force; the actin and the myosin and I even mentioned you that in future we will not follow a gross classification. When you will be teaching here, probably the classifications will go much at the molecular signature people.

We will ask for like you know tell me the myosin sub-type. Depending on the myosin and the actin and what is that kilodalton, what is their size, what is the nature it is decided or it can be concluded at least partially that what kind of force they will generate and most of the muscle disorders like you know muscular dystrophy or muscle wasting related genetic issues is nothing, but most of the time you will see there may be some form of mutation in these proteins or a related proteins. So, there are two aspects what we will be dealing today.

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First is, so let us put it together. So, this is where we ended the last class. If you remember I told you, you have these actins and the myosins which are present there, right. So, today we are starting our week 3 lecture 4.

So, let us pick up the story from here where we left in the last class. So, today we will be talking about the two aspects. One aspect what will be talking about is arrangement of actin and myosin filaments; second aspect how this arrangement. So, this is your structure. How this structure leads to the function and what is the function is force generation and in the case of muscle, this force generation is also linked to its electrical activity. Now, this is something putting a bomb there like from where this electrical activity came. I will come to this.

It has something to do with just putting this point electrical activity. So, let me digress a little before I come back to this part, the arrangement of the actin and the myosin filament in the structure. So, in our body most of the tissues, there are multiple ways by which you can classify the tissues. There are multiple techniques based on anatomy, based on anatomical feature, based on function, based on certain other sets of presence of protein or absence of it. There is another very interesting way you can classify them electrically excitable and electrically non-excitable.

So, in other word what the way you can put it is that the tissues could be classified as electrically excitable and these are non-excitable tissues. So, what does that mean is electrically excitable tissues can generate a electrical waveform what we call as action potentials, which is essentially electrical waveform due to or rather generated due to, one second, due to movement of ions across the cell. So, I will come later. We are not going to talk about this action potential at this stage because as soon as we will introduce in the nerve tissue, we will have to come to that, but what I wanted to highlight is, so we have classified these muscles into three categories; cardiac muscle, skeletal muscle what we are dealing now and the smooth muscle. Then, we went ahead and did another kind of classification in terms of the structural feature.

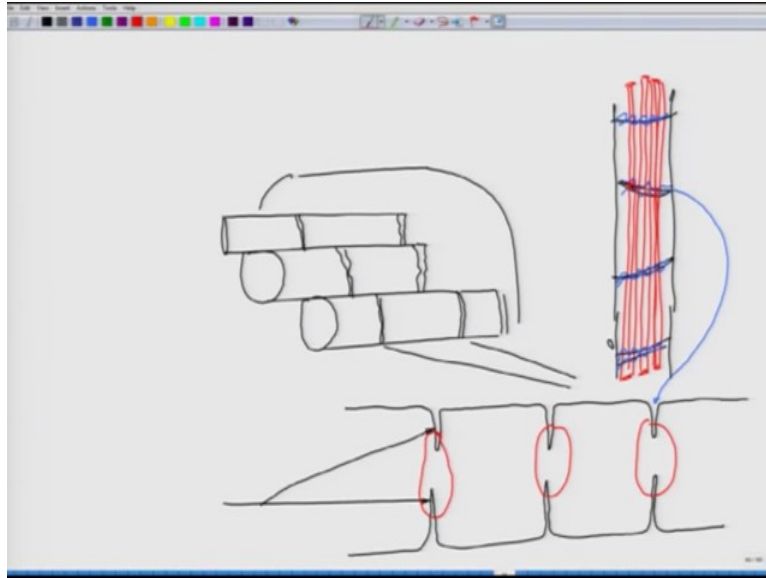
We talked about striated, non-striated muscle, right. That you remember. These are the two anatomical features we talked about as well as the presence where they are specially

in terms of the location within the body. The third classification which I generated was based on the force generated by them that was the very beginning. You remember that how I told you that you know the cardiac muscle generate a force like this. Why does this skeletal muscle generate huge amount of forces, where as the force through with the generated in the elementary canal or the digestive track you do not even feel it, right.

Now, today I am introducing a fourth classification, but this classification holds true for all the muscle, all the muscles and the nerves are electrically active. That means, in this context; that means they generate an action potential. It means in order to generate action potential they needed to have some specific family of ion channels in them and the nature or the shape of the waveform electrical waveform of the action potential of different muscle type is different. So, in other word this electrical activity could be directly correlated. Mark my word very carefully. This electrical activity could be directly correlated with the force generation of the muscle. So, these two disperse or very separate entities force generation and electrical activity could be clubbed together because we have already talked about the force generation is different for different muscle, skeletal muscle. SK for skeletal muscle, cardiac is CM and SM is the smooth muscle, right. For these three, it is different and simultaneously as we will proceed further, you will see their action potential waveforms are also unique.

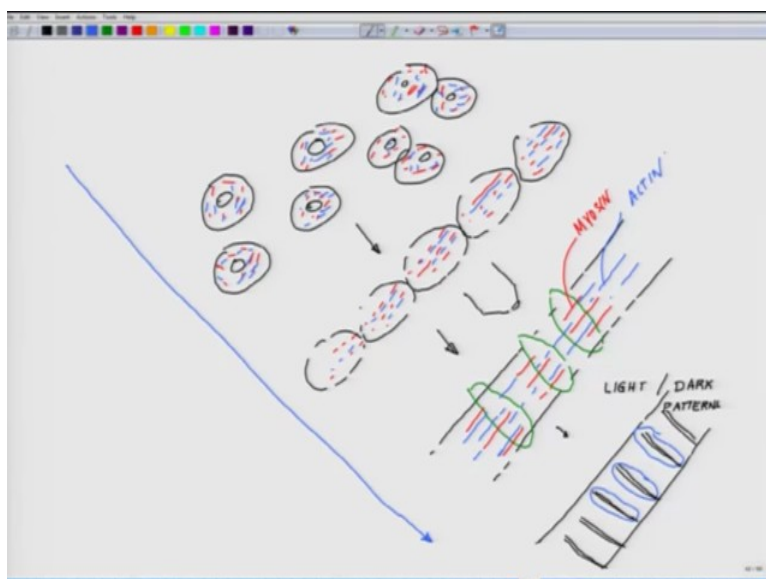
Just keep this in mind because there are two things. Now, I am telling you to carry over one.

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The one which I requested you to carry over is this feature. These structural features first thing and second thing, I request you to carry over is this part. They will come very handy. Just I am introducing them, but we will come back to this. Now, let us continue our story where we left this actin and myosin filaments. So, now coming back.

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So, you are having these individual cells or myocytes sitting here like this which are dividing, this is the nucleus, the second circle I am drawing inside the one. So, these myocytes are having I told you, these are the actin and myosin filaments synthesized and a very different, very high concentration. So, initially when these are individual cells, they have a very different kind of arrangement in the individual cells, but then I told you these individual cells come close to each other right the previous class and then, eventually would happen they form a tube like structure which is called the myotubes.

When they come close to each other slowly while they are about to lose their individual identity of the cell, these myosin and actin filaments started to rearrange themselves in a very specific geometry. Almost they are aligning themselves like straight lines in the individual cells. So, put it like this and once the myotube is formed, they come with a very different form and arrangement of a different kind. I am just putting it here. We will come to that molecular arrangement which was one of the hallmarks of muscle biology. They are arranged in an unique pattern. You see this. You could see a pattern out here in this picture and what will you observe is very interesting. There are zones. I am just putting where there will be overlaps like you see there are overlaps out here as compared to the places where there are no overlaps. So, it means there are places where the two filaments are like this. They are overlapping yet there are places they would not be overlapping. There will be overlaps, right. There is no overlap out here; no overlap on this side.

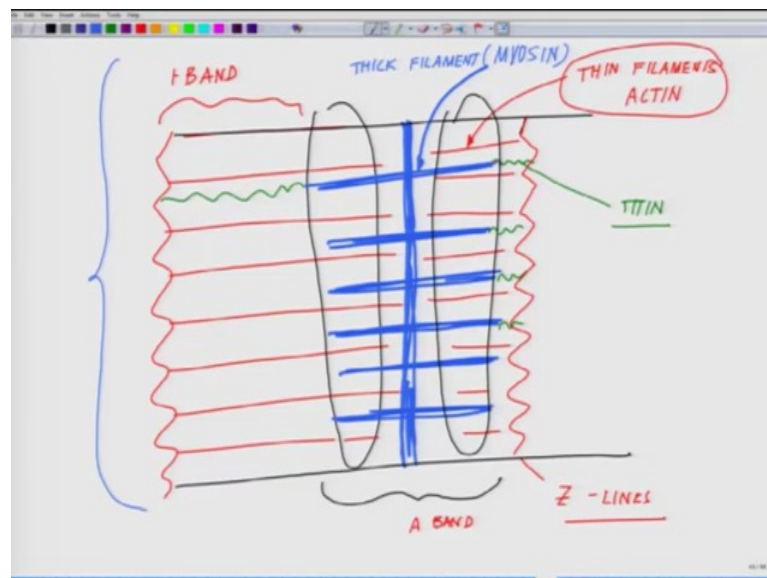
Now, if you see it under the microscope, what you will see this place, there is a overlap, right. So, automatically the lesser amount of light will pass through it because you are seeing from the top, you are seeing from the bottom, it does not matter, right. So, this point there will be lesser light as compared to the light which is falling here. So, automatically this side if you look at this side and this side, the light will be passing more. So, by the simple from if you are a cameraman, if you are looking at it, this side will look more lighter. This side will look more lighter; this side will look darker.

So, what you will you observe essentially will be a light and dark pattern. Once you see it under the microscope, if you see it under the microscope, you will see a light and dark pattern and these light and dark patterns is what led to conclude that there are some form

and striations on them. Those striations and this was very first observation and what people observe was very interesting. This is all back in 1960s 1950s, where I am talking about even earlier. You know what they observe that there is a regular pattern of striation something like this and there are, this is nothing, but an observation and then, people devoted their life to figure out what the anatomy of it is and then, followed by what I told you what the anatomy in terms of the arrangement of this actin and myosin filament is and what their functional significance is. Now let us see.

So, this is how historically this whole field had moved or it is still moving this first observation. Then, people went on to do a electron microscopy and in the electron microscopy, they could see even much better because you have the electron density. So, you see more electron dense zones here as compared to the zones which are much more empty. So, still you could see that dense and as you go further down into this, what you observe was a very interesting feature and now, I am going to draw that feature in front of you.

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If this is say for example mytotie myotube. I am talking about what people observed was something like this. First of all they observe let me change to go to a very fine thin ones because they observe there are once again there are thin and thick filaments which are

present there and there is an unique pattern.

I will come more into this pattern and on these patterns people observe something like this and in between what do you see is something like this and then, you observe was something like this. You see a thicker line. I am drawing you see something a pattern like this started to emerge. So, the first observation was there are two distinct thin threads which were of protein which we know or thin thread and a thick thread. The green one if you see the picture out here on the slide, these are the thick threads whereas, you have these threads which are the thin threads.

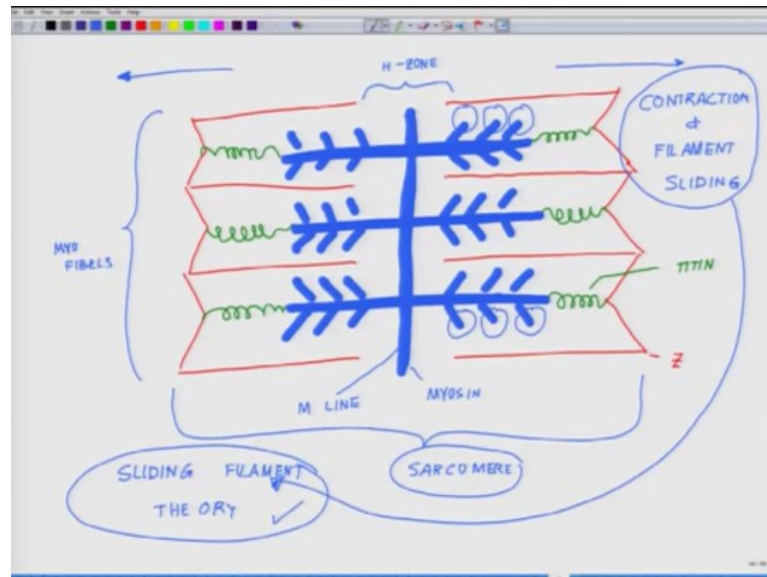
This was the very early observations and based on that the naming happened, the thick filament and thin filament and if you see this zone very carefully, you will see a lot of overlap out here, right. So, wherever there is a overlapping zones like something like this is where you see there is enormous amount of overlaps which are taking place. I am put the whole red out here. Just let me put the red. So, look at it. Now going back. So, these overlaps leads to the zone of overlap leads to a lot of pattern which started generated and this whole zone is sometime in the literature, they call it is the a band where I have put it and there is a zone where you will not find these blue lines that is called there is a very light zone which is called the I band. I do not get bog down into this, I and z band, but you just try to understand.

Now, there are lot of variations and this is called the Z lines and of course, I have marked the thin and thick filaments and apart from it, this thin and thick filaments are these thick filaments are attached by a unique kind. Just let me pick up another colour which is kind of there are attachments which are there like this and those attachment molecules which are present there are called titin.

So, I introduced thick filament, thin filaments and the Z lines and the A bands, right. Now, what are those thin and the thick filaments? Now, these thick filaments are myosin proteins and these thin filaments are actin proteins. Now going back to this structure now see. So, here you are having, so how we marked it myosin we are calling answer red. So, these are your myosin and these are your actin of course. We have just changed the colour code here. We have the actins are shown in red here and the myosin shown in

blue, but that does not matter. So, this is how the architecture started to emerge here and if you go little bit further, if we draw it little bit in a much more finer way, it will be something like this.

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Thin filament, thick filaments first. So, the thick filaments are like this, sorry. So, this is how the thick filaments look like. Now, I am kind of very microscopic level. These are the thick one. Second, these are the thick filaments and within the thick filaments you will come across some very interesting feature. I will come to that. What are those features we will come across within the thick filaments? We will see something like this. We will come to that what are the significance of those structures. So, this is about the thick filaments.

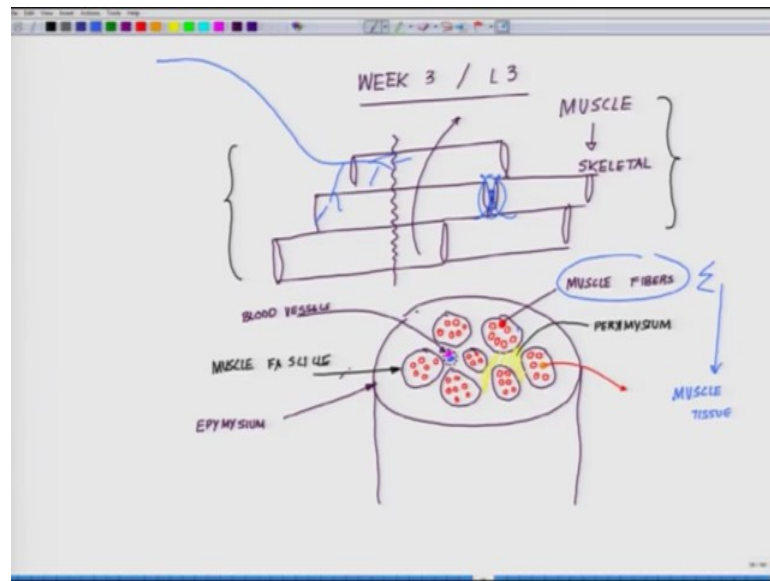
Now, I will go to the thin filaments which are present there. So, thin filaments are enclosed proximity. Let us take a simple scenario out here or another one out here, another one out here and may be another one like this. So, I am just keeping it, ok. These are the Z lines. You remember in the previous slide I talked to you about the Z lines. Just for those just recaps. So, these are the Z lines. So, now these thin filament or thick filaments are attached to a even much more thinner A which are called the A spring like a structure which are called the titin molecules. Now, here is the architecture, right. Now,

one minute I have not finished it off yet because I forgot to put, right. Now, I have the structure ready for you. So, this is how A structure looks like as if they are attached in spring. Now, this structure actually move like this. In other word, this frame work what you observe out here, this frame work, within this frame work you see this is spring. So, there is a movement of this thick filaments on the rails of thin filaments.

Again carefully listen to me. So, there is a movement of this thick filaments on the rails of these thin filaments translating it in terms of the molecules. There is a motion of these myosin filaments on the rails of the thin actin filaments. How that get executed? Once again another repeat. There is the movement of, there is a controlled movement of the myosin thick filaments or the myosin filaments within bracket the thick filaments on the rails of the actin filaments which are thin filaments. I have shown here in the rate on the slide. Now, there are few terminologies which needed to be defined. I defined this terminology the z line, we know about this titin molecule, we have talked about myosin, within myosin there are few other interesting thing, we have talked about this part and this is called H zone. This I am just introducing. I have not introduced this earlier.

This whole assembly from this end to this end is there is a name for this assembly. This is called sarcomere. This one single unit is called sarcomere. Then, this myosin, this is called M line and this I have already talked about the Z line and these are the myofibrils and the movement out here is something like this is a moment like this contraction and filament sliding. There are two words. Now, I am introducing contraction and filament sliding which is also known as sliding filament theory and I have already explained it what sliding filament theory is. Sliding filament is nothing, but which I repeat it on the rails of the thin actin filament. The myosin slides like this, but this process, a spontaneous process if it is a spontaneous process, our muscles spontaneously will twitch. No, it is not a spontaneous process. Yet there are certain muscles where it is a spontaneous process, but it is governed by lot of neural signatures and the muscle signatures.

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Now, this is where the physical movement of the muscle occurs. Now, imagine the slide which I bring. So, imagine at every level if this kind of movement are taking place, it has to be orchestrated. So, there has to be some kind of a control which is governing them the one which I am drawing now is basically a nervous control which I am introducing at this point. There are few other molecular details which I will be going out here, this zone which is called as the myosin head.

So, let us close in today and the next class we will go to the further molecular details of this structure and then, we will talk about how this sliding filament theory gets executed and how much force is generated.

Thank you.