Physics of Biological Systems
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Lecture - 45
Average length of polymers in equilibrium

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So, this is the sort of Basic Biology. And then, we will try to look at models at various levels of complexity to see how we could model this look.

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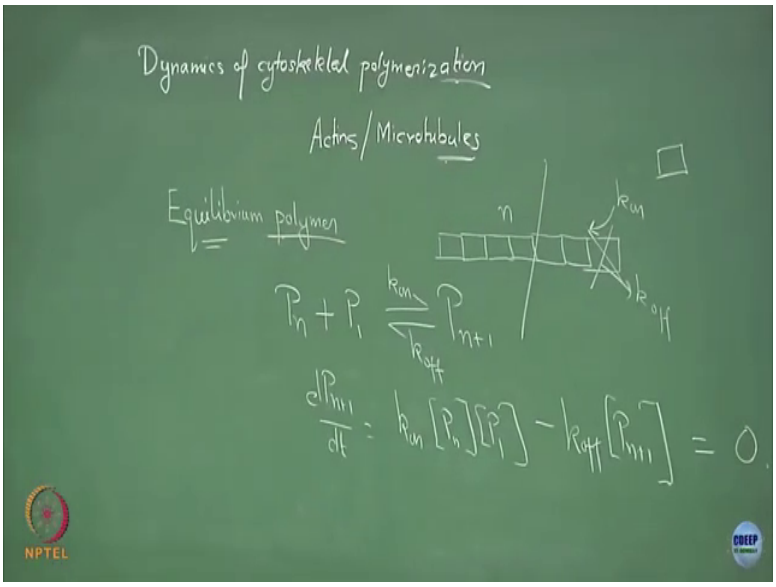

So, we will start off with the simplest sort of model and then we will see what it does and what it does not do. So, we will start off with the module of an equilibrium polymer, ok. So, here what we will see is that I will forget a lot of this complexity that I just said, I will put it back in slowly. So, I forget that there are these two states the GTP and the GDP and so on; I just say that I will consider a simple polymerization process, so I have this subunits and these subunits are being added. So, they are being added with some rate let us say k on and they are being taken off with some rate let us say k off. This could be as well a model for actin or for microtubules because it is thrown away all the relevant distinctions between them.

And I say that it only grows and shrinks by the addition of a single monomer, ok. So, if some it is to grow is let us say its n length polymer, n length actin or n length microtubule, if it has to grow it can only grow by the addition of one more subunit or if it shrinks it can only shrink

by one subunit disassociating. There is nothing like let us say a breakage from the middle where it is sort of snaps into two paths, ok.

So, I do not consider processes like that. So, in that case the relevant sort of chemical reaction as it were where a polymer of length n, adds a monomer, right and becomes a polymer of length n plus 1, right. It has some rates, so let us say it has an on rate to go this way and it has an off rate to come back from that way, right, the dissociation. So, what the.

So, let us say if I wanted to write what is this d P n plus 1 dt, right, that is simply k on times the concentration of P n, the concentration of P 1 minus k off times P n plus 1, right that is my reading. And that is true for any n that you might write.

So, what this equilibrium, this equilibrium assumption means is that I say that this probability does not change in time. So, it does read some sort of a steady state and I put this equal to 0, which means that these concentrations of these various polymers. So, I am thinking in terms of an ensemble I have many polymers or one polymer repeated many times; however, you want to think.

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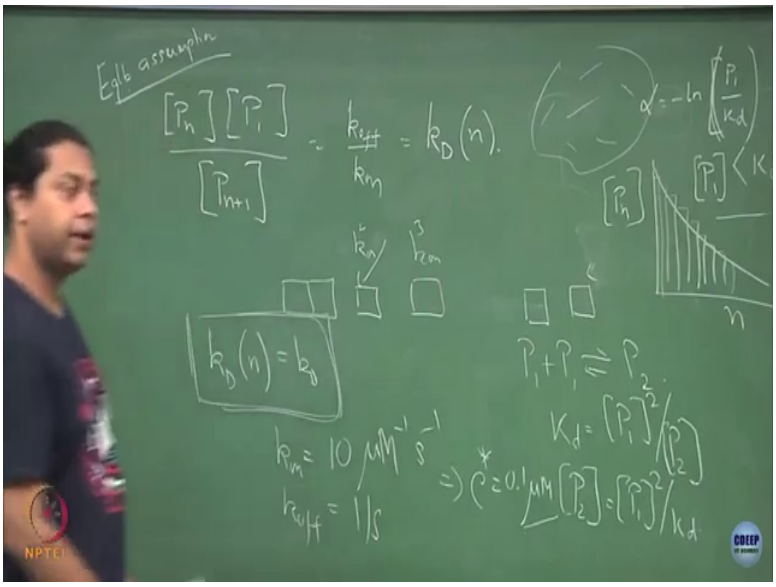

So, what I would say is that these concentrations let us say P n, P 1 by P n plus 1, that in this steady state approximation is equal to k off by k on and that it is called the dissociation constant k D, right. So, this is the equilibrium, this is sort of the equilibrium of the steady state assumption, equilibrium assumption.

Now, you could imagine that or rather more realistically, you could think that these on and off rates are actually a function of n themselves. That is if I were go if I were going from polymer of length 2 and I were to try to add one more maybe the rate would be some k on 2 and then if I were to try to add one more that would rate would be k on 3 and so on.

So, these could all happen with different rates and similarly for the dissociation. So, it in principle this k D should be a function of n. But let me make you an even more simplifying assumption that I assume that all of these k Ds are the same. So, let me just say it has no

independence. This is not really motivated by biology; it is motivated by physics way of thinking. This is what I can do this is the first step to any model that I can build. So, let me make this assumption and see what I get, ok.

So, I say that all these equilibrium constants of this dissociation constants are the same, and then I can sort of write down let us see. So, basically I will have, if I were to consider the first step that I have a monomer and I add one more monomer to it to get a dimer then that reaction is P 1 plus P 1 giving me a P 2, which means that this K d is P 1 whole square by P 2, so right. So, P n P 1 except that n is also equal to 1 now. So, P 1 whole square by P, right.

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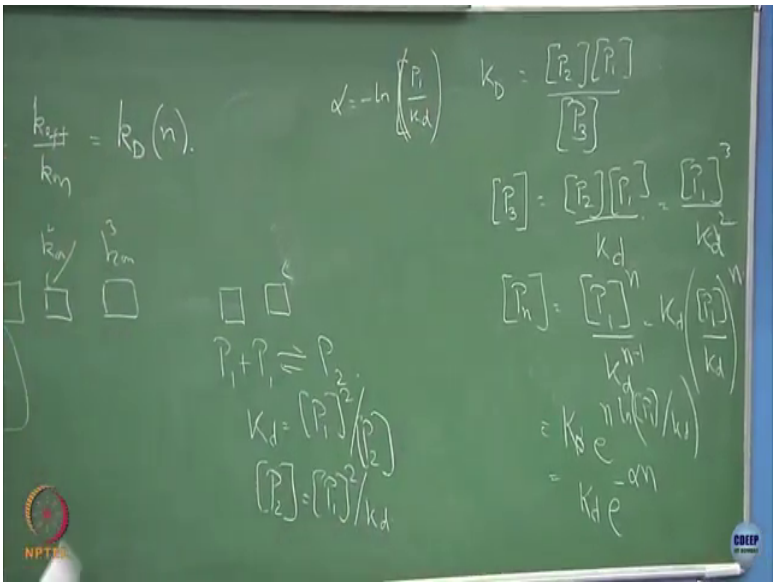

Similarly, if I continue this sort of thinking then K D, what am I write, K D. So, K D is also P 2 times P 1 by P 3; right that is when the dimer becomes a triangle for that reaction. But now I can, so let me say I want to write down what is P 3. So, P 3 is P 2 P 1 by K d and then for K

d, I substitute, so P 2 P 1 by K d, ok. So, that is my P 3 and let me say I write what is P 2 over here; P 2 was P 1 square by K d. So, if I substitute this becomes P 1 cubed by K d square, right.

So, P 2 was P 1 square by K d to the power 1, P 3 is P 1 cubed by K d to the power of 2 and so on. So, if you continue this scheme you will get that P n is equal to P 1 to the power of n K d to the power of n minus 1, right. So, let me just say this is K d times K d times P 1 by K d whole to the power of n, ok. So, let me rewrite this. So, I can rewrite this. So, this is K D, K D e to the power of n log P 1 by K d, ok; this to the power of n, I just written as exponential of.

And then if this object I call is some alpha or rather minus alpha, then this is like K d e to the power of minus alpha n; where this alpha is just that object alpha is negative log of P 1 by K d, right. What is P 1? P 1 is simply the monomer concentration, right. There is a single, so it is like g actin concentration of this alpha beta tubulin dimer concentration, the free monomer concentration divided by this equilibrium constant. So, that is my log negative log of that is my alpha and then the probability or the concentration of having a filament of length n goes as K d e to the power of minus alpha n, ok.

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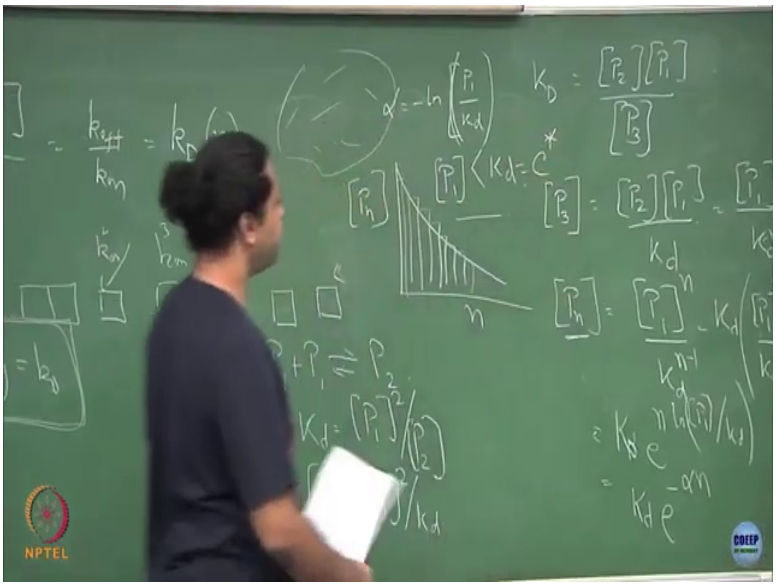

So, as long as you are as long as your monomer concentration P 1 is less than K d, you will get a distribution that looks like this, P n is a function of n you will get some sort of an exponential distribution, right. So, I have done this very simple model and what it says is that if I take all of these approximations and then I looked at a system, so I look inside my cell.

Let us say I have microtubules of various different lengths, I plot the probability distribution of those lengths, I should see an exponential and actually amazingly you do indeed see an exponential, ok. So, if we were to actually plot the length distribution, if you go to plot the histograms of these different lengths that are found inside a cell, you would see roughly an exponential distribution, ok. So, that is that is nice, in the sense that we have done really a very crude model.

We have taken this equilibrium approximation and we have taken this approximation simply for the fact matter of convenience, not without even trying to justify it biologically, but still we get a distribution that looks like an exponential which is what the experimental distribution looks like. Still it is not that all is well this is the final model. But let us stick with this for the time being and just try to calculate, so what is the average length of the polymer.

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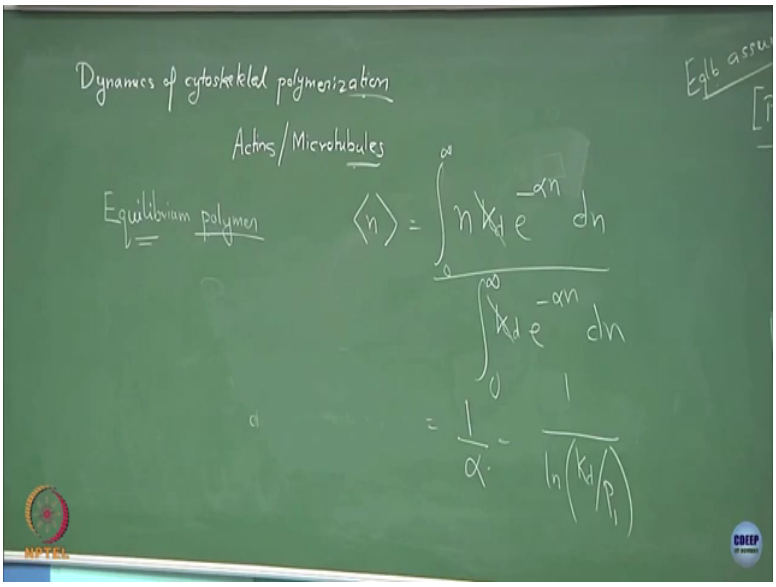

So, given a distribution like this, I can calculate what is the average length. The average length of the polymer is simply n times P of n. So, it is like K d e to the power of minus alpha n dn divided by K d e to the power of minus alpha n dn, right. That is simply the mean length of the polymers that you get. If you do the K d anyway cancels out. If you do this integration, so this is from 0 to infinity, 0 to infinity, if you do this calculation what you will get is that this mean length goes as 1 over alpha. which is 1 by log K d by P 1.

In fact, if you think about this, so this was for the case when P 1 is less than K d. So, this K d has units of concentration, right because K d is P 1 concentration around the concentration divided by another concentration. So, it has units of concentration. So, you can think of this let me call this as some C star, ok. So, as long as your monomer concentration is less than this C star, you will get on an average that these filaments will be shrinking and you will get a length distribution like this which is peaked about 0.

If you have monomer concentration which is greater than C star then your filaments will keep on sort of growing and you will get infinite length filaments, in that case this calculation will no longer hold of course, ok. This is for the case when P 1 is less than K d. And you can sort of calculate if you can just put in numbers for example, if I put in numbers for actin, roughly of course these numbers none of these numbers are gospel they differed again from cycle which point of the cell you are looking at, different proteins and so on.

But still a typical number is like 10 micromolar per second for the on rate and let us say the off rate is around 1 per second, which means that together this gives you a critical concentration or a K d of rough K d is k off by k on. So, this is roughly around 0.1 micromolar. So, it would say that if you if this were if I were to consider a model like this, then as long as my concentration of monomers was less than this if these filaments would on an average shrink and I would get a length distribution like that. If it was greater than this, then your filaments would keep on growing, ok.

Of course, you have to realize that and we will do that in a bit. This monomer concentration is not sort of a fixed quantity, right, as things sort of polymerize we are using up more of your monomers as well. So, you have to take that into account as well. Even if you started off with something which was C greater than C star, as time goes on and you polymerize and polymerize we will hit a limit where you know C is no longer greater than C star. So, we will take such a model into account, but anyway. So, this is the 0th level model in equilibrium sort of a model. But now I can calculate one more thing over here within this sort of a model which is about time scales.