Physics of Biological Systems
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Lecture - 56
Translocation ratchet

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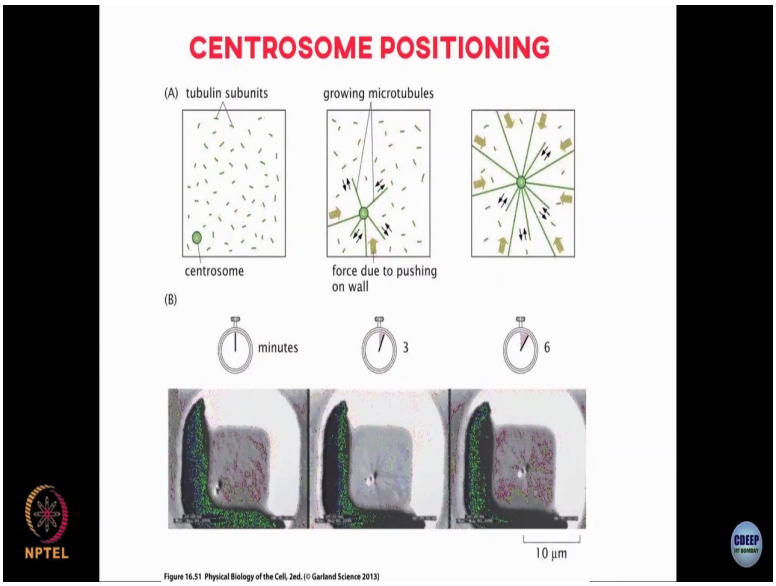

One more a different a different sort of motor that you could think of, so these were polymerization sort of motors.

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A different sort of motor that you could think of are these Translocation Motors, for example we talked briefly about this.

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For example if you are packaging DNA inside a viral capsid.

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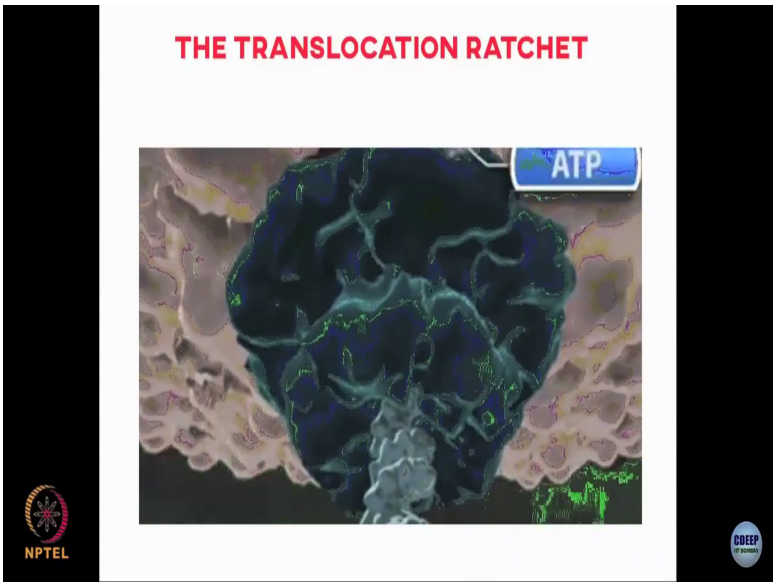

Screen is very bad, but for example let us say if your packaging DNA inside the viral capsid. This is again an ATP dependent process, where ATP has to come and bind and then you push this DNA inside this bacterial phase. Or similarly in reverse when a, you know when a virus is trying to infect something. Let us say a bacteria it has to push out the DNA into the bacterial cell.

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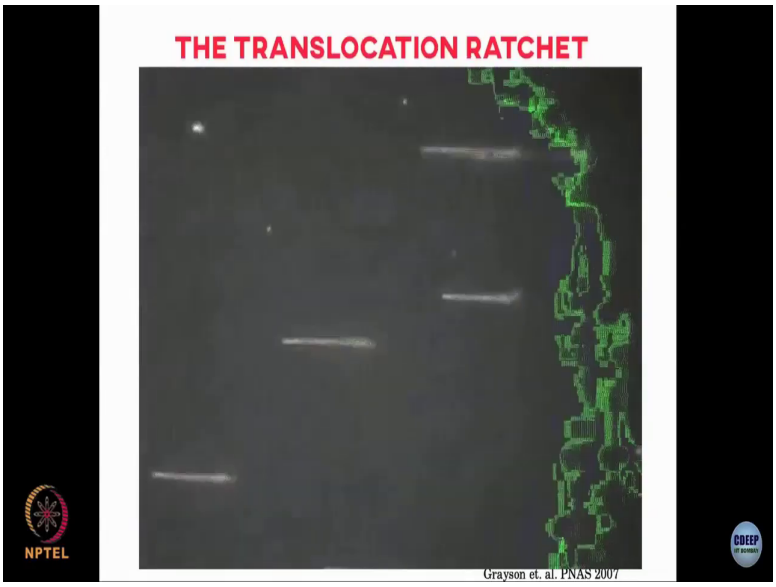

So for example, this is actually an experiment on this pushing out DNA from viruses viral capsids. So, these points are different viruses and you will see that these viral capsids are being ejected, this is there this will stuck for some time it will get ejected ultimately. And once it gets ejected so there is a flow also, this is a solution this is a solution where you take various many viruses.

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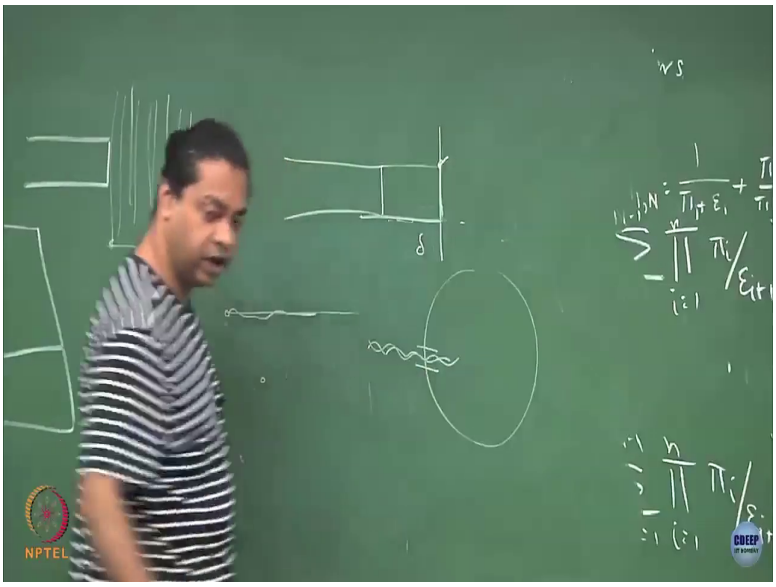

And the virus sort of ejects it is DNA and once ejected the DNA will zip out. So, you can actually so this is experiment, but you can actually measure speeds in these sort of experiments. So, these are what we call the Translocation Ratchets.

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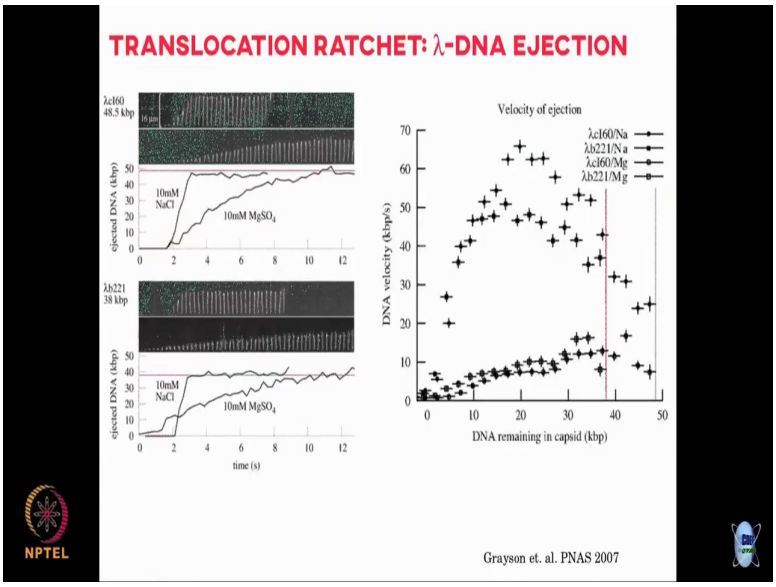

So, if you measure speeds under different conditions. So, these are for example, experiments on two different viruses lambda c 160 and lambda b 221, this was DNA of different lengths this was 48.5 kilo bases this is 38 kilo bases and what you are seeing is the ejected DNA as a function of time.

So, these are time traces of the fluorescent DNA as a function of time under two different salt conditions. So, one is a monovalent salt NaCl another is a divalent salt magnesium sulfate, again because this DNA are charged depending on the amount of salt, that you put you can control the sort of speed with these with which this DNA is ejected. So, with NaCl it is sort with monovalent salt it sort of gets ejected very fast very quickly all the DNA is ejected it reaches 48.5.

Whereas, with divalent salt it is sort of very slow, the x axis is time seconds. So, you can measure the sort of velocities. So, this is what is plotted over here the DNA instantaneous DNA velocity as a function of the amount of DNA that is remains back in the capsid and you can see that the salt has a major effect on the DNA velocity, the salt concentration, the length of DNA not so much. So, these two plots are for these 2 DNAs the 2 viruses.

So, the length does not play some rule but it is minor, on the other hand the salt plays a major role (Refer Time: 03:08) ok. So, if you were to sort of model something like this that I have let us say a cell which is being infected by this virus. So, it needs to push it sort of DNA inside over here. Can I come up with estimates of the speed in this case in this sort of scenario and again if I do a zeroth order modeling.

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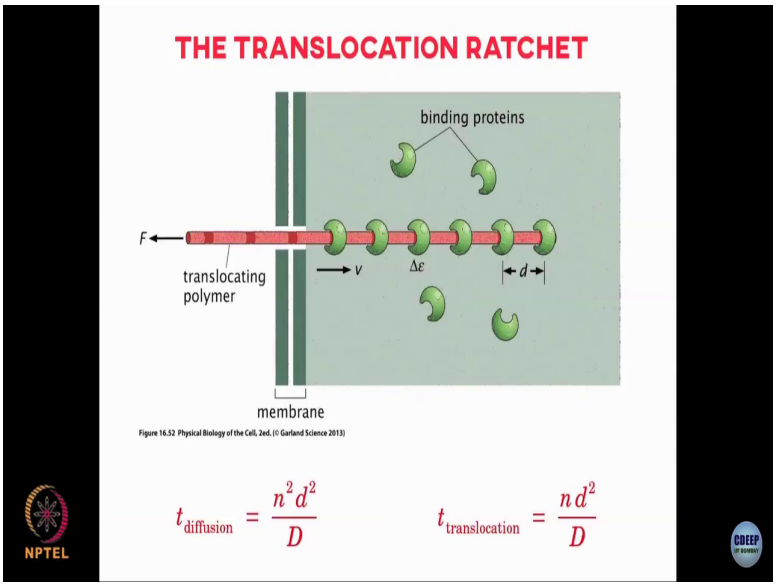

So, often what happens is that if I have this sort of a translocating polymer. So, this is how it is going in, let us say and the this DNA often will have spaces where proteins can bind. For example, ribosomes can come and bind to start the transcription process. So, the idea is this that I have the idea is this that I want to sort of get this thing in into the cell let us say, I could just try to diffuse it in and it would take some time.

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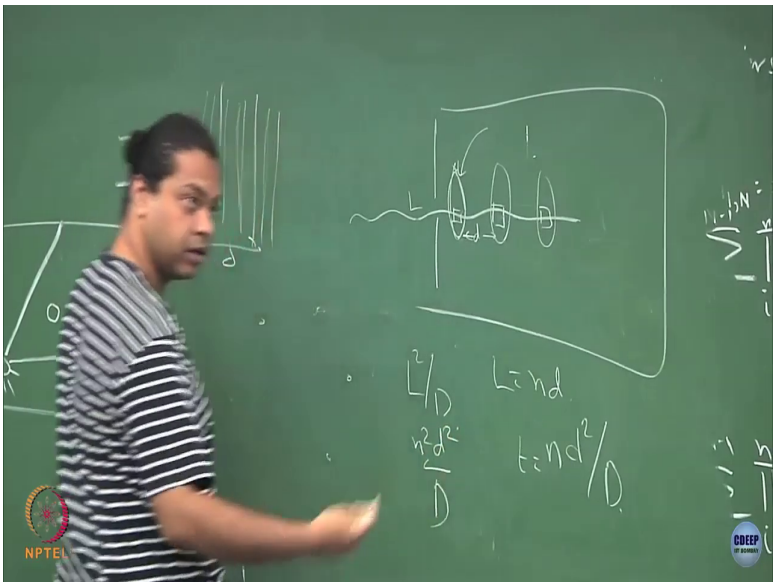

See if this polymer is of length L it would take some time L squared by D to diffuse this whole thing in. On the other hand if it has sites for binding proteins every some distance every D distance, then once the protein comes and binds this thing cannot slide back out anymore ok. Let us say a large protein comes and binds like a ribosome, then that can the DNA cannot slide back anymore ok. So, that will then speed so once we have these proteins binding over here that will then speed up this translocation process and you can estimate by how much. So, for

example the diffusion, see if this length of the polymer I call it as n times d, n being the number of binding sites and d being the space between these binding sites.

So L if I this write as n times d, then the diffusive timescale for this wholes polymer is n square d square by capital D of the order of. On the other hand if these things bind every d base pairs or every d sites whatever, then the time taken to defuse 1 unit of v base pairs is basically d square by D and once it goes in the assumption is that a protein comes and binds and it cannot come out anymore. Which means and there are n such sort of segments which means the time in this case is n d square by D and in this case it was n square d square by D ok.

So, you get a speed up of around a factor of n, n being the number of binding side. So, diffusive timescale grows as n square this translocation timescale with the help of these ratchets these binding proteins grows as n.

So, you can get significant speed up simply by this sort of simple mechanism yes, because the virus for example for the case of a virus, the virus wants to infect a bacteria right. So, the way it infects is that it injects it is genetic material into the bacteria and it injects it through these very small pores on the membrane like ion like ion channels. So, they are not ion channel, but there are pores on the cell membrane.

So, it has to inject it is DNA through these pores ok. So, with what we just inject by diffusion that would take a long time, on the other hand through some mechanism like this it could inject it at much smaller timescales.

Student: Ok sir.

If some salt the buffered salt that is being flowed from left to right. So, which is why once the virus gets ejected it just slips through, because there is a background flow of this salt in the solution ok.

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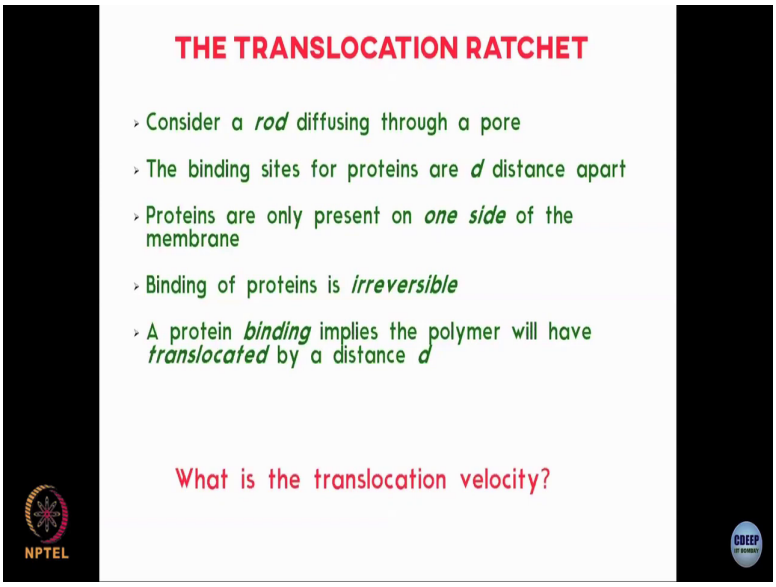

So, we can do this a little more formally again this sort of a calculation. So, formalize the model again what we say is that I consider a rod that is diffusing through a pore. So, I neglect the polymer degrees of freedom, I just say it is a straight rod that is defusing through the pore. I say that the binding sites are d distance apart, proteins are present only on the inside not on the outside. The binding is irreversible so again infinite k on 0 k off in that sense and this binding implies that the protein has this polymer rather has translocated by this distance d. An irreversible translocation because this does not come off, so it cannot come back out over there and then I could ask therefore, what is the translocation velocity ok, what is the velocity with which this polymer gets pushed in.

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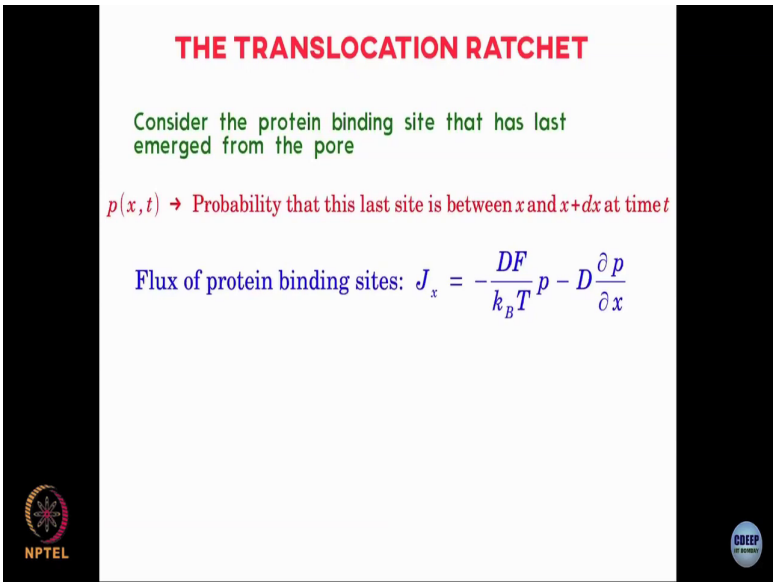

So, again I can frame it in terms of the kinetics of a binding site that has last emerged from the pore ok. So, binding site that has lost emerged from the pore, so I called p x t the probability that this last site is between x and d x at time t and again I can write down the drift diffusion sort of equation. So, the flux of protein binding sites is like this, there is a diffusive term and there is an advection term if there is some sort of a force.

So for example, the force again could be some electrostatic force, it could be some other force that these proteins exert. But let us say there is some force that is exerted on this polymer, in that case I can write down a current like this. So, again I am going to solve the diffusion equation basically I want to solve del p del T is equal to minus del J del x with J being given by minus D F times k B T times the probability minus D del p del x.

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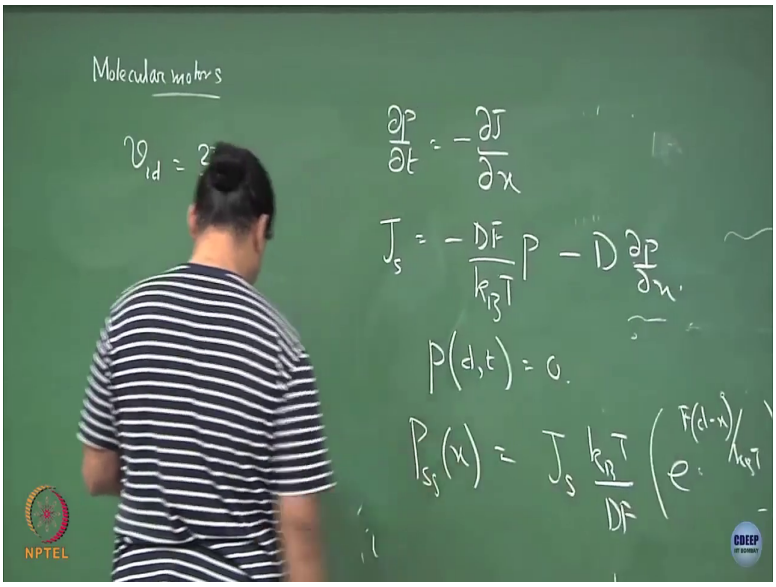

This again like F by gamma, gamma is k B T by D and I put the boundary condition again that that P d comma t is equal to 0. So, again the moment it reaches d sites a new protein will bind and it will come back to 0 exactly like in the other case. So, you can solve again you can again solve this in the steady state. So, let us say this is some steady state current you can solve this equation for P the probability in the steady state. So, P s s of x and again I will just write that down. So, this is some steady state current k B T by D F e to the power of F d minus x by k B T minus 1.

You can normalize this to find what is J s, steady state current and from there again you can find out what is the translocation velocity. This is very similar formalism to what we did for this polymerization ratchets.

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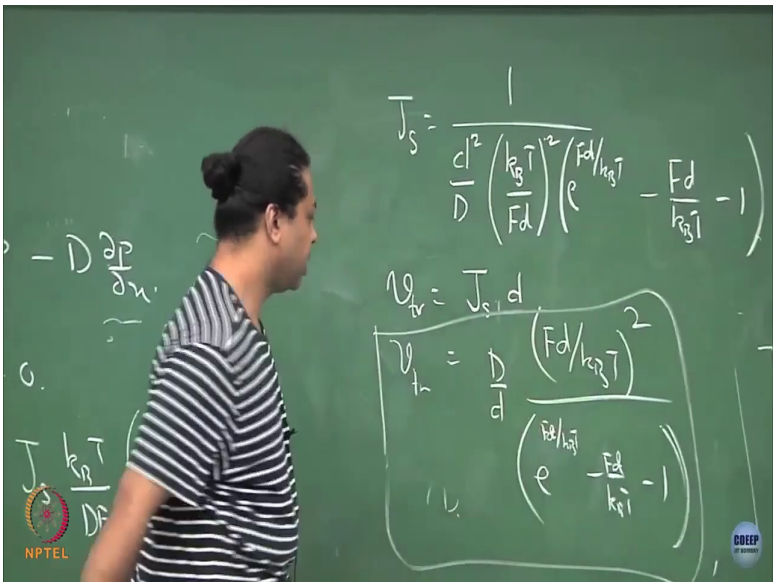

Just some steady state current if you normalize it comes out to be 1 by d square by D k B T by F d whole square e to the power of F d by k B T minus F d by k B T minus 1, which means that your translocation velocity. The translocation velocity is thus the steady state current times the distance that you have covered which is the distance between binding sites.

So, that is nothing but D by d F d by k B T whole square and then this object e to the power of F d by k B T minus F d by k B T minus 1 ok. So, again you can find out the translocation velocity in this sort of a model in the presence of some sort of a force F positive is an assisting force. If you have repelling force, then F would be negative and accordingly the translocation velocity would be.

So, you can have all of these sort of different things molecular motors polymerization motors or even these sort of translocation motors all of which depend on ATP. But they do very

different things and for these different objects you can calculate these different quantities like velocity of translocation or the velocity of polymerization.

For example, using this sort of advection diffusion formalism, that we learnt way back ok. I think I will stop here for today there are many other things that I did not cover. For example, I did not do rotary motors which I said I will, but I do not think I will have time.

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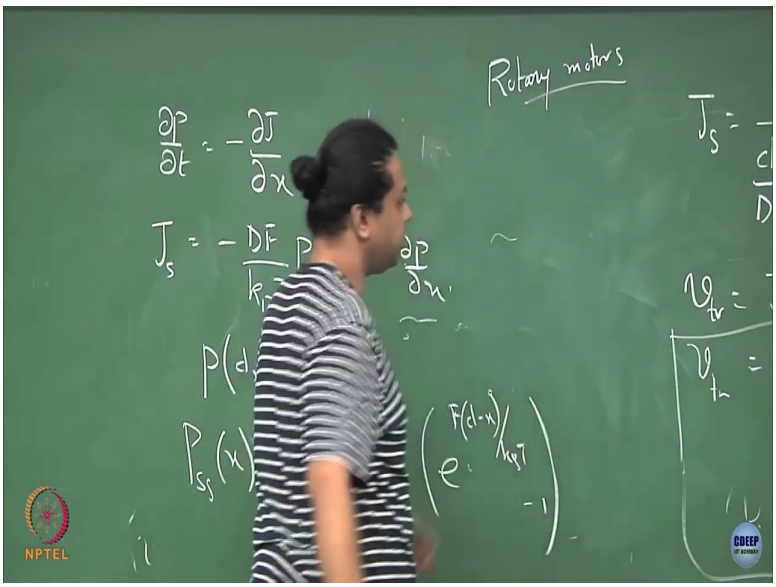

So, if you are interested in these sort of flagellar motors, the rotary sort of motors, you can look up Philips as a good discussion on this sort of rotary motors. What I will do for the next two or whatever classes remain is that I want to move on to these reaction diffusion systems and see how patterns form in these reaction diffusion. So, we have done chemical kinetics. So, reactions we have done diffusion, we will put these together to look at reaction diffusion systems and how patterns form via these reaction diffusion systems and how these patterns

affect various biological processes in particular development of organisms early embryonic development of organisms ok. So, that is what I will do for the next couple of classes.