Biomathematics

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Lecture No. # 34

Statistical Thermodynamics of Biological Systems Part - I

Hello, welcome to this lecture of on biomathematics. Today, we will try and think and discuss, how do we apply many of the mathematical techniques that we learnt to understand a bit of thermodynamics and, because… So, basically we have to learn or discuss a bit of thermodynamics, because thermodynamics is a very essential feature of a if a essential tool to understand various biological systems. So, the today's title is basically, statistical thermodynamics of biological system, and the question is why why statistical thermodynamics, why why should we why should we learn this, why first of all, when we say, when is a statistical thermodynamics, you can see there is, this term called statistical.

So, something that we learnt, so far including biology sorry the probabilities, averages, standard deviations; all these things we learnt in statistics and probabilities. So, this will all be applied will be applied here, and we will be using all these tools to understand statistical thermodynamics, and in turn various biological system. So, basically thermodynamics involves some amount of mathematics and some amount of physics. So, we have to discuss bit of physics also while while we are discussing various biological system, but the focus will be, how do we apply the techniques that we learnt to understand all these biological system.

So, now when we say thermodynamics, first of all, let us quickly discuss why do we need thermodynamics, and in particular statistical thermodynamics, because basically all the biological system, they are at first at a given temperature, mostly in our case is 37 degree Celsius. So, any protein or any bimolecules that you think of, they are at 37 degree Celsius, and they are in a medium typically like mostly water. So, one has to whenever we say, whenever we have to understand or think about bio molecules or biological systems, we have to think of that some objects or some molecules or a system at 37 degree Celsius in some medium like water.

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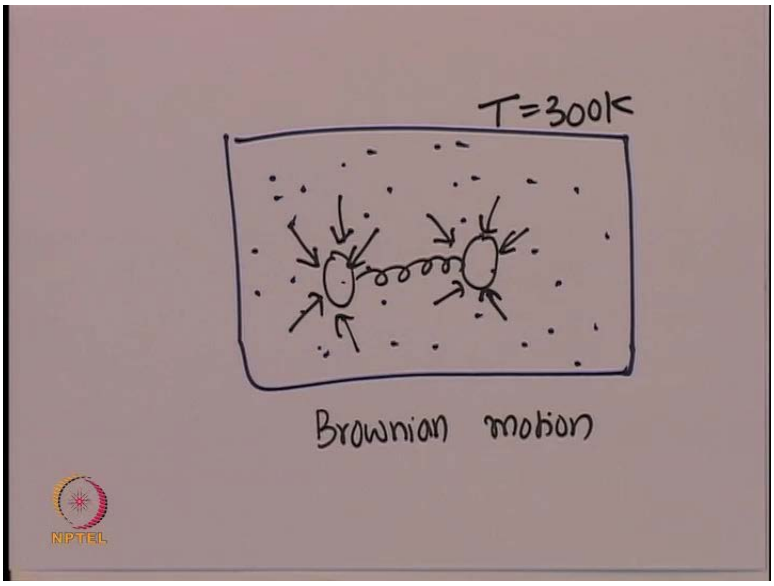

So, let us let us think of let us think of some molecs some. So, for simplicity, let us even think of, there is water (no audio from 03:14 to 03:19) and there is a bunch of particles. So, atoms like, these are connected. So, you could think of, the simplest model of any protein could be like two balls connected by some springs. So, think of some molecule like this, like two atoms interacting via a spring like potential. So, the two molecules two atoms, they are interacting like a spring what does it mean what what does it mean is that, these two atoms would like to be at a certain distance and there you do not, when you when they are taken apart, they will be attracted and when they are taken too close, they will repel.

So, this spring has this property that, if you take them too close, they would, you will have a resistive force. So, this will resist, coming together, it will also resist, going away because spring pulling is also need force and this spring pushing is also needs force. So, such, this is a good example of simplest case of of biomolecule would be something like, this two atoms connected by a spring. Now, this is the model, this is the something that we mimic to mimic a biological system, this is the simplest model we can think of.

Now, imagine there is water there is water and these dots are what, these dots represent water and all these water molecules do Brownian motion. So, these water molecules do

Brownian motion, why do they Brownian do Brownian motion because these are all at some parti particular temperature T, which is typically like three hundred Kelvin or around so, like something around three hundred Kelvin.

So, at this temperature, all this water molecules do zig zag motion, when they do zig zag motion, they go and hit these atoms from all sides. So, this is, these arrows represents water molecules going and hitting this atoms. So, when water molecules go and hit these atoms, they will also start vibrating. So, essentially what happens is that, these molecules will have to vibrate, they will have to fluctuate, their position of these atoms will fluctuate.

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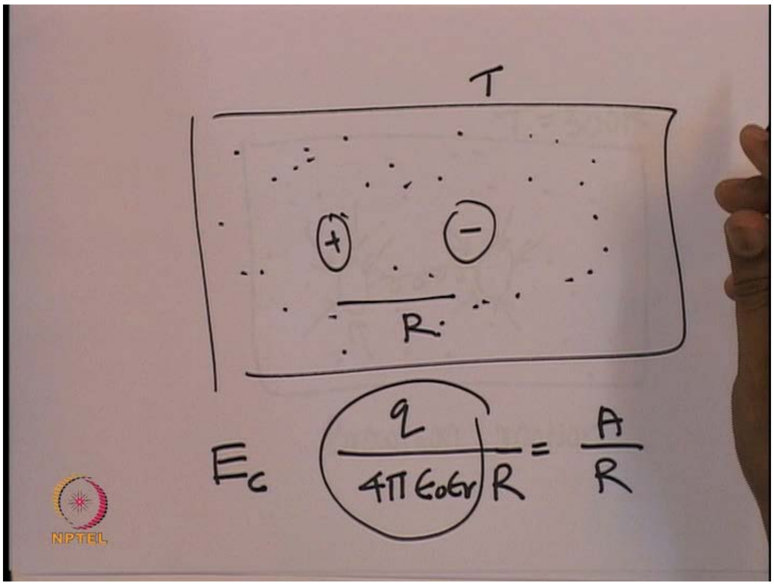

Now, think of certain cases for example, let us think of, there is some two charges in water So, think of two charges in water, plus charge and minus charge, they are at certain distance R apart and from physics you know that, the energy will be like q by 4 pi epsilon 0 epsilon r R, energy will have one over R relationship. So, this is basically, we do not need to worry about all these constants, in some constant do not worry about any of this, this is some constant divided by R.

So, this will be some constant, let me call this A divided by R. So, this is the typical energy of coulomb energy right. So, So, now, there is water and water will do Brownian motion at a temperature T. So, when they do Brownian motion, there is an energy which we can call thermal energy. So, there is this thing of thermal energy. So, what is thermal energy, thermal energy is the energy due to the browni thermal motion.

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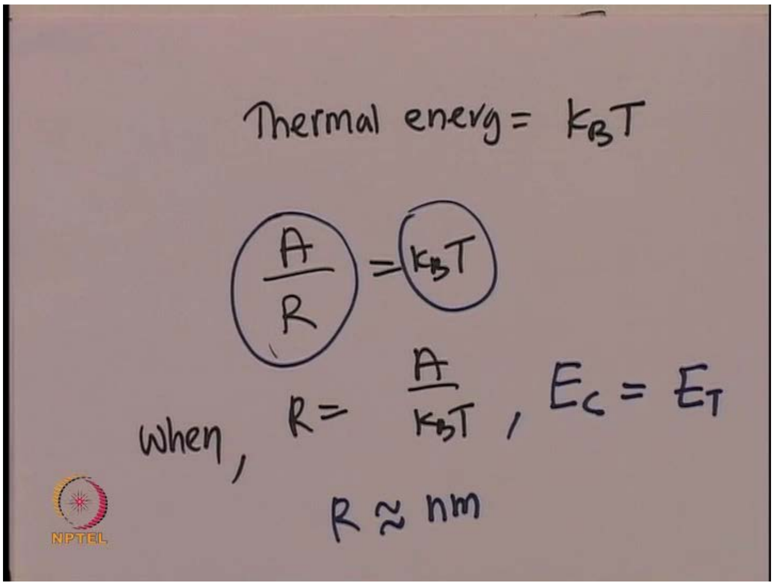

Thermal energ = k_BT

$$\frac{A}{R} = k_BT$$

when, $R = \frac{A}{k_BT}$, $E_c = E_T$

$R \approx nm$

So, the thermal energy is K B T. Now, where K B is Boltzmann constant and T is temperature. So, this is the rough amount of thermal energy will be one K B T. Now, coulomb energy is some constant divided by R and thermal energy is K B T. So, it turns out that for partic some value of R when R is equal to A by K B T when R is equal to A by K B T, these two thermal energy and coulomb energy will be equal. So, when R is equal to when R is equal to here, you can see that, if you substitute R is equal to A by R K B T this two will be equal.

So, this is basically coulomb energy. So, this is coulomb energy and this is thermal energy. So, when R is equal to A by K B T, coulomb energy is equal to thermal energy. So, now it turns out that, this R, if it is order of nanometer, this will be equal, if if this is so, it turns out that when R is of the order of nanometer, these two will be equal, that is what, when you typically substitute these numbers and see, you will you will find that the R is the order of nanometer, these two will be comparable, thermal energy, coulomb energy and thermal energy will be approximately equal.

So, what does this mean, in biology all the length scales, nanometer, the typical length scale like, what is the one base pair of D N A is 0.34 nanometer, like typically, nanometer is the distance between atoms or molecules various distance, varying molecules in the molecular size, the size of the typical distance in biological biomolecules is basically of the order of nanometer, what does that mean is that, at this length scale, the thermal energy is comparable to for example, here the coulomb energy.

If this is even true, even if you take some other energy like elastic energy, the bending energy, if you take the bending energy, some lengths of the order of, if you take the D N A bending energy, if when the length is about fifty nanometers, these energies are comparable or hundred nanometers of the order of fifty, hundred nanometers, these two energies will be comparable. The thermal energy and the bending energy, the energy near the elastic energy needed to bend D N A will be comparable to the thermal energy, if we will will have we can have a quick look at this.

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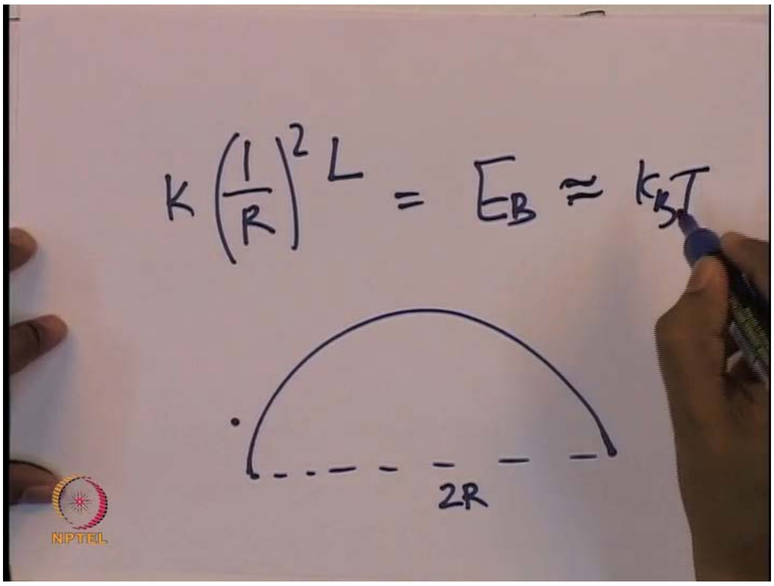

So, it turns out that, the bending energy of the D N A can be written as, 1 over R square into L, it is some constant (( )), this is the bending stiffness. So, this is the bending energy and when will this E B equal to K B T. So, this is the bending energy of D N A, D N A of length L. So, if this is the energy, we have a D N A of length L, this is the this this if you take as 2 R. So, then you have to bend it to a circle. So, let us say, you have to bend it to a circle of. So, let let us let us draw this little more carefully.

So, let us draw a circle. So, the if you want to bend it to a circle of radius R, this will be, this you can ask the question, what will be the, when will this two bending energy will be equal to K B T and I would not go into the detail of this because it is not the important point is now this here, but I just want to say that even for the bending of the D N A.

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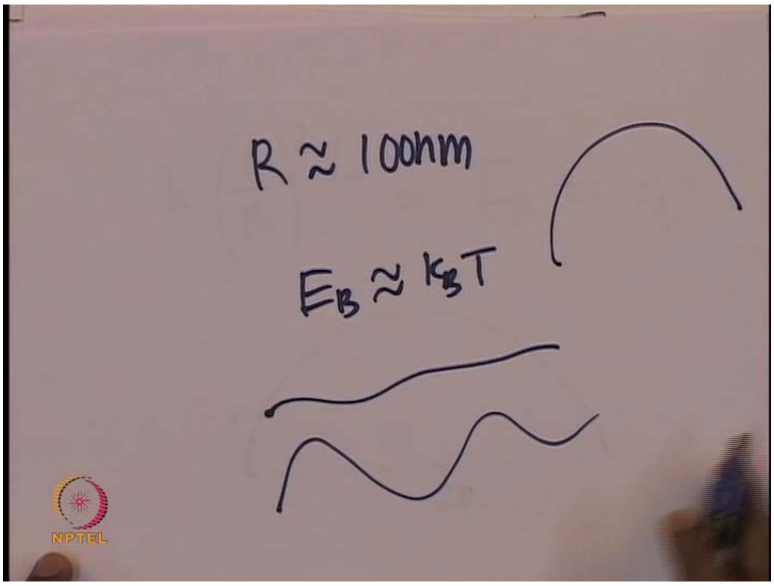

You will find out that, when distance when R is of the order of about 100 nanometer, you will find that the bending energy is comparable to K B T. So, that means, what does it mean is that, even if a D N A will at at that temperature which is about three hundred Kelvin will start bending. So, D N A will not be straight any more, if the D N A is of the length of 100 nanometer, they will start bending. So, what does this mean, this means that all the position of the molecules will start fluctuating.

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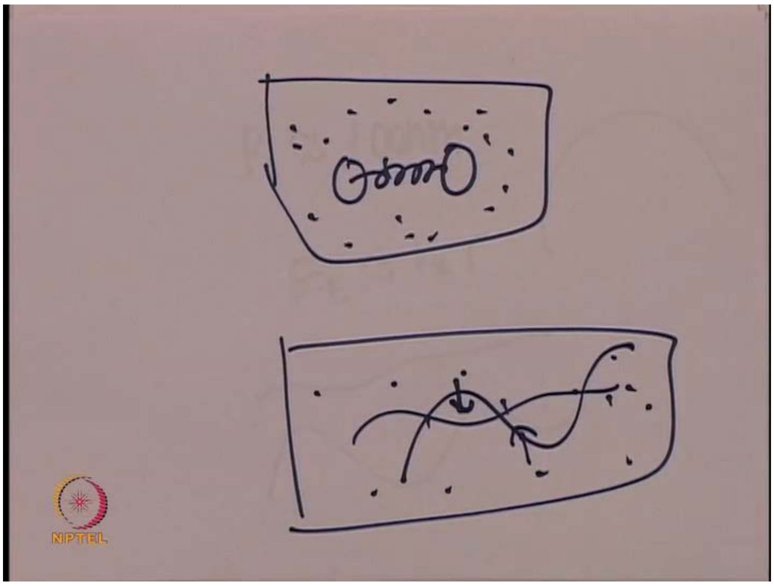

So, we saw that, if you have in water, if you have molecules connected by a spring, their position will start fluctuating because they get hit from all directions. If you have a filament like D N A in water because of this thermal motion, because of this molecules coming and hitting this, this will start bending. So, all the biomolecules will start fluctuating. So, if you think of the biomolecules, they will just start wiggling in water. So, there is, this thing is called thermal fluctuation.

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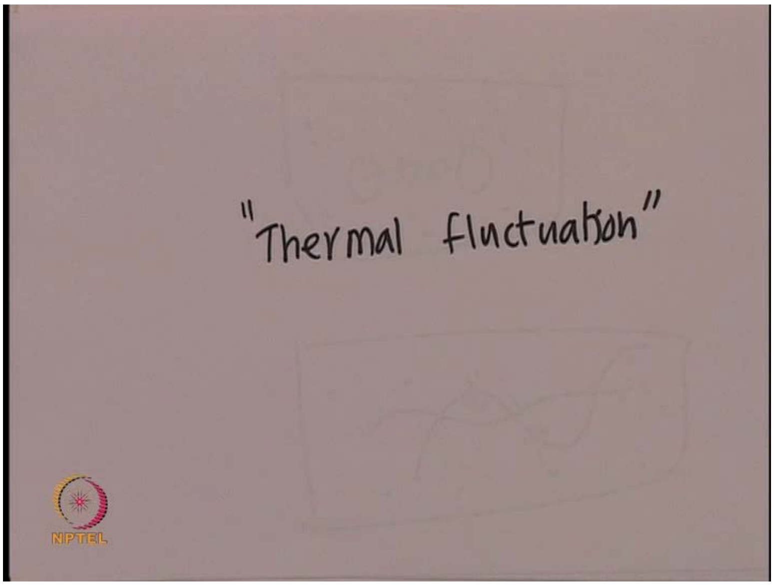

So, let me tell this word Thermal fluctuation, what is thermal fluctuation means, is that the fluctuation position of atoms of biomolecules due to Brownian hit thermal motion, due to thermal energy, the fact that, the water molecules and the molecules around do Brownian motion will lead to the fluctuation position of various molecules atoms in biomolecules. So, this biomolecules will start fluctuating the D N A or the proteins will be will have their position, that they will bend and they will do wiggly motion, the atoms will start vibrating or moving around or the charges will start moving around.

So, they will all, they will be very dynamic and the reason behind that is basically the thermal motion. So, given this fact, that given that they are not static any more at temperature of three hundred Kelvin, this atoms in biomolecules are not static any more, they keep fluctuating all the time. So, if you want to talk about the distances between two ends of a D N A or the distance between two parts, you have to always talk in terms of statistical averages, what is the average distance between two atoms, what is the average. So, that is, where you want, you would need to use ideas from statistical thermodynamics.

So, there is the need of statistical thermodynamics. So, to understand the configuration of biomolecules for example, we need to use statistical thermodynamics. Now, let us go and think of some stuff that we know, already know something we have heard in thermodynamics, you have heard terms like energy, entropy, enthalpy, free energy. So, let us quickly look at it because there is very interesting mathematics behind all this and I will briefly discuss.

So, this statistical thermodynamics is a course in itself, but in a few lectures, I want to give you a just of, how do we apply various mathematical techniques to understand, this quantities in a better way, various you might have studied various formula like h is equal to e plus p v, g is equal to h minus t s and so on and so forth, what is all this behind this formula, like like like can we understand this in a better way and yes we can and we will let use some ideas from mathematics and then this will be much more clear. So, let us think about this, as well as, first discuss some of the terms, that we already came across, in biology in in in thermodynamics. So, that is what, today, we will do, we will discuss some of this.

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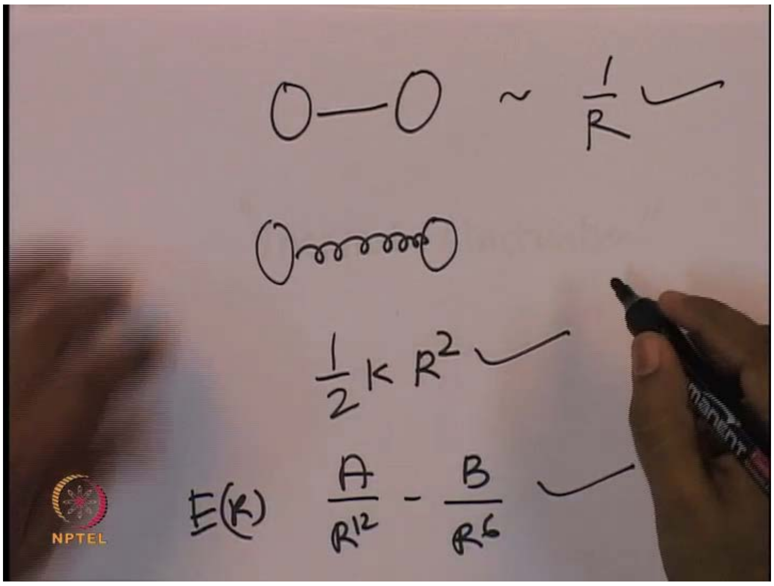

So, we will start with this term energy, which you all know, what is energy. So, we said that, we will first think of the system, we we we said that, we can think of proteins as two balls connected by a spring, this is a way of thinking about proteins, this will help us two balls, you can think of as two atoms and they are connected, they are interacting by some kind of spring like interaction. Now, you know that the energy for this system has to be half K into R square, this is the spring energy.

So, this is the energy for such a system, if you have instead of this, if you have two charges, that is distance R, we said that the energy is coulomb energy, which is goes as 1 over R. So, always in some other cases, you might have had like wanderwaals interaction, that the interaction energy will have some particular form, A R power 12 minus B R power 6. You might have seen such a formula for energy. So, energy is all this, depending on the interaction you will have different energy, but all this energies coulomb energy, spring energy, wanderwaals energy.

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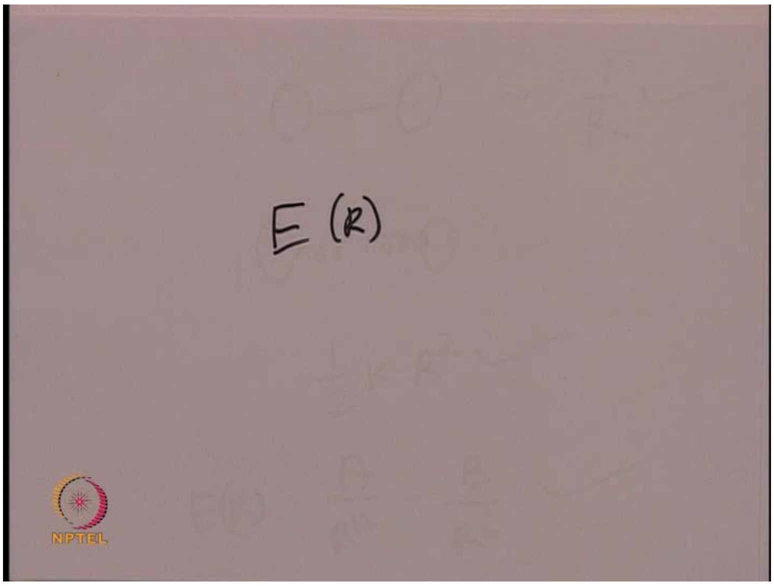

In all this cases, it is important to know that, energy is the function of, the distance R. This is what typically happens, E is the function of R. So, now, you can even think of bending energy and this also will turn out to be function of R; we will discuss this a bit, little more in detail later, but for the moment, let us think of the energy that we know. So, whenever we say energy, we would mean the interaction energy, the coulomb energy or spring energy or Lena john's energy or that is called the wanderwaals interaction energy.

So, energy will be typically the function of the distance or the positions of the atoms because interaction will depend on distance. So, therefore, E is the function of R. So, when I say energy, this is what examples are this. Now, another term, that we all have seen and which is not very clear to many of you, might be this term called entropy. So, what is entropy? So, we will take a bit of time and then discuss this in detail and the mathematics associated with this entropy and how do we calculate entropy.

So, we know how to calculate energy, energy we know that the formula, K R square half K, if you know K and if you know the R, K R square can be calculated. Q by q 1 q 2 by 4 pi epsilon 0 R, this can be calculated. So, the energy can be calculated the once we know the formula, but how do we calculate entropy and what is entropy. So, it is said that, entropy is basically a measure of disorder, this is something that we all learnt, entropy is a measure of disorder and how do we quantify disorder, when we started this lecture of mathe biomathematics for , we said that our aim is to quantitatively say, this is exactly this is how, what it is.

So, when we say disorder amount of disorder, we need some measurement, some quantity to really quantify and say for this case, the disorder is this much. Mathematics, we would like to say everything in numbers. So, we would like to say disorder is 3.157 disorder is twenty three point something. So, we know that, if disorder is twenty three and disorder is ten, one system has disorder ten and one system has disorder twenty three. We know that, one has more disorder than the other.

So, we would like if possible to represent disorder as a number. So, that we can compare. So, how do we tell, entropy as a number, can we do that. So, that is what, we will discuss first, how we do that. So, let us think of, a bit of disorder first. Now, so, for this, let us think of some example, let us let us think of books in library. So, if you go to a library and if you look a particular stack, there will be a set of books.

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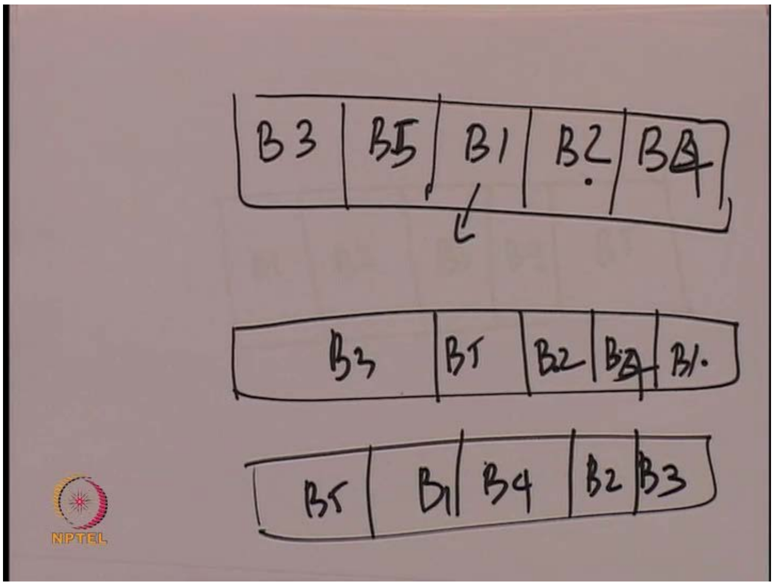

So, let us say, you have a stack and this stack has like five books, one, two, book one, book two, book three, book four and book five and these books in the library will be arranged in a particular order, according to either their serial number or accession number, there will be some particular number given to each book and in this particular, in a rack of in a in a particular rack, this books will be arranged in a very in a particular order.

So, you go to library today and have a look at this stack of books and you will see that, this arranged B 1, B 2, B 3, B 4, B 5, you come back tomorrow and again, they will be arranged in the same manner. So, you keep taking photo of these books day and each day, you will see that they are arranged in that particular order. So, this is highly ordered arrangement the books in library. Now, you imagine that, you take all these books, all these five books and take to your home then you arrange these books in your shelf. So, in library, if somebody takes out this book to read, after reading they will be kept back in the right exactly in the same position.

So, librarian will make sure that, there books set in that order. So, that is easy to easy to access this book, easy to get this books. Now, at home, we do not, we have like only few books, we do not really care about keeping in a particular order like, we do not need, we do not know which is first book, second book, we do not really care about accession numbers or serial numbers at home. So, at home, we take all these books and then we will put may be in some particular order, we will put like B 3, B 5, B 1, B 2, B 3, this is the way, we will arrange in my in my in our home our home, we will arrange in a in a in our rack, in the book shelf, we will arrange the books in this particular fashion.

Now, we take out some book B 1 to read and the next day, when we keep it back, we keep the B 1 at the end after B 3. So, let us say we keep (no audio from 24:25 to 24:30) so, B 1 you kept B 3, B 2 then B 5 sorry there is there is B 4 here actually, B 3, B 5, 1 2 3 4 5. So, we kept this B 1 here, there is B 4; there is B 2 then B 1 is removed then B 5 and B 3. So, one, two, three, four, five books. So, the order changed, it became B 3 B 5.

So, this is not, there is no particular now, some another day, we might take all the books to read and when we keep it back, we need not remember this order, we will we will keep in some fashion, we will keep may be B 5, B 1, B 4, B 2, B 3, we might keep in this order. So, there is no particular order for us to keep this. So, the arrangement at our home is less ordered compared to the arrangement in the library.

So, now how do we quantify this, this is less ordered and more ordered. So, if you take this pack of five books and if you look at the position of the books, in the library, all of the each book will have only one position, first will be B 1 like the particular arrangement in the library will be B 1, B 2, this is the exact arrangement. So, there is only one particular way, we can arrange these book, on the other hand at our home, we have many ways of arranging this book. So, let let us let us simplify this and make it only three books. So, that is easier to write down all the arrangements.

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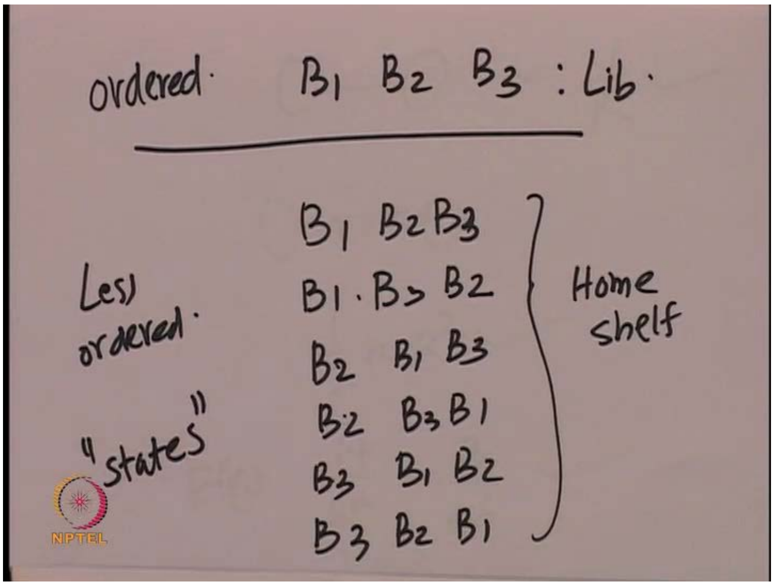

ordered · B_1 B_2 B_3 : Lib·

Less ordered·

"states"

B_1 B_2 B_3

B_1 · B_3 B_2

B_2 B_1 B_3

B_2 B_3 B_1

B_3 B_1 B_2

B_3 B_2 B_1

Home shelf

So, in the library, the books will be arranged, B 1, B 2, B 3, this is what in library, but at our home, one day, we might be arranging in B 1, B 2, B 3, next day, we one, we might be arranging B 1 then B 3 and then B 2, another day, it could be B 2, B 1, B 3 or B 2, B 3, B 1 or it could be B 3, B 1, B 2 or B 3, B 2, B 1. So, we can all this possible arrangements are possible. We can arrange the books in this way or in this way or in this way. So, this is at home. So, home shelf.

So, what, first day, we might arrange in this way, but we take out all these books and and we read and keep it back, one day it could be like this, another day it could be like this, another day it could be like this, another day it could be like this, another day. So, there are one, two, three, four, five, six, six possible arrangements here, just check carefully look at it, did I forget any arrangement, I think I have not. So, there are this many possible arrangements I think yeah.

So, this is all the day, it will be one arrangement only here, there are six possible arrangement we discussed. So, we, this we call ordered, this we call less ordered. So, library is more ordered, this is less ordered. So, entropy for this library is this way small, entropy is a measure of disorder. So, this will be more entropy and this will be less entropy. So, this particular arrangements, we can call as states, we can call this as states.

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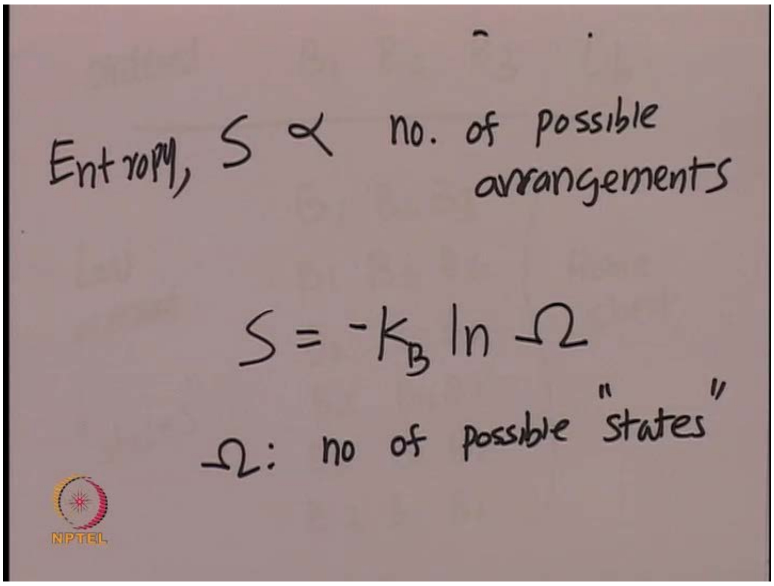

Entropy, $S \propto$ no. of possible arrangements

$$S = -k_B \ln \Omega$$

Ω: no of possible "states"

So, it turns out that the way to define entropy, that entropy S. So, this is the notation, we will use for entropy, entropy S is proportional to number of possible arrangements. In the library, there is only one arrangement, but at home we had many possible arrangements. So, this is more entropy and it turns out, that the correct definition of entropy in biological thermodynamics is basically or in thermodynamics is minus K B log number of states. So, let me call this omega as a number of states, omega is number of possible states or arrangements.

So, we will discuss, what do we mean by states. So, what in our in our case when we in states, this is position of books. So, in biology states means, typically would mean position of atoms, if one protein molecule has like three atoms or two atoms, if it can get arranged positioned in different different positions, many many arrangements are possible. So, let us let us quickly even discuss another example of order and disorder that we see. So, you might have seen like parking lots where cars are being parked. So, what what what is the one feature that you have seen in parking lots.

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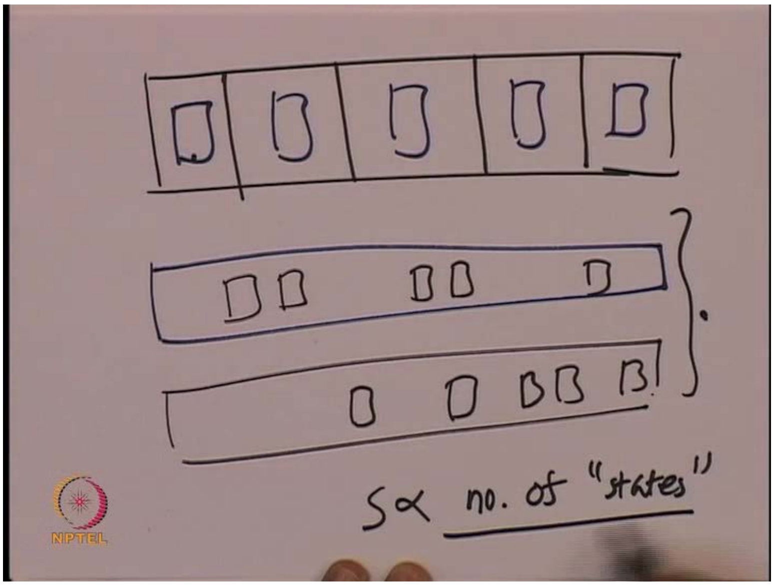

So, many of the parking lots will have like lines drawn like this for cars to park. So, the first car, one car will park here, next car will park here, next car will park here. So, there are parks are very, cars are very well organized here, if you did not have this lines if you did not have this lines then someone car could park here, another car could park here, another car will park here, this could be some such arrangement or you will see that, one car is parked here, one car is parked here, one is parked here and some such arrangement.

So, here, this is very very ordered arrangement, less entropy, here is highly disordered, no ordering. So, this is more entropy. So, each of this car, here, this car can have only one position between because this is restricted by this blocks, this, this, this lines. So, you should not park, beyond this lines, only within these lines, you can park. So, there is only one position for this car, inside this box, but here, there is no particular restriction here, you can take any position you want. So, then people start parking anywhere you want.

So, there are too many possibilities. So, entropy is proportional to, the number of arrangements, the number of states. So, this is one state; this is another state, you can think of all states and the more the position for each car, more the states. So, there are large number of states you can think of. So, this is one state; this is another state. So, this is another example of disorder and order. So, more entropy for this case and less entropy here. So, now we have to think of this number of states.

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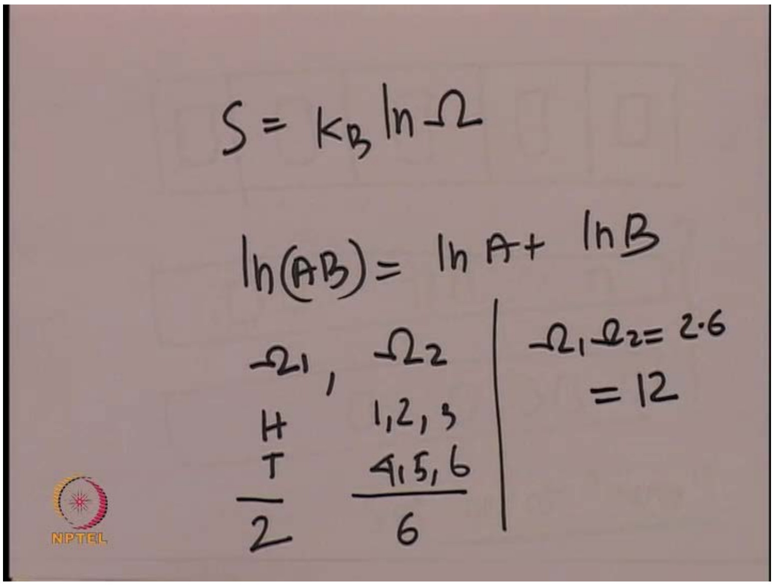

$S = k_B \ln \Omega$

$\ln(AB) = \ln A + \ln B$

Ω_1 ,	Ω_2
H	1, 2, 3
T	4, 5, 6
2	6

$\Omega_1 \Omega_2 = 2 \cdot 6$

$= 12$

So, if you know the number of states, we can get entropy and is proportional, but how is it proportional, it turns out, that as we said the formula is, S is K B log omega, it is logarithmic relation and there is some particular reason because if you have two systems like, a log has a particular property that, log of A B is log A plus log B. So, if you have a system like which has omega one state and some other system is omega two states and the total state will be like, so, the this, we can think of this as like, let us say, you are tossing a coin, when you toss a coin, it has two states head or tail, so, omega one.

So, let us this is this is head or tail, this is two states, omega is, you can think of some other system which is throwing a dice, when you throw a dice, here a six states like one, like you know, you might have played snake and ladder and play things like this. So, where you throw a dice and will have six faces and each face is a state. So, there are six states for throwing for the dice. So, this has one, two, three, four, five, six, there are six states possible for a dice. So, now, imagine that, you have a dice in one hand and a coin in another hand and you are throwing each of them at the same time, both of them at the same time.

So, the coin will come head or tail, dice will have six of these one, two, four, five or six. So, now, you ask the question, what is the total number of states, when the coin is head, the dice can have all the six states, one, two, head one, head two, head three, head four, head five, head six, when coin is head, dice can have all six states, when coin is tail, the dice can have six states. So, there will be twelve states. So, there will be like omega one, the total number of states will be omega 1, omega 2 which is 2 into 6, there will be 12 states. Now, entropy, the total entropy of this two systems together will be sum of this entropies.

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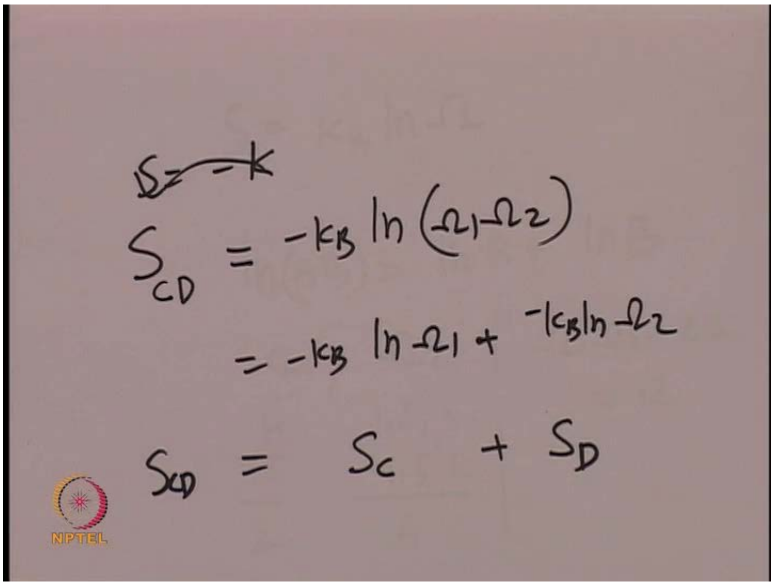

$S = -k$

$$S_{CD} = -k_B \ln(\Omega_1 \Omega_2)$$

$$= -k_B \ln \Omega_1 + -k_B \ln \Omega_2$$

$$S_{CD} = S_C + S_D$$

So, this property that, S is total system of, so, S of coin and dice C D let me write is, minus K B log (omega 1 omega 2), this is two into six. So, this is minus K B log omega 1 plus minus K B log omega 2. So, this is basically, entropy of the coin plus entropy of the dice entropy of the dice that we. So, throwing dice will have some particular entropy and this sum of this will give you this.

So, this particular property that, the sum of this two will give you the combined entropy, to have this property is good to have log, any function having log has this nice property that, if you combine this two systems, the entropy of the combined systems will be the sum of this entropies of this individual systems, so that and such a property is being entropy has such a property and therefore, to have, it is good; it is appropriate that we have this function as log, that is the reason why there is a log .

So, now we know, if we can count the number of states, we can understand that, we can understand entropy. So, entropy is K B log omega in simple cases, but there is an assumption here, this is only true for such systems where all the states are equally probable, when when we toss a coin, head and tail are equally probable, when you toss a dice, when you throw a dice, all these states one, two, three, four, five, six are equally probable, if they are not equally probable, let us say, head is more probable than tail or if it is a bias coin or if it is a dice which has some bias like

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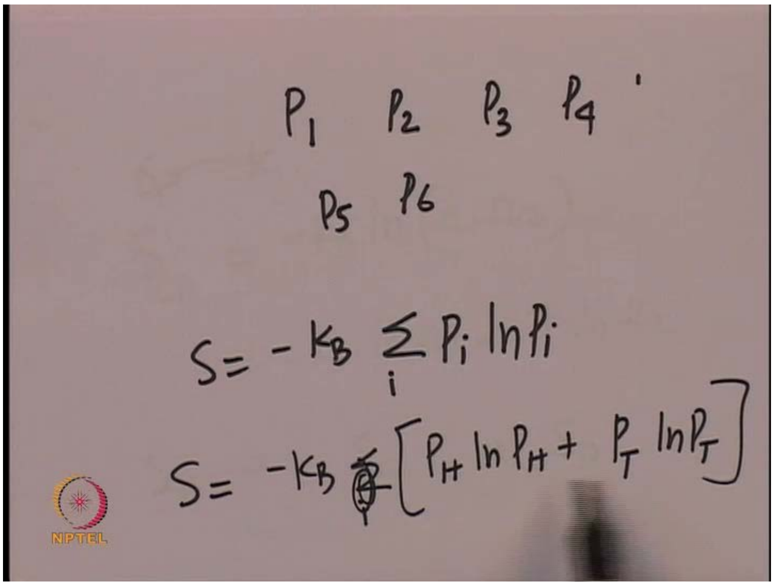

If there is probability of 1, different from probability of 2, p 3, the probability to have all this is different, if if they are different then the entropy is given by this formula, sum over i p i log p i, where p i is the probability to have state i. So, if it is for the case of coin, S will be, if minus K B sum over i, so, sum over, this sum here, will would mean probability of head log, this is one state plus probability of tail log probability of tail. So, this is the example for, if this p H and p T are equal, you put p H is equal to p T equal to half.

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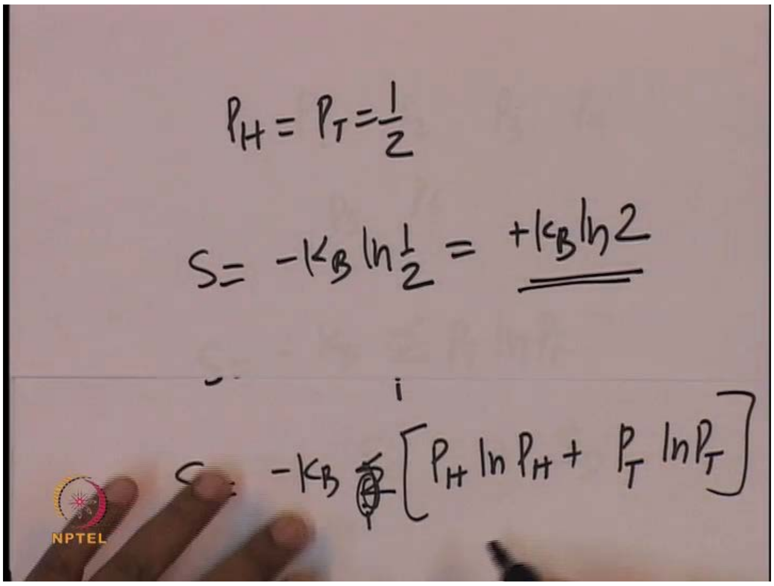

$$P_H = P_T = \frac{1}{2}$$

$$S = -k_B \ln\frac{1}{2} = \underline{\underline{+k_B \ln 2}}$$

$$S = -k_B \cancel{\sum_i} \left[P_H \ln P_H + P_T \ln P_T\right]$$

So, you take this case, this formula and here, you put, p H is equal to p T is equal to half, what do you get, half log half plus half log half. So, you will get, S is equal to minus K B half log half plus half log half will be one log half, this is log half is log one minus log two, this will be minus K B sorry this will be plus K B log 2. So, this is, if the probabilities are equal, you will get the whole formula that, log of number of states times K B, there are two states, head or tail and K B log 2 will be the answer.

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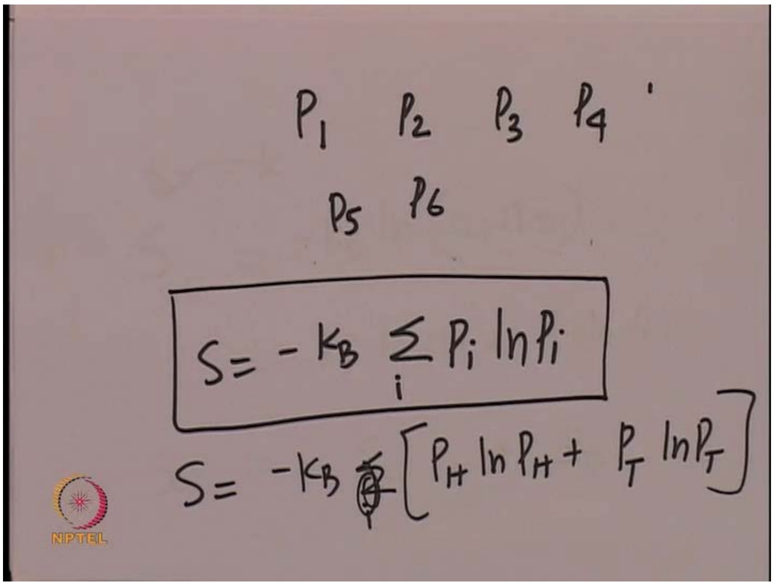

$$P_1 \quad P_2 \quad P_3 \quad P_4$$

$$P_5 \quad P_6$$

$$\boxed{S = -k_B \sum_i P_i \ln P_i}$$

$$S = -k_B \cancel{\sum} \left[P_H \ln P_H + P_T \ln P_T\right]$$

So, when probabilities are equal, this formula will be equivalent to the formula of K B lan omega otherwise, the general formula for entropy is basically this, this is attributed to a famous scientist called Shannon; however, this is the formula when the when the probabilities are different for each state. So, we understand, we know know how to calculate entropy. So, if we know the probability of the state and then if we know how many states are there, we can calculate the entropy and by state, we mean position. So, let us quickly do, let us do some quick calculation of entropy of some in some cases.

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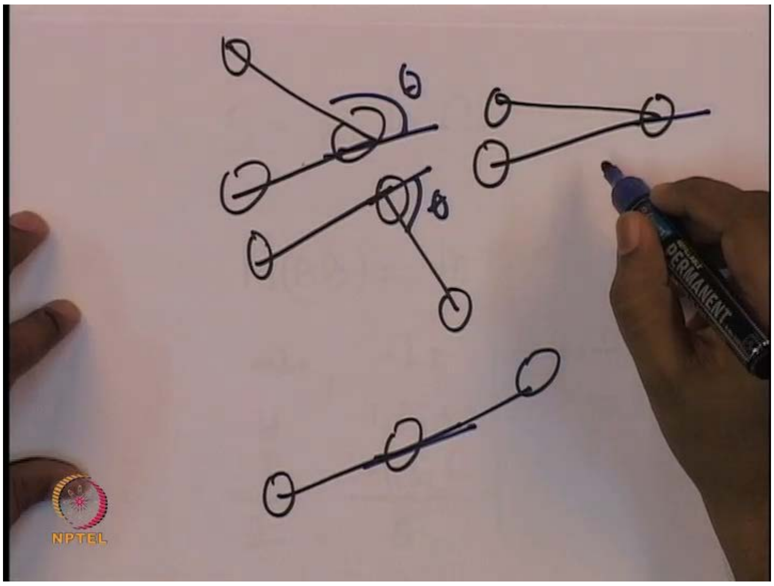

So, let us think of, the simplest example that is, let us think of a protein and a very simple case for a protein which is basically three atoms connected by some bonds. So, let us think of, this is one atom; another atom; another atom and they are connected by some bonds, what is the entropy of this system. So, we know that, if do not depending upon the interaction, you can always calculate energy. Now, we can ask the question, what is the entropy of this system? So, now, this three atoms can have any position, we want.

So, let us imagine that, this can have any position that we want, what does this mean, this means that, this can have this particular configuration. Now, let us say this atoms moves here, this is then it can take some positions like this, it can take some other position. So, this two atoms like, this is third atom moved here, you can think of some position like this (no audio from 41:43 to 41:47) like this. So, you can think of many many positions, in all these cases, what changes is, in this simple case, this angle between this two lines they change.

So, if you think of this angle. So, let us say if you call this angle as theta, in this case, each of this angle between, so this angle can take any value, starting from 0 to two pi. So, the total number of states will be all possible sum of all this conformations So, you can take theta any value from 0 to 2 pi. So, if we take this into account, we can get the entropy of this.

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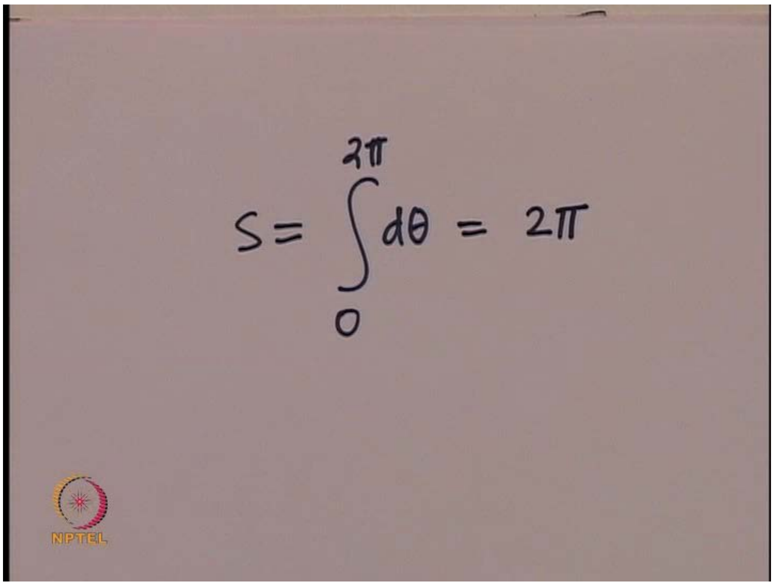

$$S = \int_{0}^{2\pi} d\theta = 2\pi$$

So, let us do this. So, entropy will be, we can write entropy S, as integral 0 to 2 pi d theta, this theta can go from any value from 0 to 2 pi. So, this will turn out to be the answer will be turn out to be of course, 2 pi. So, the entropy will turn out to be 2 pi.

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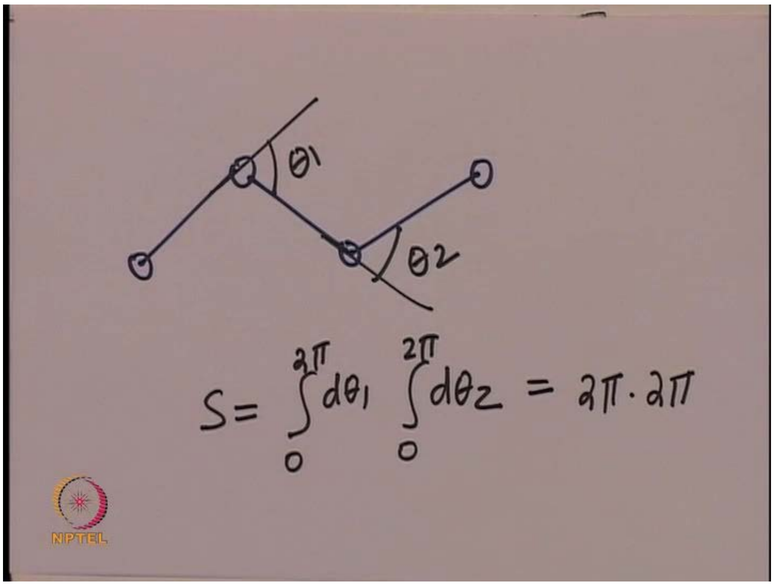

$$S = \int_0^{2\pi} d\theta_1 \int_0^{2\pi} d\theta_2 = 2\pi \cdot 2\pi$$

Now, if you think of two atom, two such molecules. So, let us think of. Now, there are two angles, we can think of, this angle can be anything and this angle also can be anything. So, there is theta 1, theta 2 and theta 1 can be any value, theta 2 can be any value. So, the entropy S, in this case will be integral 0 to 2 pi (d theta 1) 0 to 2 pi (d theta 2). So, basically, the answer will be 2 pi into 2 pi. So, four pi square. So, we can generalize this two ends such angles. So, we can draw more lines.

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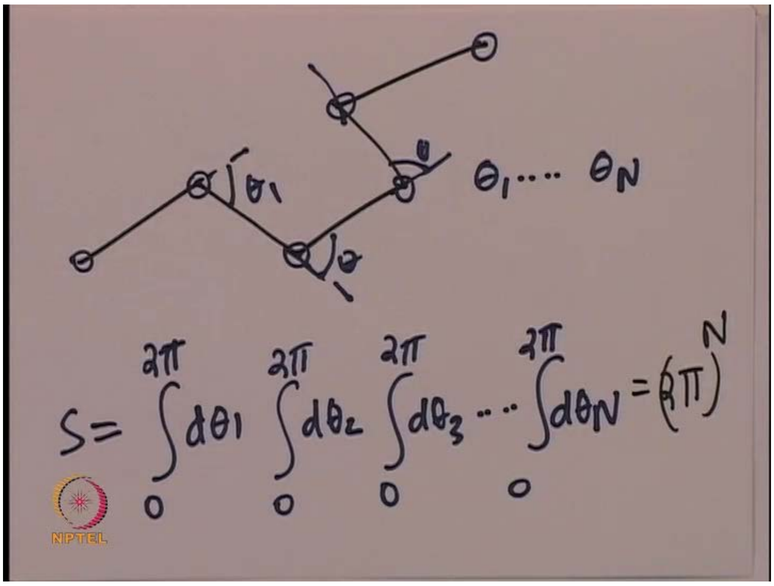

$$S = \int_0^{2\pi} d\theta_1 \int_0^{2\pi} d\theta_2 \int_0^{2\pi} d\theta_3 \cdots \int_0^{2\pi} d\theta_N = (2\pi)^N$$

So, we can now think of one protein molecule, which has N such bonds. So, this is connected by n plus 1 atoms n plus n plus 1 atoms connected by bonds, each of this angle let us say, theta 1, theta 2, theta 3, theta and so on and so forth. So, there will be like N angles, theta 1 up to theta N, there will be N such angles and the entropy will be given by (d theta 1) 0 to 2 pi, each of this angle, can take any value. So, the total number of confirmations will be this integral 0 to 2 pi (d theta 2) 0 to 2 pi (d theta 3) up to 0 to 2 pi (d theta N) and the answer will be 2 pi whole power N. So, the entropy will be 2 pi whole power N.

So, this is the way, we can calculate entropy. Now, think of something called something in protein bio physics, that you know, that you know that, this theta cannot actually take any value, you want. So, in most of the cases, having you might have heard of something called Ramachandran plot. So, most of the proteins, I mean between the angle between the amino acids, there are some restrictions, they are known, it is like. So, you know Ramachandran, professor Ramachandran, who was one of the eminent scientist from India like, he discovered that certain atoms, they have to be certain planes have to be in a particular restricted manner.

So, that are particular angles, which people call dihedral angles are more like phi and psi, you might have studies phi and psi in biophysics. So, if you know that phi and psi, they are restri the value of this angles are restricted, all the states are not equally probable then the entropy is not all possible states, but basically they, if you know then those the states with those angles are more probable, then the entropy will be slightly different.

So, then you have to use the formulae of p i log p i. So, we will we will discuss that, but if all states were equally probable, there is no restriction then we we know how to calculate entropy. Now, we will we will come back to other case of, when there is a restriction, how do we calculate entropy, we will we will come to that. So, once we know energy, once we know entropy, there is a important quantity in thermodynamics and that is known as free energy. So, this is the next quantity, which is basically the quantity known as free energy.

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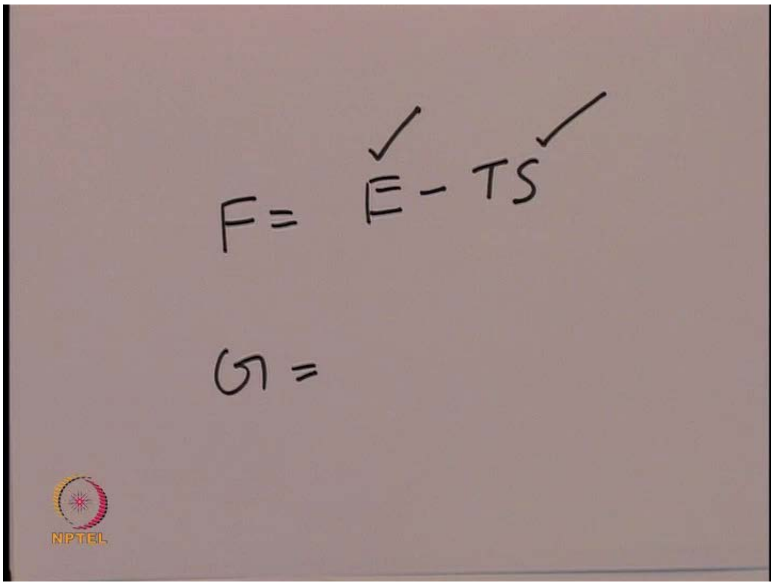

So, free energy is typically, the definition of free energy is sometimes written as F, sometimes written as G. So, we will today discuss F and we will come to G and we will see the difference between these two in the next class, but G F is basically energy minus temperature times entropy, F is E minus T S. So, if we know how to calculate entropy, we know how to calculate energy which is either half K R square or q 1, q 2 by R or this is some value, with this we know how to calculate and we know how to calculate T. So, we know how to calculate free energy. So, if you calculate free energy, why is it useful? So, it turns out, that, in thermodynamics, if we have a system, that system will reach equilibrium when the free energy of the system is minimum.

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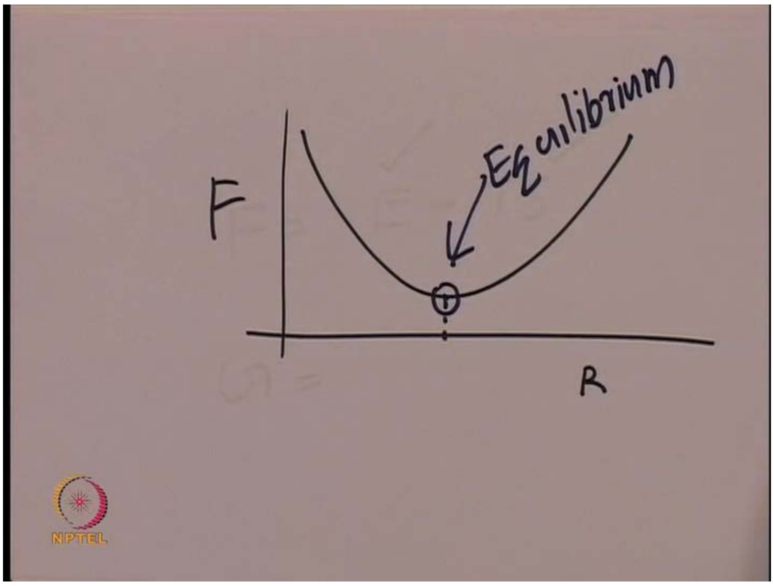

So, when you plot free energy typically, some that some occasions we have seen, free energy as a function of some variable, there will be some minimum like minima like this, in a... So, this point where the free energy is minimum. So, with some variable, let us say R. So, then there is a particular state where this free energy is minimum. So, this state will be the equilibrium state. So, equilibrium. So, in thermodynamics equilibrium is a state, when I say state, it is the confirm confirmation of protein or a configuration or a position of atoms in a positions of molecules in a protein. So, the molecules will take this particular position, those particular position such that, the energy, the free energy F is E minus T S is minimum. So, that will be the most preferred configuration.

So, when I say equilibrium that will be the preferred confirmation. So, we will discuss about this free energy equilibrium etcetera in the coming classes in little and we will go and understand the statistical concept here, in little more detail, but what one thing we saw is that, there are many confirmations possible because of the thermal energy and the hit due to the Brownian motion of water particles for example, or the particles in the medium, each protein or each biomolecules can have large number of states or large number of confirmations and therefore, one has to talk about statistical quantities and we will be using ideas from statistics here and we will see, we will discuss little more in detail, how do we how how do we calculate free energy and how do we use it to predict some things.

So, today we learned about energy and entropy, and briefly discussed about free energy, so, three things - energy, entropy and free energy. We will discuss about the free energy in detail little more tomorrow, but the idea basically, I want to convey, today is that one has to use ideas from statistics and mathematics to understand thermodynamics, and which in turn will tell us about bio molecules, and this is biology various biological systems.

So, many things we discussed so far actually, without discussing involve some amount of thermodynamics like Nernst's equation or Einstein's equations, but today we will discuss some more, some other in the in the coming lectures, few lectures, we will discuss few other quantities formally, and we will see how do we use mathematics for that. So, with this, I will stop today's lecture, and see you in the next lecture. Bye.