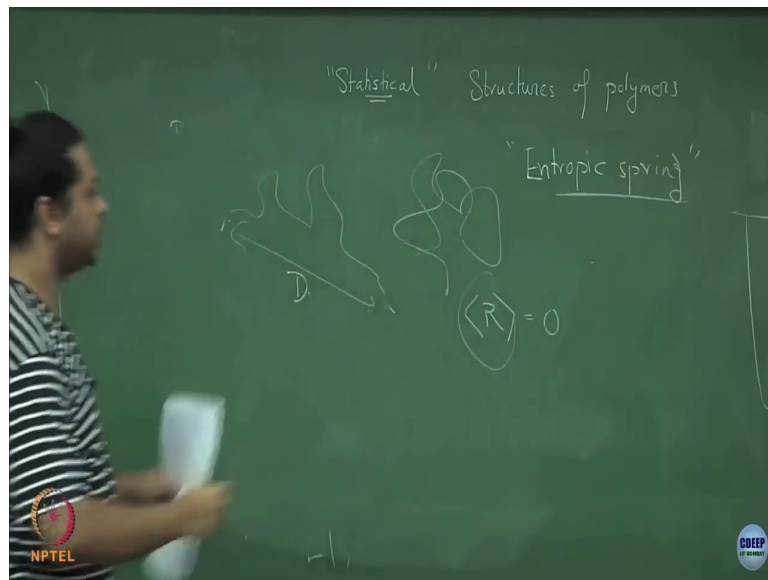


Physics of Biological Systems
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Lecture – 30
Entropic Springs and Persistence Length

This is mathematics, but this is nice consequences. For example, let me say that I take a polymer.

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So, let me say that I had some polymer, the DNA whatever you have and let say somehow you have two optical tweezers or whatever, you have kept these, if pull these this end of the DNA apart from this end or this end of the polymer apart from that, ok. So, you have taken this,

taken hold of these two ends and you have stretched them apart to some distance right, let us say capital D, ok.

Now, you let go of this polymer, ok. You let go of this. So, whatever was holding it apart at this distance you let go of it and again you let it come to an equilibrium. And then you ask that what is the end to end distance of this polymer going to be, ok. What would that be? So, if taken the polymer you have stretched it, I have stretch the ends to ends apart by some distance D. Once I have done that I let it go, and then I let it equilibrate and I ask what will be the equilibrium sort of end to end distance of this polymer again. What would that be?

Student: (Refer Time: 01:36).

Student: (Refer Time: 01:37).

Yes, sorry.

Student: (Refer Time: 01:38).

For the variance, for the mean.

Student: (Refer Time: 01:43).

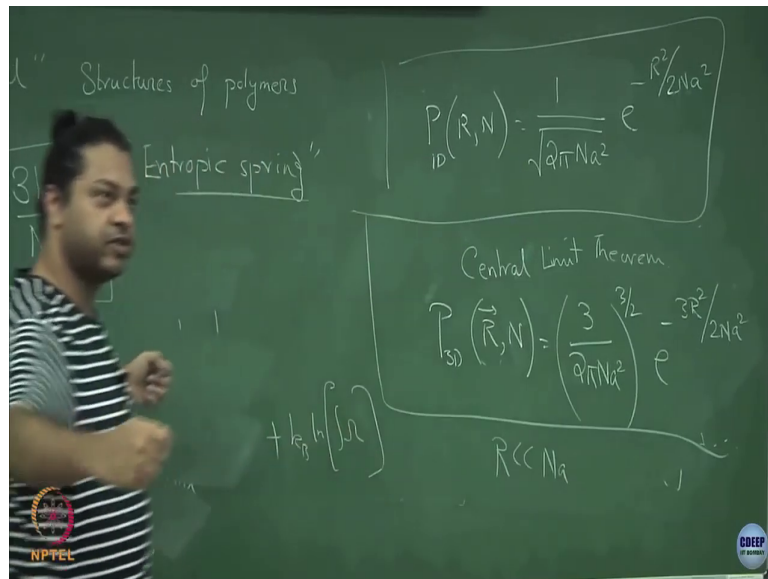
It would still come back to 0, right; then, the first moment is 0. So, if you stretched it apart by a distance D and then you let it go, after some time you will see some confirmations whatever. If you take an average of all of those confirmations again you would find that your end to end distance this is my end to end distance. The mean end to end distance would again come back to 0.

What does it sort of remind you? Of that sort of behavior reminiscent of a spring right I take a spring and I stretch it and I let it go and it comes back to its resting state x equal to 0.

Similarly, here if I were to take a polymer and stretch it and I let it go, it sort of comes back to a state where you again you have your mean end to end distance coming back to 0, ok.

But in a spring, unlike a spring where you have an energy which is trying to be its trying to pull you back to the origin here it comes back to 0 simply because if you think about the probability or if you think about the number of states, the maximum number of microstates that you have is at this R equal to 0 conformation, right, or if you think about the probability this probability is peaked at R equal to 0, ok.

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So, it is a spring, yes, but the origin of the spring is entropic. So, which is why a polymer is often behaves as what is called as an entropic spring. So, if you pulled it and you let it go, it would come back to 0, but it would come back because of entropy. It has the maximum

number of microstates at this R equal to 0 point, ok. Can we formalize this little more? This concept of the, this springiness of a standard polymer, and it turns out we can.

So, let say, let me say that can I write down what is the free energy of a of this sort of an ideal polymer. We start off with writing what is the entropy.

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Polymers in biology

Entropy of this ideal polymer?

$$S = k_B \ln \Omega(\vec{R}, N)$$

$$P_{3D}(\vec{R}, N) = \frac{\Omega(\vec{R}, N)}{\int \Omega(\vec{R}, N) d\vec{R}}$$

$S(\vec{R}, N) =$

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So, let me ask what is the; what is the entropy of this, entropy of this ideal polymer? Right, ok. So, what is entropy? S is $k_B \log$ of ω , right. S is $k_B \log$ of ω . And this ω is of course, a function of the end to end distance and the number $R N$. How do I get this ω ? Anyway, I know this probability. So, I can just write down what is ω .

So, probability of let us say for this 3-dimensional polymer, you have an end to end distance R to the polymer of length N is simply this ω of $R N$ divided by integral of this ω $R N$

dR, right. This is the definition of the probability. So, now, that I know the probability then just write down the omega in terms of that. And this is whatever that that expressions P 3D, ok.

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"Statistical" Structures of polymers

"Entropic spring"

$$S(\vec{R}, N) = k_B \ln P_{3D}(\vec{R}, N) + k_B \ln \left[\int \Omega(\vec{R}, N) d\vec{R} \right]$$

$$= \frac{3}{2} k_B \ln \left(\frac{3}{2\pi N a^2} \right) - \frac{3R^2}{2 N a^2} k_B + k_B \ln [\Omega]$$

$$= -k_B \frac{3R^2}{2 N a^2} + S(0, N)$$

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So, if I wanted to write down this entropy S is k B log of omega. So, this entropy is S of R given N is k B log of this P 3D R given N plus k B log of this integral, plus k B log of this integral omega R N dR, log of this whole thing, right. This I will not worry about, but anyway, we will, let us keep this for the time being. So, this is my full expression for omega from here and then I have just taken k B log of that.

So, now I can substitute for this whatever expression that I have for P 3D. So, then I would get log of that first term is 3 by 2 k B. So, 3 by 2 k B log of 3 by 2 pi N a square, that is my

first term. Then the second term I would get minus $3 R$ square by $2 N$ a square times k_B , right and then I would have this k_B log of this integral, plus k_B log of this integral ω .

Notice that this term and this term, the first and the third are both independent of R , right. So, they do not have R in them. So, I can just say that this S of R comma N is minus k_B $3 R$ square by $2 N$ a square plus the entropy at 0 comma N , right, that is independent of R in many case. So, let me just put everything in that in this term S of 0 comma N , ok.

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Polymers in biology

Entropy of this ideal polymer?

Free Energy.

$$F(\vec{R}, N) = E(\vec{R}, N) - TS(\vec{R}, N)$$

$$= \frac{3}{2} k_B T \frac{R^2}{Na^2} + F(0, N)$$

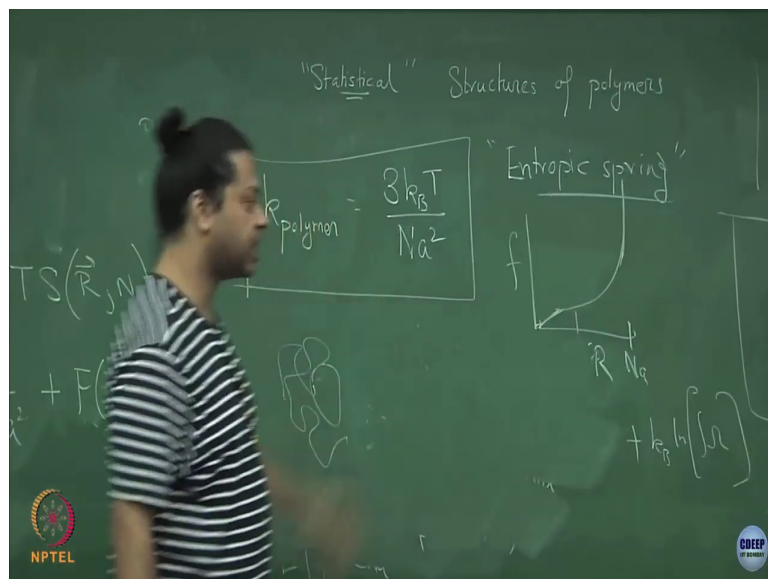
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So, now, that I have the entropy of course, I can also have the free energy, free energy is E minus $T S$. So, I can also have the free energy which is like, so F of R comma N is the energy of R comma N minus T times the entropy at R comma N , right. And now, I will use this ideal this thing that I have called as an ideal polymer. But an ideal polymer means.

What is ideality? Ideality means that these monomers do not interact with each other, ok, there is no interactions between them which means that there is no energy term in over there. So, this E_{RN} is independent of R . So, I could might as well this write this thing as a minus T times that, so $k_B T$. So, $3/2 k_B T R^2$ by $N a^2$ plus whatever else remain let me just lump it into this F_0 comma N all that S_0 comma N , so right (Refer Time: 08:40).

So, the free energy as a function of this end to end distance R is something $3/2 k_B T$ by $N a^2$ times this R^2 , right, plus a constant term this is independent of R , ok. So, even here, if I were again if I were to go back to this spring analogy the energy goes as half of k times x square, right, which means that from here I can define what is an effective spring constant of this polymeric spring, right. So, I can define what is an effective spring constant of this polymeric spring $k_{polymer}$. What is that $k_{polymer}$?

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So, what would be the effective spring constant of this polymer? If this is like half $k \times \text{square}$ right, then k is this thing over here $3 k B T$ by N a square, right. So, the stiffness of the spring constant of this polymer is like $3 k B T$ by N a square, ok. You can also just do this by doing $\Delta F / \Delta R$, or (Refer Time: 09:59).

So, yes, if you sort of stretch a polymer it will try to come back to this R equal to 0 state and the stiffness of that, so that that response is going to be given by the stiffness of this polymer which I am define, which comes out to be this $3 k B T$ by N a square. What does it mean? It means that, so for example, if I took polymer which is let say I take a DNA which is 100 base pairs versus which is 10,000 base pairs.

Which DNA would be easier to stretch? The 10,000, ok. The longer the DNA remember this N comes in the denominator the easier it is to stretch. The longer a polymer let me not say DNA, any polymer which behaves like this the easier it is to stretch. The lower the temperature the easier it is to stretch. Is this always troops.

So, for example, what is the limit of valid when will this sort of a spring description of the polymer break down? For example, so let say I have this polymer right, I have this very coiled sort of a polymer and I take the two ends and I start pulling it, ok. Claim is that it will behave with like a spring with this sort of a spring constant. But when do you expect this sort of a behavior to break to fall apart?

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In what limit?

Student: (Refer Time: 11:34).

In what limit did we derive this probability distribution?

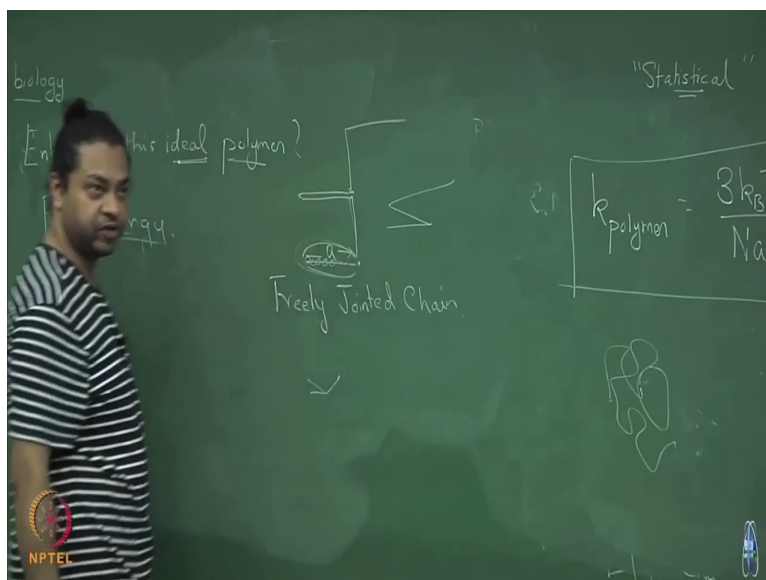
Student: R much much.

R much much less than $N a$, but of course, if you keep stretching this polymer you will approach the limit where this end to end separation is of the order of this $N a$ itself, right, and there of course, it will not no longer behave like a (Refer Time: 11:57) spring. So, if you were to plot this F against the extension of the polymer, let us say the end to end distance R , for small extensions, yes, it will behave like a spring, but you know that you cannot stretch this polymer or at least you cannot stretch it by keeping it intact beyond this R equal to $N a$ because that is the maximum extension.

So, there I know that this force is to blow up, right, it has to go up to infinity. So, this description will no longer be valid when this R becomes when this condition no longer holds true. So, therefore, it is true for small extensions, but it is not true for any general extension. In general, as you pull it more and more this force sort of relationship will become highly non-linear, it will no longer behave like (Refer Time: 12:39) spring. But at least for small extensions of a generic polymer you will see this sort of this entropic spring sort of a behavior, ok, all right, right

Now, let us try to think about we talked about this ideals or a polymer this random walk or a Gaussian polymer. It is called the Gaussian polymer because the probability distribution comes out to be a Gaussian or it is also called freely jointed polymer. Let us just think about what that means, right, ok. So, how am I constructing this polymer?

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I am saying that well. I take a step of length a and then after I have taken this step I take another step let say I am drawing it in 2D, a 2D polymer. I can take another step in any of these other four directions, right. So, I could take a step here then maybe I take one here and then maybe I turn back and take another one here and so on, ok.

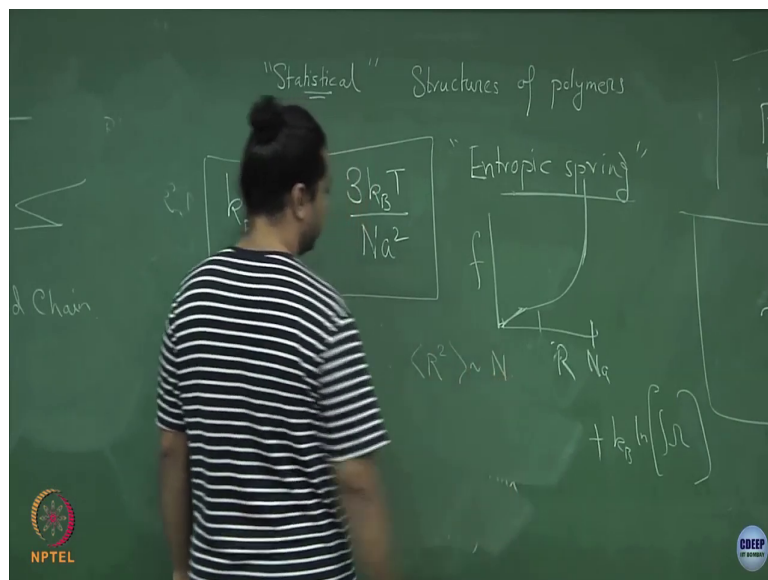
What it means is that there is no correlation between one step and the next step, right. It retains no memory of what my previous step was. So, it is also what is called freely jointed chain. So, this sort of a model is also what is called freely jointed chain. If you this side draw it on a lattice, but if you were to draw it on a continuum, you draw one bond, the next bond has this whole 2π angle available to it and so on and so forth, ok.

So, there is no restrictions on these angles. But if you think about what a polymer is of course or any, so any of if you really peered down at this length scale the length scale of these

monomers, these are ultimately chemical compounds, right. If I think about DNA and so on, these are ATCG or whatever. So, you have some sort of chemistry that is going on, that is going to generally tell you that well I cannot really take from one bond to another chemical bond. I cannot really go any arbitrary angle that I wish, while preserving the structure of the molecule itself, right.

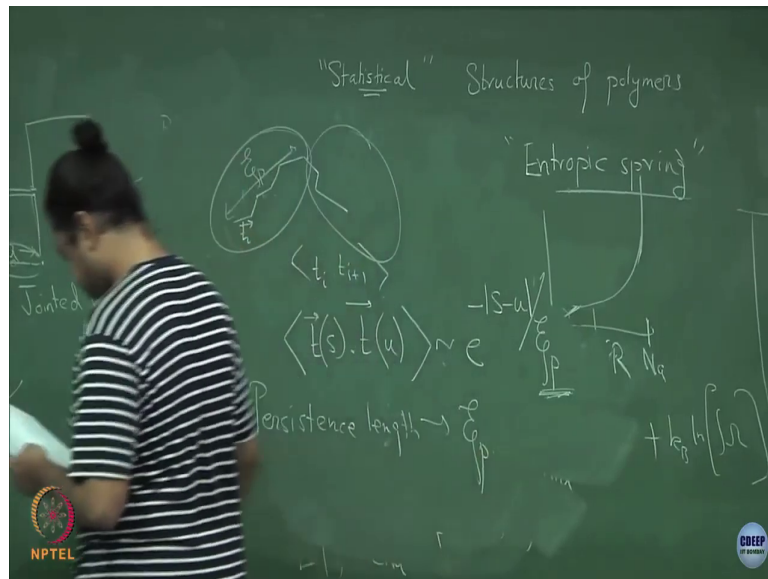
So, how do I reconcile that? That for a generic chemical compound that I think of I cannot feel you alter my bond angles randomly, right, versus the description versus the fact that actually if you calculate this R square the end to end distance of many polymers including DNA in certain approximations, you will see that it indeed does behave like this it grows as a number of monomers of this DNA.

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How do I square these two facts? And I squared these two facts by saying that this monomeric subunit the time placing is not really the same as a single chemical subunit, ok. So, the chemical; there might be many many chemical subunits over here. I come, I put many of them into one big unit and that is my monomer unit for constructing this freely jointed chain, ok. What do I mean formally?

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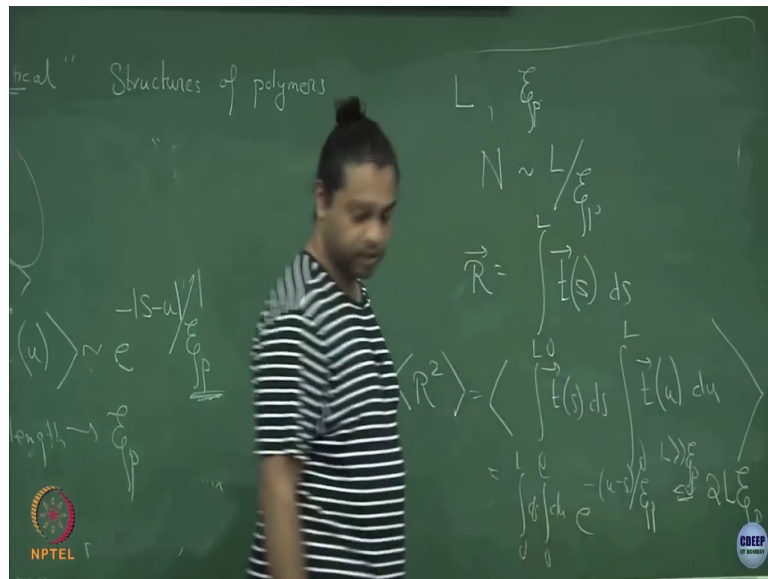
What I mean is that let me take that, ok. So, I have these sort of chemical compounds and so on which maybe you want to maintain a certain sort of an angle between them, ok. So, let me denote each of this by let say the tangent vector t_i , ok, the tangent vector t_i . So, generally when I am looking peering at the molecular scale that the level of these bond with these individual monomeric units there will be some sort of correlation simply because of the chemistry and the bond structure right.

So, there will be some correlations between let us say t_i and t_{i+1} , right. But as I move further and further away, I would expect these correlations to sort of decay, right, and the way it generally decays is that if I write around the tangent vector at some location s and the tangent vector at some other location let us see u , and I take an average over conformations over possible conformations it generally decays as some e to the power of minus the distance between these s minus u by some sort of a persistence length.

So, this ξ_P is called the persistence length. So, this is the length over which you retain memory of these molecular conformations of these chemical bonds of your polymer. So, if I construct my monomers my coarse grained monomers in some sense to have a length scale that is of the order of these ξ_P , then I can say that these coarse grained monomers no longer retain a memory from one monomer to the next. So, once I have replaced this; so, let say that this is my ξ_P . So, over here I obtain some memories of what this previous bond conformations were, if I put all of this into one big monomer then the next monomer I can place in an arbitrary way, so in this equivalent description this would be a freely jointed chain, ok.

So, you would have to construct blobs to go from a real polymer into this sort of a freely jointed picture or this random walks sort of a picture, you must construct blobs which are off the order of this persistence length, of the order of this persistence length this is my ξ_P . And we can calculate what this ξ_P is, actually in terms of this step length a .

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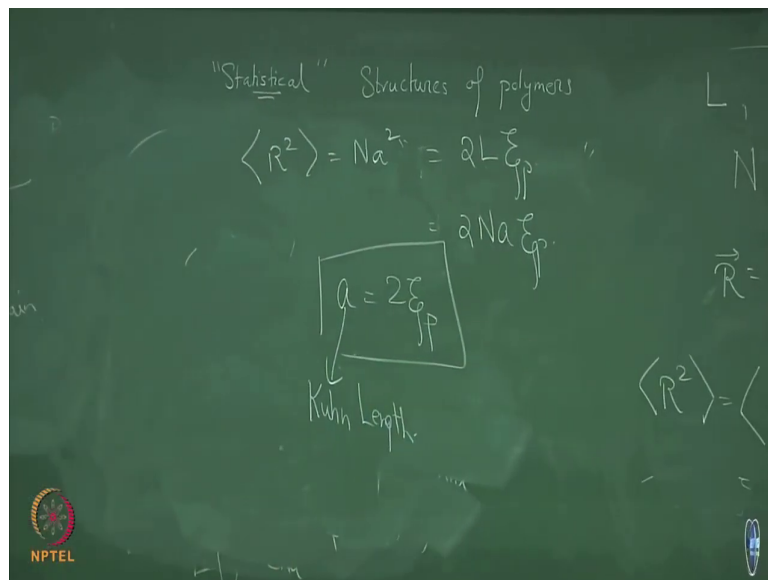
So, let say I have a chain of length L this is the actual length of my polymer, and this chain is characterized by some sort of a persistence length ξ_P , ok. What that means, is that I will model this chain if I wanted to model in this sort of a random walk since, I will model it using some N coarse grained monomers where this N will be of the order of L over ξ_P , right, each ξ_P length object is going to form one of these coarse grained monomers. I will have these many of these effective monomers in my chain, ok.

So, let me try to calculate for example what this end to end distance is. So, remember my end to end vector I can write down as in terms of the tangent vector for example, the tangent vector at the location S and I integrate over ds from 0 to L , L being the contour length of the polymer. And then if I want to do R^2 , R^2 of this average squared, average of the

N to N vector then what I will have is this 0 to L t of s, d s and then another t, so let me say t of u du 0 to L, ok

So, this is like two 0, two integrals 0 to L d s du, d s du average of t s dot t u, right. And I have a sort of hypothesis for how this average correlation decays, it decays as e to the exponential e to the power of minus s by u by xi P. So, let me just put that over here minus minus s by xi P, ok. You can now do this integration and what you should be able to show is that given this the end to end this R square average comes out as of the order of, let me not write exactly 2 L times xi P. Again, in this is again in the limit that l is very large compared to xi P, ok. So, this is again in the limit that L is much much larger than xi P.

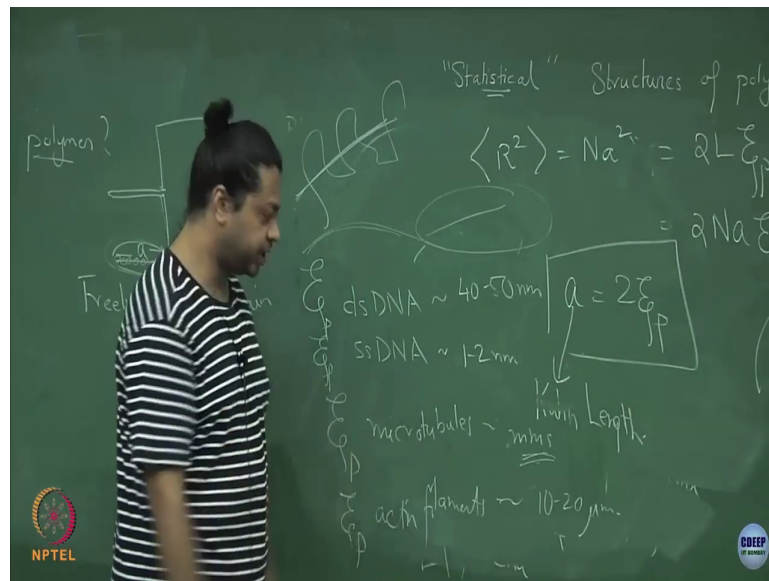
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And I know that if I have N segments, N segments of a freely jointed chain then this R square average is just N a square, this R square average is just N a square and it is equal to from here

$2L$ times the persistence length. L is nothing but, L is what? L is $N a$; $N a$ times ξ_P which means that a is simply nothing but $2 \xi_P$. This a , the size of each of these effective monomers is what is called in polymers is the Kuhn length, as the Kuhn length and this ξ_P is the persistence length. So, you can write down your end to end distance in terms simply of this persistence length of the polymer and the total contour length $2L \xi_P$.

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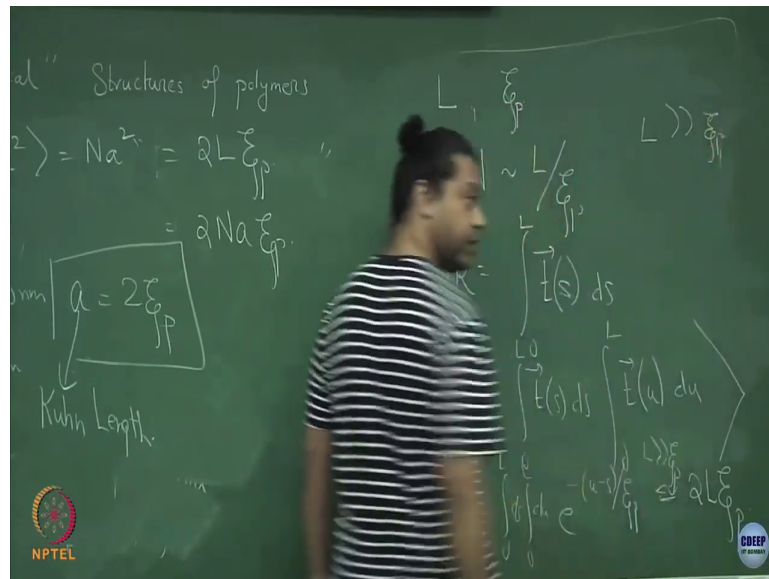
What does this persistence length say? Remember the persistence length is the length over which tangent correlations decay, right. So, the length scale over which you sort of lose memory of the structure, so the larger this ξ , in some sense larger this ξ_P the persistence length in some sense stiffer your polymer is the larger the length over which it retains memory, right. So, for example, if you think of DNA, let say if you think of double stranded DNA versus single stranded DNA which would you expect to have a larger persistence length?

Student: Double.

Double stranded, right because it has these additional bonds for on the (Refer Time: 22:35) strand. And if people have calculated or will have measured rather from experiments what are the persistence lengths of these, so ξ_P of this double stranded DNA is roughly around 40 to 50 nanometers, whereas, ξ_P of this single stranded DNA you remember correctly is around 1 to 2 nanometers, ok. What is it again? What do these numbers mean?

It means that if you take a DNA strand which is let us say I do not know a 1000 nanometers long then you could very well treated by this equivalent freely jointed chain model, the large scale properties would be given by whatever the freely jointed chain model predicts. However, if your total length of your DNA strand was itself of the order of this persistence length, if it was 50 nanometers or 100 nanometers then whatever this theory says is no longer going to be valid, right. Because I am going to be violating that condition that this L is much much larger than this ξ_P .

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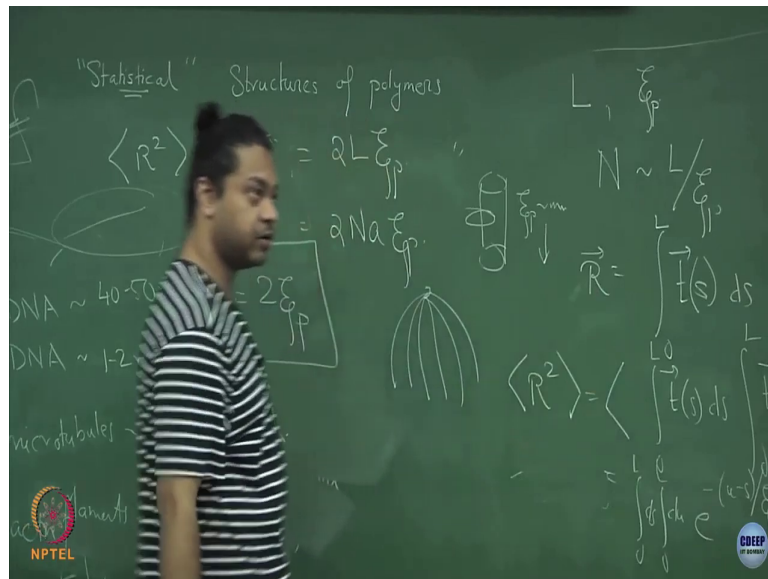
In fact, if you look, let say if you look at a DNA which is 20 nanometers that would roughly look like a stiff rod right, because it is much smaller than the persistence length over there you have this tangent, the tangent correlations are pretty strong, so it would not at all look something very floppy. It would look like some stiff rod.

So, the sort of theory that you would use to describe a polymer a real biological polymer or any real polymer would sort of depend on what is the persistence length of that polymer, and that depends on the chemical structure. Once you know that that, the whole amount, the whole information of the chemical structure at least from this perspective is encoded in the persistence length, once you know that you can decide what sort of a theory is appropriate to describe the polymer in that length, ok. Just because I am writing down let me write down a few more persistence lengths.

Let us say what is the persistence length of these microtubules that we saw: what is the persistence length of microtubules as opposed to what is let say the micro persistence length of actin filaments. Remember, microtubules and actin filaments for the cytoskeletal filaments inside the cell. So, the persistence length of actin filaments is of again these are all rough numbers, is I would say around 10 to 20 microns some millimeters. So, microtubules are actually very stiff, it is difficult to bend them whereas, actins are; so, if your cell is of the order of some 10 microns or 30 microns or something like that you would expect to see actin filaments which are bent, on the other hand you would expect to see microtubules which are fairly straight, right because this the persistence length is much higher than the length of the cell itself.

Now, that is slightly misleading, because often if you look at these pictures of microtubules let us even in the spindles and so on, you know when the cell is dividing and these microtubules come out you will often see this microtubules are bent or even if you look at the cytoskeleton structure often you will see that the microtubules are bent.

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So, all of these persistence lengths you have to understand, that often when people quote these persistence lengths, these are persistence lengths of pure objects, so pure microtubule would have persistence length of the order of millimeters let us say. On the other hand, the properties of these of these polymers can be modified drastically by whatever proteins come and say, come and attach to these polymers.

So, if you have some microtubule which is which has a persistence length of the order of millimeters maybe you have some proteins coming and binding which can drastically change this persistence length and bring it down to the order of maybe 10s, 10s or 100s of micrometers. So, it can reduce the persistence length by 1 to 2 orders of magnitude.

Still, so you should always keep that caveat in mind that these numbers that one quotes are of these pure polymers, but biologically you can often modify these properties by interactions

with different proteins or with different components of the cell. So, if this numbers explain what you are trying to see well and good, if not you should keep in mind that these numbers themselves are sort of subject to change depending on what environment it lies in.