Biomathematics

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Lecture No. #36
Statistical Thermodynamics of Biological Systems Part – III

Hello, welcome to this lecture on biomathematics. Today, we will discuss and compute certain quantities for DNA, and understand how do we apply statistical thermodynamics ideas from thermodynamics to understand various properties of DNA. So, today we are again continuing the same theme, that we have been discussing same module that we have been discussing basically in statistical thermodynamics of biological systems. And what we will be computing at the beginning is partition function for Double stranded DNA.

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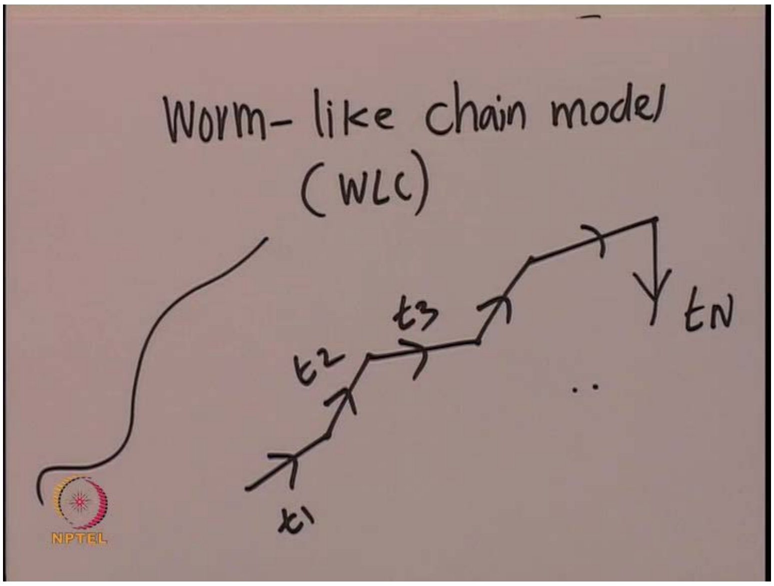

So, there is, this model for DNA known as worm like chain module, and so this is worm-like chain module let me write it here, worm-like chain model, in short this is known as WLC. This model is DNA is thought of as a line inaccessible line with a bending energy, the only energy is bending energy, and the discrete version of this is thinking of DNA as a set of vectors. So, this is tangent vectors t 1, t 2, t 3, and so on, and so forth, there will be some similar N tangent vectors.

So, up to there will be like t N, there will be N tangent vectors and this orientation of this tangent vectors in 3 D will decide the configuration of the DNA. So, now the energy of such a system is given by in a certain certain manner. So, but just before that orientation of this in 3 D, whatever way this is tangent vector orients will decide the orientation of the DNA and one of the properties that the DNA would not like to bend, there is an energy cost to bend the DNA to make a loop out of D N A, there is a cost of you have to spend some energy.

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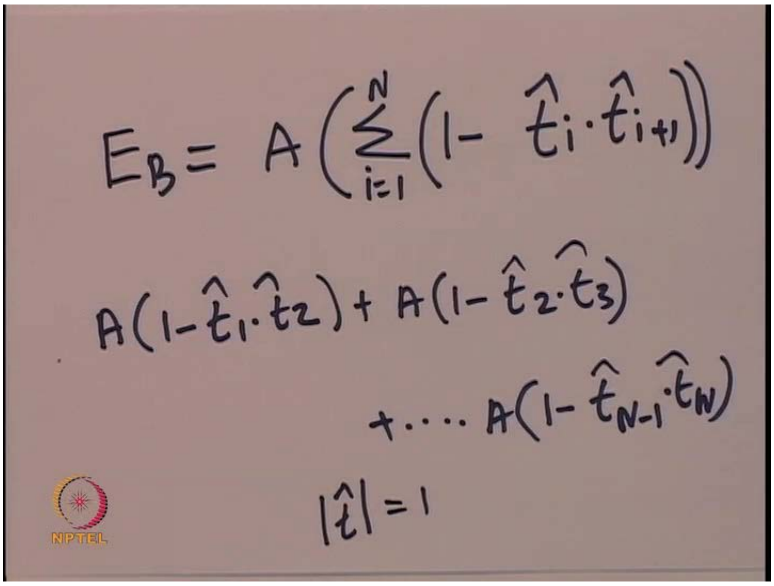

$$E_B = A\left(\sum_{i=1}^{N}\left(1-\hat{t}_i\cdot\hat{t}_{i+1}\right)\right)$$

$$A(1-\hat{t}_1\cdot\hat{t}_2)+A(1-\hat{t}_2\cdot\hat{t}_3)$$

$$+\dots A(1-\hat{t}_{N-1}\cdot\hat{t}_N)$$

$$|\hat{t}|=1$$

And that energy is basically the bending energy which is given by some constant A which is called the bending stiffness times, sum over all tangent vectors, i is equal to 1 to N, there are N tangent vectors, 1 minus t i dot t i plus 1. So, this is basically the this is basically the bending energy of a D N A, sum over i 11 minus t i dot t i plus 1. So, if you, if there are three of if this if this DNA of like three base pair, this will be, A into 1 minus t 1 dot t 2 plus A into 1 minus t 2 dot t 3, there are three tangent vectors only then this will look like this, t 1,t 2 and t 3 then if there are many, there will be plus dot dot dot A into 1 minus t N minus 1 dot t N.

So, this is the energy, the bending energy, this is the only interaction here is the bending interaction and this is the bending energy of a double stranded DNA which has N tangent vectors and each of this unit vectors and the mode the the each of this unit, this has a particular, so, more t is 1; that means, we take all this vectors unit vectors. So, now given this, we want to calculate the partition function and we said that the partition function is basically sum over all states.

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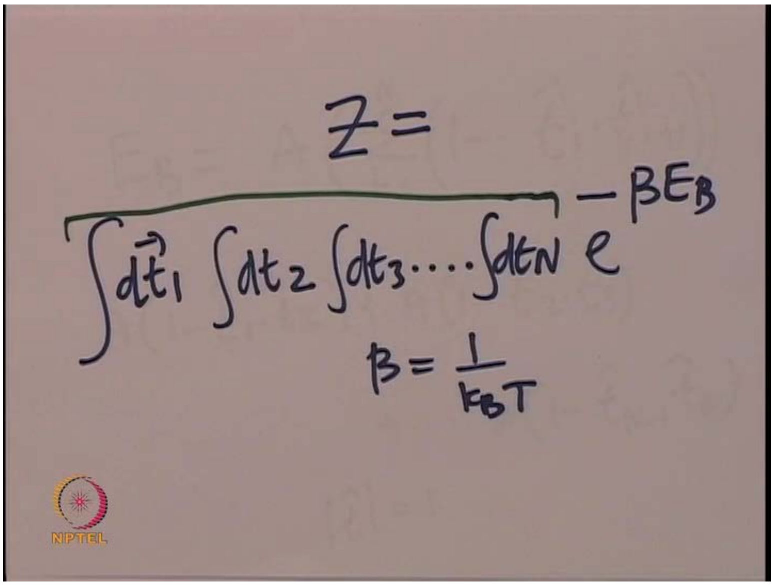

$$Z = \overline{\int d\vec{t}_1 \int dt_2 \int dt_3 \cdots \int dt_N}\, e^{-\beta E_B}$$

$$\beta = \frac{1}{k_B T}$$

So, that means, you integrate over all possible d t 1, the first tangent vector can take any orientation. So, this is vector in 3 D. So, it can take all orientation in 3 D, it can it if you if you have this vector and this vector, the first vector t1 can orient in any way, this t 2 is fixed this particular way and t 1, the green 1 can orient any way, you want. So, d integral d t 1 means, you sum over all these orientations and integral second one, integral d t 2, integral d t 3 and so on and so forth, integral d t N e power minus beta E B where beta is 1 over K B T

So, this is the partition function so, this is the partition function z for the double stranded DNA which is an energy E B and this partition function is given by this formula, integral d t 1, this this means sum over all possible confirmations e power minus beta E.

So, this this this integrals here, mean that sum over all possible confirmations, first tangent can have all angle, all orientations; second tangent can have all orientations; third tangent can have all orientations and end second tangent have all orientations.

So, each base pair, you can you can imagine, each tangent as each base pair. So, each base pair can orient in any way or this can be thought of as in general, if you can imagine, DNA as a polymer, each monomer can orient in any direction and this into sum over all this will give you, the partition function. Now, we said that, what is d t 1, d t1 is you can think d t 1 as a vector in 3 D. So, the basically d t 1 can have any orientation means, if you imagine one reference point, reference line as for example, if you take X axis and y axis, the vector which you are interested in can take any angle.

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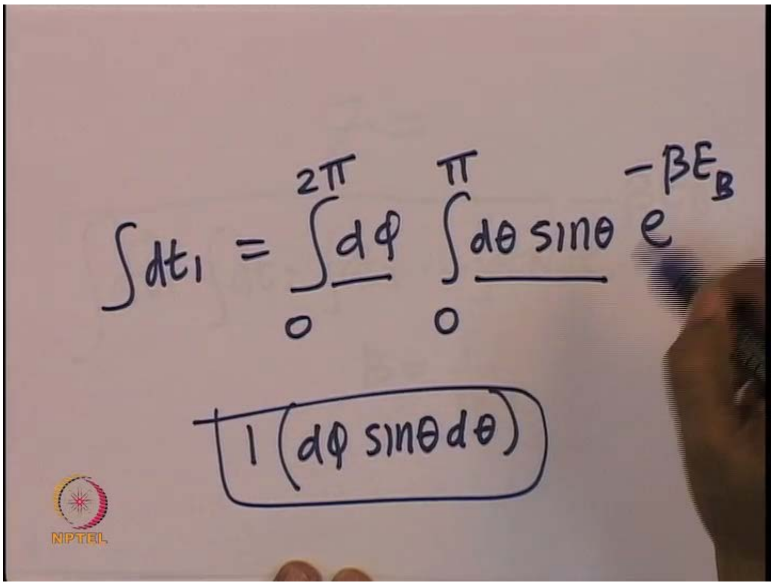

$$\int dt_1 = \int_0^{2\pi} \underline{d\phi} \int_0^{\pi} \underline{d\theta \sin\theta} \, e^{-\beta E_B}$$

$$\boxed{1 \, (d\phi \sin\theta d\theta)}$$

So, this can be described by set a of angles, theta and phi, just like we know from spherical polar coordinates and since the length of the tangent vectors is a constant, this d t 1 is nothing, but integral angle from 0 to 2 pi and integral over theta from 0 to pi. So, this is the integral and the this will have sorry there will be sin theta here. So, this is sin theta d theta sin theta e power minus beta E.

So, as you might know, that the volume element in spherical polar coordinates is basically, d phi sin theta d theta with so, the only angle change happens only phi angle can change, theta angle can change in this particular manner, given that the length is constant and unit vector 1, this will be the and length does not change, this will be the volume element, so, that is why, this integral is d phi and sin theta d theta. Now, sin theta d theta can be written as d of Cos theta sin theta d theta can be written as d of Cos theta.

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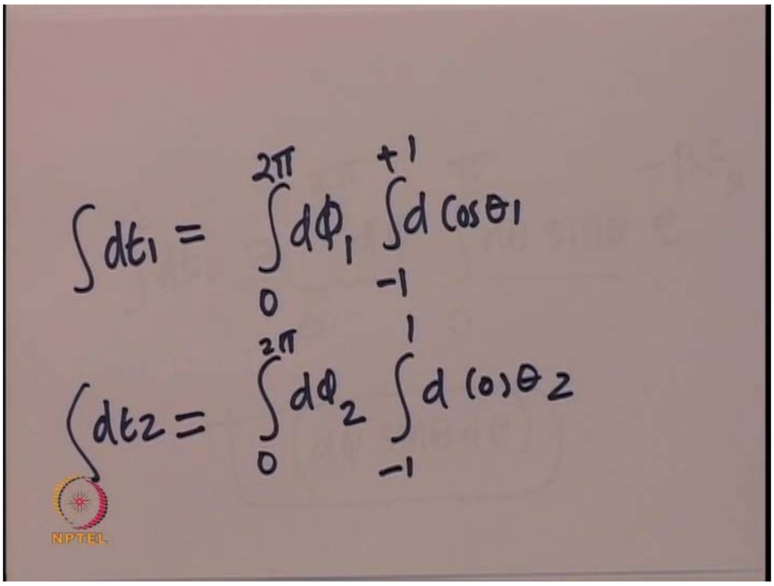

$$\int dt_1 = \int_0^{2\pi} d\phi_1 \int_{-1}^{+1} d\cos\theta_1$$

$$\int dt_2 = \int_0^{2\pi} d\phi_2 \int_{-1}^{1} d\cos\theta_2$$

So, you can write this as d of Cos theta and then accordingly change the limits and this d t 1, if you do that, you will get that integral d t 1 can be written as integral d phi. So, since there is d t 1 lets lets also call this d phi 1, the first phi angle d Cos theta 1. So, this will be 0 to 2 pi and this will be minus 1 to plus 1, if you change the limit appropriately, you will get that, this is from minus 1 to plus 1. So, and then you have similarly, you have 0 to 2 pi d phi 2. So, this is d t 2, you can write integral d t 2 as d phi 2 minus 1 to plus 1 d Cos theta 2. So, if you know d t 1, d t 2 like this, you can write everything like this.

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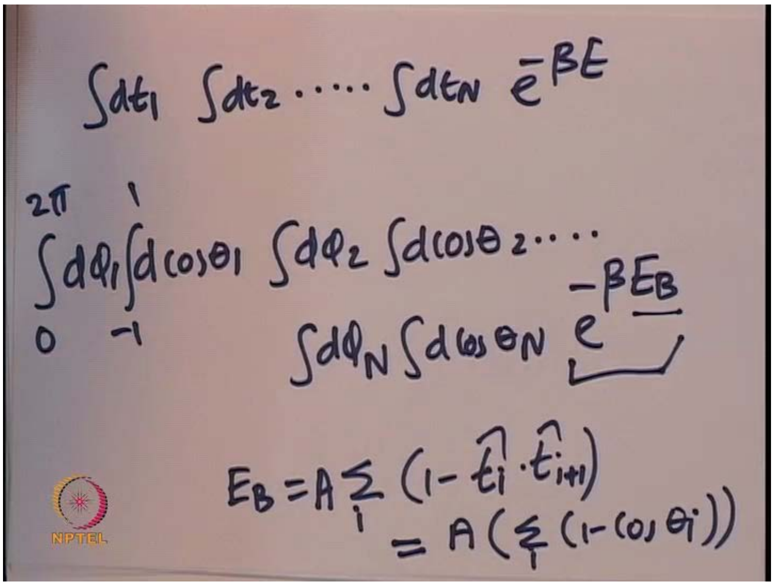

$$\int dt_1 \int dt_2 \cdots\cdots \int dt_N \, e^{-\beta E}$$

$$\int_0^{2\pi} d\phi_1 \int_{-1}^{1} d\cos\theta_1 \int d\phi_2 \int d\cos\theta_2 \cdots\cdots \int d\phi_N \int d\cos\theta_N \, \underbrace{e^{-\beta E_B}}$$

$$E_B = A \sum_i (1 - \hat{t}_i \cdot \hat{t}_{i+1})$$
$$= A\left(\sum_i (1 - \cos\theta_i)\right)$$

So, essentially, the partition function will turn out to be, so, partition function essentially is integral d t 1 integral d t 2 and so on and so forth, integral d t N e power minus beta E or this is the bending energy and this can be written as integral d phi 1, integral d Cos theta 1, integral d phi 2, integral d Cos theta 2, dot dot dot integral d phi N, integral d Cos theta N e power minus beta E B, this is the bending energy. Now, all these limits are same, here, this limit is 0 to 2 pi, here, it is minus 1 to 1.

So, now what is E B, E B is sum over i, some constant A times 1 minus t i dot t i plus 1, t i dot t i plus 1 can be written as a Cos theta because this is two unit vectors and the product is Cos theta and the magnitude is 1, each has been unit magnitude 1. So, this is just nothing but, 1 minus Cos theta. So, you can write this, 1 minus Cos theta here. So, this E B depends only on Cos theta. So, this is nothing, but A into sum over i 1 minus Cos theta. So, this depends only on Cos theta. So, the whole integral does not depend on phi at all. So, because this this this function does not depend on phi at all only theta it depends. So, we can take out all the phi integrals out and you can do all the phi integral.

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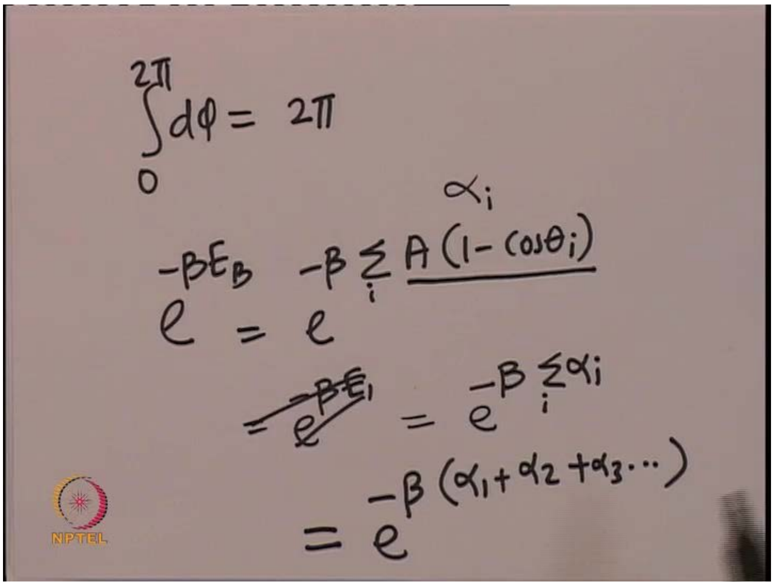

$$\int_0^{2\pi} d\phi = 2\pi$$

$$e^{-\beta E_B} = e^{-\beta \sum_i \overset{\alpha_i}{\underline{A(1-\cos\theta_i)}}}$$

$$\cancel{= e^{-\beta E_1}} = e^{-\beta \sum_i \alpha_i}$$

$$= e^{-\beta(\alpha_1+\alpha_2+\alpha_3\cdots)}$$

So, integral 0 to 2 pi, d phi is just 2 pi. So, we can do this and if you rewrite this, you can see that e power minus beta E bending energy can be written as e power minus beta sum over i A times 1 minus Cos theta i. Now, if you take this sum. So, this is basically e power minus beta E 1. So, if you if you call this this part A into 1 minus Cos theta as alpha i, A into 1 minus Cos theta i let us call it as alpha i. So, this is basically, this is nothing, but e power minus beta sum over i alpha i. So, this is nothing but, e power minus beta into alpha 1 plus alpha 2 plus alpha 3 dot dot dot. So, e power anything sum can be written as product. So, e power minus beta alpha 1 plus alpha 2 plus alpha 3 etcetera can be written as the product of this.

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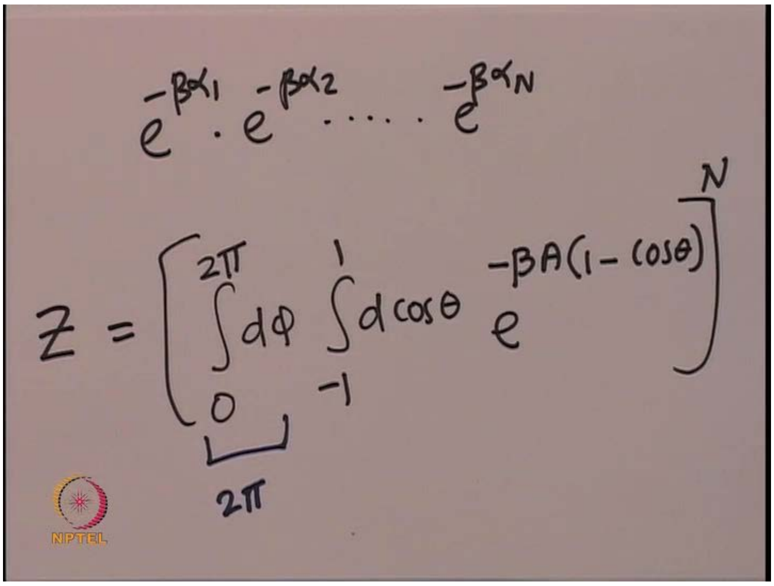

$$e^{-\beta\alpha_1} \cdot e^{-\beta\alpha_2} \cdots\cdots e^{-\beta\alpha_N}$$

$$Z = \left[\underbrace{\int_0^{2\pi} d\phi}_{2\pi} \int_{-1}^{1} d\cos\theta \; e^{-\beta A(1-\cos\theta)}\right]^N$$

So, if you rewrite this, you will get e power minus beta alpha 1 dot e power minus beta alpha 2 dot dot dot. So, this is the sum can be written as so, this sum can be written as a product of alpha N. So, essentially, the partition function can be written as, so, this is a product of N such terms. So, it turns out that, you can think about it and you will see that, the partition function is essentially integral d phi, integral d Cos theta, d phi goes from 0 to 2 pi, d Cos theta going limit minus 1 to plus 1 e power minus beta A into 1 minus Cos theta whole power N.

So, there are N such terms and this the product of N such terms and that will give you the partition function. So, if you take calculate just this two integrals and find the product of this N times, you will get the partition function for a double stranded DNA So, this is very easy to do, this is 2 pi as we know and we can easily calculate this integral. So, here itself e power minus beta, this A term will come out. So, that e power minus beta A into 1, this term will come out and we can call Cos theta as x, let us call Cos theta as x. So, if we rewrite this a bit, what do we get, let us let us quickly rewrite this. If you rewrite whatever is seen here, what do we get.

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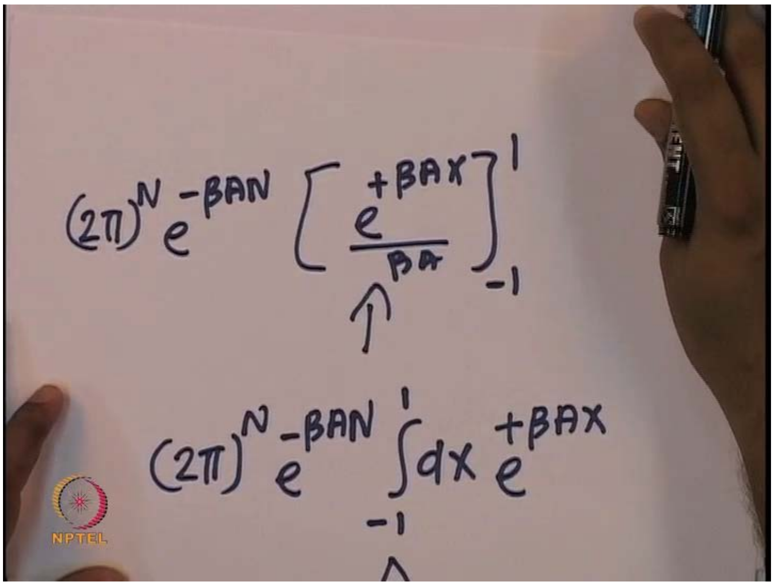

So, let us rewrite these terms. If we rewrite this, this is basically 2 pi. So, there will be 2 pi power N because integral 0 to pi, this is 2 pi. So, and there is N whole power N. So, there is 2 pi power N and there is e power minus beta A N times. So, there is e power minus beta A N times So, this is e power minus beta A N times and then there is, this integral a Cos theta, let me call this s minus 1 to 1 d Cos theta as d X and there is e power minus beta A into minus Cos theta, this minus minus becomes plus. So, this e power minus minus becomes plus beta A X.

So, this is the integral, we we have to do, integral d X minus 1 to 1, e power beta ax, this is easy to do. So, this is basically, 2 pi whole power N, e power minus beta A N and this is integral of e power beta A X d X is basically, e power beta A X divided by beta A in the limits minus 1 to 1.So, if you apply the limits, this will become minus and minus. So, sorry this is plus here. So, you can apply the limits. So, if you apply the limits, it will be e power beta A minus e power minus beta A. So, let let us apply this limit properly. So, if you apply the limits what do we get.

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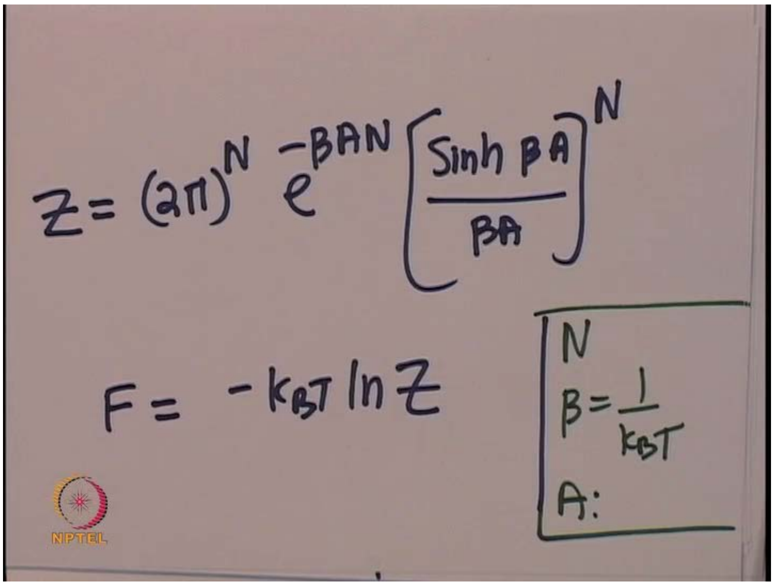

$$Z = (2\pi)^N e^{-\beta A N} \left[\frac{\sinh \beta A}{\beta A} \right]^N$$

$$F = -k_BT \ln Z$$

N

$\beta = \frac{1}{k_BT}$

$A:$

So, if if we do this and apply the limits, what you will end up getting is basically, the partition function, you will get as 2 pi whole power N, e power minus beta A N. you will get sin hyperbolic beta A divided by beta A whole power N. So, this is the partition function you will get and log of z minus K T log z will give you the free energy. So, the free energy of a double stranded D N A, F is minus K B T log z. So, from this, we can calculate the partition function and the free energy.

Now, this is the answer to parti this is where the partition function for a double stranded DNA is 2 pi power N e power minus beta A N sin hyperbolic beta A by beta A whole power N. So, it depends on the this is quality called A, which is the bending stiffness of the D N A, it depends on K B beta, beta is basically 1 over K B T . So, depends on the temperature. So, it only depends on two thing three things, it depends on three parameters.

So, let us note this parameter, it depends on this N, it depends on beta which is 1 over K B T which is temperature, it depends on A, which is the bending stiffness. So, there are three parameters, the property of the DNA will depend on three parameters, how many monomers are there, how many based pairs are there, N is the basically the length, related to the length of the D N A, it depends on the temperature of course, it depends on A which is a bending stiffness.

So, all property, free energy will give you all property of the D N A, you can derive all the properties of the DNA from free energy and we will see some examples immediately, we will discuss for even simpler case of single stranded DNA we will discuss, what is the, how do we get free energy and from free energy, how do we get various measurable quantities, but at this moment, what we learn is, how to calculate free energy and immediately we will learn, how to get measurable quantities from the free energy. So, before, so, this is what we discuss now is, how do we get free energy and partition function and free energy for double stranded DNA .

Now, what we are going to learn is, how do we get something useful from this, what is the use of knowing free energy, what is the use of knowing partition function, the answer is, we can get all measurable statistical quantities from this. So, let us think of very simple example first and then we will go to the case of DNA again and then we will do a calculation and see that something, which you did not know till now, can be estimated, can be calculated, sitting here by knowing what we learnt so far.

Very simple idea, if you know, how to calculate partition function and free energy, we can calculate the few things, that we did not know so far, related to DNA for example, here and any other system that you can think of. Now, let us think of first a simple spring like protein which is our favorite example for describing or discussing any statistical statistical thermodynamics idea because this the, if we imagine a protein like a spring will help us thinking ahead and then will help us to simplify a lot of things and have the basic have the have the important idea seen in the examples.

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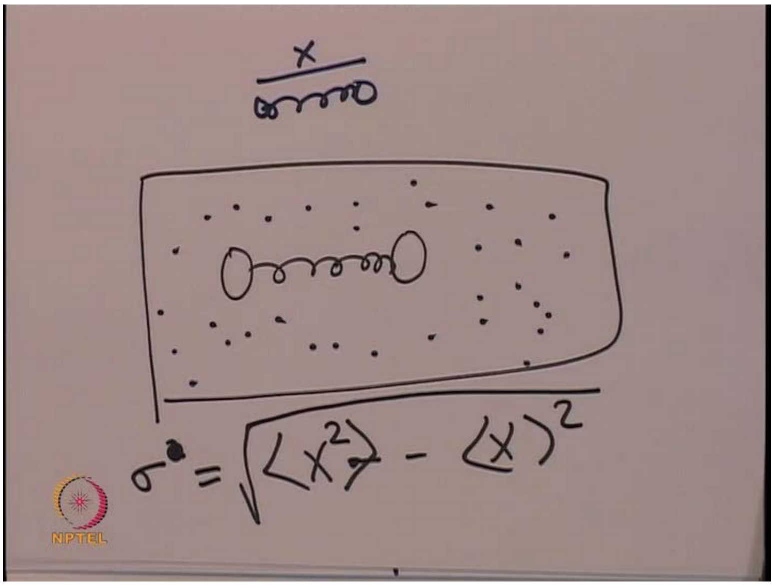

So, let us think of two atoms character by spring, just like we have been thinking two atoms connected by a spring like interaction and this is in water. So, this is water here. So, as we said, since the due to the Brownian motion, this spring will be extended and compressed. So, this atoms will be doing this molecules will be doing Brownian motion. So, if you imagine, they will be just doing this vibrating like this because they will be hit by Brownian water molecules doing Brownian motion. So, essentially this atoms will be doing vibrating like this.

Now, you can ask the question, what is the distance between this two root means square distance between this two, like will it be how much it will fluctuate, how much this distance will fluctuate, this answer, this is given by this quantity which is basically, you know this X square average minus X average square, this quantity is called the sigma square which is basically, the stand sigma which is a sigma square is a variance and sigma is the square root of this is the standard deviation.

So, this will give your X, if X is the distance. So, X is basically, this distance from here to here. This distance is X and if you calculate X square average minus X average square, this will tell you how much this protein will fluctuate. So, how do we compute this from partition function ,we can compute this and that will tell us, how much this will fluctuate and what will be the position of this atoms on an average, we we will be able to calculate. So, let us take. So, what is the energy of a spring? So, the typical the energy of a spring is basically, half K X square.

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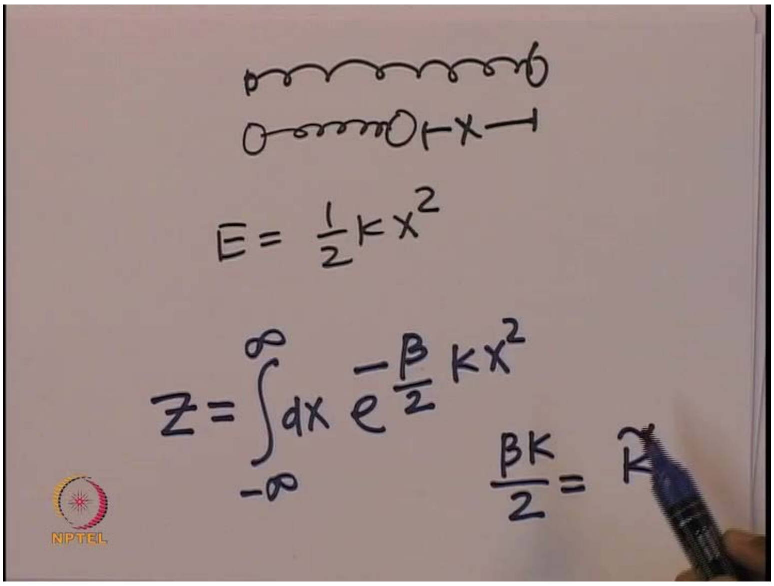

$$E = \frac{1}{2} K X^2$$

$$Z = \int_{-\infty}^{\infty} dX \, e^{-\frac{\beta}{2} K X^2}$$

$$\frac{\beta K}{2} = \tilde{K}$$

So, energy of a spring like (( )). So, if you have a spring like this, the energy we know is half K X square, X is basically the distance from, so, let here, let us take X as basically some. So, let let us call this, X is basically the distance from equilibrium. So, at equilibrium let us say let us say, if you have the such spring, this can get stretched then this distance, we can call it X here. So, then how if it stretch by distance of X then the energy is half K X square, even if it is compressed by a distance of X, the energy is half K X square, if you compress the spring by an amount X, this energy is half K X square.

So, now what will be the partition function, the partition function will be z, will be e power minus beta which is 1 over K B T half K X square, this is e power minus beta E and all possible X. So, the X can go have all possible values, so, integral over X. Let me take minus infinity to infinity that means, I can take this coil, this spring from all way, all the way from minus infinity to the infinity throughout this. So, this way, if you if you do this integral, the answer of this will give you the partition function.

So, we will have a look at this once more. So, the partition function for a spring doing Brownian motion, the fluctuating spring will be d X e power minus beta by 2 K X square. So, this will be the partition function and if you calculate this, from this, you can calculate free energy and from that, we can calculate various useful qualities. So, let us think about this a minute. Now, let us let us do this calculations.

So, if you think about this this is an something some, so, beta is a constant, K is the constant. So, this beta K by 2, I can call this. So, let me call this, beta K by 2 as some new notation, let me call this K tilde. So, K tilde is basically, beta K by 2. So, this is e power minus K tilde X square. So, this is like Gaussian integral. So, this is like Gaussian function, e power minus some constant into X square. So, integral of a Gaussian function we know.

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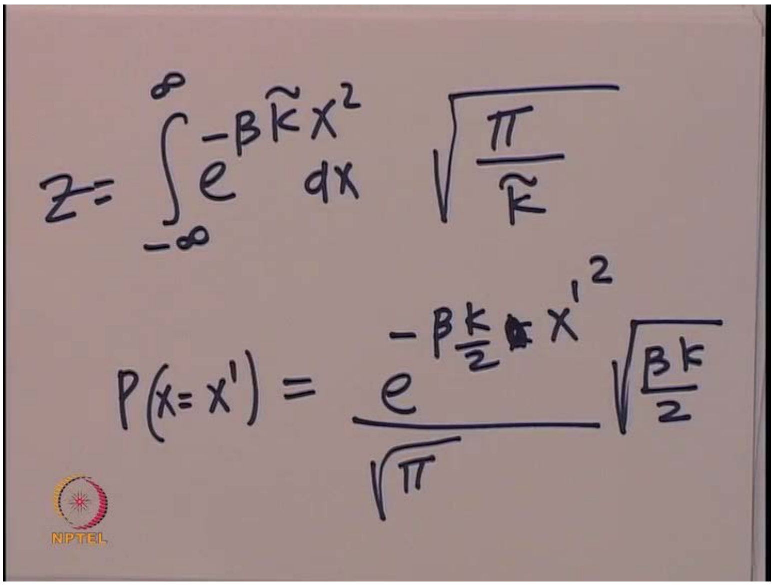

$$Z = \int_{-\infty}^{\infty} e^{-\beta \tilde{K} x^2} dx \qquad \sqrt{\frac{\pi}{\tilde{K}}}$$

$$P(x = x') = \frac{e^{-\beta \frac{k}{2} x'^2}}{\sqrt{\pi}} \sqrt{\frac{\beta k}{2}}$$

So, let us say that, integral of the Gaussian function, integral e power minus beta K tilde X square minus infinity to infinity d X is our and this answer is root of pi by K tilde. So, this is the answer, if such an integral, this is called a Gaussian function and this is the function which looks like normal distribution something something we discussed. So, this answer integral of this from minus infinity infinity root of this. So, this is this is basically the answer.

Now, you can ask the question, what is the probability of finding the spring at particular distance X equal to let us say, twenty unit or you can ask, what is the probability to find the DNA at a distance 35 units and the answer will be this. So, the probability of finding the spring when X is equal to let us say X is equal to X prime, X prime is some number, some some particular value which could be two nanometer, three nanometer, five nanometer. So, this is, e power minus beta half K X is equal to X prime square divided by root of pi by root of K tilde, root of K tilde 1 over K tilde, I can write us root here and K tilde, we wrote as beta K by 2.

So, this will be the , what is the probability of finding the spring at a distance, if you put substitute X X prime is equal to three nanometer and the appropriate spring constant is beta K by 2 X prime X square, there is no extra K here. So, this is energy and if you substitute X prime K and beta appropriately, you will get the probability. So, from this, we can get the probability. Now, you can ask the question, if you know the probability, we can calculate X square average.

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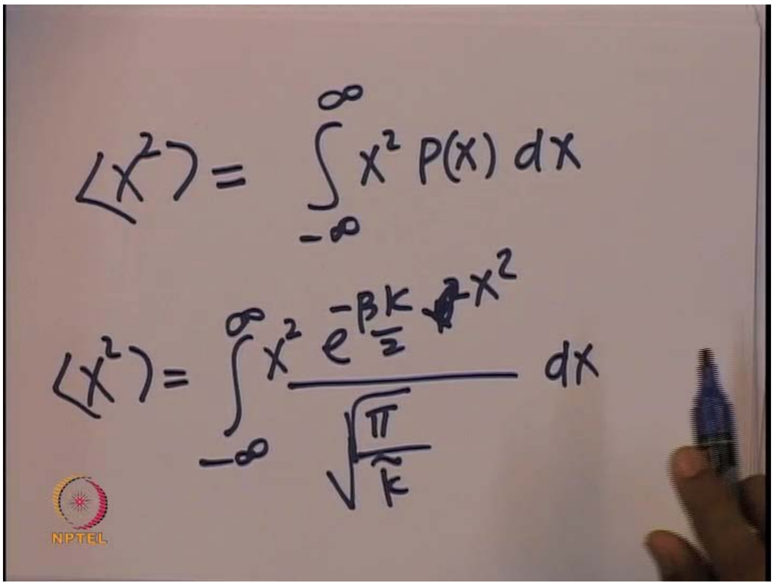

$$\langle x^2 \rangle = \int_{-\infty}^{\infty} x^2 P(x)\, dx$$

$$\langle x^2 \rangle = \int_{-\infty}^{\infty} x^2 \frac{e^{-\frac{\beta K}{2} \cancel{2} x^2}}{\sqrt{\frac{\pi}{\tilde{K}}}}\, dx$$

We said that the definition of the X square average always is basically, X square average is defined as integral X square p of X d X minus infinity to infinity, this is X square average. So, let us calculate X square average, X square average is equal to minus infinity to infinity, p of X will be e power X minus beta K by 2 into X K by 2 into X square divided by root of pi by root of pi by K tilde. So, now here, you have you have root of pi by K tilde and you have to multiply with X square and integrate over this. So, again let us call this part as K tilde beta K by 2. So, this integral will turn out to be, if we do this correctly, what do what it is a very simple integral.

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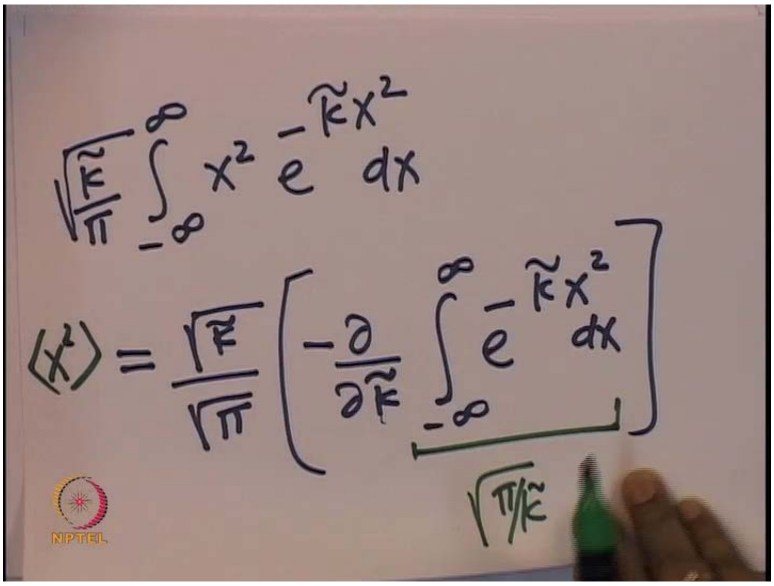

$$\sqrt{\frac{\tilde{K}}{\pi}}\int_{-\infty}^{\infty} x^2 e^{-\tilde{K}x^2}\,dx$$

$$\langle x^2\rangle = \frac{\sqrt{\tilde{K}}}{\sqrt{\pi}}\left(-\frac{\partial}{\partial\tilde{K}}\underbrace{\int_{-\infty}^{\infty} e^{-\tilde{K}x^2}\,dx}_{\sqrt{\pi/\tilde{K}}}\right]$$

So, what do we have, what we have is basically, what do we have here is, integral minus infinity to infinity, that one over z which is root of pi by K tilde will take out. So, this is root of K tilde by pi, X square e power minus K tilde X square, this is the integral d X, this is the integral we have to do. So, it turns out that, there is trick to do this integral, there is an X square here and if you take the derivative of this, with respect to K tilde and put a minus sign, you will get this. So, it turns out that, just see this carefully and try to do this yourself.

So, this is nothing, but is equal to, root of K tilde by root of pi into minus del by del K tilde, you do this yourself after seeing this and see what I am saying is correct or not, del by del K tilde integral minus infinity to infinity e power minus K tilde X square d X, it turns out that, if you dare take derivative with respect to K tilde and X square will come out, that X square is same as this X square. So, you can rewrite this in this particular manner, you can do this carefully.

So, if you do this, you will get this answer and we know that the answer for this, this is again a Gaussian integral. The answer for this is again, root of pi by K tilde, root of pi by K tilde is answer for root of pi divided by K tilde is answer for this. So, once we have this, we can calculate the derivative of this and then get this answer which is basically, this this will give you X square average, this is what we are calculating and X square average is this. So, let us do this slowly. So, this is very simple algebra nothing complicated.

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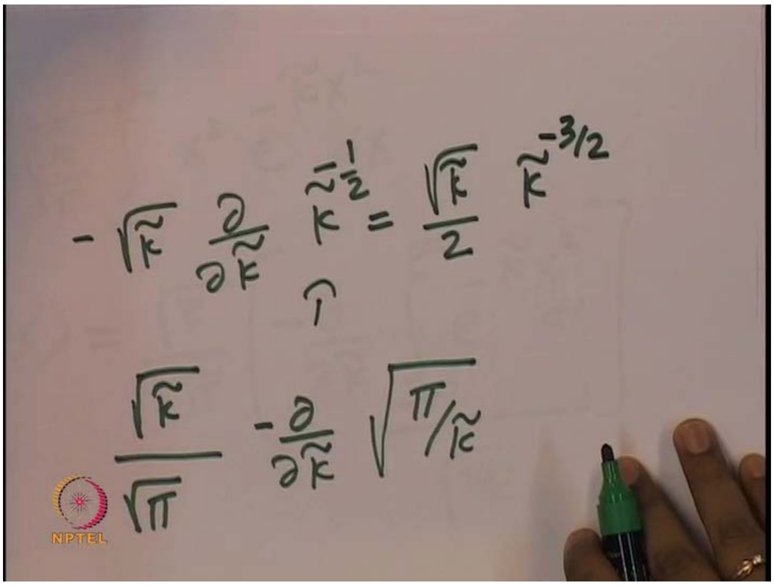

So, if you think about it. So, you have here, root of K tilde by root of pi and this is root of minus del by del K tilde or root of pi by K tilde. So, this is the answer and root pi comes out and what you have is basically, if you do this, root pi and root pi cancels and you what you have is, root of K tilde del by del K tilde into, there is one over root of K tilde which is K tilde power half minus half. So, this will turn out to be and there is a minus sign here, from here. So, this minus half and then so, this this will turn out to be root of K tilde into half, minus half minus 1. So, basically, what you have here is K power minus 3 by 2. So, K power minus half minus 1 which is K tilde power minus 3 by 2.

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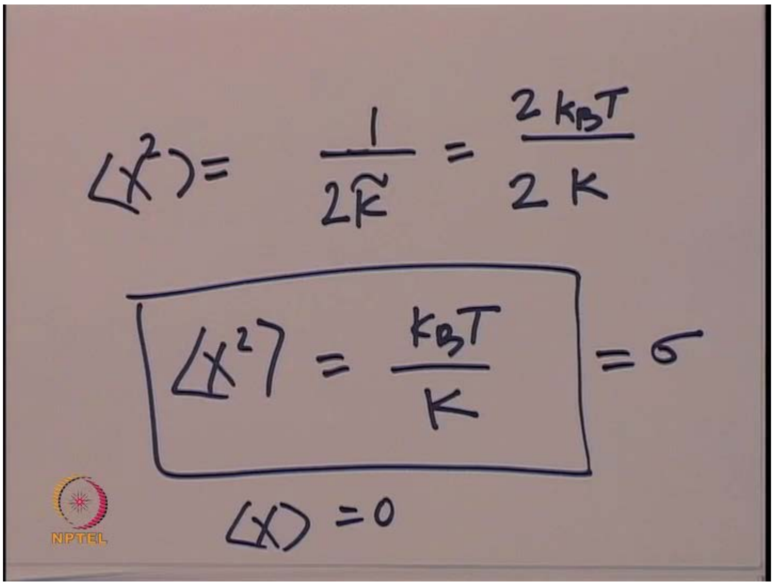

So, basically, this will turn out to be the answer, final answer will turn out to be X square average is equal to 1 over K tilde with the half sign, this is the X square average, what is K tilde, 1 over 2 into K tilde is beta which is 1 over K B T, so, you can take K B T are here and K and there is a by 2. So, half, so, there is a 2 here. So, this 2 and 2 cancels. So, this is basically, K B T by k. So, it turns out, that the X square, the average X square is K B T by K, the more the temperature, the more the X square averages, the less, the more the spring constant, less the X square averages. So, it turns out that, the X average will turn out to be 0, you can see this similar way, X average will turn out to be 0.

So, the standard deviation is nothing, but X square average. So, we have this same thing as standard deviation. So, we have X square average is equal to K B T by k. So, this is something some interesting quantity that we can calculate, how much protein will be fluctuate because the the whole fluctuation is because of the hitting by water and statistical we have to calcu calculate quantities, that is statistically nature like X square average and the sigma the standard deviation, essentially, what we computed here, what the quantity here, K B T by K physically tells you, what is the meaning of this, it means that, if you have a protein in water, it can fluctuate depending on the temperature, it will fluctuate.

So, it is K B T divided by K which is basically the elastic prop, K depends upon the decides the elastic property of this protein. So, if depending upon the elastic property of the protein, we can say that, this K is K this the fluctuation will vary. Now, think of, let us think of, quickly think of a DNA . Now, and let us see, what is what do we mean by such such things, we can calculate for DNA also and let us let us think of a long chain in a water. So, for a minute, let us think of a single stranded DNA .

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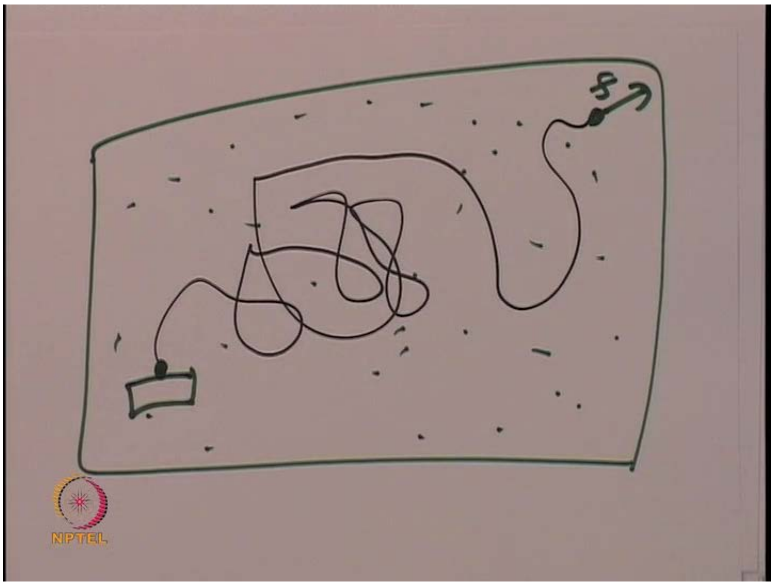

So, so a single stranded D N A, a long DNA can be thought of as d of as a filament like this and this is in water and there is water everywhere (no audio from 36:15 to 36:19), the appropriate buffer and think about this end and this end and imagine that, you are holding this end, you are fixing this end at some particular place and pulling the other end. So, as you pull this, you can imagine that the distance from this end to this end will keep increasing. So, imagine that you are pulling a rope which is like this, slowly, very slowly and if you imagine that you are plotting the distance from one end to the other end, how will the graph look like. So, let us think about this is, how will the graph look like. So, the graph will look like.

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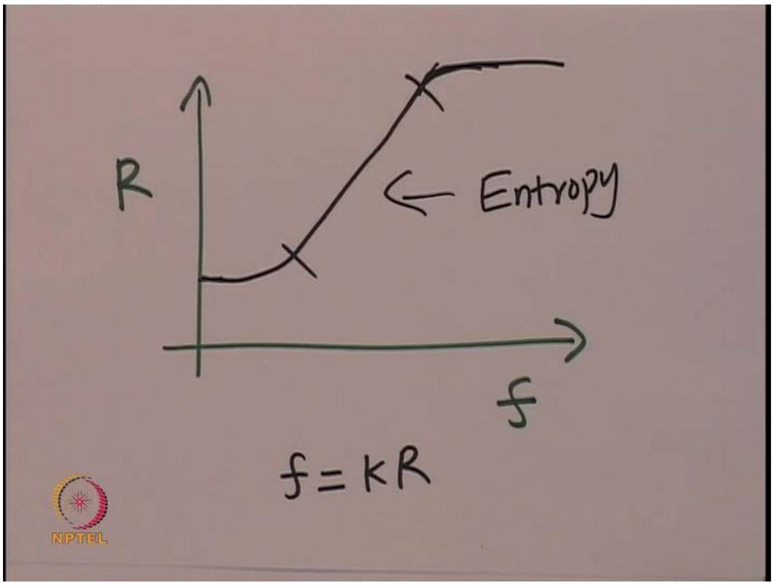

So, let us play say, we are plotting this, the force we apply and pull it and the distance from one end to the other end. So, let me call this R, distance from one end to the other end. So, it turns first, the distance from one end to other end is a constant then it will slowly increase and then finally, it will reach maximum length. So, this is smooth, this is smooth, this is pretty smooth. So, this will like, but look at this particular region, here this is almost like a linear part, in this region between this and this, it appears as if force is proportional to the distance.

So, what is here, is force is equal to some constant times R. So, this constant this this this like a spring, this is like a f is equal to K X, it is like a spring equation. So, in this regime, the DNA behaves or any polymer for that matter would behave like a linear spring, like f is proportional to R, there is a regime where any protein will behave like a linear spring and what is the reason for this, the reason for this essentially think about this a minute, this reason for this is entropy, if you did not have any entropy, if you they are at 0 temperature, the DNA would take the, it would not like to bend.

So, it would like, it would it would take basically a very straight straight filament, it will be like only one configurations, but due to entropy, it can go to various confirmations and this elasticity, this can be also, this is often often called entropic elasticity. Now, imagine that, we are doing this for a single stranded D N A, pulling a single stranded

DNA with some force f and we can calculate, how much this K will be, how much this spring constant will be. So, this is this is just like…

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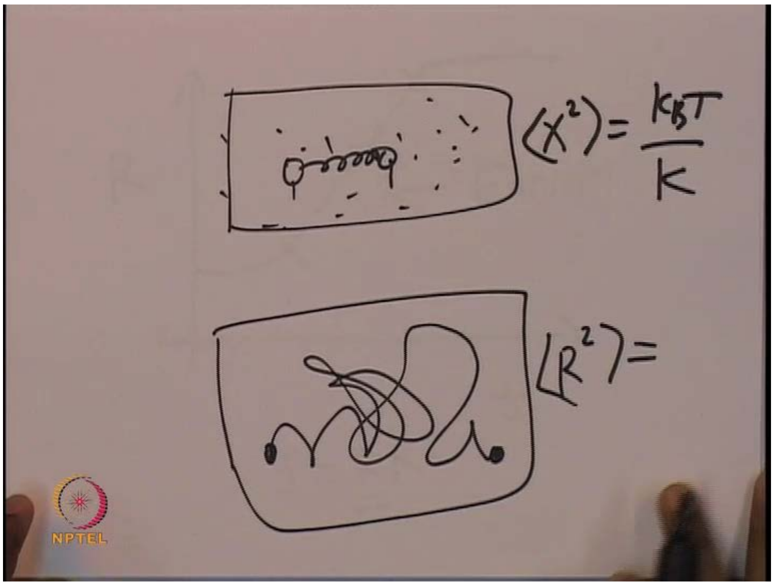

So, imagine that for a moment, this is your just like we discussed an example of spring in water in a exactly like similar way. You can think of a DNA in water, it is a coiled DNA and the distance between this and this end is equivalent to the distance between this end and this end of the DNA. So, if you got here a relation, we said X average square is K B T by K. Similarly, what will be the end to end distance square, what will be the R average square, it turns out that the R square average can be computed in a similar manner.

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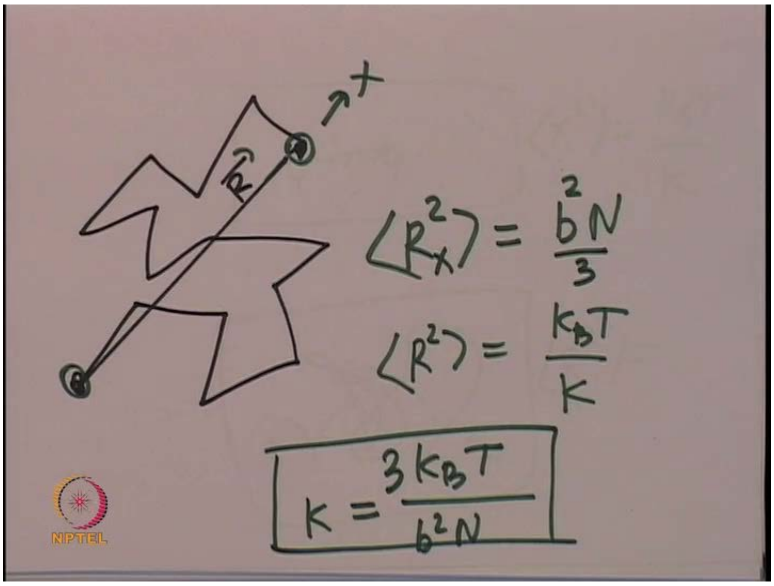

$$\langle R_x^2 \rangle = \frac{b^2 N}{3}$$

$$\langle R^2 \rangle = \frac{k_B T}{K}$$

$$\boxed{K = \frac{3 k_B T}{b^2 N}}$$

And we can say that, this this is something which we discussed before that, if you had random orientation for each of this monomer, the distance from here to here, this distance let me call R, this is basically the distance from one end to this other end, if you call this R, this R square average will turn out to be b square which is the length of this each sub unit times N. This will turn out to be this; this is something we discussed before.

So, this will turn out to be R square is b square N and we also saw that for a spring R squ, we said that K, the R square average, if it is like a spring will be equal to K B T by k, we quit this two and it turns out that actually, there is a, if you if you think of this only in one direction fluctuation only one direction, there this can be, there will be only one third of this in each direction. So, you can think, this is only one in one direction then it will be one third of this, but if you take of this whole thing, you will get, equate this two, you will get that K is nothing, but K B T by b square N. So, this is in 3 D. So, if you one third of this, if you take, you will get a three here because this is, so, if you take R X square only in one direction.

So, according direction let, if we call this X axis; X direction, we can put a one over three here. So, then this will turn out to be 3 K B T by b square N. So, this can be thought of as without doing much of calculation, we can think of, we can we can just equating a couple of things that we already know. We can guess, how much will be the spring constant for a, if you think of it as a spring, the DNA that can be pulled like this, which will behave like a spring with the spring constant can be estimated here.

We can calculate this exactly, but (( )) without doing much of calculation we can estimate, we can we can guess, what the answer will be. Now, what is the use of all this again, this all telling some property of D N A, if the DNA is in the medium and the thermal behavior due to this thermal motion, thermal Brownian motion, DNA will behave as if like a spring and the spring constant can be estimated and from this we can know, how much force you need to pull, if you know the K which is a spring constant, we can know how much force you need to pull the DNA and straighten them.

This is of course, what I said is for only for single stranded D N A, for double stranded D N A, this is much more complicated, whatever I discussed in this part, is for single stranded DNA where you do not need energy to bend and for double stranded DNA things are more complicated. So, now we will do a detail calculation later by applying real force to a single stranded DNA and calculate the partition function and from that, we can calculate something called this is exact relationship between force and R.

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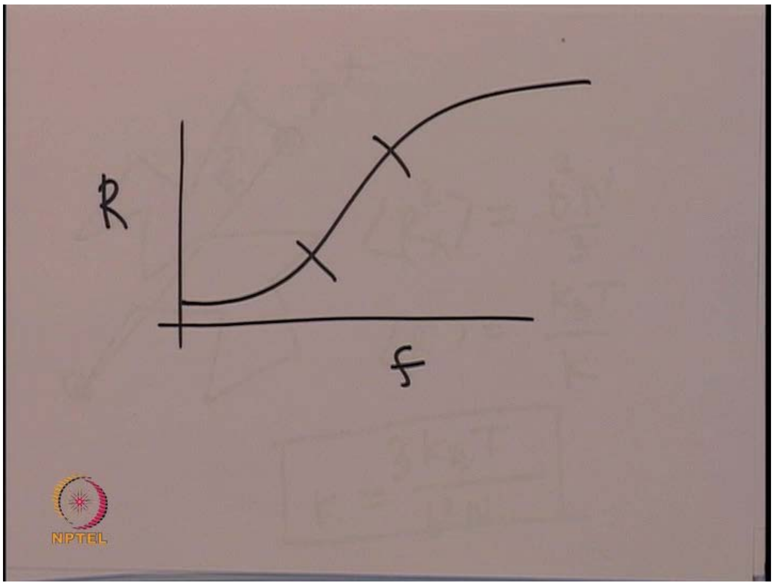

So, we can we can calculate, what will be this relation, f versus R relation which will look like this, we can calculate this full, we only guess we only estimated this part, but we can calculate this full part for for small forces the you, for large forces, there will be a slightly different behavior and we can calculate all this all this in detail. So, we will this is also against simple statistical mechanics, statistical thermodynamics calculation. We will do that calculation and we will estimate this pulling of DNA and then there is result from that, we will we will we think about we will think about this.

So, basically what we have been doing so far is applying ideas from statistical thermodynamics to calculate partition function. Now, one more thing, I should say that, we have calculated partition function and if we calculate partition function, we can get free energy which is a log of a partition function and it turns out that the derivative of the free energy will give you various quantities. So, if you calculate the free energy as a function of force or a function of some other quantity, if you take the derivative of the free energy, you will get various measurable quantities. So, it turns out that there are two types of free energy that you typically come across two or three. So, one is called Gibb's free energy which is represented by g.

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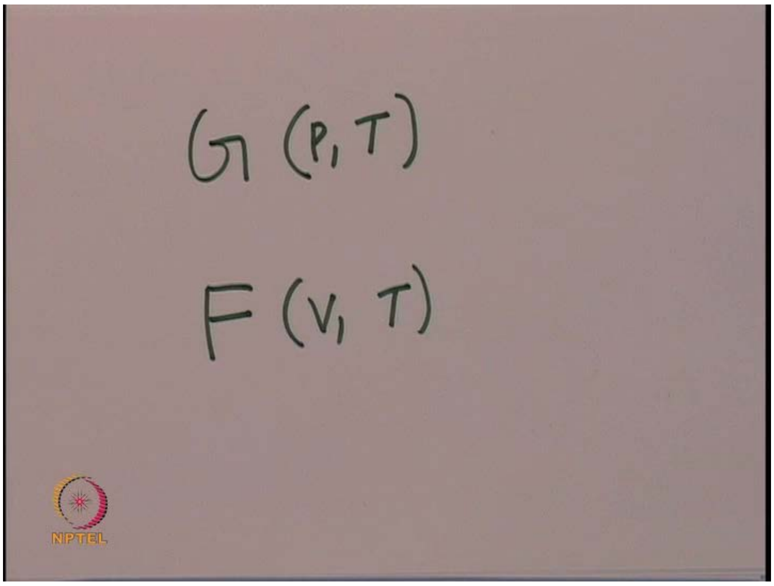

$G(P,T)$

$F(V,T)$

So, Gibb's free energy G and Helmholtz free energy F. This Gibb's free energy is a function of typically is a function of pressure and temperature and this is the function of a volume and temperature, what this is the difference between this two, what does this mean is that, if you fix the pressure and if you fix the temperature and if you also fix, in the case of total number in the system which we are not discussing here. We always take it as fixed. We will get this free energy, if you do the experiment and by fixing the volume and temperature, you will calculate, what you will be calculating is this F. Now, what is pressure, pressure is basically force per unit area. So, pressure and force are equivalent. So, when you think of pulling DNA, pressure is like force.

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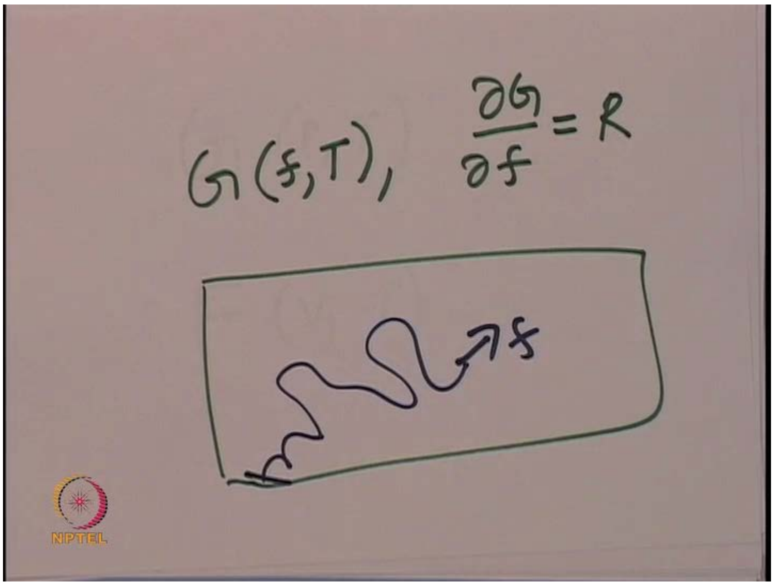

So, in the case of pulling DNA experiments, you can say that the G, the (( )), if you take a DNA, and fix one end. So, you have a DNA and apply a force at the other end, and ask the question what is the free energy of this system? What you will be calculating is the Gibb’s free energy, because you are calculating it as a given force, and a given temperature. And it turns out that if you know this G by taking the derivative del G by del f, you will be getting this end to end distance R along a particular axis. So, by doing del G by del f, you get this end to end distance.

So, basically knowing this free energy, you will by taking the derivative of free energy, we can call get all measurable quantities, if you ever to calculate the do the experiment at a with fixed length, fixed the distance between the end to end of the DNA and calculate the free energy from that case and take the derivative with respect to length, you will get the equivalent of force. So, basically, we can calculate free energy and by finding the derivative of the free energy, we can calculate the various measurable quantities. So, think about a few things like, you might be heard, you might have heard of various things in thermodynamics, let us list a set of things that you have heard in thermodynamics.

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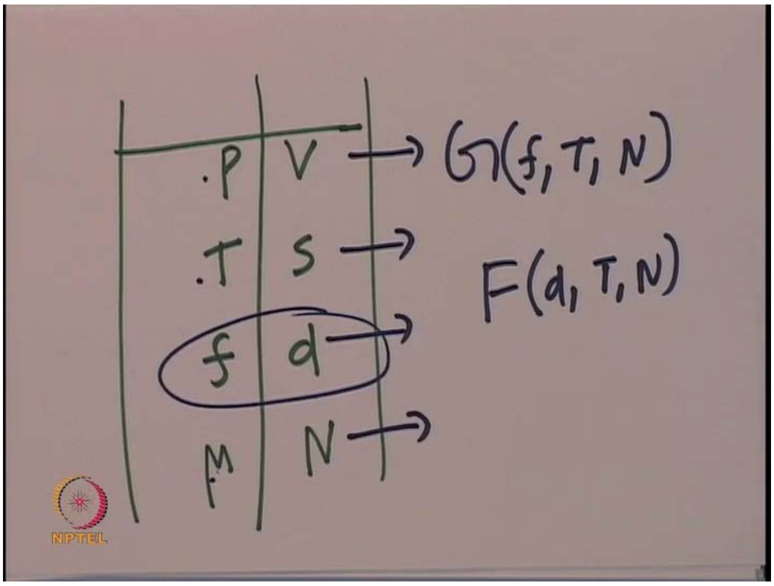

So, you have heard pressure and volume, temperature entropy, force distance. So, all of this has a property that P into V has a dimension of energy, T into S has a dimension of a energy, f into d has a dimension of energy. We can also say something about mu which is chemical potential; N is the number, this also has dimension of the product is the dimension of the energy. So, there are two things here, see you can, there are two quantities all this belong to one set of quantity and all these belong to another set of quantities, set that their product is has a dimension of energy.

So, this basically, the P V is one pair, T S is one pair, f d is one pair, mu (( )) one pair. So, this is just like, this is like forces, you can call this as generalized forces and this is some kind of conjugate variable to this, but just enough to remember that, there are many pairs in thermodynamics pair one, pair two, pair three, pair four. Now, we can do an experiment any experiment by fixing any one quantity from each of these pairs. So, when you say some free energy G, we can fix basically pressure and force are same. So, there are only three pairs essentially. So, you can either fix F from this, T from this and N from this.

This will give you some free energy, you can cal compute some other free energy which is basically fixed, instead of f, you fix d, the distance or length, you can fix T and you can fix N, this will be another free energy and you can think of many other free energies by fixing any three, any one quantity from each pair. You can fix either f or d, mu or N, P or V, one of the take three pairs basically, this pair and this pair are same. So, this pair is kind of redundant because pressure is missing, but force is nothing, but pressure in one dimension.

So, 3 D, there are only three pairs one, two and three. So, you can fix one of these from each pair and calculate appropriate free energy. So, and by taking the derivative of the free energy with any of these quantities in the bracket, we can get the conjugate variable. If you take the derivative of free energy with respect to f, you will get the average distance, if you take the ,calculate this free energy and take the derivative with respect to N, del f by del N, you will get mu. So, in this in this in this manner, we can think of computing various quantities and the measurable quantities, all these quantities can be computed by computing free energy.

So, we will continue the discussion in the next class. So, for this moment, we will stop here, so, what we discussed is basically a model worm like chain model for double stranded DNA, then we discussed how to calculate partition functions for this. Then we discussed, partition function for a spring in water and we calculated the fluctuation, how much it will be fluctuating, and the spring constant for a single stranded DNA, the effective spring constant, if you were to pull this. So, with this, I will stop today’s lecture, we will continue the next lecture. Bye.