Physics of Biological Systems

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Lecture - 47
Dynamics treadmilling of microtubules

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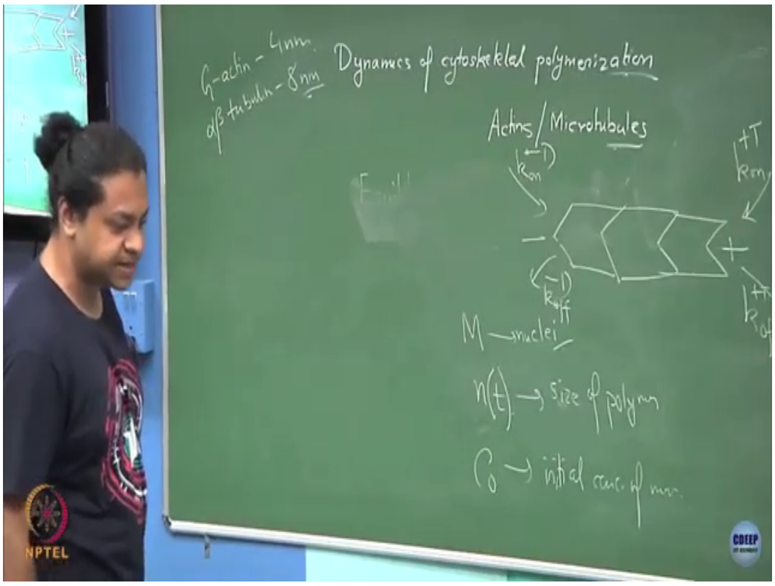

This was actin, so let me do a model little more specific for microtubules. So, instead of treadmilling of actin let me do a model for dynamic instability of microtubules. So, this is just to systematically show that you starting from this very basic model, you can build in layers of complexity.

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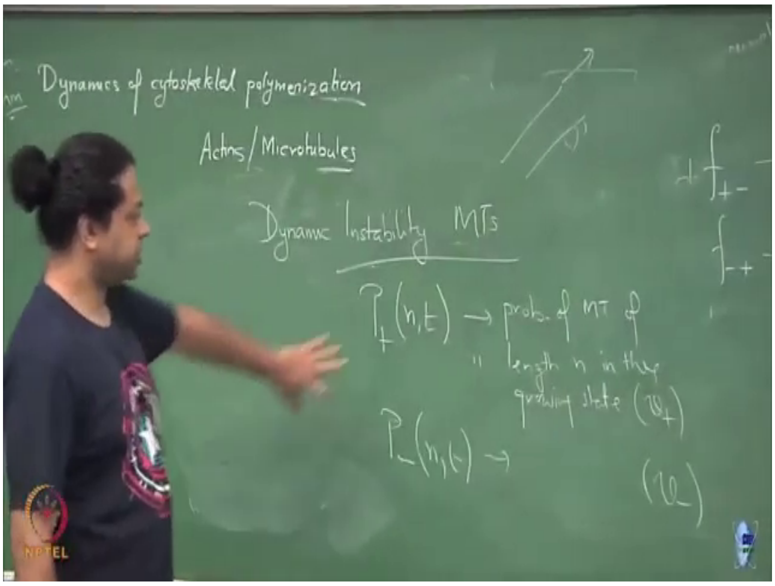

So, that you ultimately approach the biological situation Dynamic Instability Microtubules. So, let me say that I my microtubules let me have a probability distribution P plus of n comma t ok, this is a probability of MT of length n in the growing state in the growing state. And similarly you can write P minus of n t which is similar except that this is the probability of a microtubule in the shrinking state.

So, I say that I have these microtubules, these microtubules can either be in the growing state where they are adding monomers or it can be in the shrinking state where it is sort of losing monomers ok. And it converts from one state to another with certain frequencies which let me say are f plus minus and f minus plus. So, f plus minus is the frequency at which a growing microtubule shifts to the shrinking state. So, this is like the frequency of catastrophe.

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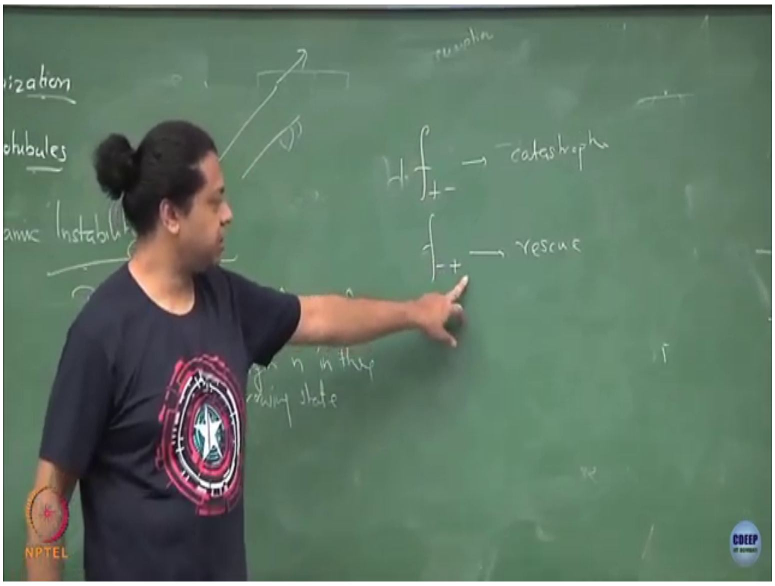

So, this is my catastrophe and f minus plus is like my frequency of rescue, frequency at which a microtubule in the shrinking state changes back to a microtubule in the growing state. So, these are all my these are the rates and what else. So, when it grows let me say it grows with some rate v plus. So, it is adding subunits with some rate v minus v plus and when it shrinks it is losing subunits with some rate v minus.

So, that is my full model, my microtubules can exist in two states given by the probabilities are given by P plus and P minus, they can switch between these states with these rates f plus minus and f minus plus. And in each of these states they grow or they shrink with the velocity v plus or v minus. So, given this I can write down how these probabilities will evolve with time. I can write down how this probabilities will evolve with time.

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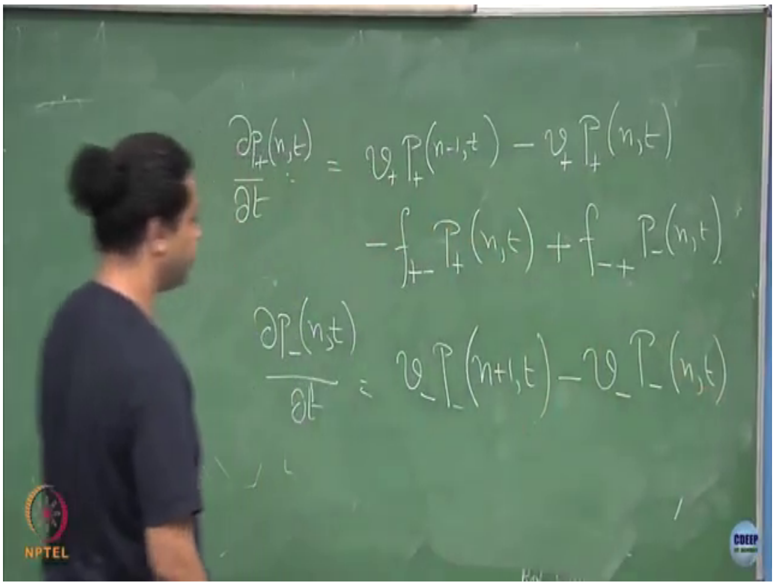

So, let me write d P plus d t, let me be specific this is P plus of n comma t. So, from what state can I reach this n t? If my microtubule was in the in the growing state then it can have added a monomer. So, I can have come to this state from the n minus 1 state right and the rate of that is v plus right. It was n minus 1 it has added a monomer it has come to n and similarly if it can go from this n to the n plus 1 also, so that is a loss term.

So, again a v plus P plus n t right this is a growth from the n minus 1 state this is a growth from the n state. Then of course you can switch states. So, from the plus you can go to a minus, so that is again a loss term. So, the rate for that is f plus minus P plus of n comma t or you could come from the minus to this plus states so, f minus plus P minus of n comma t right. There are the only four ways you can come to this plus a growing microtubule with n filaments.

Similarly, you can write down how the probability of a shrinking microtubule with n filaments changes with time, that is v minus in this case from n plus 1 ok. From n plus 1 it can come to n with a rate of v minus and then P minus of n comma t from n it can go to n minus 1 which is a loss term and then these two things.

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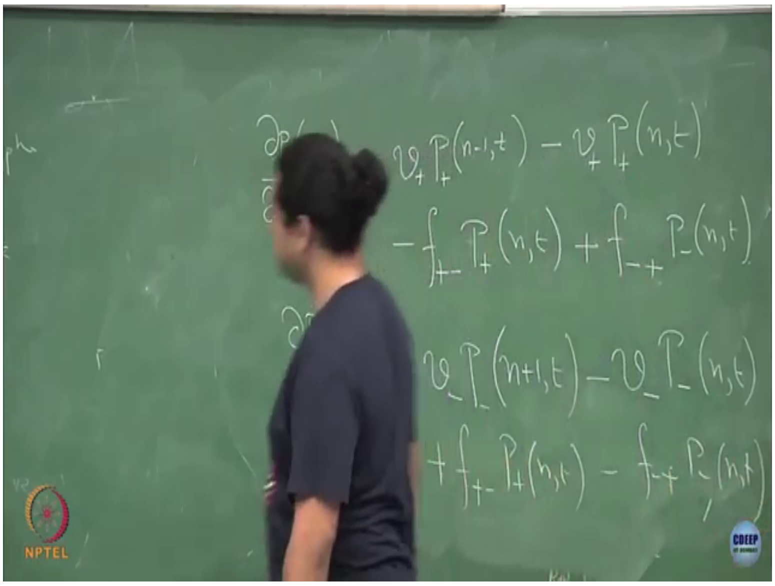

So, this will be a plus f plus minus P plus of n t minus f minus plus of P minus of n t. So, these are my evolution equations for a model like this a model for this dynamic instability of microtubules. So now, what I can do is that I can take these n minus 1 and n plus 1 P and expand them in a Taylor series.

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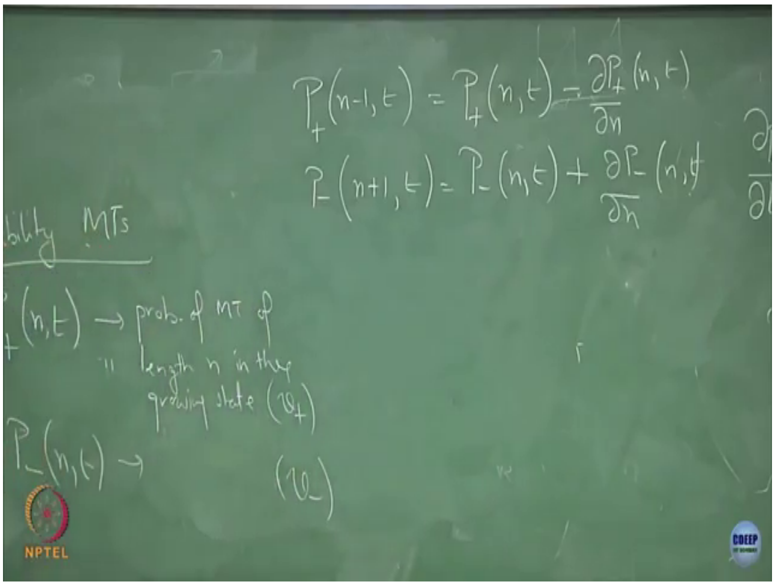

So, we can expand this let us say I have a P plus of n minus 1 comma t, I do a Taylor series, we can expand this let us say I have a P plus of n minus 1 comma t I do a Taylor series expansion.

So, this is P plus of n comma t minus del P plus del n n comma t I just keep terms of the first order and I have P minus of n plus 1 comma t. So, this is P minus of n comma t plus del P minus del n comma t ok.

So, if I substitute I substitute this P n minus 1 over here, the first term which is v plus into P plus will cancel this. What I will be left with is a minus v plus del P plus del n right.

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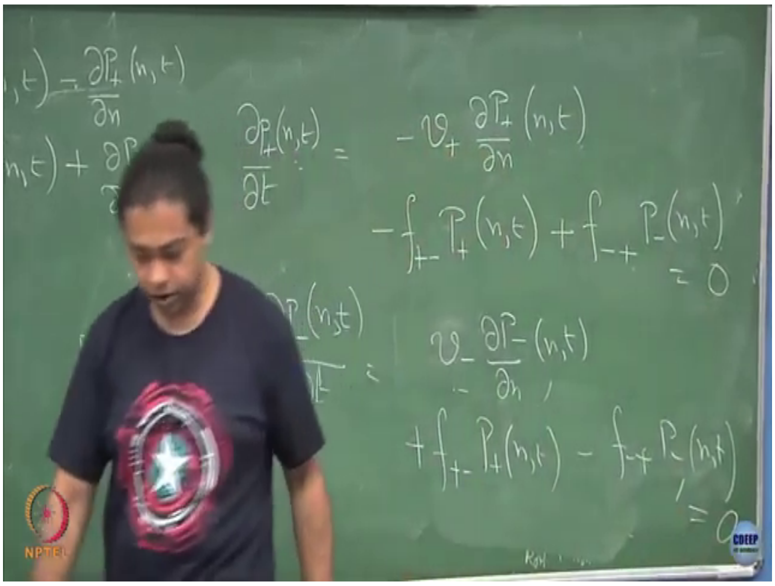

So, what I will be left with over here these two terms writing, I will be left with a minus v plus del P plus del n of n comma t. And similarly if I substitute for P n plus 1 with this equation again what I will get is v minus del P minus del n of n comma t right. Now let me say that I will solve this equations in the steady state, which means the I will say that these probabilities do not change with time. So, let me say this is equal to 0 this is equal to 0. What that gives me is an equation for this del P del n? So, let me just write down that equation.

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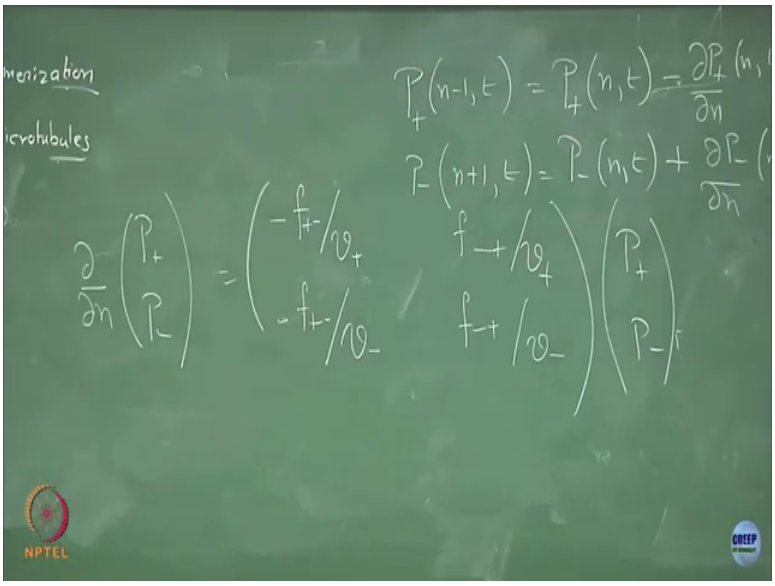

So, what I have is a del del n del del n let me write it in a matrix form P plus P minus P plus is equal to plus I think no minus. So, minus f plus minus by v plus and then f minus plus by v plus and then over here f plus minus by v minus with a minus sign again and f minus plus by v minus and then P plus P minus.

So just written that the same equation with this del P del t 0 in a matrix form and now I can solve this equation. So, 2 cross 2 matrix you can find out the eigen values and eigenvectors and so on. So, let me so this I will not do. So, let me just write down the solution you can you can show that the eigen values. For example R0 and f minus plus v plus minus s plus minus v minus by v plus v minus; these are your two eigen values and you can find out the corresponding eigen vectors for this.

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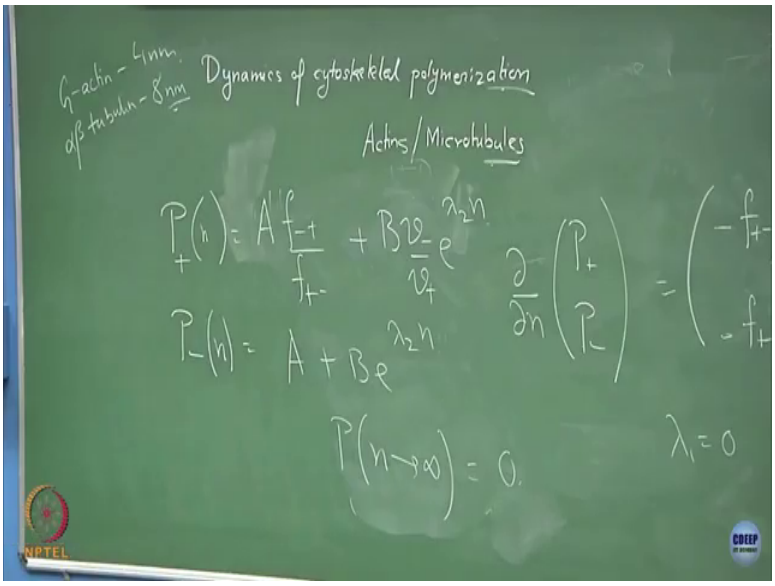

So, once you do that you can write down your P plus of n is some constant A into f minus plus by f plus minus plus B into v minus by v plus e to the power of lambda 2 times n and P minus of n is equal to A plus B e to the power of lambda 2 comma n.

So, these are two undetermined constants so these are my eigen vectors. So, I have just written down the eigen vectors and use that to construct the solution. Now let me say I am looking at scenarios where the lengths of the microtubules are finite. So, it is some sort of a bounded growth which means that if I took the probabilities of this n a very long microtubule n tending to infinity that I say should be 0. What that means, is that this A term basically should be 0; so that will drop out and then you can use the normalizations to determine what this B is and that B will come out to be something.

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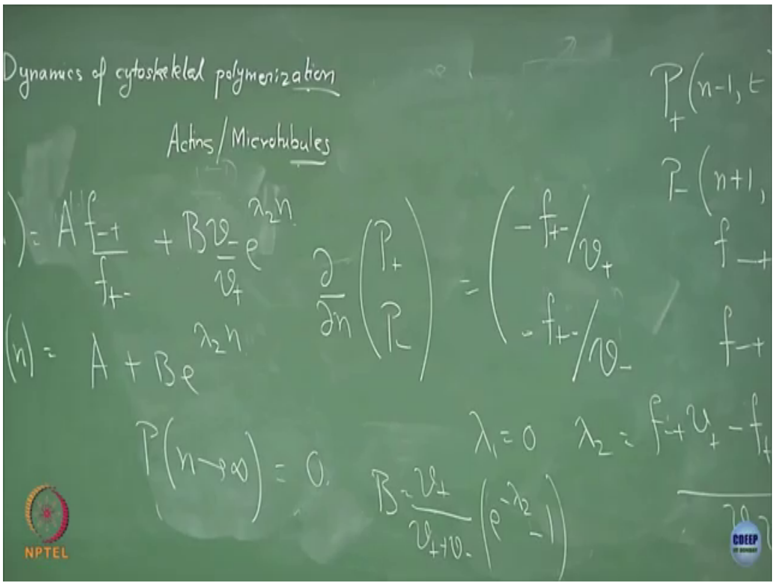

So, that B will come out to be v v plus by v plus plus v minus e to the power of minus lambda 2 minus 1 ok. And also you can see that if you want to have this bounded growth basically, this lambda 2 term must be negative right, otherwise this will blow up. So, this lambda 2 must be negative what it says is this ratio it gives you a relation that if. So, this is my lambda 2.

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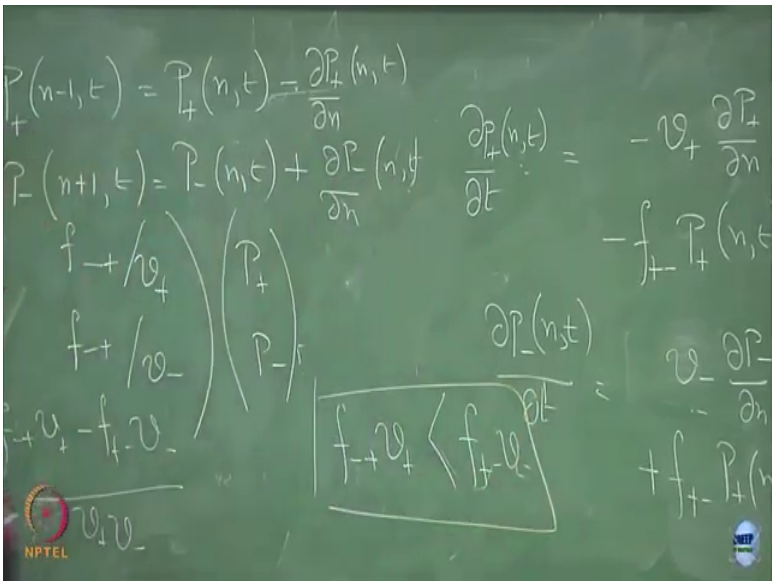

So, what it says is that f minus plus v plus must be less than f plus minus v minus, in order to have bounded growth. And if you satisfy this criterion what your length is a function of time is going to look like is something like this length is a function of time it will look something like this ok.

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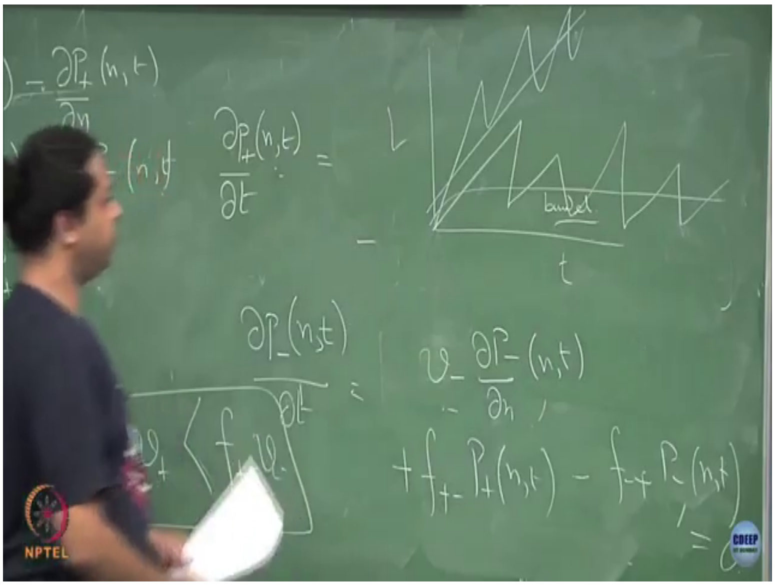

It will grow and it will shrink, if on the other hand if you have unbounded rules if you violate this condition this will keep growing like this and until it reaches sort of infinitely large microtubules. So, here it is this sort of a steady length here it is just going to keep on increasing. So, this is bounded growth and given that this is roughly what you see, that sort of tells you even experimentally to a certain still. Of course, against you can build more complicated models where at least in the context of this model.

How should these ratios of switching from this plus to the minus state versus, the velocities of this growth and shrinkage how should they be related in order to get bounded growth. And these you can sort of calculate or measure not calculate from experiments and see whether this holds are not. You can measure how fast the microtubule grows you can measure fast it shrinks and how fast it switches from 1 state to another and like I said you can.

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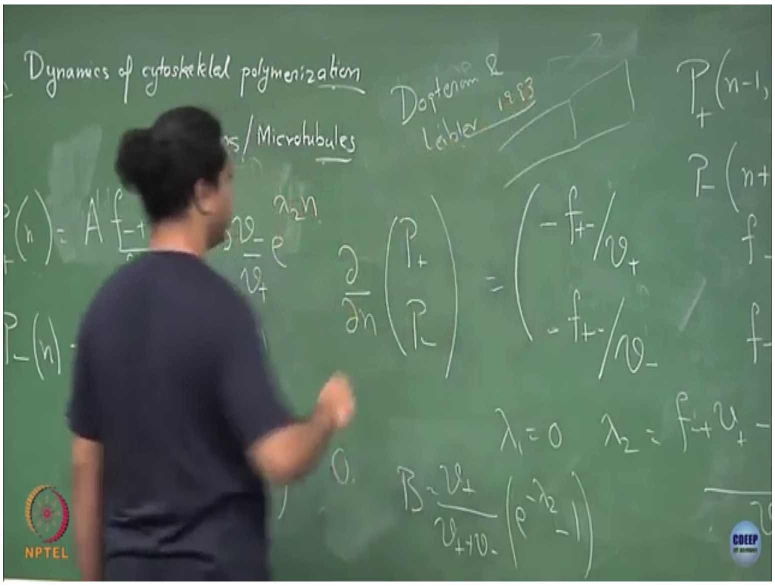

So, you can keep building complexity you can build in this cap idea that you have this g t P subunits at the end of the microtubule which form a sort of stabilizing role and so on. And all of those as you add more and more complexity you will see that you will get better and better match with experiments.

But this model this is a very classic model actually this is a model by Dogteram and Leibler in 1993. It is a classic model for the dynamical instability for microtubules for any of you who are interested. You can calculate other stuff as well.

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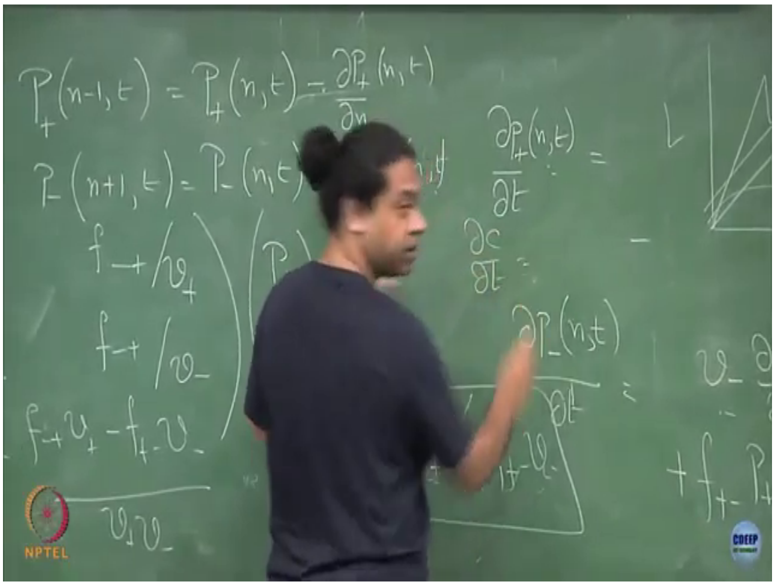

So, for example, you can couple these equations to an equation for the concentration of free monomers right. That that I still have not done, but in principle you could couple these to a concentration of free monomers and then see what that gives you ok. So, let me stop here for the day and then I will continue on Friday.