Physics of Biological Systems
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Lecture – 07
Random Walks and Passive Diffusion

We will quickly sort of recap most of us are familiar with diffusion, but we will quickly recap how to derive the diffusion equation, and then we will look at some biological context in which diffusion is applicable.

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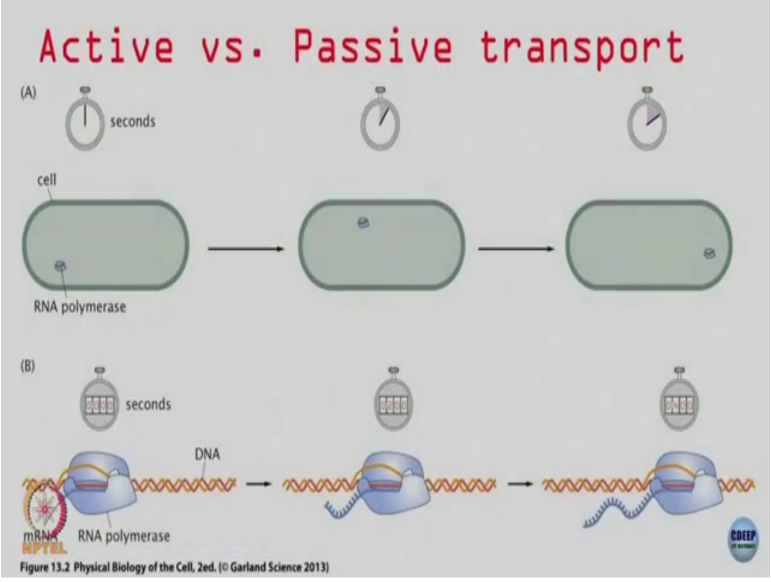
Active vs. Passive transport

Figure 13.2 Physical Biology of the Cell, 2ed. (© Garland Science 2013)

So, here is for example, the same molecule RNA polymerase ok, when it is just floating around in the cell what is performing you is passive diffusion. So, it is just floating around in the cell and the timescales of that are like tens of seconds to go for. So, this is again like it is let us say a typical E coli cell and the timescales of this are tens of seconds to cover from one end of the cell to another that is what it is doing when it is not actively sort of producing proteins from the mRNA or rather when it is not producing mRNA from the DNA.

On the other hand when it is attached to the DNA molecule, and it is sort of reading the sequence of the DNA and producing the corresponding mRNA that motion is an active process, in that it takes in energy, it does not do a jiggling motion. So, if this is my DNA track, if this is my DNA track, and this is my RNA polymerase which is bound to this is DNA track, it does not sometimes move this way and sometimes that way it moves in a directed so it moves in a directed fashion only along one direction it reads the sequence in that direction and produces the corresponding mRNA. So, the same molecule can perform active or passive motion depending on what function it is trying to achieve.

Similarly, if you look at E coli trajectories, like I said the E coli trajectory is what is called a run and tumble motion, it is a run and tumble motion. So, it will often move in some direction in directed fashion, then spend some time change direction, and again move in a in another randomly chosen direction again spend some time and so on.

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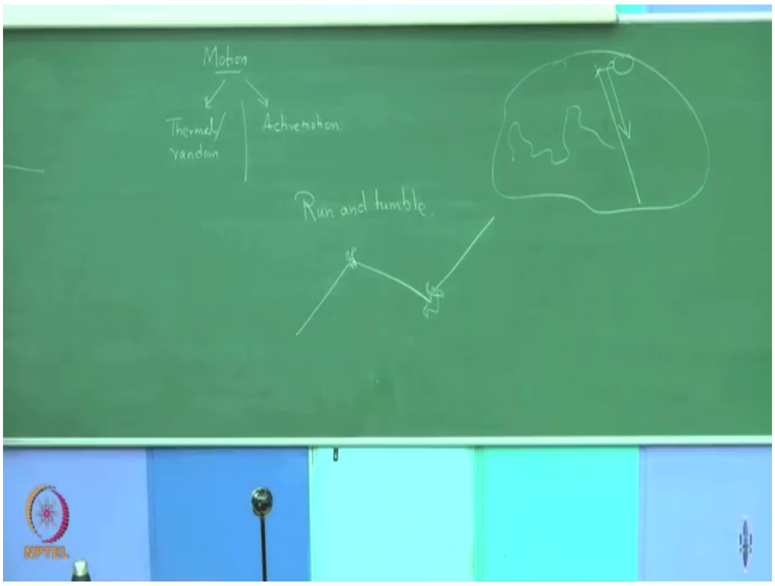

So, if you zoom out and look at the E coli trajectories, it looks like a random walk in space. If on the other hand, you were to focus on any one of these sort of long runs, this is an active process which is driven by motor proteins which is driven by the flagellar motor protein. The flagellar motor protein like I said it sort of winds up together and helps the E coli move in a directed fashion.

So, again depending on the time scales that you are looking at or what at what scale you zoom in to this process, you can think of an active description if you are looking at just these runs or a passive description if you are looking at this whole trajectory as this trajectory as a whole ok.

So, what we will start by focusing on for the first couple of lectures is this process of passive diffusion. So, let us start with a random walk. Let us start with random walk. So, at it is heart that is the most basic definition of a random walk is a process that takes successive steps in random directions.

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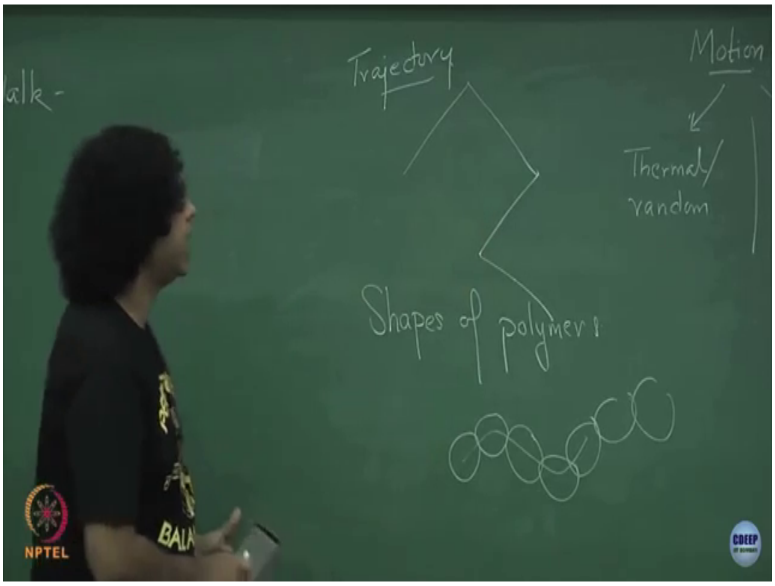

So, just like that the diagram over there it takes one step in this direction, then another step in another direction and so on, So, that is my basic random walk. It arises in many contexts, for example, in the context of E coli or other proteins, it could arise as a trajectory. So, it could arise as a trajectory all right, and that is what we look at today. But you can use the same formalism to sort of study shapes of long shapes of long molecules, shapes of polymers right.

So, if you have polymers which are made up of many, many repeating subunits called monomers, so I add one monomer, I add another monomer I add another monomer and so on. So, this is like my backbone which is like my random walk. If I build up all of these monomers together, what I get is a long polymer object polymeric object. So, if the same formalism that will sort of develop, you can use to look at shapes of polymers as well which we will do when we look at DNA and so on later on in this.

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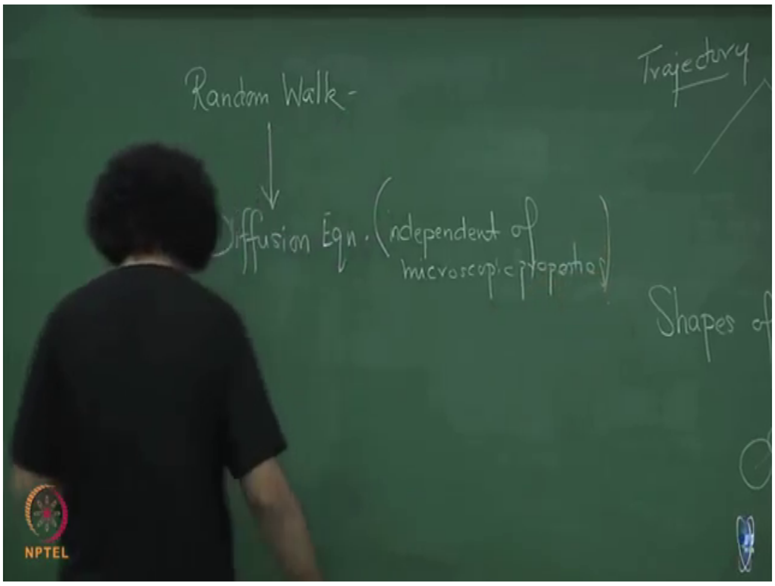

So, we will start with this microscopic process where each step is uncorrelated from the other from the previous step and in success in random directions. And we will try to and we will try to go from this microscopic description to a continuum description, and the continuum description of the random walk is the diffusion equation is the diffusion equation right.

So, if you take large numbers of long random walks, what we will end up with is the diffusion equation. And this is all this is independent of the microscopic properties of the walk; this is independent of the microscopic properties ok. So, before we do it formally, let us just look at couple of simple things, let us start off with the simplest example which is that of coin tosses.

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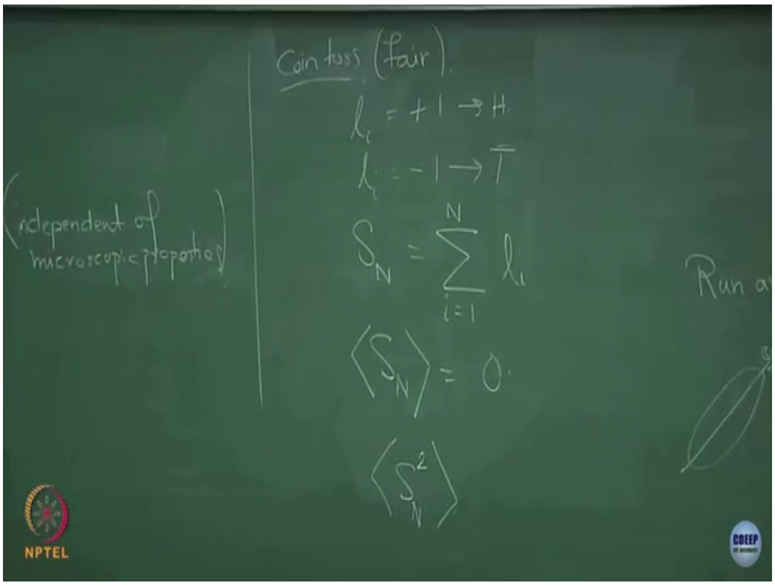

(independent of microscopic properties)

Coin toss (fair)

$l_i = +1 \rightarrow H$

$l_i = -1 \rightarrow T$

$S_N = \sum_{i=1}^{N} l_i$

$\langle S_N \rangle = 0$

$\langle S_N^2 \rangle$

Run a

So, let us start off with a coin toss right. So, let us say I toss many, many coins. If a coin comes out is heads, I say that I record that object as plus 1; let us say for heads; if it comes out as tails, then I record that object is minus 1, so this is for tails ok. i is the i th coin toss. So, this is the outcome of the i th coin toss this variable l i measures the outcome of the i th coin toss which can be either a head or a tail, and I represent a head by plus 1 and I represent the tail by minus 1 ok.

Let me construct the sum of all of these random variables. Let me construct the sum of all of these random variables as. So, if I do capital N number of coin tosses, then i equal to 1 to n sum over i l i ok. So, look at the sum of these individual random quantities l i which can be either plus 1 or minus 1 with probability half, let us say it is a fair coin. So, each head or tail comes with a probability half ok. So, what I can ask is that, what do I expect the average value of this sum to be right, what do I expect the average value of this sum to be after n such coin tosses. And what is that, 0 ok.

So, the average is often not a good measure because plus, these plus 1s and minus 1s will cancel out ok. So, what is a good characteristic measure is offering the variance of the standard deviation. So, if I do S N square, then what is that, so for n coin tosses I take the square of the sum and it take the average of that what is that?

Student: N square.

N square.

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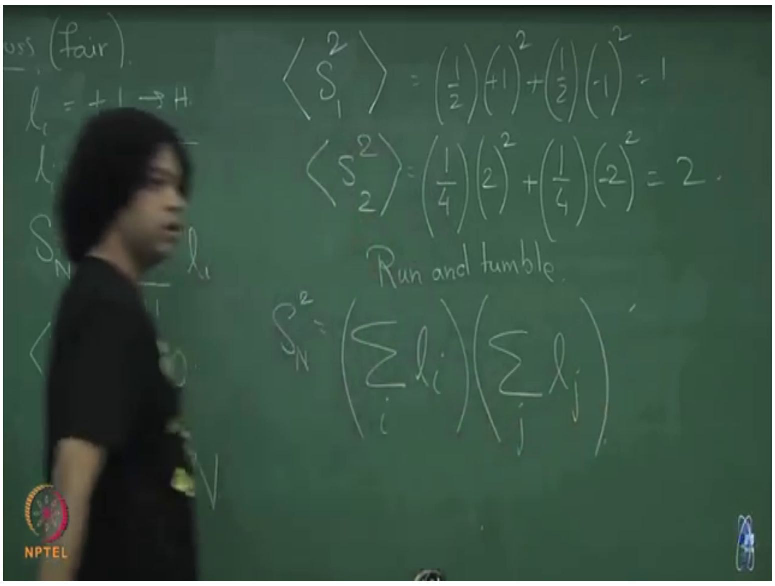

So, let us see if it is I have only tossed one coin right, so I do S 1, if I measure the average of S 1 square with probability half, it could have given me plus 1 so plus 1 square, with probability half it could have given me minus 1, so that is 1. If I do, if I have tossed two coins, so S 2 square then what can I get I can get head head, head tail, tail head, and tail tail.

What will that give me? So, if I do a head head, so one-fourth into 2 square plus the head tail and the tail head will give me S 0. So, I do not consider that the minus 1 minus 1 holds, so minus 2 square is this. So, what is that 1 plus 1 that is 2 right and so on. So, what is S N square N, not N square right ok, yes.

Student: How do I?

How do I?

Student: How do I define S N square?

How do I define S N square? So, it you understand how I construct the sum right. So, I just take the square. So, S N square it is just the square of this object right, sum over i l i sum over j l j ok.

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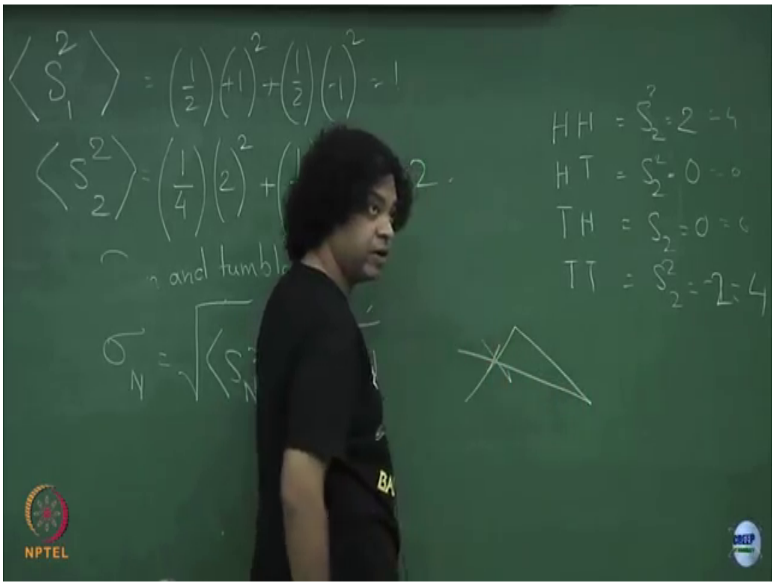

Or if you want to spell it, so if I were tossing two coins, I can get a head head, head tail, tail head, tail tail. The S N for this is so S 2 for this is 2, S 2 for this is 0, S 2 for this is 0, S 2 for this is minus 1, i square each of these. So, S 2 square is 4, here this is still 0, here, sorry this is minus 2. So, this is still minus 4, I take the. So, these are the four possible outcomes that I can have for two point doses.

I take the average of all of this, this event has probability one-fourth, one-fourth, one-fourth, one-fourth and so on or formally this is what it is you take this summation you would take the product that gives you S N square ok. So, the standard deviation therefore goes as the square root of N right.

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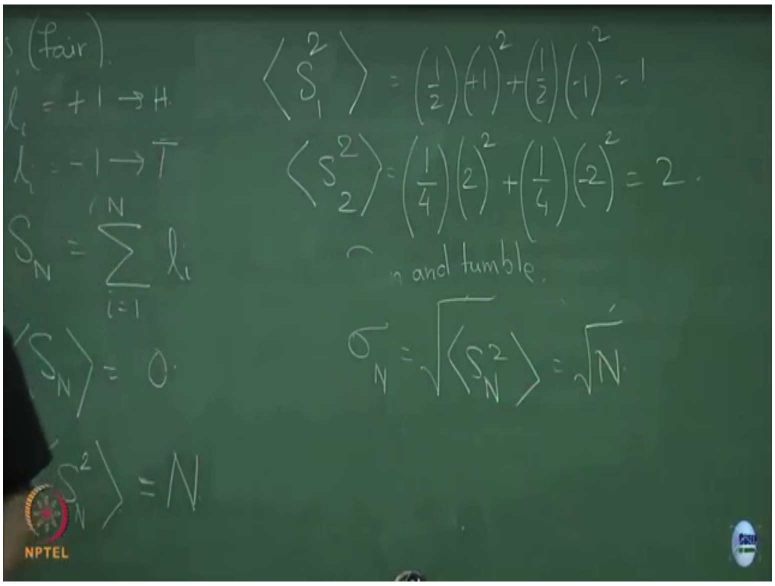

s (fair)

$l_i = +1 \rightarrow H$

$l_i = -1 \rightarrow T$

$S_N = \sum_{i=1}^{N} l_i$

$\langle S_N \rangle = 0$

$\langle S_N^2 \rangle = N$

$\langle S_1^2 \rangle = \left(\frac{1}{2}\right)(+1)^2 + \left(\frac{1}{2}\right)(-1)^2 = 1$

$\langle S_2^2 \rangle = \left(\frac{1}{4}\right)(2)^2 + \left(\frac{1}{4}\right)(-2)^2 = 2$

n and tumble

$\sigma_N = \sqrt{\langle S_N^2 \rangle} = \sqrt{N}$

Sigma N which is square root of this S N square goes a square root of N for this coin toss process ok, so that is like a simple example. We can now actually take random walks. So, if we think about an actual project, so let us say I am talking about trajectories of particles.

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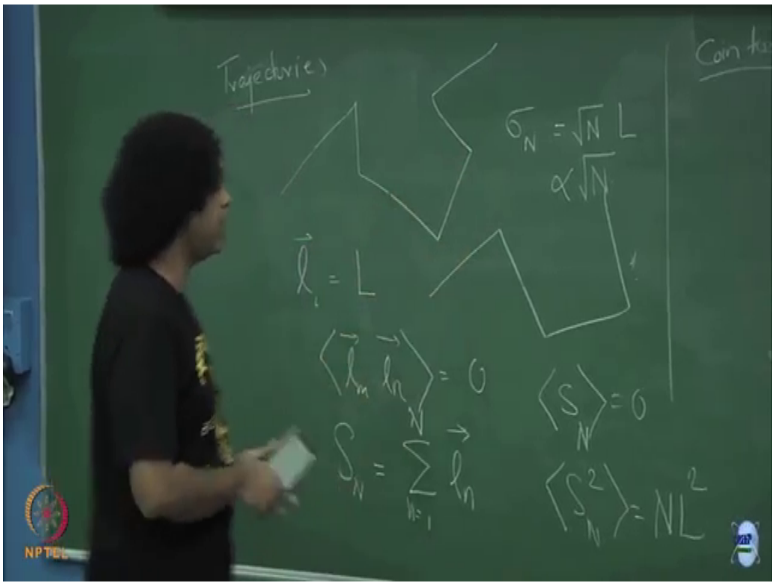

If I think of an actual trajectory such as that of an e coli, it might look something like this. So, each step might in be of different lengths right they would be in different random directions they can have different velocities and so on. Let me simplify this a bit. So, let me say that each I fix the length of each step ok. So, let me say each. So, I still call represent each step by this variables l i. So, each step has some fixed length L.

So, my simplified random walk is like this, assume that these are all of same length, what is random is the direction ok. So, this is step 1, this is step 2. Step 2 direction is uncorrelated from the step 1 direction ok. So, it starts off at some point at time t equal to 0, and I let it continue for some time. The steps are uncorrelated means that if I take this average lm dot ln let me put a vector sign, so lm dot ln is 0. So, it has no dip this one step has no correlation with any other step. So, these are completely uncorrelated.

So, again I look at the sum. So, I look at how much distance it has covered after N steps. So, again I look at this sum S N which is the sum of these individual steps that you take n equal to 1 to capital N ok. So, I construct this sum. And again what will be the average of this sum, so what will be the average of this sum 0 right, because on an average you will not really travel anywhere. What will be this variance of this sum S N square?

Student: (Refer Time: 13:00).

N L square right. So, again if I look at the standard deviation sigma N that is square root N times L. So, again it is proportional to the number of steps square root of N right. So, you will find that for a large class of objects like this independent of whether I took equal steps or I did not take equal steps and so on.

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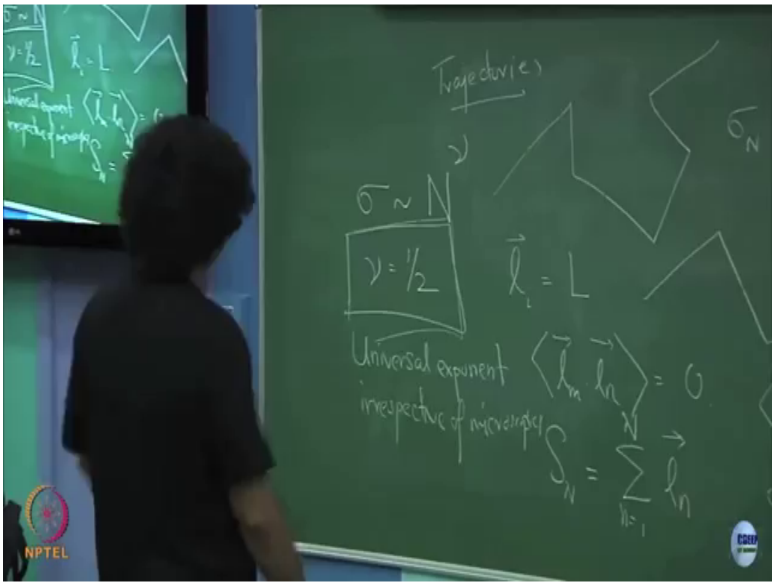

What I will get is that the standard the standard deviation will vary with the number of steps as N to the power of nu, where nu is equal to half. So, this is an exponent which is universal irrespective this is an universal exponent for this class of processes irrespective of the microscopic details, irrespective of the microscope details all right. So, you could take variable times, you could take variable speeds, you could even have some time correlations, you would still get this nu is equal to half.

So, all processes which follow this sort of a standard deviation N to the power of half, we will see they fall on the same universality class. If you get a different nu for some process that is described by a different sort of physics, so it falls under a different universal universalality class. For example, if instead of taking this sort of a walk, if instead of taking this sort of a random walk, you took random walks, which was self avoiding right. So, you have said that your trajectories could not cross each other.

So, you could not have something like this if you had self avoiding walks, then you would no longer have this nu, you would have a different nu and that would fall under a different universality class ok. So, with this fine right this is sort of basic. So, let us try to quickly derive the diffusion equation. Remember the diffusion equation is the continuum limit of these microscopic random walks.

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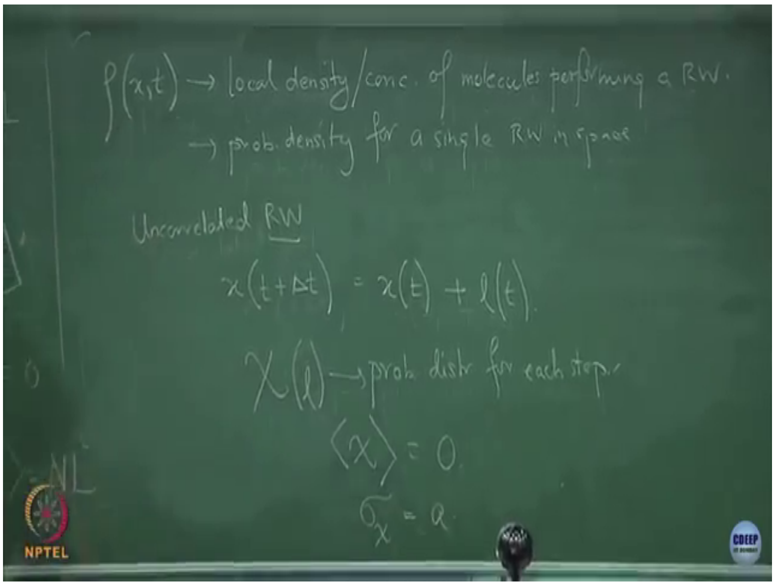

$\rho(x,t) \rightarrow$ local density/conc. of molecules performing a RW.

$\rightarrow$ prob. density for a single RW in space

Uncorrelated RW

$$x(t+\Delta t) = x(t) + l(t).$$

$\chi(l) \rightarrow$ prob. distr for each step.

$$\langle x \rangle = 0.$$

$$\sigma_x = a.$$

So, let me define this quantity rho of x comma t. Let this could be like the local density local density or concentration of molecules performing a random walk. Or if you have a single random walker then this could be like the probability density, this could be like the probability density for a single random walker in space.

So, if you have many, many random walkers, all doing their own random walks happily, then you could think of this is a density or concentration, if you have a single random walker you could think of this is the probability density to find that random walker at position x at time t ok. So, let me consider uncorrelated random walk, let me consider an uncorrelated random walk right which evolves according to this equation that x at time t plus delta t, the position of the random walker at time t plus delta t is whatever it was at time t.

So, x of t plus this step that it takes at time t l of t, where the steps are drawn from some distribution. So, with let me call as chi chi of l this is the probability distribution this is the probability distribution for each step. So, every time I take a random step l of t, which l of t I draw from some distribution which I call chi of l ok. The only constraint that I put is that this mean of this chi is 0. And let us say the standard deviation of this distribution sigma I call some quantity a.

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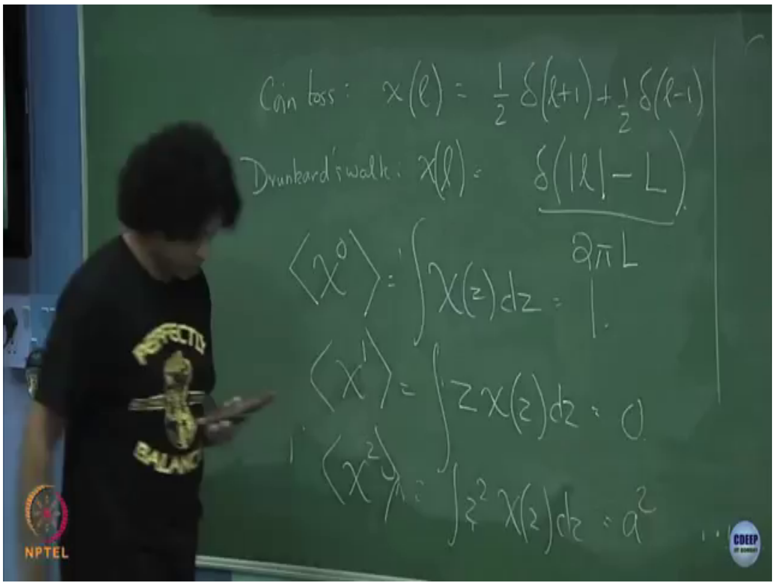

So, just to clarify for example, if I am thinking of this, if I was thinking of this coin tosses, then what would this say if I thinking of coin toss coin tosses, then what would the chi of l be what we values could that random variable take for the coin tosses it could be plus 1 or minus 1 each with a probability half. So, therefore, this distribution chi of l in that case would be half delta l plus 1 plus half delta l minus 1 right, it could take two values plus 1 and minus 1, each with probability half ok.

If I were thinking of this equal length random walk which is often actually called a drunkard's walk, drunkard's walk, then what would that chi of l be for example,. So, again all steps remember: what was the constraint that all steps were of equal size, which means that and that was equal to capital L right. So, mod l would be equal to capital L, and let us say it is in 2 d. So, it can choose any direction any random direction within a circle of this radius right. So, 2 pi L each direction is equally likely right it is a completely random. So, then that would be my corresponding probability distribution for that drunkard's walk.

So, you can have any distribution depending on what is the microscopic process that you are trying to model. Each process would have a different chi of l, I do not care this description is valid for any microscopic process as long as the mean is 0, and the standard deviation is some value which let me call as a ok. So, basically the moments of this distribution are, so the 0th moment is integral chi of z dz.

What is that? What is integral chi z dz? Who said 0? What is the property of the probability distribution 1 right. So, it has to be normalized. The first moment chi one is z chi z d z that is 0, because that is the constraint. The second moment chi 2 is z square chi z tz is a square ok, all right, so that that is that is how I define my process.

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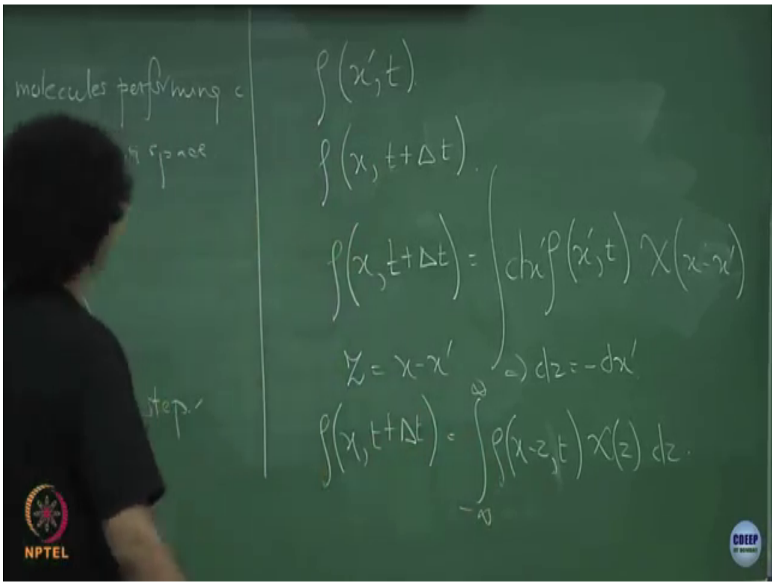

So, now, what I want to ask is that given what I want to ask is that given some probability distribution at time t x prime comma t: what is the probability distribution at some time t plus delta. So, given some probability distribution at time t what is the probability distribution in the next instance of time t plus delta t ok. So, how do I go from here to here, so rho of x t plus delta t ok.

So, I was at x prime at time t, I was at x prime at time t right, I need to be at x which means that my step length should be x prime minus x. What is the probability for that that is chi of x prime minus x right, so chi of x prime minus x right. You were at x prime you take a step of length x prime minus x that brings you to x ok.

What do I need to integrate over x prime you could be at any position at the previous instance of time. All I need is that you reach x y integrate over x prime right ok. So, now, let me do some change of variables and so on. Let me call this z as the this I wrote [FL] all right, let me write x minus x prime, let me call this z as x minus x prime ok, so dz dz is minus dx prime right. So, then rho of x t plus delta t is equal to integral rho of x minus z comma t chi of z dz minus infinity to infinity ok, ok.

So, now, I will expand this row of x I will assume that the step z is small compared to x, and I will expand this row x minus z in a Taylor series.

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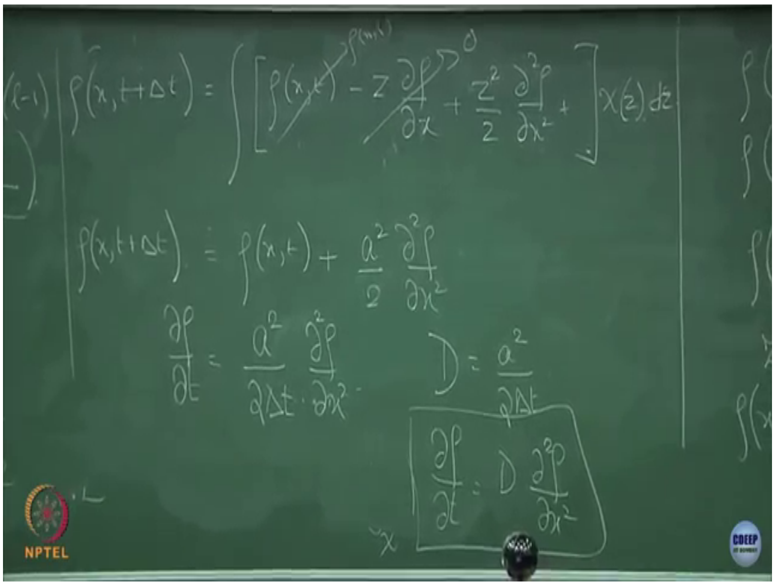

So, let me expand, so rho of rho of x comma t plus delta t is equal to integral, I will expand that rho x minus z. So, rho of x comma t minus z del rho del z right del x del x plus z square by 2 del 2 rho del x 2 and so on. I will keep only terms up to second order, and then I have that chi of z dz all right. So, now, I can do each of these integrals one by one. The first integral is just integral rho of x comma t chi of z dz. So, what is, so this will come out. So, what is integral chi of z dz that is simply 1 right, actually it mean instead of writing individually let me just.

So, this term when I do an integration will give me a rho of x comma t. What will this term second term give me, that will give me a 0, because the z integral is z chi z which because I have chosen the mean to be 0, will give me a 0. What will this will give me this will give me the variance right. So, if I bring it all together this term gives me a rho of x comma t, and then I get a square by 2 del 2 rho del x 2. So, this is rho of x comma t plus delta t.

I can bring this to this side divide by delta t throughout then the left hand side would become a del rho del t right. The right hand side would become a square by 2 delta t del 2 rho by del x 2 right. So, I call this object as my diffusion constant, so I call this object as my diffusion constant D is a square by 2 delta t, it has units of l square over time, and then this equation continuum version of this equation becomes del rho del t is equal to d del 2 rho del x 2 which is nothing but my diffusion equation. I could do this, and of course, in any I did this in one dimension, but I could row could be a function of x y z and so on in which case this would be del square right v del square rho.

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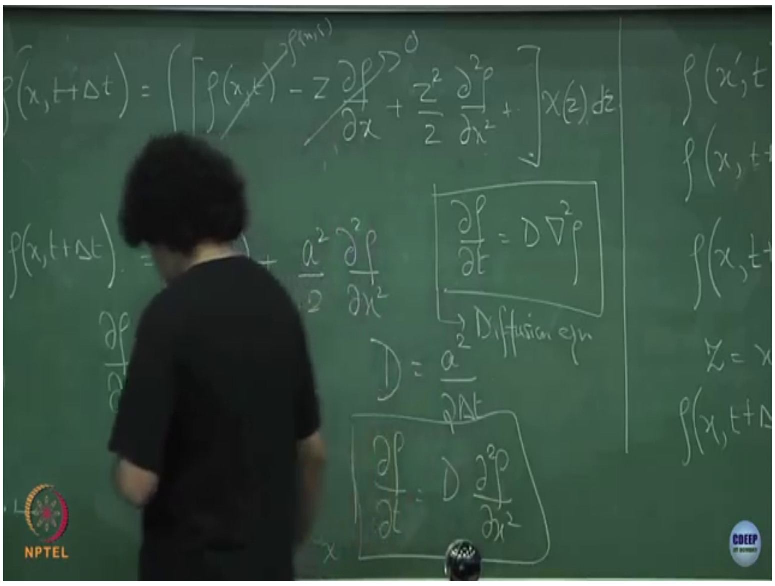

The in general I would get del rho del t would be D del square rho. So, I started off from a microscopic random walk, I imposed only the condition that the steps are uncorrelated. And the steps were drawn from a probability distribution with zero mean and constant variance, and I tip the continuum limit of that equate of this microscopic walk, and what I reach is the diffusion equation.

So, this is my diffusion equation ok. What does the diffusion equation tend to do, the diffusion equation is one of those equations which are very boring at it is heart it is sort of tends to even out any hills or valleys that you might have.

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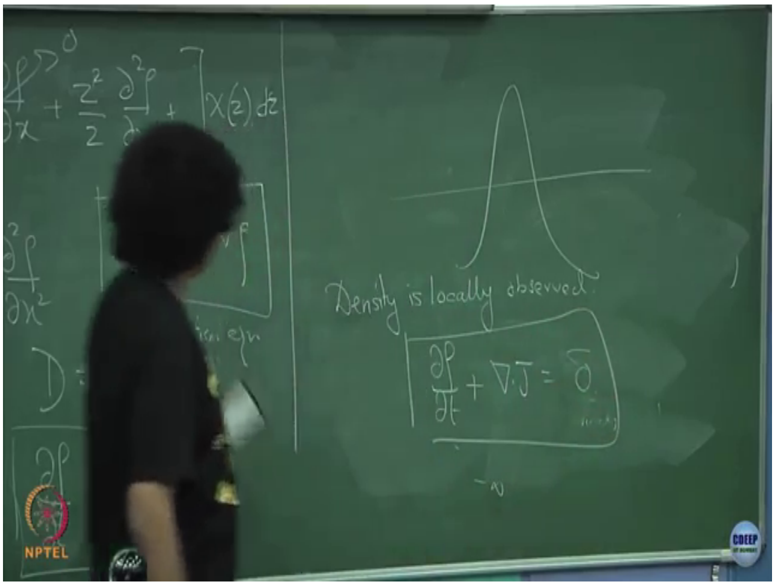

So, if you started off with a concentration distribution concentration or a probability distribution that looked like this and things were diffusing, then over time what you would reach is a sort of flat profile right, so that is what the diffusion equation would tend to do. The diffusive dynamics will flatten out any hills or valleys that you might have. If your particles your object which are undergoing this diffusion are not created or destroyed, so if these are conserved objects, so if your density is locally conserved if your density is locally conserved that is the random walkers are neither created nor destroyed.

Then you can write the continuity equation which is what which is del rho del t which is del rho del t plus divergence of j is equal to 0 right that is my continuity equation in the absence of any sources or sinks. If you had sources or sinks you would get some contribution from sources over here right. But in the absence of any sources or things you can write this continuity equation which together with the diffusion equation implies with the diffusive flux or the diffusive cut into j is nothing but.

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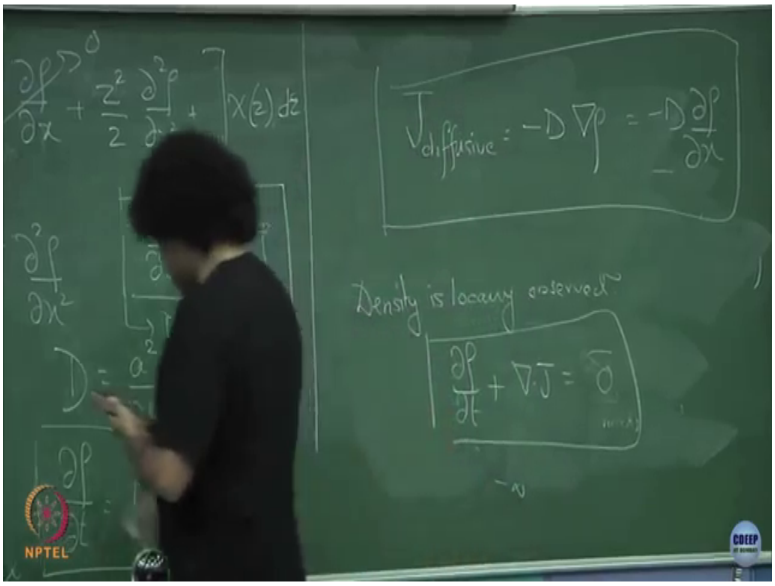

The diffusive j diffusive is nothing but minus D gradient of rho or in one dimension it is minus D del rho del x right if I put this j over here I will get back to the diffusion equation. So, this is my diffusive flux.

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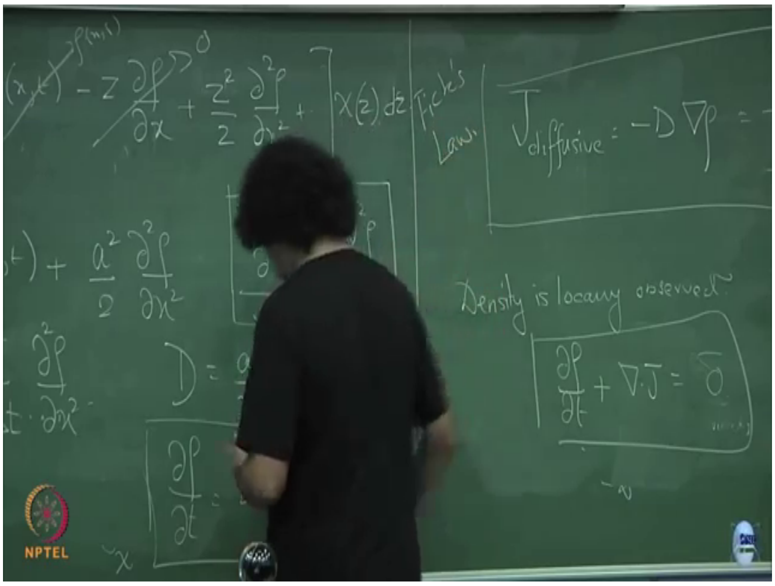

This also has a name it is called Fick's law. Hopefully all of this is roughly familiar at least you know if the derivation is not familiar the diffusion equation should in itself be familiar. Is this sort of clear? Ok good. So, with this background let us just see in what contexts diffusion arises in biology and then let us try to work out one of these cases.