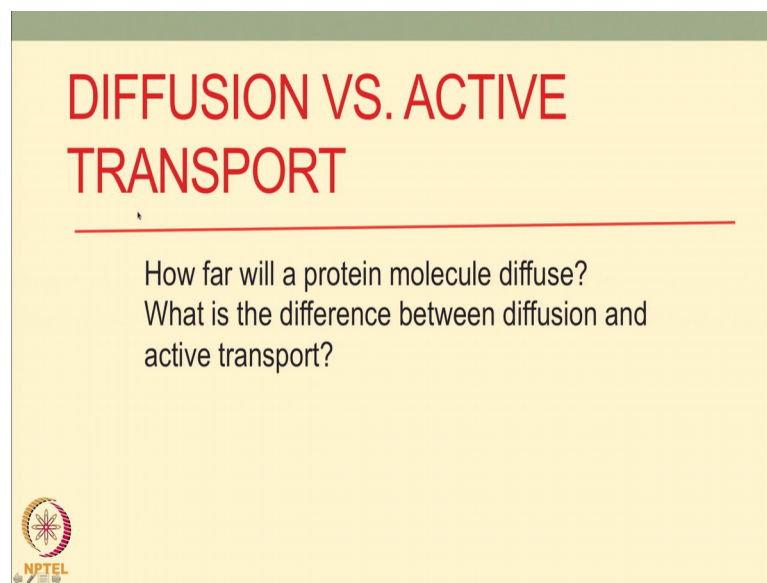


Introductory Mathematical Methods for Biologists
Prof. Ranjith Padinhateeri
Department of Biosciences & Bioengineering
Indian Institute of Technology, Bombay

Lecture - 30
Diffusion vs. Active Transport

Hi. Welcome to this lecture on mathematical methods for biologists. We learned about diffusion and we learned that how to use calculus to understand the diffusion and the diffusion equation. Today we will learn one more thing about will try to learn to calculate some things from the equation that we learned which would be very useful in a in biology and to estimate various co estimate quantities about like how far apart protein will diffuse and so on and so forth.

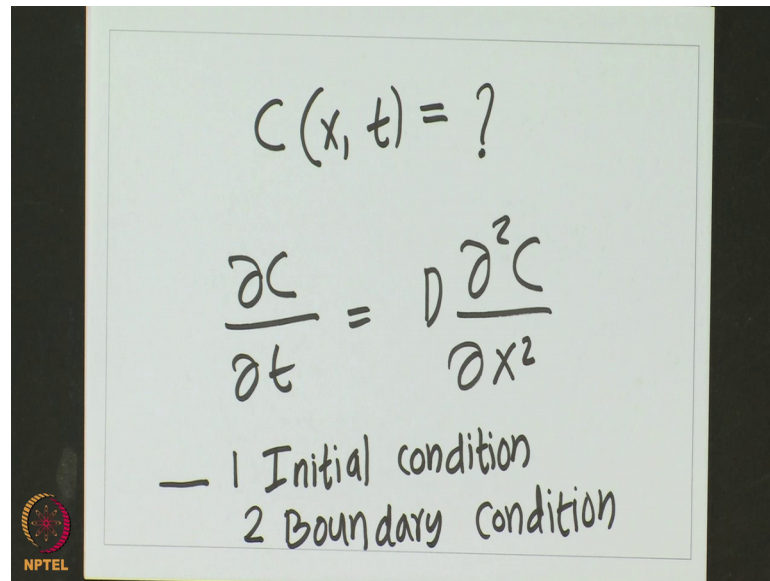
(Refer Slide Time: 00:58)



So, that and today's topic therefore, is diffusion versus active transport. So, that is what we will discuss today and the question will try to answer in this lecture is how far will a protein molecule diffuse and what is the difference between diffusion and active transport. So, this is something that we will discuss, we will I try to answer these 2 questions that how far will a protein molecule diffuse in a typical condition and what is the difference between diffusion and active transport.

So, what we learned is an equation which describes the diffusion of protein monomers. So, and the question we described was that.

(Refer Slide Time: 01:39)



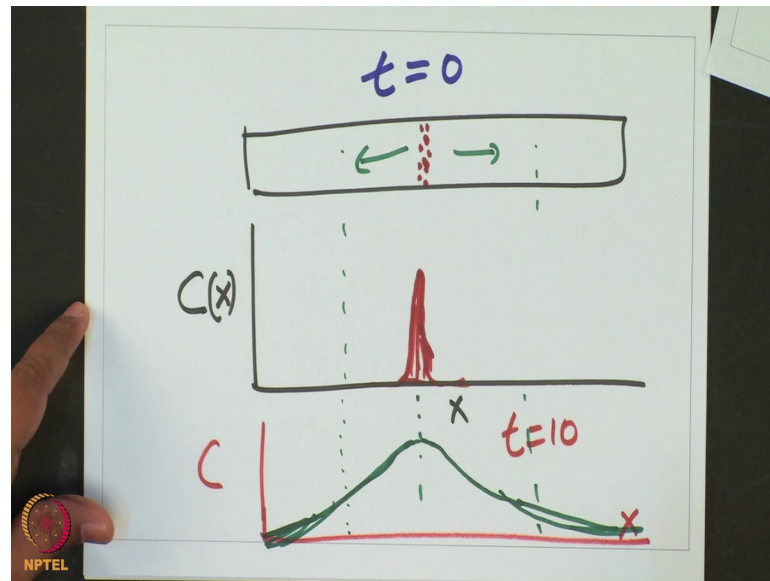
The image shows a whiteboard with handwritten text. At the top, it says $C(x, t) = ?$. Below that is the diffusion equation: $\frac{\partial C}{\partial t} = D \frac{\partial^2 C}{\partial x^2}$. At the bottom, it lists two conditions: "1 Initial condition" and "2 Boundary condition". In the bottom left corner of the whiteboard, there is a small circular logo with the text "NPTEL" below it.

If C is a concentration of protein molecules as a function of x and time instead of x , it could be x, y, z , if we know this, if we want to know the concentrations of function of x of x and t , if we know some quantities this C would can be obtained by solving this equation $\frac{\partial C}{\partial t}$ is equal to $D \frac{\partial^2 C}{\partial x^2}$. So, this is the equation that we learned for this C , this is the diffusion equation and by solving this by; so, by solving this; the equation we will get C as a function of time. So, this C is a solution of this equation.

So, to get this; to get C as a function of x comma t , we have to solve this equation and what we know is that to solve any differential equation. We need something called initial condition. So, here there is a derivative of in time therefore, we need a we need some initial condition and we also there is a 2 derivatives in x therefore, we would need 2 conditions for that which we would call typically boundary conditions. So, we would need 2 boundary conditions to solve such one initial condition and 2 boundary condition if we provide this we would we able to solve it.

So, let us think of the following situation which is important to understand this imagine.

(Refer Slide Time: 03:24)



That you have a cell as we have been imagining along one dimensional cell which is very long and if you imagine a time is equal to 0. So, time is equal to 0, we assume that all the protein molecules are just 1 point here. So, only at this particular point we have protein molecules only here.

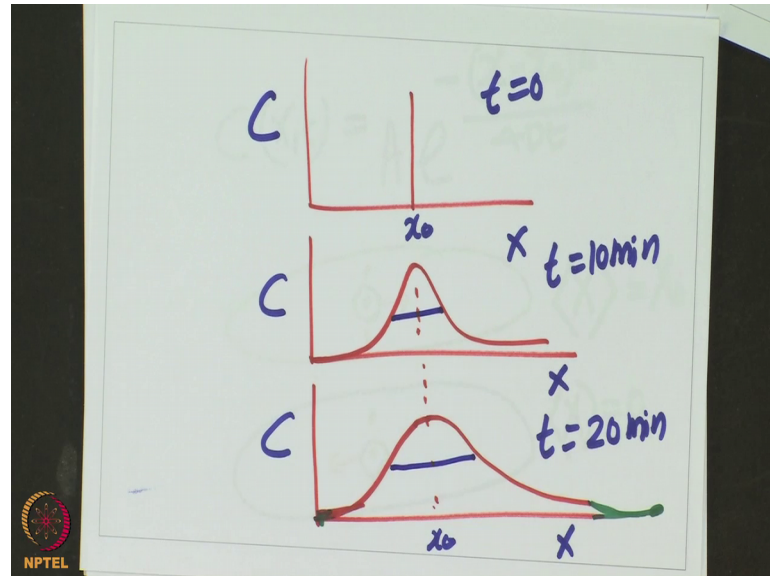
So, if I plot concentration versus x at t equal to 0 this would be almost like a delta function almost will be a function only has value here everywhere is a function as 0 such functions are called delta functions Dirac delta functions if you want to assume this is a very you can even imagine this is a Gaussian with a very small width. So, you could imagine this is a Gaussian with a very small very small width. So, you can imagine this is a Gaussian with very small width if you want. So, you essentially have a dist concentration which is a peak at essentially at one point.

Now, after 10 minutes if we look at this. So, when you look at t is equal to 10 minutes how will that concentration versus x will appear it turns out that as the time progresses this would diffuse this way and this would diffuse this way and the concentration at this x values. For example, the concentration here and the concentration here would be slightly higher it will be non-zero.

Therefore, after long time after sufficiently long time you would get some. So, this would be this you would expect some function something like this something some

symmetric function something like this, this should be symmetric on either side, I can draw this better a symmetric nice function like this.

(Refer Slide Time: 05:51)



Now, let us imagine this further. So, as the if I start with a t equal to 0, we have a delta function and as time goes, it would be a function like this and as it goes further, it will spread further. So, let me draw this it would spread further and further and further.

So, you could imagine concentration versus x concentration versus x concentration versus x . So, this is t equal to 0. So, this is equal to t is equal to 10 minutes this is further like t is equal to 20 minutes or 30 minutes. So, as the time progresses the concentration would have a functional form something like this naively speaking.

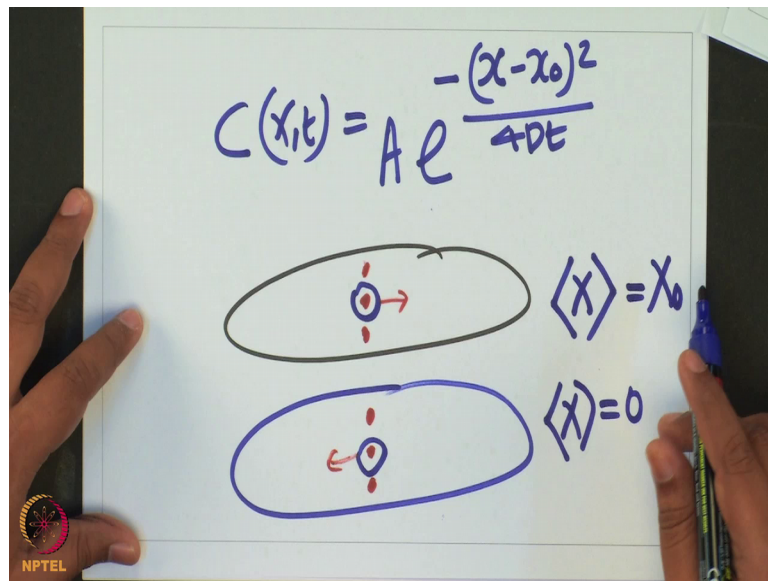
Now, mathematically how do we get it, we can get this by solving this equation for appropriate boundary conditions and initial conditions depending on various boundary condition initial condition one will have various solutions this need not be the solution always this is a typical solution. So, such solutions are obtained by assuming 2 things 1 is at t equal to 0.

The concentration is like only the concentration is highly peaked at one point the concentration at delta function and as time at far away that is here at this boundary is like if far away here the derivatives and concentrations are 0 and the assuming this kind of conditions at infinities the derivative in the concentration is 0 and at t equal to 0, it has a

delta function if you assume such boundary conditions one will get nice symmetric functions.

So, a symmetric function which represents this is a Gaussian function. So, typical solution for this kind of a diffusion equation is a Gaussian function which is C of x comma t .

(Refer Slide Time: 07:54)



The image shows a whiteboard with handwritten content. At the top, the equation $C(x,t) = A e^{-\frac{(x-x_0)^2}{4Dt}}$ is written in blue ink. Below the equation, there are two diagrams. The first diagram shows a red dot with a red arrow pointing to the right, enclosed in a black oval, with the text $\langle x \rangle = x_0$ to its right. The second diagram shows a red dot with a red arrow pointing to the left, enclosed in a blue oval, with the text $\langle x \rangle = 0$ to its right. An NPTEL logo is visible in the bottom left corner of the whiteboard.

So, if you assume nice initial condition and boundary condition one would get a typical solution which you would read in textbook which has some functional form like this e power minus x minus x_0 whole square divided by $4Dt$ at x equal to x_0 which is this location. So, this is my x_0 . So, at x equal to x_0 you will have a peak and it will be symmetric around x_0 and as time goes this denominator term will increase and which would make this spread.

So, this is the solution for the diffusion equation under some particular; so, initial and boundary conditions. So, I urge you to read about it learn this a little bit more, but does not matter what you should know is that by solving those equations one can get a C as C as a function of x comma t and one would be able to know the concentration at any point.

What we are further interested is the following imagine that you have a cell like if you imagine a at t equal to 0 as we just said there is the protein molecules are only at one point. So, this is a t equal to 0 as the time progresses this would spread as we know. So,

ill I do one experiment let us say I did one experiment and I saw that if I focus. So, I have the situation I will focus on one molecule.

So, let us focus on one protein molecule and if I track this protein molecule I would see that this going in some random direction. So, let us say it went in this direction first and then it took various random directions in some other experiment. If we repeat the experiment if I repeat this experiment exactly under same conditions, I repeated exactly same experiment same condition and I tracked another molecule this time this might as well go this way we do not know.

So, on an average if you average over many experiments it is a fair question to ask what is the average position of particles of a over a given particle as the time proceeds or at any time and it turns out that if you average over many realizations since things are symmetric the x average will be x_0 or if x_0 is 0 the x average will be 0. So, x average would be 0 if $x_0 = 0$, otherwise on an average, it would be at the peak at this at this initial position itself it would as if that on an average the position would be the x_0 which is the initial position itself.

Now, how would it how much would it spread how much is this spread this is calculated how much it would at any given time at 20 minutes; how much it would spread this spread is basically calculated by this quantity call root mean square distance as we would learn little bit in the statistics or anybody who has learn statistics would know that the spread which is x^2 average minus x average square.

(Refer Slide Time: 11:27)

The image shows a whiteboard with handwritten text in blue ink. At the top, the equation $\langle x^2 \rangle - \langle x \rangle^2 = \text{variance}$ is written. Below it, a double arrow points down to the word "spread". At the bottom, the equation $\sigma^2 = \langle x^2 \rangle - \langle x \rangle^2 = 2Dt$ is written. A hand is visible on the left side of the whiteboard, and a blue marker is on the right side. In the bottom left corner, there is a small circular logo with the text "NPTEL" below it.

$$\langle x^2 \rangle - \langle x \rangle^2 = \text{variance}$$

↓
spread

$$\sigma^2 = \langle x^2 \rangle - \langle x \rangle^2 = 2Dt$$

This is the spread which is the standard which is the variance. So, this is the variance and this basically tells us that how much would a molecule spread after some time the amount of spread the width of this distribution is essentially given by this and it turns out this quantity which let me call sigma square which is x square average minus x average square and it turns out this is equal to in one dimensional it is 2 dt. So, x square average is 2 Dt, if x average is 0 if I can take x 0 equal to 0. So, then it says x square average is 2 dt.

So, interesting to note that the square of space variable x square is proportional to time this is important to remember. This is a very important property of diffusion that x square average.

(Refer Slide Time: 12:45)

The image shows a whiteboard with handwritten mathematical derivations. At the top left, the equation $\langle x^2 \rangle = 2Dt$ is written in blue ink. An arrow points from the text "mean, average" to the angular bracket in $\langle x^2 \rangle$. Below this, the equation $\overline{x^2} = 2Dt$ is written. To the right of a vertical line, the root mean square distance is derived: $x_{rms} = \sqrt{\langle x^2 \rangle}$, followed by $= \sqrt{\overline{x^2}}$, and finally $= \sqrt{2Dt}$. In the bottom left corner of the whiteboard, there is a small circular logo with the text "NPTEL" below it.

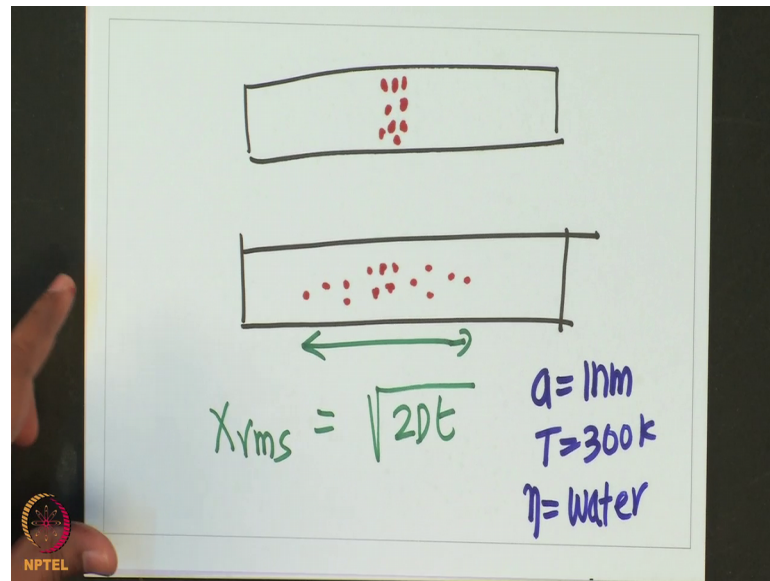
So, this angular bracket would mean or average mean average this the angular bracket means this is equal to $2Dt$ in 1 dimensional and depend in three dimensional it will be $6Dt$ in 2 dimensional like $4Dt$. So, x square average is $2Dt$, this is also sometimes written as x square bar; bar would also mean average or mean. So, this is $2Dt$ is important remember the square is proportional to time the root of this which is called the x rms the rms distance.

So, this is let me call this x rms root mean square distance. So, I find root of mean and square in other words some someplace it will be written as x square bar like this which would of course, be root of this it will be root of $2Dt$ square root of $2Dt$.

So, this is an important relation that one should remember to calculate the spread how far the protein would the concentration would spread if I start from one point. So, if you using this one can estimate the distance a typical distance the root mean square distance is the typical distance typical distance protein would spread given some time t this is answered by this formula.

So, let us calculate this x rms which. So, let us let me physically explain this once more this is very important for all of you to understand.

(Refer Slide Time: 14:36)



If we imagine a cell as we have been imagining and if we consider at t equals 0 lot of proteins accumulated at one point and as the time progresses this protein would spread. So, let us say this is after 10 minutes the protein has spread to a larger this. So, you have few here and this has spread to a larger distance; how far the spread is. So, this distance over which this has approximately spread this is the physical measure of X_{rms} which is root of $2Dt$ this is the root mean square distance in one dimension this is $2Dt$ in 2 dimension its $4Dt$ and three dimension it is $6Dt$.

So, this we will let us compute this spread the distance over which a protein would spread given a time and a diffusion coefficient we can compute this and let us do this for a particular protein. So, let us do the let us assume these are protein molecules having a size of 1 nanometer. So, let us assume protein having diameter one nanometer at 300 Kelvin and let us assume viscosity of water which is 10^{-3} si unit.

So, then we will ask the question how much it will spread what is the spread can we measure and this spread is measured by calculated by this. So, let us calculate this $2Dt$. So, in one second, if I take t is equal to one second root t , d will $2d$ will give me the distance the spread over one second. So, root $2d$ will give me the distance over spread over one second. So, let us do that calculate here.

(Refer Slide Time: 16:45)

$$D = \frac{k_B T}{6\pi\eta a} \approx 10^{-10} \frac{\text{m}^2}{\text{s}}$$
$$\sqrt{2D \times 1 \text{ sec}} = \sqrt{2 \times 10^{-10}}$$
$$X_{\text{rms}} \approx 10^{-5} \text{ m} \approx 10 \mu\text{m}$$

So, let me calculate x square. So, d for a protein is $k_B T$ divided by $6\pi\eta a$ and if I substitute these values this will be approximately 10^{-10} meter square per second root $2d$ and if I take one second as the time, this will be root 2 into 10^{-10} meter square. So, this is approximately 10^{-5} ; 10^{-5} si unit is meter. So, this is going to be the x_{rms} .

So, in other words this is approximately 10 micrometer. So, in one second the spread would be approximately 10 micrometer. So, this is the an interesting answer that we would get that if I take a one nanometer protein and ask the question that if I take a concentration of one nanometers protein and ask the question how far it will spread in one second the answer is approximately 10 micrometer.

So, this is one interesting point another interesting point one should remember is that let us consider 1 second and 100 seconds.

(Refer Slide Time: 18:16)

$$t=1s, X_{rms}(t=1s) = 10\mu m \leftarrow 1s$$
$$t=100s, X_{rms} = \sqrt{2Dt}$$
$$= 2 \times 10^{-10} \times 10^2 = \sqrt{2 \times 10^{-8}}$$
$$\approx 10^{-4} \approx 100\mu m \leftarrow 100$$

$X \sim \sqrt{t}$

NPTEL

So, let us do this X_{rms} t is equal to 1 second, we found this is 10 micrometer now if. So, this is t is equal to 1 second, if t is equal to hundred second X_{rms} will be root 2 d hundred root t is hundred. So, this is approximately equal to 2 times 10 power minus 10 times 100 which is 10 power 2. So, this would be approximately root 2 times 10 power minus 8.

So, this is let me approximately write it as 10 power minus 4 and this is basically hundred micrometer. So, this is approximately 100 micrometer. So, in one second it was 10 micrometer in either when the time was increased by hundred times. So, time was increase from 1 to 100; 100 times the distance increased by 10 times. So, the x is like increases like square root of t this is the hallmark of diffusion when I increase time by hundred times the x only increases by 10 times it change from 10 to 100, 1 to 100 here.

(Refer Slide Time: 19:57)

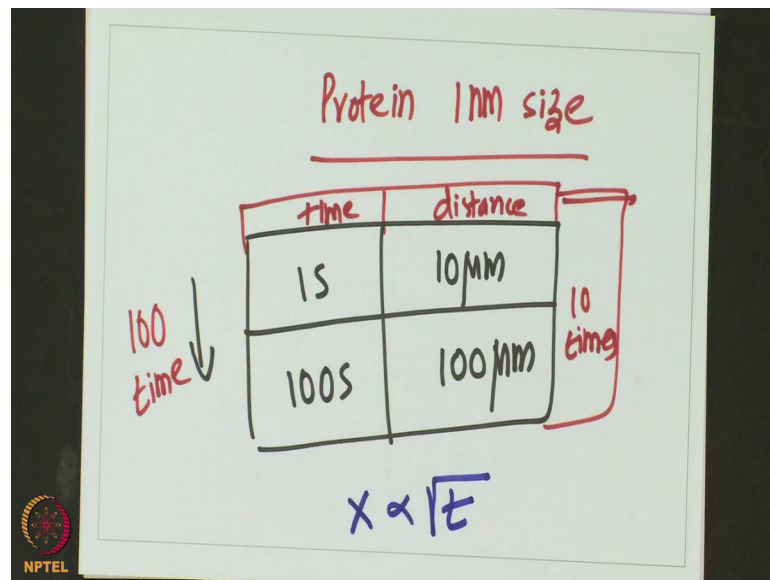
Protein 1nm size

time	distance
1s	10μm
100s	100μm

100 time ↓

10 times

$x \propto \sqrt{t}$

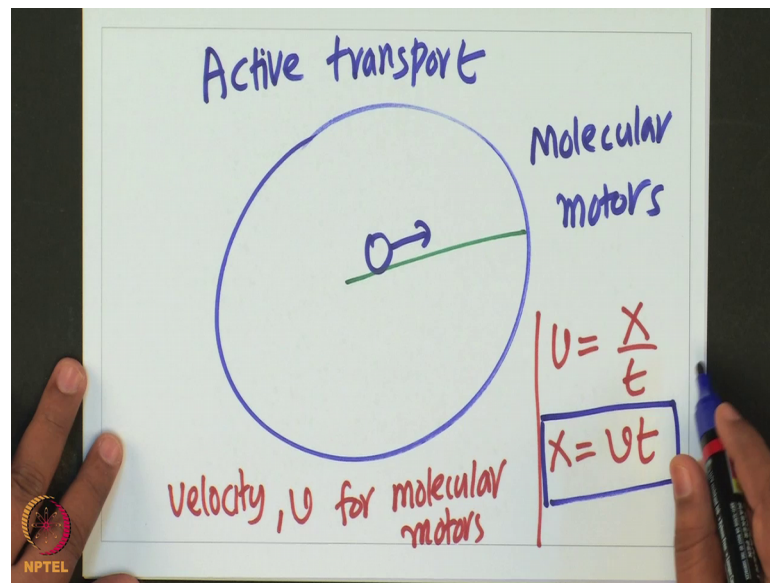


Let me say this in if I take protein one nanometer size if I take this protein and ask the question how far it will diffuse in 1 second, 10 micrometer is answer in 100 seconds 100 micrometer.

So, the time was increased by hundred times. So, the time 100 times the distance. So, this is time, this is the distance spread this increased by 10 times in other words the distance variable x , the spread is proportional to square root of time this is the hallmark of diffusion which all of you should remember if I increase the time by t times n times this will increase only root n times. So, that is the hallmark of diffusion that all of you should remember.

Now, as oppose to diffusion there is active transport inside the cell for example, there are molecular motors which would carry and transport things. So, if you consider a cell there are 2 kinds of transport one can imagine.

(Refer Slide Time: 21:26)

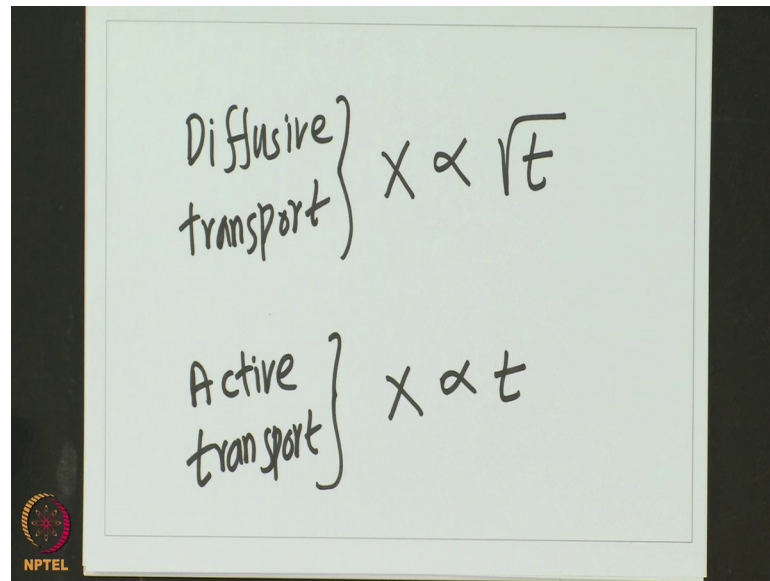


So, you have a cell and there are molecular machines which would carry particles vesicles along a microtubule. So, there is an active transport. So, this is are called molecular motors this molecular motors will transport using atp; they will use atp and transport things and how far will this go in as a function of time.

So, these molecular motors have a velocity. So, velocity of molecular motors molecular motors has a velocity. So, velocity v for molecular motor molecular motors, have a velocity; velocity is distance by time right it is like x by t . So, x is vt . So, here in the active transport, this is transport by molecular motors are call active transport. So, let me call this active transport what do I mean by active transport this is transport by molecular machines. So, they apply some force and carry something. So, there is a force typically applied at the they use energy from atp hydrolysis or the food we eat and it transport things.

So, there are a typical transport molecular motors move along microtubule a typical molecular motors names are Kinesins and Dynein. So, they walk along microtubules and transport vesicles this is this should be contrasted with diffusive transport. So, here just remember x goes as vt ; there x went like $\sqrt{2Dt}$. So, let me contrast this transport active transport versus diffusive transport.

(Refer Slide Time: 23:46)



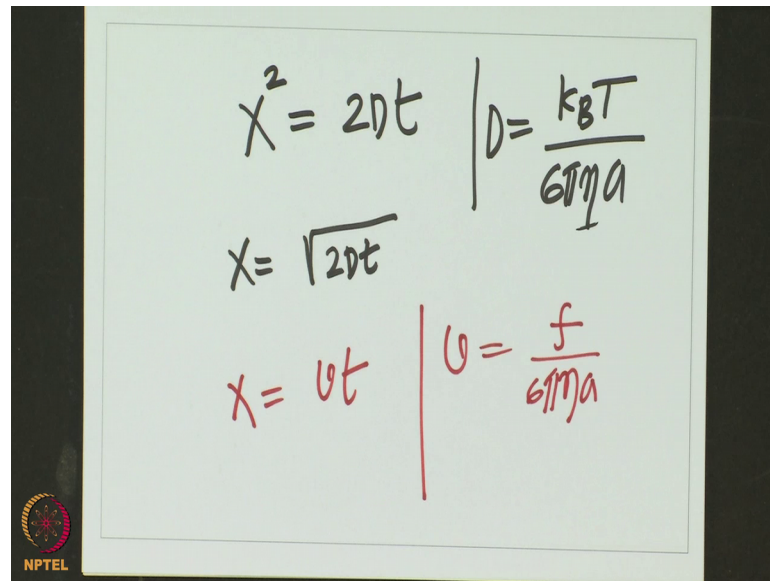
So, in the case of diffusive transport; so, this is diffusive transport of protein what we learned is x is proportional to root time; this is the thing that we learned and in the active transport where the transport happens because of either some external force or molecular motors x is proportional to t . So, this is the difference.

So, if I increase this by 100 times, this would increase only by 10 times the distance traveled if I have molecular active transport if I increase this by 10 times, this would increase also by 10 times if I increase this by 100 times this will also increased by 100 times.

So, this in the active transport the distance traveled x is proportional to time here the distance traveled is proportional to square root of time this is an important difference that all of you should keep in mind and one interesting thing that all of you should do is use this idea and calculate the time it takes for a particle of protein of your interest to move rougher for example, across the long neuronal cells how long, it would take what is the time it takes, I urge all of you to calculate you would see that diffusion is very slow and what would need an active transport to take things a far away.

So, now the interesting thing here another thing to remember is that in one case.

(Refer Slide Time: 25:38)


$$x^2 = 2Dt \quad \left| \quad D = \frac{k_B T}{6\pi\eta a}\right.$$
$$x = \sqrt{2Dt}$$
$$x = vt \quad \left| \quad v = \frac{f}{6\pi\eta a}\right.$$

The x was $\sqrt{2Dt}$ and the d is controlled by temperature which is a fixed quantity in a cellular environment viscosity is also kind of fixed the size of the protein also fixed. So, this is not at all in our control d is not at all in control. So, if I have one hour time this can only go that much sorry x square here x square. So, x is $\sqrt{2Dt}$ the x is $\sqrt{2Dt}$ since d is a constant given a biological environment this can only go this much.

On the other hand, the velocity which is the active transports x is vt , here the velocity is not really constrained. So, if there is an external force we saw that this is f by $6\pi\eta a$. So, as I increase the external force I can increase the velocity or I could drive this by hydrolyzing atp. So, the more atp, I consume I can drive it a faster.

So, this velocity only depends on the availability of atp and so on and so forth. So, I can move much faster using the active transport as opposed to the diffusive transport. So, this is important to understand this difference between active transport and the diffusive transport and this gives us some basic details about these 2 different types of transport and the mathematics behind this.

So, with this I will stop this lecture and continue in the next lecture. Bye.