Physics of Biological Systems
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Lecture – 48
Introduction to molecular motors

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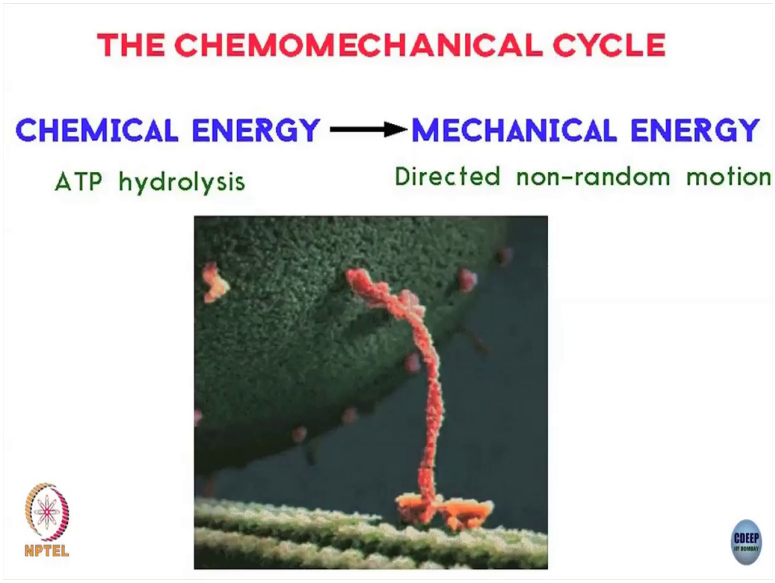

So, what I will do today is that I will give an Introduction to this molecular motors. I will not do a lot of math's today I will keep that for next class. But, I thought I will just introduce what motors are and in what context we want to study them ok.

So, here is one of the most famous examples of a molecular motor. This is the kinesin motor which is walking on a microtubule. So, this orange thing over here is kinesin, this green track over here is the microtubule and this darker green sphere of which you can only see a part is the cargo that this motor is carrying. So, it is very nice in that. So, this is the protein basically.

It walks along this microtubule track by using ATP to bind and unbind this microtubule binding domain. So, which are let us say it is legs ok.

So, it places its legs one after another and it walks. And, on its head it is attached again chemically to this cargo. In this case a vesicle it can attach to different types of cargo and it transports this cargo inside this vesicle it might have different proteins or whatever that needs to be transported from one end of the cell to another. So, it just carries this cargo along these tracks and it does so processively and repetitively many many times over the life cycle of the cell.

So, it takes in what it does is that it takes in chemical energy in the form of ATP hydrolysis. So, these are active processes they require an input of energy ATP binds with hydrolyses from ATP plus phosphate plus energy, that energy is utilized into converted into this mechanical energy which results in this directed non-random motion.

So, this is not like a random walk where this motor you know sort of does takes one step this way or the other, another step the other way. These motors move along because these microtubules you remember have a polarity, it has a minus end and a plus end. So, there is a directionality to the real way track of this microtubules and then they move directedly on this underlying real way track. So, this is one motor.

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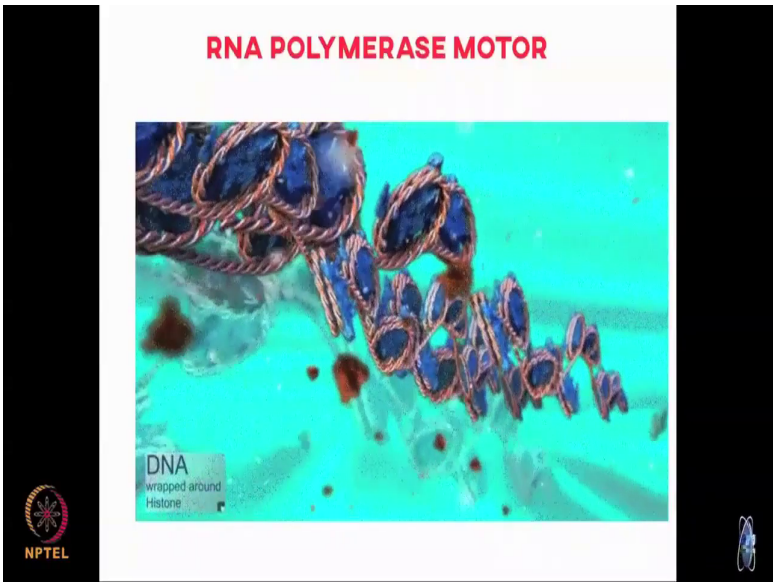

There can be other types of motors for example, this RNA polymerase motor. So, again this is nice video. So, here is my DNA the DNA is wrapped around this histone proteins forming the nucleosome right. If you do not remember this you should go back and recall it. It is also part of the quiz question.

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So, when this DNA needs to be transcribed you need to form the mRNA, then this RNA polymerase then comes and binds to this DNA. It first opens up from the histones, so that it can be read then this RNA polymerase comes and binds to this. And, then it moves along this DNA track while forming this mRNA by reading the sequence. And, again this movement of this RNA polymerase is an energy driven process. It takes in chemical energy in the form of ATP, it converts it to directive motion as it moves along the DNA backbone and it produces this RNA transcript.

So, again this is an example of a motor. So, anything that takes in this chemical energy and converts into some sort of mechanical work this what I will call biological motor. And, they can be of different types as we you will see as we go along, but for this RNA polymerase

which we have seen in the context of this DNA transcription that also fits our definition of the motor.

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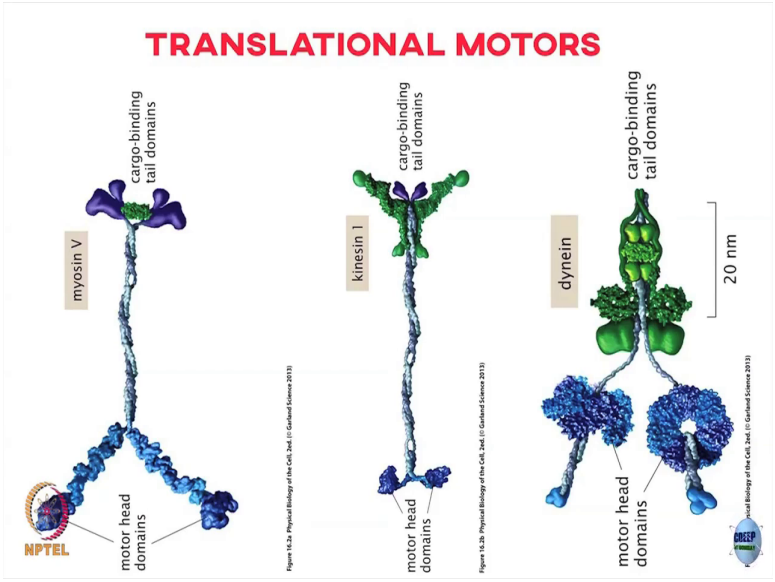

So, for the first part what I will try to focus on are these translational motors, families of translational motors. There can be other types. So, will talk I do not think I will talk about them today.

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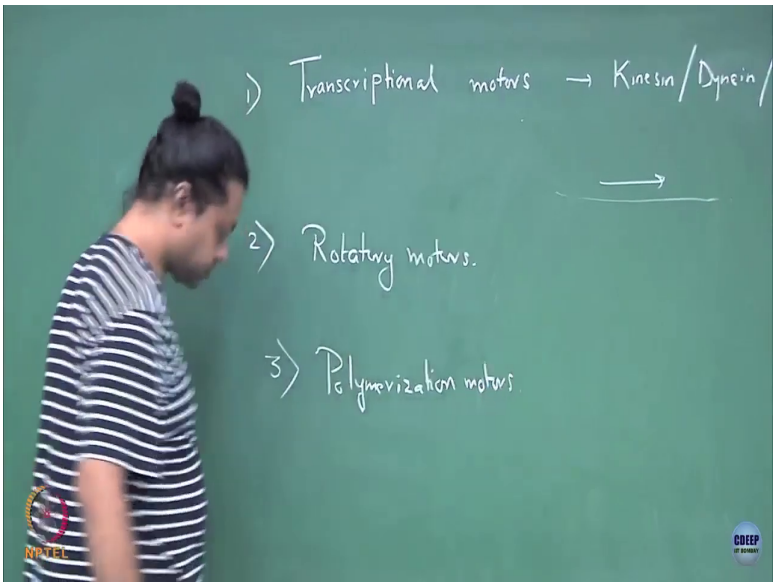

Let me just say that roughly or broadly you can say that I categorize my motors into may be three classes. Transcriptional motors like this kinesin or this RNA polymerase motor that we saw or these other motors we shall discuss, kinesin, dyneins, myosins whatever. So, these are motors that takes in chemical energy and it sort of uses that chemical energy to produce directed motion along different substrates in different contexts, but produce directed motion linear sort of motion along a track is something like this. So, that is one sort of motor.

Another sort motor could be rotate rotatory motors; rotatory motors and where have we seen a rotatory motor?

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The helical flagella. For example, in the E. coli where the motor that rotates the helical flagella, that is an example of a rotatory motor. Again, it takes in chemical energy, but it converts that not into linear motion, but into rotational motion. So, that is a different class of motors. Or you could think of stuff like polymerization motors, for example, microtubules and actins themselves. They can take in energy, they polymerize and in the process of that polymerization they can do some work by exerting forces on different substrates. So, that is a different class of motor that is called polymerization motors.

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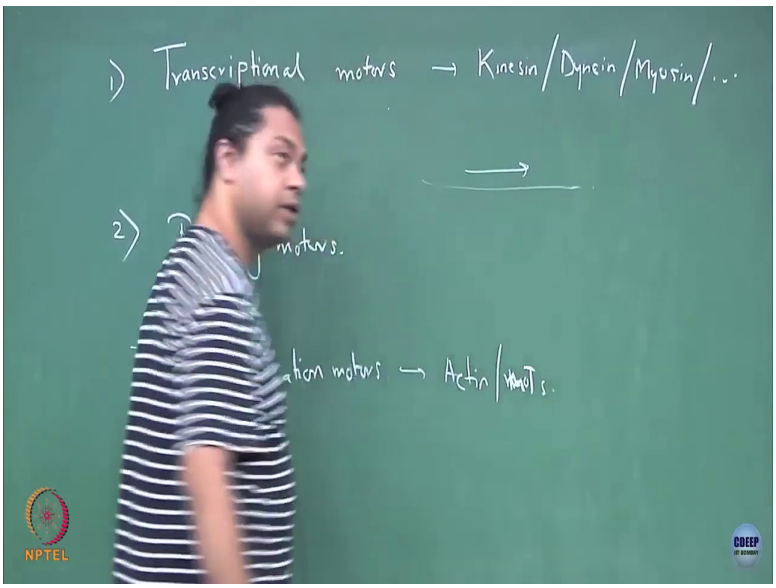

So, this would be actins microtubules and so on microtubules so on ok. So, all of these are motors because broadly they fall under the class of active processes. So, these are systems protein complexes that take in chemical energy in the form of ATP or GTP or something, and converts into some sort of motion.

So, for today what I will deal with is mostly these translational motors and in particular motors that walk on microtubules and on actin. So, here are three representative motors. So, this motor over here is what is called the is example of a myosin category of motors. So, myosin's are motors that walk along actin filaments.

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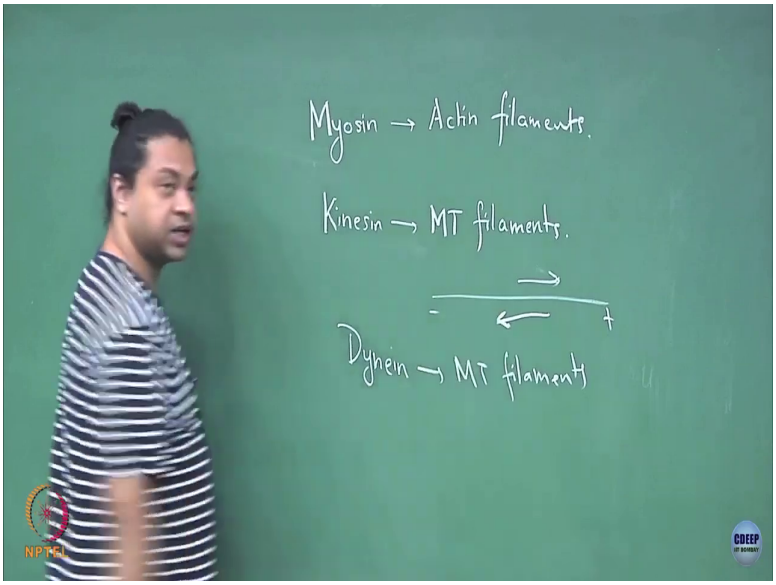

So, myosin's will walk only along actins. Myosin's these walk along actin filaments. If you see the structure there is the stock of the motor, then over here are these two head domains and over here there is something called the tail domain ok. The tail domain is the one that binds the cargo and the so, the vesicle like the vesicle in the previous animation the head domain is what binds the stock or the track along which the motor walks.

Here in the middle is something it is a example for kinesin motor and kinesins is opposed to as opposed to myosin's. They walk along microtubules; they walk along microtubule filaments

and not only that they walk in a specific direction along microtubule filaments. The microtubule you remember has a minus and a plus depending on whether alpha tubulin is exposed or beta tubulin is exposed. It is a chemical polarity and then kinesins walk towards the plus end of microtubule always. Whenever you have a kinesin motor they will walk towards the plus end of the microtubule from the minus end towards the plus end ok.

And, again it is roughly similar it has these head domains where the head domains are much smaller the tail domains are different. So, structurally this is different from the myosin family, but functionally it is somewhat the structure is somewhat conserved in that you have this head domains which bind to the track microtubule in this case the tail domains which bind to the cargo.

And, finally, there is this other class which is dynein's which is dynein's these also walk along microtubule filaments this also walk along microtubule filaments except they walk in the reverse direction. So, they walk from the plus end of microtubules towards the minus end as opposed to kinesins. The dynein structure is somewhat more complicated than the kinesins or the myosin's and as a result it is functionality also has some complications we will come to that later.

But, at the simplest level it is again the same you have this head domains which will bind to the track the microtubule in this case and the tail domains which will bind to the cargo ok. I call it examples of myosin, kinesin and dynein because these are basically not a single motor, but these are a family of motors ok.

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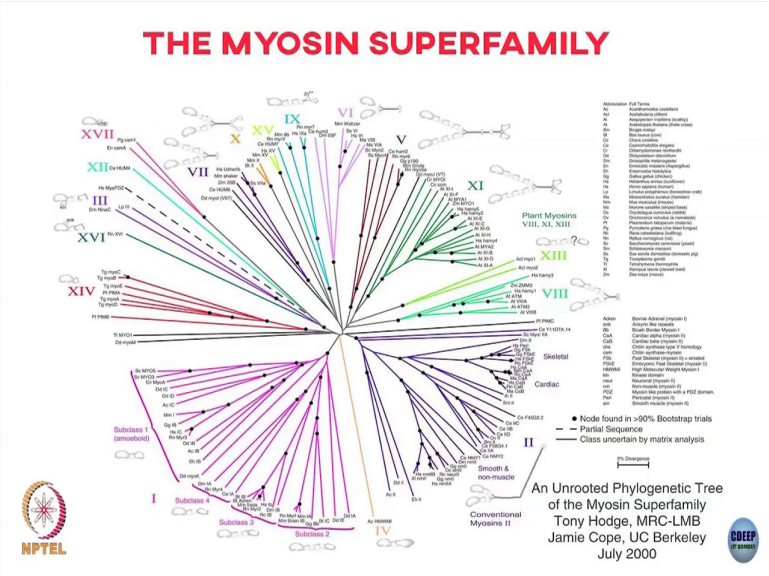

So, for example, if I think of myosin here is the myosin fam super family of motors. So, these are all different proteins all different myosin like proteins occurring in different organisms or in even in the same organism in different cell types ok. So, there are myosin 1 and myosin 2 and so on and even within one there are subclasses of myosin motors. They might differ by amino acid residues, but they will all roughly do the same thing in that they will bind to an actin filament and they will walk along the actin filament.

The actin the myosin I have not written whether it is a plus walking motor or a minus walking motor because in myosin's there are categories which walk towards the plus end of actin and categories which walk towards the minus end, but they are not different proteins as such unlike in the case of kinesins and dynein's. See, when kinesin you would have a super family

like this there are different types of kinesins what is shown here is a particular kinesin, kinesin 1 there can be other types of kinesins.

But again and they will differ in the sort of cargos, they can bind they will differ in the organisms in which they are found, but they will all bind to microtubules and they will all walk from the minus end to the plus end. Similarly, there will be different types of dynein's, but again they will all bind on microtubules and walk from the plus end to the minus end.

So, these are if you think about the diversity these are quite complicated objects ah, but as long as we were talking in terms of a modeling context, I will often use kinesin as something that just you know I will not care about what particular cargo it binds and so on. And, I will just consider it to be a motor that binds to microtubules and walks along the plus end. How do I say that these motors are different? One is of course, by looking at the structure in the amino acid residue and so on. So, the chemical level you can see that these this protein is different from this protein is different from that protein ok.

But, physically one can also show that these motors behave differently by using different experiments. For example, one common experiment that is used to characterize the properties of a motor I what I call this force velocity curves.

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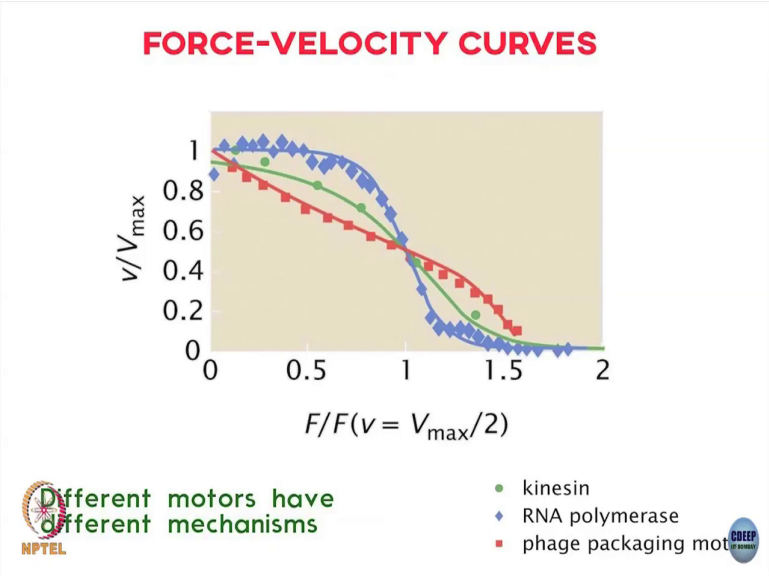

So, you apply a sort of force. So, let us say this here is my kinesin.

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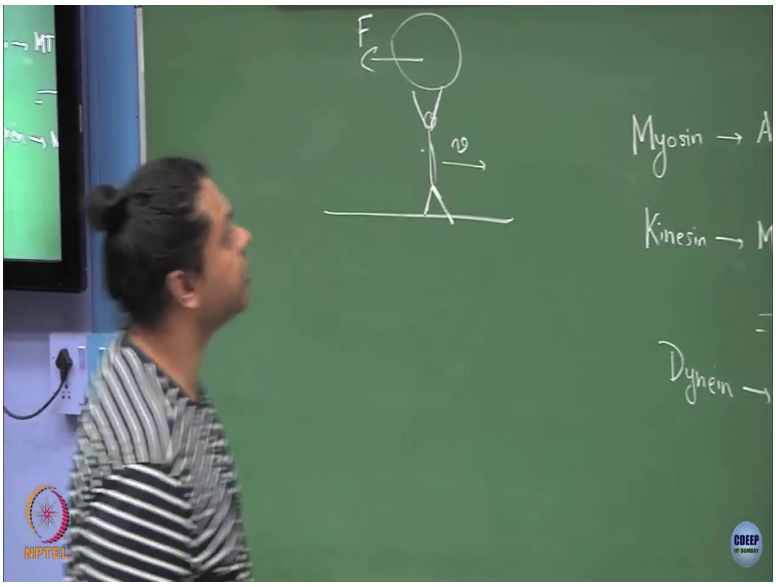

Let us say here is microtubule on which I have this kinesin is a very bad kinesin, but this kinesin motor binding ok, here is my cargo. And, what I can do is that I can it walks with some velocity some average velocity it will walk along the microtubule. What I could do is that I could pull back on this cargo with some force, let us say the cargo is let me just draw it on the cargo. So, let us say pull back of the cargo with some force. Generally, these experiments are done using optical traps to trap the cargo bead and you pull on it with some opposing force and you see how this velocity changes as a function of force; how does this velocity change is the function of the force that you apply.

And, if you look at it for different motors this curve will look different. So, these are all not the force axis is are all normalized by the force at the half maximal velocity because the forces that are produced by these different motors are very different. But, I just normalized it, so that

when F is equal to 0, whatever it is that y-axis is normalized with the maximum velocity so that all points in the y axis for these different motors all fall on one.

So, this is data for three different motors – one is this kinesin motor that we have been talking about, the second is the blue curve is this RNA polymerase motor that is showed and the third one is this phage packing motor ok. The phage packaging motor is in viruses like bacteriophage you need to package your DNA inside this viral capsid and that again happens through a motor. So, that is this phage packing motor. So, that is the one shown in the red curve.

And, of course, when force is very high all of these velocities will drop to 0. So, if you apply a counter you apply an opposing force eventually provided you apply a large enough force all of these motors will stop ok. And, so, the velocity in each will drop to 0, but how it drops to 0 is very different for different classes of motors. So, kinesin so, for example, RNA polymerase has this very strong sigmoidal curve. So, for small forces it does not really affect the velocity that much then beyond the certain this critical force it sort of very quickly and very sharply drops to 0.

Kinesin is somewhat of a more of a less steeper sigmoid, whereas this phage packaging motor it sort of drops linearly with force almost for a very long range. The more force we apply the more develop the more slower the velocity and then it is fully drops to 0. And, you would do it for different motors you will see different sorts of curves that emerge and you can use this sort of force velocity curves to characterize.

So, the internal working of all of these motors are different and what this force velocity curve shows you is sort of a macroscopic manifestation of the differences in this internal architecture or the internal machinery of these motors. So, it is a reflection of the fact that these different motors have different mechanisms ok.

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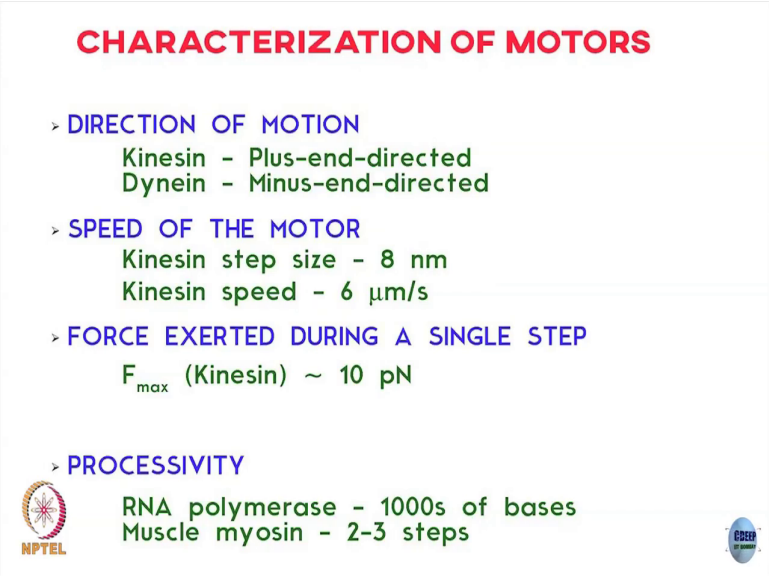

So, how do I how can I characterize motors for example, what is the different quantities that I can use? So, one is this thing that we have been talking about direction of motion right. So, for example, kinesin is plus end directed on microtubules whereas, dynein's are minus end directed ok. I can talk about the speed of the motor. So, for the speed of course, depends on the depends on the forces we saw.

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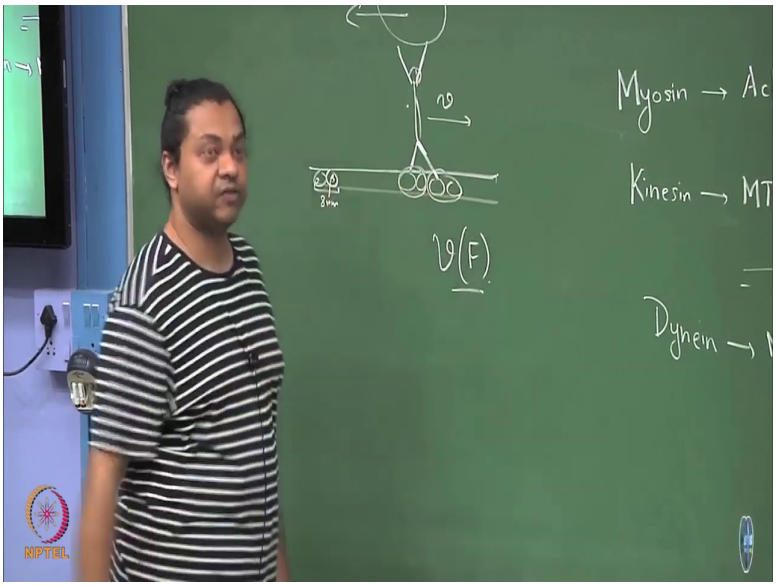

So, this V is the function of F, but I could talk about the zero-force velocity right say in the absence of any opposing load, how does this what is this velocity with which the motor works?

So, for kinesin for example, the step size is 8 nanometers and this 8 nanometer step size is nothing, but the size of the underlying lattice basically. You remember this microtubule consist of this alpha beta dimmers right and the size of this alpha beta dimers is 8 nanometers. What it means is that these kinesins bind hopped from one of these alpha beta tubule in sub units to the next one and therefore, the step size of this kinesin motors is 8 nanometers. The speed is some of the order of microns per second so, some 6 microns per second for the case of kinesins.

Again, these are all sort of typical numbers in the sense that if you did different if you look at different kinesin motors for example, you would maybe find some differences, but roughly of that order.