Animal Physiology
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Lecture - 15
Function of Actin and Myosin

Welcome back to the 5th lecture of the 3rd week which is last lecture of this week. So, let us have a little recap what we did in the last 4 lectures.

So, this week we have completely devoted on the muscle, starting from the development of the muscle, classification of the muscle based on force, based on morphology, based on the myosin and actin which eventually lead to the force generation and we talked about the hierarchy of the muscle in terms of molecular to tissue organisation and then, in the last class we talked about the molecular architecture of the muscle.

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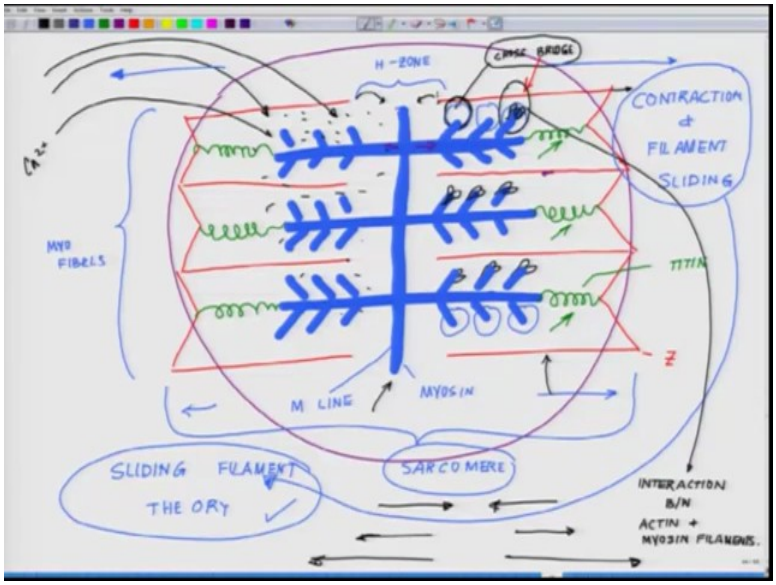

So, this is the picture where we ended, where we have the Sarcomere. You could see the Sarcomere out here. We have the Z lines, the red you have the Titin molecules attaching to the myosin filament, thick myosin filament and thin actin filament which are shown in red.

So, let us start this class with a small recap of the organisation of muscle and after that we will come back to the molecular details of this individual structure. I told you there is something very interesting out here, the interaction between actin and myosin filaments and generation of something which is termed as power stroke.

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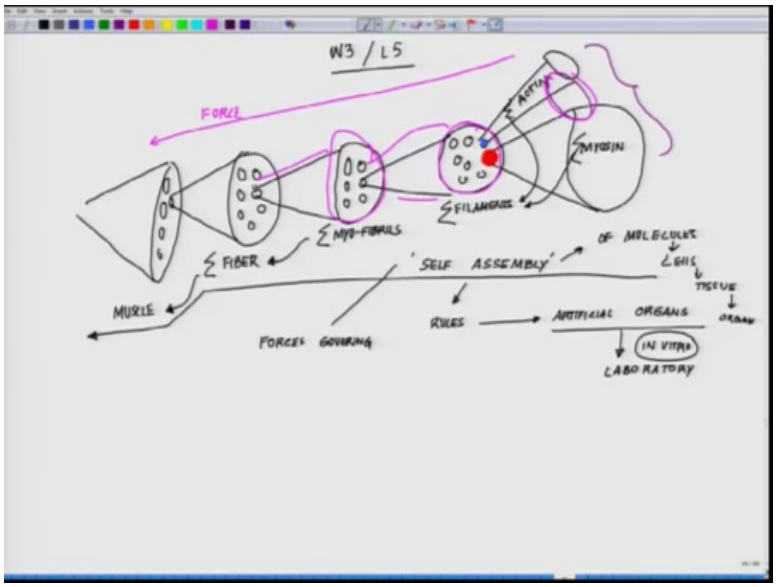

So, we are into week 3 and this is the final lecture, the lecture 5 of week 3. So, in terms of the organisational level, this is where we are. If this is what we call as muscle, this is how we should be able to remember. So, we pick up the fibres, the smaller unit of it. The individual fibre attaching together to form muscle, right from there we pick up another smaller unit which is the myofibrils muscle and fibrils myofibrils making fibre fine.

From the myofibrils we have now narrowed down our search to filaments, thick filament and the thin filaments. So, let us colour them differently. This is a red coloured filament and we have these blue coloured filaments. So, these red coloured filament which are thicker in diameter, they form the myosin filaments and thin colour or lesser diameter filaments which are blue in colour form the actin filaments. So, if you look at this picture very carefully, you will realize the level of hierarchy what is being followed in nature from self-assembly of some big molecules like actin and filaments which are proteins. Essentially they align in a very unique self-assembly to form what we call as filamentous

assembly, what we call as myofibrils. These myofibrils then form even much more complex assemblies called fibres and these fibres eventually form even a much more higher self-assembly called muscle.

So, what is the central theme in this whole process? If you look at it, there is one word which explain this process and that is self-assembly. So, if you look at it at every level in nature, there are certain unique rules of self assembly which is dictated to led to the formation of such complex structure and the future lies in understanding these kind of self assemblies because these self assemblies or understanding these kind of self assemblies will one day make us to dream or maybe will help us to achieve the dream of developing something called artificial organs, where we will be able to develop structures according to our needs and requirements in the laboratory, but in order to do so or you can call it in vitro outside the system self assembly. As a matter of fact our very core of understanding our own self depend how into the minutest or the finest detail we understand the forces, governing forces, governing self assembly of molecules to cells to tissue to organ.

So, keep this picture as a part of your brain map even if you forget. It should be able to figure out and the easier way to remember the way we used to remember was suppose there is a huge pipe and a hollow pipe, smaller pipes inside that even smaller pipes inside that even a smaller pipes. So, it is kind of a barrel those of you are opened up gun or something, you must have seen the barrels. It is like a barrel and within a barrel there is another barrel, inside another barrel likewise or those of you have seen the Russian dolls you know those wooden stuff. So, inside one doll there is another doll. You open that doll, there is another doll. It is something like that. It is a very unique structure to look at and especially when you look at in tissue culture dishes, how these myotubes or forming myofibrils. It is a joy to see them.

Now, coming back to the self assembly of these 2 things, where in the previous class we ended that they form something like this a Sarcomere like a structure out here which is called a Sarcomere unit. Now, today we will talk about even further self assembly of these myosins and these actins.

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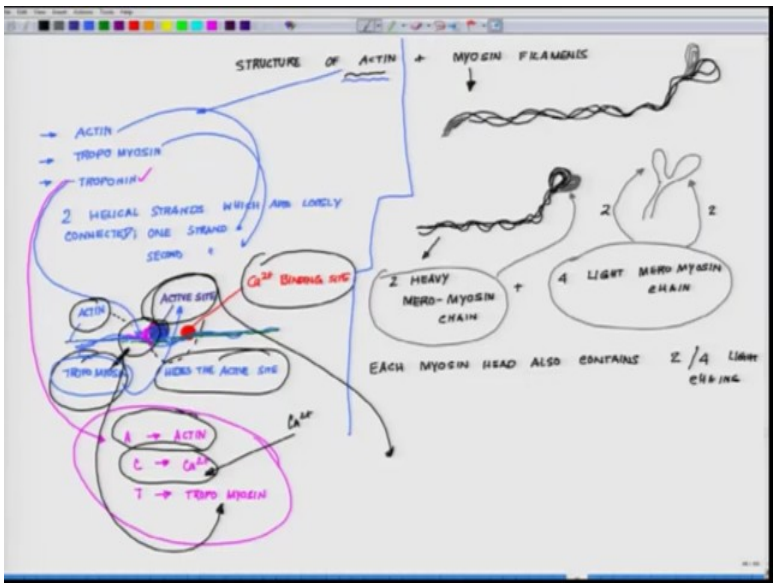

Essentially we talk about the structure of actin and myosin filaments. So, that is what we are going to start today, structure of actin and myosin filaments. So, talking about the myosin filaments, let us start with the myosin filaments. Myosin filament are composed of numerous myosin molecules that are bundled together say a multiple such molecules and they are bundled together like this, like this along with a globular protein head protruding out. So, that globular protein head is here. So, out here this head is like this which yesterday I just left it like this. So, structure is more or less like this. So, if you look at this structure, this structure eventually forms something like this. This is the globular head. So, the structure what I drew yesterday was something like this. Essentially it has like this. I did not purposefully did not do that. It will be confusing. So, now I am just putting it together and these are nothing, but filamentous proteins. There are thick and a thin segment which makes this structure and each individual myosin molecule is made up of 2 heavy Meromyosin chain. So, what you have is 2 heavy and this is called Meromyosin. It is just a terminology, Meromyosin chain plus 4 light Meromyosin chain.

So, some total there are 6 chains, Meromyosin chain. The 2 heavy chain wound around each other to form the 2 heads at one end. So, there are actually just 2, there are 2 heads which are formed here like this. The head looks like this and they are formed by these 2

Meromyosin; so this head. Now, I add one more information and that was the reason I did not tell you yesterday. So, this head is actually something like this is kind of a fork as if there is a flower with 2 petals. Of you have to remember, it is something like this. This is how it looks like whereas, the 2 heavy chains wound together to form the 2 heads, one end and the tail at the other. So, this is where the tail is, where they are attached, fine. Each myosin head also contains 2 of the 4 light chains that make up the part of a cross-bridge. So, these are split up into two. So, what essentially these are doing? So, each myosin head is this is 2 and this is 2. Each myosin head also contains 2 of the 4 light chains which makes the part of the cross-bridge.

So, I will come later what is the cross-bridge, what we are talking about the cross-bridge. So, cross-bridge essentially is let me go back here, this zone. The zone what you see here, this is termed as the cross-bridge. This is the zone which is called a cross-bridge and the movement here is like this either Sarcomere will shorten. So, the option is that Sarcomere length, either it will become shorten or it will remain in a normal relax position or it will remain in an extremely relax position. So, if you follow this drawing, so when it gets shorten, there is maximum amount of interaction, but then these redlines move here when it is getting shortened, right because you are shortening it though they there will be more cross-bridge area accept it whereas, if they go further away, then this redline will shift further outward. So, automatically the number of cross-bridges if the interaction is something like this. So, if they are close into each other, this is where there is a shortening. There is a maximum amount of interaction among each other and if they relax like this, there will be a minimum amount of interaction and there will be a zone of optimal interaction, right.

So, not there very close like this which is shortened version, very shorter or they are very relaxed like you know kind of you know chilled out from each other or something like this. So, there are three possibilities. They may have a kind of say for example, I say let us give it a number. If I say there are 50 connections between these 2 palms like this, there are 50 something like this connections like this. So, now let us put it like this. There are 5 connections like this. Now, if we move away, there may be only 2 connections left or if were somewhere between, there will be 3 connections. So, 3 is somewhere in between 5 and 2, right. So, something like that. So, there is a change in

length of the Sarcomere. They come too close. Maximum interaction between the cross-bridges and cross-bridge is essentially is this area. So, now let us correct this drawing little bit further, improvise this drawing like this. So, these heads are fork kind of thing. So, number of cross-bridges decides the interaction between the 2 and now, if you look at the actin filament, now coming back.

So, we talked about the myosin filament, details of the myosin filament and if you look at the actin filament, actin filament is even much more interesting. The actin filament contains three proteins. Let us put another colour to this. So, we talked about the myosin. Let me talk about the actin filaments. They form actin contains three protein; one is actin itself, then you have tropomyosin and troponin; tropomyosin and troponin. It is made up of 2 helical strand that has loosely connected, made up of 2 helical strands which are loosely connected, 2 helical strand which are loosely connected, 1 strand composed of actin filament. On the other hand, the other strand co consist of the tropomyosin. So, second strand is tropomyosin molecule. The tropomyosin strand covers the act. So, actin filament if you look at it, actin has multiple sites actin if you look at the actin filament. So, this is something like this. So, you have actin tropomyosin. Then, you have something called active sites on it. Let us put a different colour out here active site and then, you have calcium binding site which is this is something and something new I am introducing now called calcium binding site.

So, I think at this stage you people need to know only 4 things. So, it has actin filament. Let us put a different colour to this which is in green the actin filament and then, you have a trpo, tropomyosin filament which is in blue, the tropomyosin this one and then, you have a active site which is present out here. An active site is the site where this interacting with the myosin filament and then, you have a calcium binding site, right. So, tropomyosin strand covers the active site under a normal condition. So, active site has certain binding pockets. Those are covered by the tropomyosin molecule is something like it. It is like this. So, tropomyosin hides the active site. Now, a troponin molecule is attached to the tropo tropomyosin molecule and tropomin is made up of now this is there is another molecule which is present there which I have noy mentioned yet which is the troponin. So, this particular molecule is attached to the tropomyosin. So, let us put another colour to this. Let us pick up this or may be this colour something like this.

So, there is a tropo troponin molecules and troponin molecule attached to the tropomyosin molecule, this troponin and it has three binding sites. It has troponin a which has affinity for actin, it binds to the actin and then, you have troponin c which affinity for calcium ion binds to the calcium ion and troponin t which binds to the tropomyosin . So, now tropomyosin adheres to the troponin molecule.

So, now again let us re-summarize it. Actin filament made up of actin one tropomyosin 2 and another molecule called troponin which is a third one. Now, troponin interacts with the tropomyosin. Troponin has a binding site with actin which is called a side troponin. Then, troponin has a affinity for calcium ions which is called troponin C and troponin has a binding with tropomyosin which is called T, fine and you have an active site out here which is hidden by the tropomyosin molecule.

At rest if you see there are no chemical reaction between actin and myosin filament and the molecules are strict without much resistance, but in the presence of calcium ions. So, I showed you a calcium site, right but now suppose in this matrix, now let us get now if you are introducing calcium, we will talk later from where calcium is coming. This is another very fundamental problem. We will come to that now when you are introducing calcium ions, so say for example, this melue is now filled with calcium under that situation what will happen is actin and myosin bond bind strongly to one another. It is believed that binding of calcium ion to troponin physically most the troponin tropomyosin complex, so that the active site on the actin filaments are exposed. What does that mean? Let me put it together once.

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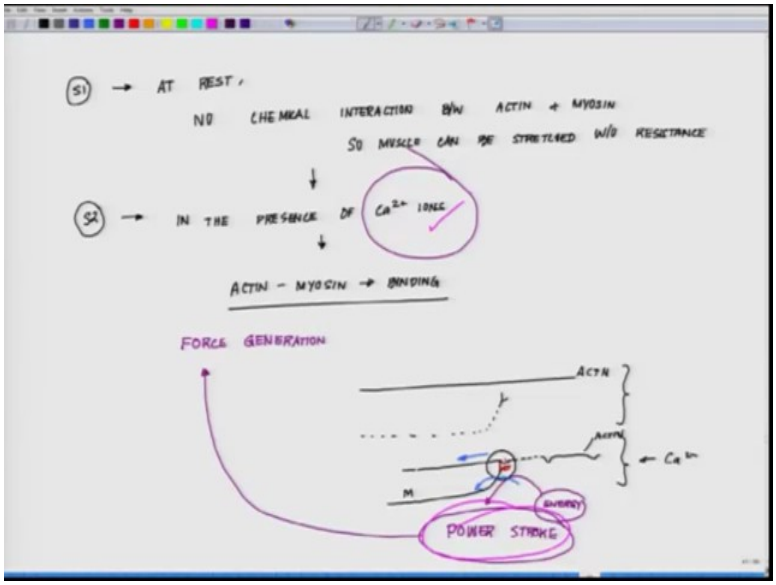

So, say for example, at rest let us break down talked about at rest no chemical interaction between actin and myosin filament.

So, the muscle can be stretched without any resistance. So, muscle can be stretched. So, we are making statements. Now, S1 statement 1 can be stretched without WO, without resistance statement. Now, we are moving onto statement, 2 statements. 2 is in the presence of calcium ion. Now, calcium is introducing to the system. The actin and myosin binds strongly to one another. Actin and myosin binding happens. We will come later about all these bindings and the generation of the power stroke and all that stuff. Actin and myosin strongly bind to one another and it is believed that the binding of calcium ion to troponin. So, coming back here to the binding of calcium ion, I told you that troponin has a binding site for calcium. As soon as the calcium binds to the troponin, it exposes this active site and export by exposing the active site. Just try to understand it first of all.

So, this is the myosin head, right. So, if this; the myosin, this is the myosin head which is present there something like this on top of it, you have the actin filaments. So, my right hand, this hand with this kind of this is the myosin. This is the actin and here you have the myosin head under neck, this is. So, this is the myosin head. Follow me this is the

actin fair enough.

Now, under normal condition there is no interaction. So, they are not touching each other and I told you on this actin, you have tropomyosin filaments, troponin filament and an active site which is hidden by the tropomyosin and you have this troponin molecule which can bind to calcium. Now, this is the normal interaction at this stage. You can stretch the muscle as much as you can because there is nothing to hold on to this, fair enough. Now, as soon as calcium comes into play, suppose it is raining. Imagine the rains are the calcium. As soon as it rains, what will happen? The troponin will bind to the calcium and will remove or expose the active site on these actin molecules and as soon as that active site is exposed, the myosin head binds to that exposed site. Now, see this is the stage, stage 1, stage 2 like this is the bind and after binding, there is a reaction which takes place, whereby there is a energy release which leads to the bending of this head like this and during that head, it moves this actin filament like this, something like this. Does it make sense?

Let me draw it for you because this is the fundamental concept you have to understand. So, you have this. This is your actin filament without any interaction and this is your myosin head. There is no interaction, right. Now, stage 2 when there is an calcium ion coming, as soon as the calcium ion comes on these actin filament, there are sites which are supposed to bind to, this is actin which are supposed to bind to the myosin filament. So, now this myosin head, this is myosin binds to this active site. So, this is the zone of active site. If you remember in this picture here, I told you the cross-bridge. So, this is that zone where the cross-bridge I am talking about. So, here the cross-bridge, the binding takes place. So, some form of let us put another colour here. So, there is some form of binding happens here and during this phase, this head makes a moment like this, the head. Look at my hand. So, head moves like this, myosin head moves like this was the myosin heads moves like this. So, what it does? If this is the actin on top of my hand; when it does, so it moves the acting along with it because it is attached.

Now, imagine that there is glue here. I have some glue, some sticky glue and it just gets attached here. What it will do if I pull my; this hand along with it? It is going to pull this one. So, what will happen is that while I am pulling this one, pulling this myosin

filament because its head is moving like this, it will pull the actin filament along with it. Once again actin filament along with it and this is a energy intensive process. This needs energy and this process is called the term is power stroke and this is that first step of force generation, but then when I introduce force generation, I have left with you with lot of confusions from where this molecule came, right from where calcium came. I have not told you from where calcium is coming, but this leads to something called a sliding of actin and myosin on top of each other and this is what I explained or what I started in the last class called Sliding Filament Theory of Muscle.

What we will do from here, it is just the beginning of understanding these forces. When they have a direct link to the nervous system, there will be a spill over. Now, next week from this power stroke we will figure out the force generation curve of the muscle. Though I am supposed to finish in this week, but do not worry. Let us understand the basic concept once and for all. Once you understand this, I know rest of your life you will never have any confusion. You will build up the story.

So, next week what we will do? We will talk about how this individual power stroke. Now, think of it for a minute while I draw this. So, at individual level there are power stocks which are getting generated. Think of it how beautiful it is. So, there is a huge power stroke happening here and that get translated into here is a huge amount of force here, and eventually this whole thing moves with a force and it all start with a molecular machines. These are the real molecular machines, but there is a small some nanonewton something, force is generated there, but that eventually leads to what you see. Today exercise everything what all we do, but it starts at the atomic resolution level.

So, I will close in here today and the next week, we will again take up from where we ended here, the power stroke. From power stroke, we will resume the story of muscle which will take us to the domain of neuroscience which will help us to explain from where these calcium ions are coming. So, apart from it, there is another very interesting thing what we will be dealing with which I have not dealt, which will start in the next class about Excitation Contraction Coupling Apparatus.

Thank you.