Physics of Biological Systems
Prof. Mithun Mitra
Department of Physics
Indian Institute of Technology, Bombay

Lecture – 52
Free energies of motor for stepping

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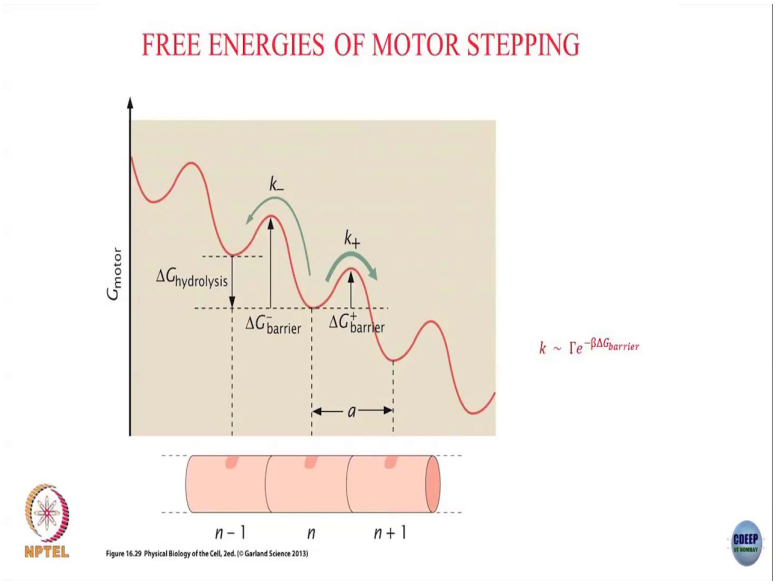

So, here is my sort of a picture that this is my free energy landscape as the motor is moving. At every step with the minimize somewhat lower which is why the motor wants to step forward in this direction right. And there are these barriers course in the difference between these barriers is coupled to this hydro energy of ATP hydrolysis.

The impetus to sort of move forward in its preferred direction come is coupled to this ATP hydrolysis step. So, ATP or GTP whatever, it must bind and then hydrolyze and release the energy in order for the motor to move forward. And in a simple sort of Arminius picture these

rate if I think of this barrier this free energy barrier sort of or free energy landscape sort of a picture.

Then these rates are sort of proportional to e to the power of minus beta of delta G of the barrier the free energy difference of the barrier. This tau is something like the frequency with which you attempt these barrier crossing moves. So, if I now want to couple it to this hydrolysis what I can do is that, again at a very zeroth order very the simplest sort of way I can try to calculate this is to go back to this lattice picture.

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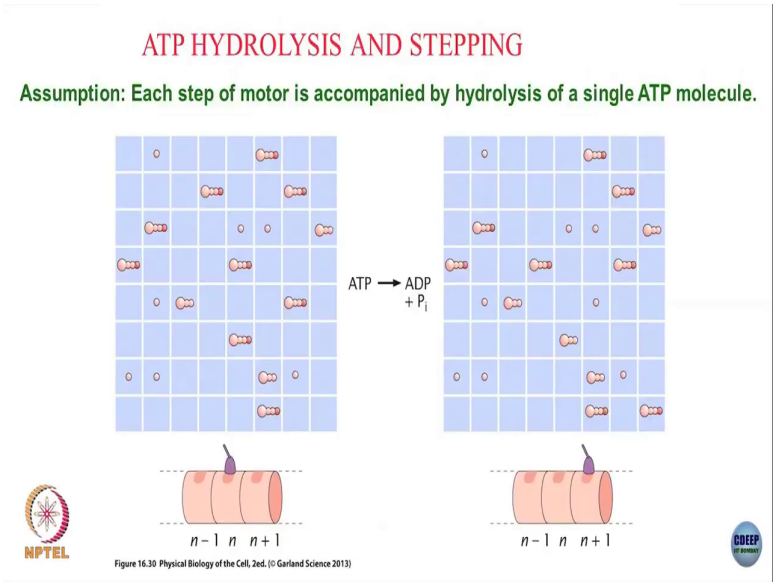

And say that here is my assumption that I say that every step of the motor is accompanied by hydrolysis of a single ATP molecule ok. So, which means that here is my motor sitting on here on this nth lattice site, and then in solution there are these ATPs and ADPs and P i is floating

around right. So, something which is like this is my ATP if it just as 2 or 3 of these blobs is ADP and the single bounce is my phosphate ions.

So, I go back to this lattice gas sort of a model and then I say that when reaction like this happens that an ATP goes to ADP plus P i that is when the motor speaks a step from n to n plus 1. So, in this lattice model then coupled to this motor stepping the number of ATP molecules would have decreased by 1 and the number of ADP and phosphate molecules would have increased by 1 each right.

So, I can calculate the free I can calculate the entropy difference between these two states or the pre energy difference between these two states. And that would give me my free energy of hydrolysis of these ATP molecules right. So, if I wanted to calculate this state for example, if the motor is in this lattice site n and let us say I have some I put some numbers I do not care I have A number of ATP (Refer Time: 02:50).

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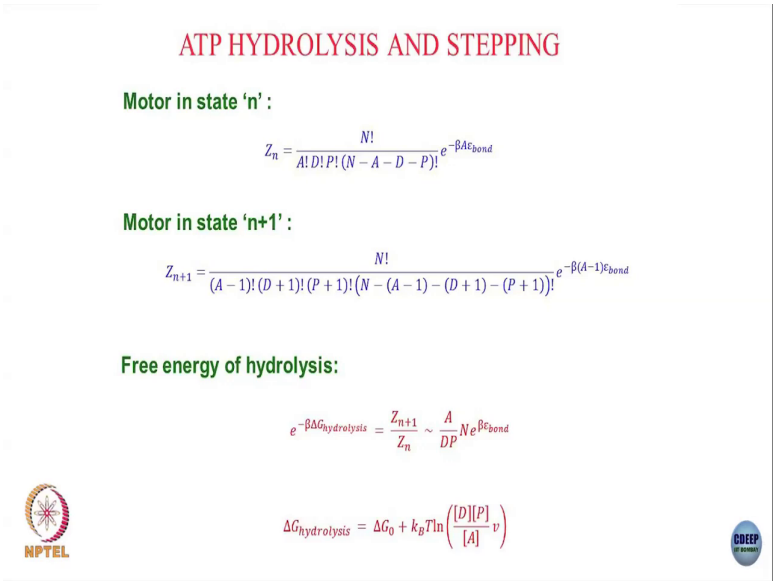

So, my I divide my solution into n boxes out of which I have a filled with ATP; D number of boxes filled with ADP and P boxes filled with phosphate. And the rest are empty then this is the weight of that state and I have these many triphosphate bonds A number of bonds, so beta into A into epsilon of the bond right.

So, this is my partition function corresponding to this n x th state the motor being in the nth state. If the motor now takes a step such that which is coupled to hydrolysis the number of ATP molecules would decrease by 1, the number of ADP and phosphate molecules with increase by 1. And the number of bonds would become A minus 1 right, because one has been dissolved.

So, I can write down the partition function for that state as that the here is A minus 1, D plus 1, P plus 1 and here is A minus 1 just here 1. Then I can calculate given these sort of partition

functions I can calculate the free energy of hydrolysis. Remember G is nothing but minus k B T log z right, G is like minus k B T log Z. And therefore, delta v I can find out given that I know that Z n and Z m plus 1.

So, e to the power of minus beta delta G hydrolysis is Z n plus 1 by z n which is nothing but you pick up an A and pick up ADP over here. You pick up 1 beta times epsilon bond because this difference and you pick up basically you pick up this thing which I have just approximated as N. So, the assumption is that this N is much larger than A or D or P and each of these is much larger than 1.

So, you have macroscopic number of ATP, ADP molecules, but you have an even more larger number of solution boxes ok. In that limit this N minus A minus D minus P I just approximated as just for ease of writing. Anyway do not care much because they are mostly focused on the ATP dependence; how does how does this hydrolysis? And therefore, the barrier crossing rates, how do they depend on the ATP concentration? That is what I want to answer.

So, therefore, if I take this formula then this what this says is that delta G hydrolysis is some delta G naught which contains all of this I subsume all of this. And then a k B T log concentration of ADP, concentration of phosphate divided by concentration of the ATP. And v is just the solution volume specific volume solute. So, what I have is that using this sort of very simple again lattice picture I have calculated how this free energy of hydrolysis depends on the concentration of ATP.

Now, I will try to couple this two ways stepping weights and see what then this predicts for the motor velocities again. Because again that is something I can measure just like I measured velocity as a function of force; I could in principle in experiments measure velocity as a function of ATP concentration. And then I could try to see what sort of a model makes sense ok.

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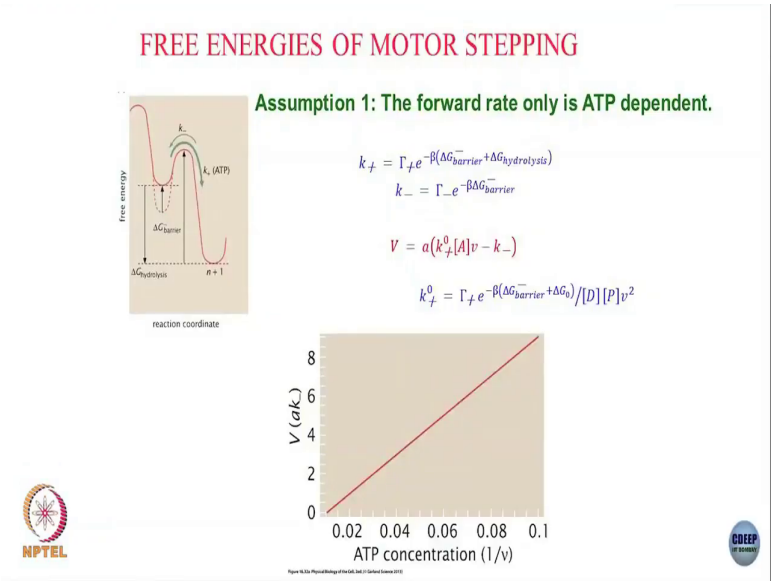

So, again I will make two of these simple approximations. Again without any biological motivation simply because it is easier for me to do the math's, one is that I will say that only the forward rate depends on the ATP concentration the backward rate does not. And of course, correspondingly the second assumption is only the backward rate depends on the ATP concentration the forward rate does not.

So, here is then my picture, so I say that first let us say that the forward rate is ATP dependent which means that here is my forward rate. So, it means that this valley sort of moves up and down as I change the ATP concentration. This one the height of this barrier stays constant which means my k minus stays constant right.

So, because this one stays constant this barrier, so let me call that delta G minus ok. And k minus is e to the power of minus beta delta G minus ok. And k plus is this barrier minus this

hydrolysis difference, so, delta G minus plus delta G hydrolysis. Remember delta G hydrolysis is negative because you get out some energy of hydrolysis of ATP is this is clear. So, I have this sort of a landscape right, so this height over here is my delta G minus right and this height over here is my delta G plus.

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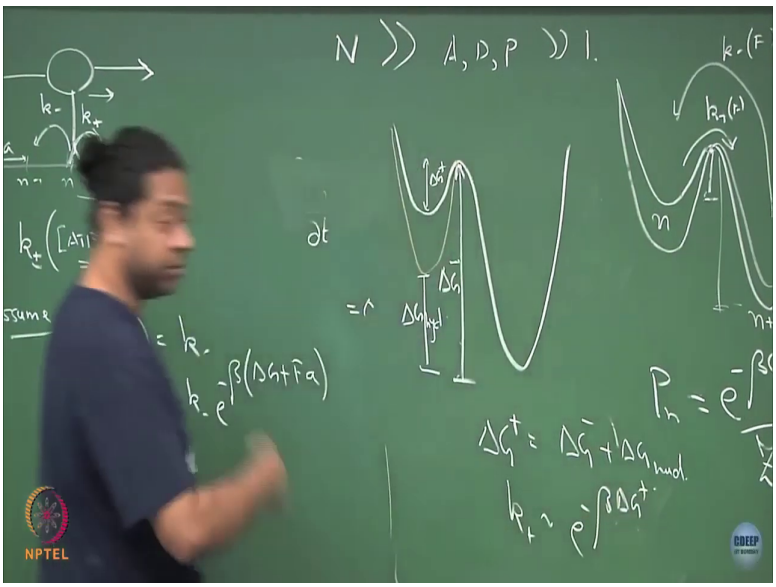

Now, this barrier can change depending on your ATP concentrations which can become something like this maybe at a different ATP concentration without changing this barrier height ok. And this difference is what I call as the difference in the free energy minimus is what I call as my delta G hydrolysis ok. So, my delta G plus is the difference between this delta G minus and the delta G hydrolysis.

So, my delta G plus is basically delta G minus plus delta G hydrolysis and then I called calculate the corresponding k plus. k plus is right e to the power of minus beta delta G plus

and similarly for k minus. So, if I do that right, so if I do that this is what I get and this delta G hydrolysis, remember I have now written in terms of my ATP concentrations using this simple lattice cursor come on.

So, I can substitute that in I can substitute that and calculate what is my velocity? Again by substituting it in this formula this k plus and k minus; I put everything else that comes in this k plus 0 term ok. So, this k plus 0 contains this delta G minus barrier this delta G naught this ADP concentration, phosphate concentration. Whatever else comes I just clubbed it together into this k plus 0, I just single out the ATP concentration dependence.

So, this is how this sort of an assumption says about the velocity is a function of ATP concentration. And then what it simply says is that the velocity sort of increases linearly with a ATP concentration right. It is just some k plus 0 times ATP concentration and minus something, so this is an intercept. So, effectively what it says is that this velocity if you plotted it as a function of ATP concentration would go as something like this ok.

And immediately you can sort of see that this is not a very good model, because the motor has some inherent speed limit. If you keep increasing the, if you were very low ATP concentration, so where ATP is therefore, the concentration of ATP or rather ATP hydrolysis is a rate limiting step. Then of course, you could say that yes, as I increase my ATP concentration I would expect my velocity to increase maybe.

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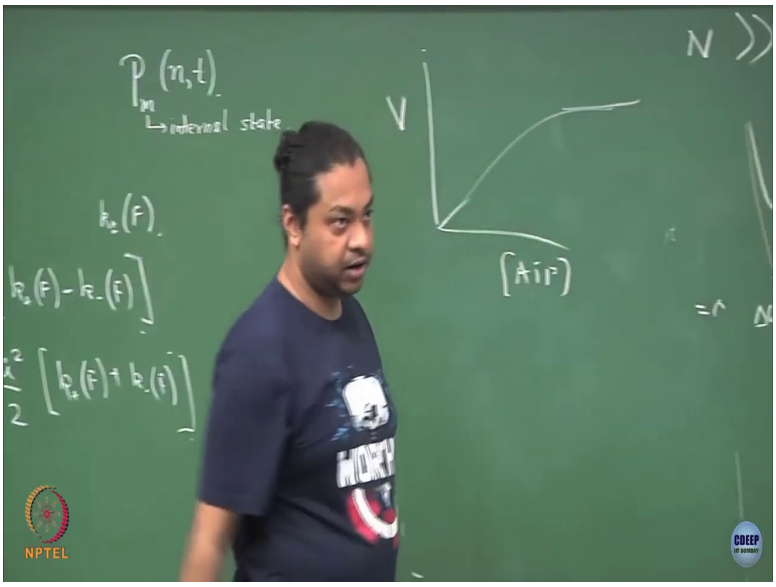

But beyond a certain point when ATP is sat at saturating concentrations you will get something; but you cannot keep increasing indefinitely right. The motor has some biochemical constraint that what is the maximum speed it can achieve which is not captured by this sort of an assumption that if I say that the entire forward rate. So, sorry the entire ATP dependence is in the forward rate then that is not a very good model. Because, even naively you can see that that is not going to fit in with what you measure in experiments.

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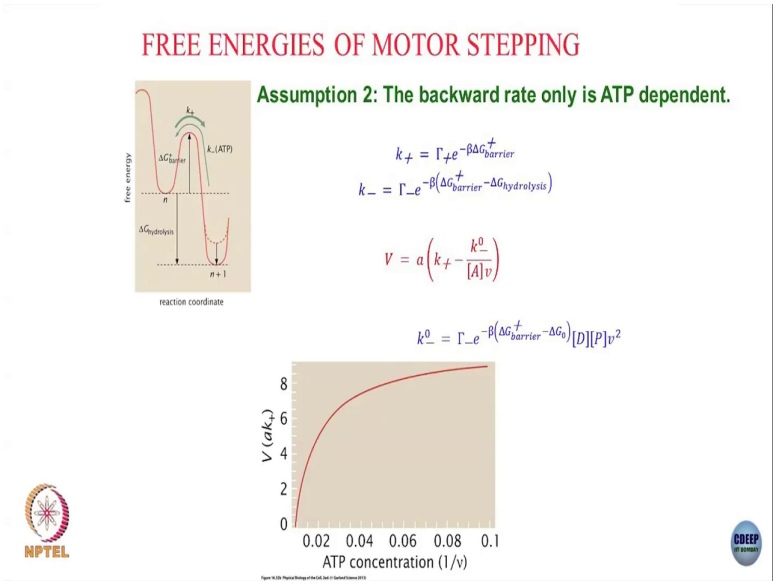

How about the other limit? So, you can say that well only the backward rate is going to be ATP dependent which means that I will keep this part of my free energy landscape fixed I change the depth of this minimum right. So, that this k minus is now going to become a function of ATP this k plus is going to be constant. So, again I write this, so now, my thing which is stays constant is this delta G plus. So, express my delta G minus in terms of delta G plus and the delta G hydrolysis, yes.

Student: It is not the (Refer Time: 11:36).

I agree, so what you are saying is I drawn something like this. So, let us say I go with this forward rate assumption that this only this thing will change this I change ATP and therefore, I go from here to here with some step.

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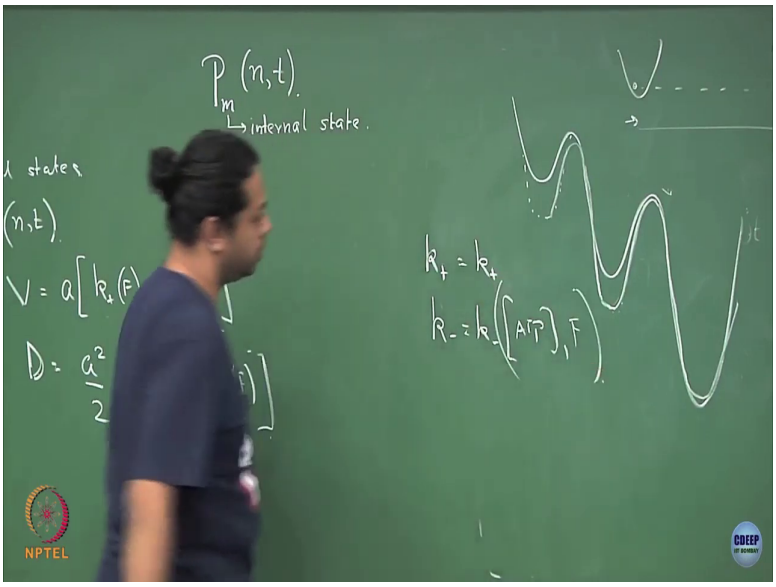

For this sort of transition where this one would not change.

Student: (Refer Time: 12:13) last expression would change.

Student: By definition if it is a (Refer Time: 12:18).

2 delta g and so on.

Student: (Refer Time: 12:21).

Yeah, But the problem is that ah, so its slightly different I understand what you saying. But the problem is that if motor is walking on a trap and I am applying some force let us say I have an

optical trap, then as the motor walks more and more my force gets propagated. So, I shift sort of everything by f n f times n times k. In the case of ATP binding and hydrolysis that is not the case it is not that I am supplying ATP from this end. And therefore, I get something which is linear with n and I get a shift it is binding throughout the bulk, so that is not going to work.

Yeah so, the answer is I probably I guess I will think about it, but I guess answer is that this is not a very good set of assumptions to begin with. We just doing it simply to see what sort of things can be captured, I will think about how to make this a little more realistic at least within this context yeah as of now. So, in the if I just go on with this, so in this case if I took that the backward rate only was ATP dependent then again I would get some sort of a dependence on this of the velocity on this ATP concentration. And again everything else is plugged into this k minus 0 and then if you plotted this, this looks something like this, it grows and then it saturates to a value which is like a k plus.

So, that again is slightly more realistic than this other case. So, at least within the context of these models what it says is that k plus is simply k plus and the k minus if I put everything together is some going to be a function of ATP and force f is ok. That at least within this simple family of models that is what sort of makes sense these sort of rates would get you closest to these experimental measurements.

It would still not explain all the measurements like we saw and it has at least this one has some internal inconsistencies. But that is because in some sense we are we have started out at the very how to say you started out with a very wrong assumption which will never physically hold which is to say that I have said that my motor has no internal states right and. So, its let us say in this side versus this side.

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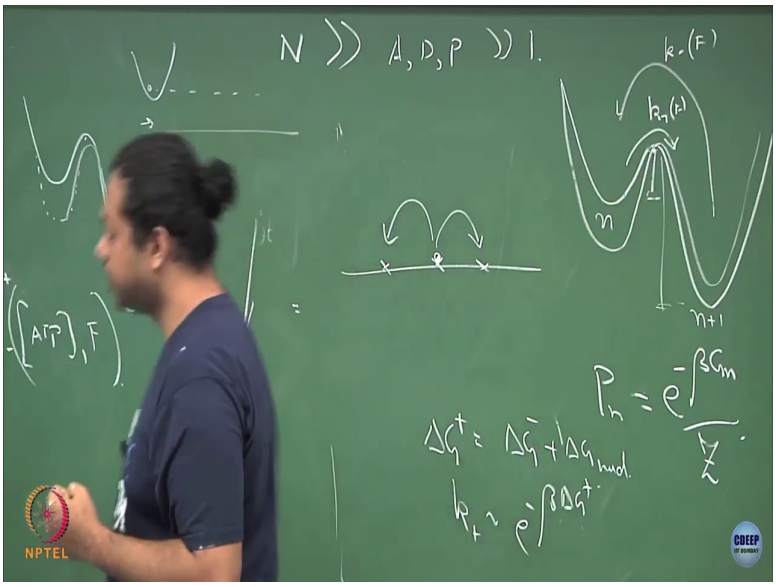

So, if the motor has no internal states they really under sort of an equilibrium under sort of an approximation they really should be no way of distinguishing this hop from that hop ok. Obviously, this better yes asymmetry in motor can do this thing, but at least in this class of models what sort of motor asymmetry do you mean for example?

Student: It is not the (Refer Time: 16:10).

Exactly, so the thing is that until and unless we actually introduce some sort of an internal variable which could be structured or which could be the state of ATP bound ATP you there is hydrolyzed or non hydrolyzed. It is difficult to actually square the physics with the biology because you are starting off from a place which does not really make much sense.

We are saying that there run there is nothing that distinguishes one state there are no multiple states of the motor. But, still I am saying that this forward rate is different from the backward rate, which is not very consistent with equilibrium approximations. The moment you say that no the motor has an internal degree of freedom, which could be this ATP hydrolysis it would be confirmations then a lot of these problems actually go away.

So, which is actually what I will try to do next. So, these sort of models are fine if you wanted a sort of qualitative understanding of this force velocity or this ATP concentration velocity dependences. But, in order to do a little more realistic models what you need to necessarily consider is that these motors do; in fact, have internal states.

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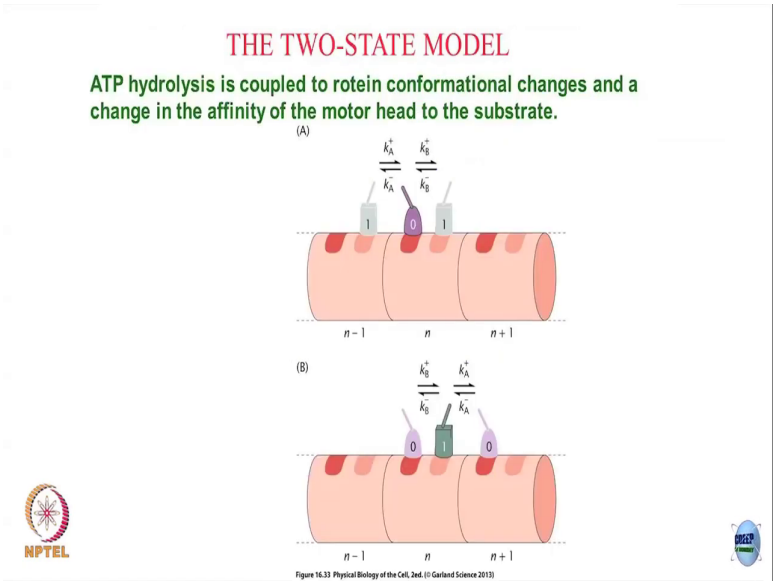

And then try to take write down a model that takes into account those internal state.