**Physics of Biological Systems**
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**Lecture - 43**
**Timescale Separation in Enzyme Kinetics**

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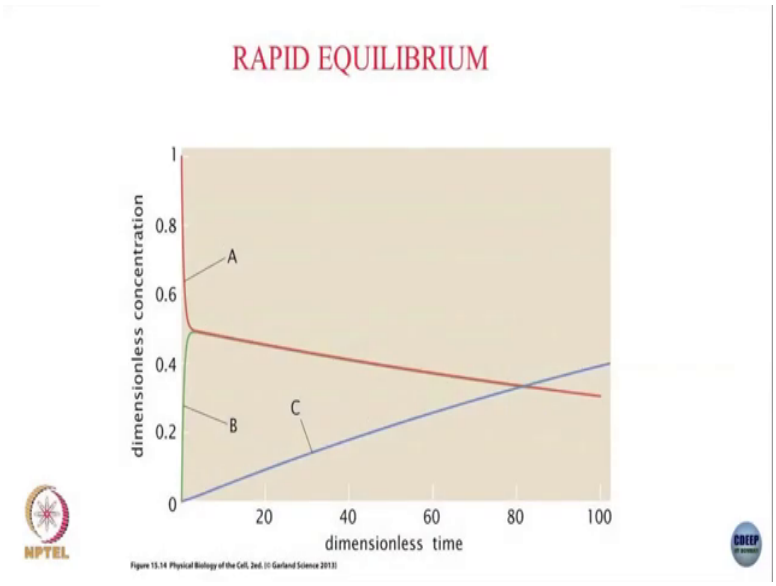


So, where would I come across something like this? So, a sort of example of an equation that looks somewhat like this, where I have this separation of time scales is if you consider let us say enzyme kinetics; if I consider enzyme kinetics.

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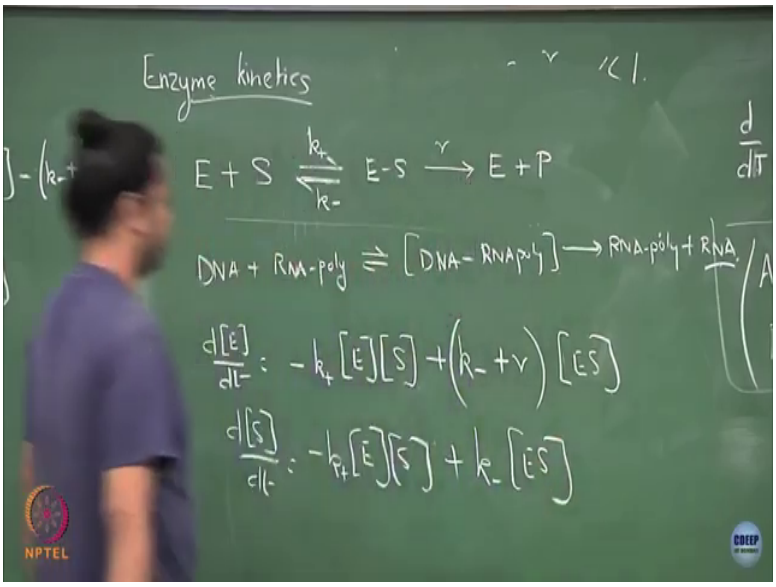


So, let us say I consider this set of equations that I have an enzyme plus a substrate which reacts to give me a complex which I call this enzyme substrate complex. And then from there I get this enzyme plus a product. So, what is essentially happening is the substrate is going to a product; but through the action of this enzyme, which I recovered back at the end ok, the enzyme does not get depleted.

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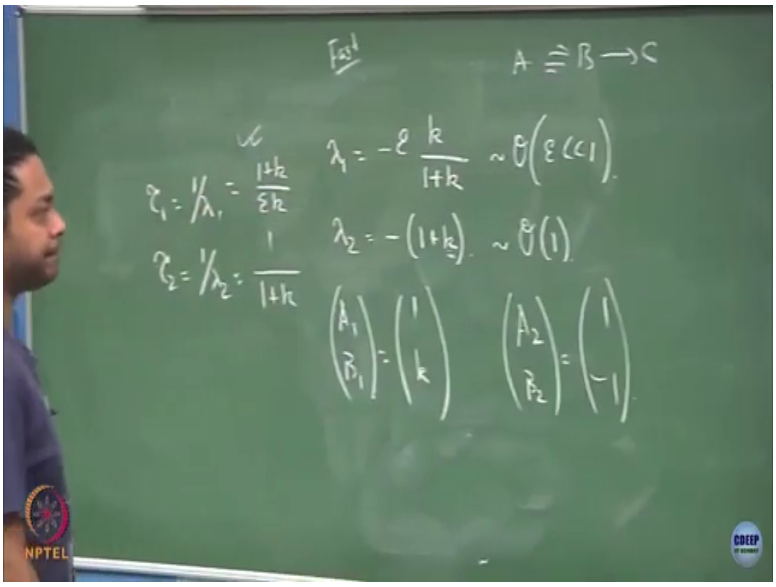


And again if I think of putting some rates, similarly rates k plus and k minus and rate r; then this has the same sort of structure as this thing that we are talking about A going to B going to C, ok. Where would I see this, so for example, if I had; let us say DNA. So, let us say I have DNA plus this RNA polymerase; RNA polymerase, that reacts to form this complex; so this RNA polymerase binds onto this DNA, DNA RNA polymerase complex. So, and then you get back your RNA polymerase plus you get back your RNA plus you get production of RNA this way.

So, this is like the transcription way, equation transcription reaction written in this sort of a language. And you can write indeed many sort of wherever you have an enzymes of the kinetics, you can frame it in this sort of a language that you have some substrate whatever the substarte is in this case DNA and something that transiently binds in order to facilitate the

reaction. For example: RNA polymerase at this and ultimately at the end of all of this will get some product out of it and the enzyme sort of comes back.

But, once I write down an equation like this, once I write down written down a schematic like this; I can again write down the rate equations exactly like I did for A and B, right. So, let me I will not solve the whole thing, but let me at least write down the equations. So, if I write down the equation for the enzyme, the enzyme d t, right. So, that has decays with the rate k plus when an enzyme and a substrate comes together; it is formed back with a rate k minus from this enzyme substrate complex and with a second rate r might as well just to write it just k minus k minus plus r from this enzyme substrate complex that takes in compressive reaction plus this reaction.

For the substrate I would have again a k minus k plus enzyme and a substrate and that is it, right.

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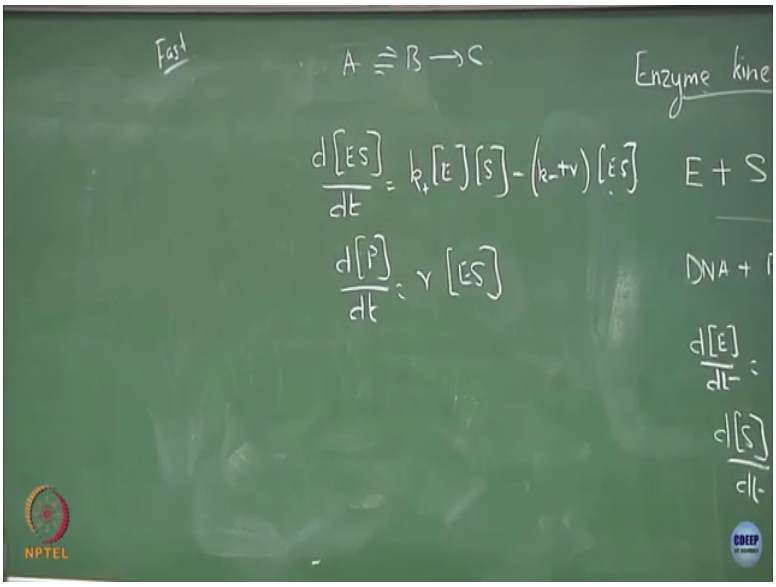


Then for this enzyme substrate complex, d enzyme substrate d t it is produced at a rate k plus from this enzyme and the substrate and it decays with the rate r, all right; r over there and another k minus will here. So, k minus plus r enzymes substrate and finally, I have the product d P d t which is simply produce. Anything else I am missing, the substrate has another term, right. So, it is produced back with this minus k plus plus k minus substrate. So, that is my full set of equations.

So, given a set, given a chemical reaction you should be able to write down the corresponding rate equations. The solution of this is somewhat more complicated; but what I will do is that I will make an approximation just to give you an idea. So, let me say that I make this approximation; that I say that this again this sort of a Quasi-equilibrium.

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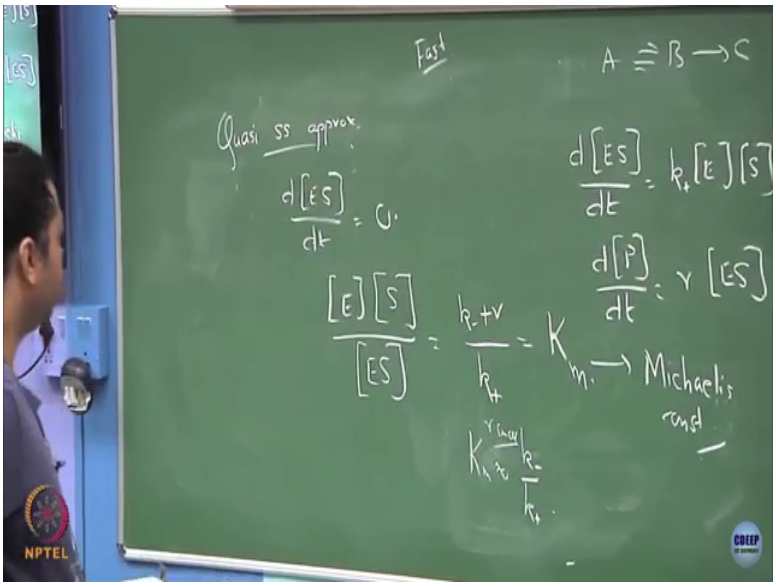


Now this enzyme substrate complex that is formed, that reaches some sort of an equilibrium, so this sort of Quasi Steady State approximation that this enzyme substrate complex which is some sort of a steady state. And what that immediately means is that I have the ratios of this from this equation the ratio of this E into S by this enzyme substrate concentration that is equal to k minus plus r by k plus.

And this thing I call as K m, this thing is the name it is called this Michaelis mine Michaelis constant. And again if I say that this rate r is much much less than k minus, then this K m is simply like k minus by k plus, provided this r is small r small. So, then what I have over here is, if I were interested in the rate at which product is forming is ultimately what I want to calculate; how fast is this product form, then I can just write this product equation d P d t.

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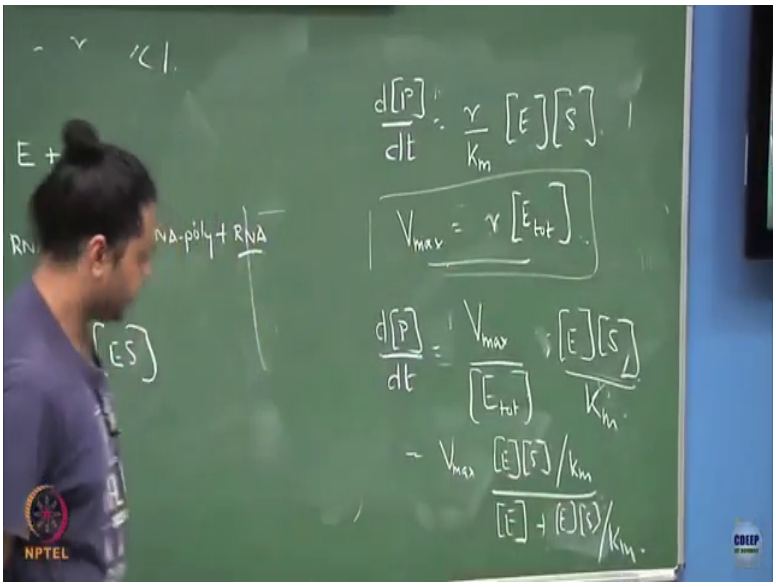


D P d t the rate of formation of product was r times this enzyme substrate which in this Quasi Steady State approximation is E into S by K m is r by K m enzyme type substrate. Let me write the maximum of this, the maximum rate of this equation as some V max. So, let me call V max is the maximum rate of this equation and let me say that this is r times E t o t.

So, I am looking at this d P d t, it is goes this r times the concentration of the this enzyme substrate complex. So, if I say that all up with my enzyme whatever I had was bound to the substrate and available for this reaction; then that would give me this maximum rate of this reaction, so that is half times the concentration of this total enzyme that I have. So, this gives me the maximum rate of this reaction. I will just write it in terms of this. So, I will write this d P d t. So, I will write this d P d t.

I just want to cost it in some familiar form. So, V max is r is V max by E total r is V max by V total by E total into r into r E times S sorry, E times S by K m. This is V max into enzyme concentration substrate concentration by K m by the total enzyme concentration which is E plus E S. So, this total enzyme concentration again I break it up into two parts; one is the free enzyme concentration and the other is the enzyme substrate complex, the concentration of the enzyme which is bound in the substrate. So, this E total I break it up into two parts and this E S, I again right using this equation S is S plus K m. So, this is again E times S by K m, ok.

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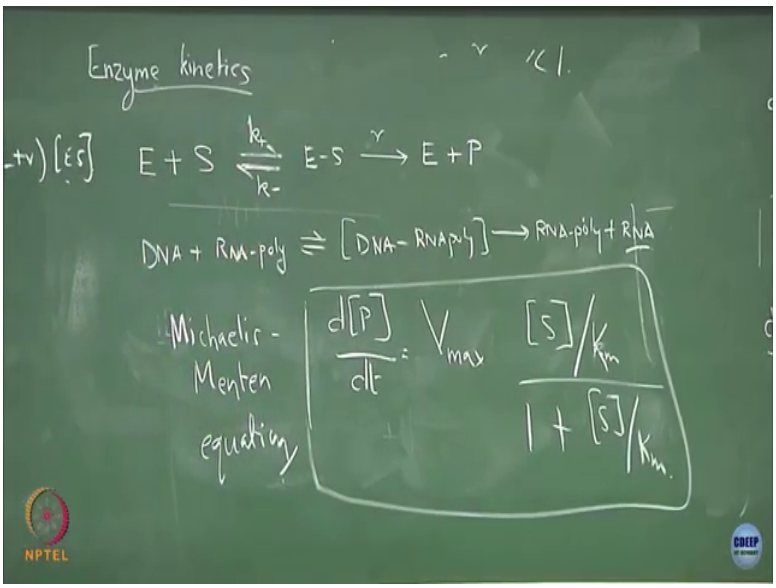


So, effectively if I now cancel out this E S; what I get is that this product, the rate of formation of product that goes as the rate of formation of this product d P d t goes as the maximum possible rate into S by K m divided by 1 plus S by K m. This is a very famous equation, this is called the Michaelis Menten equation or the Michaelis Menten Kinetics.

And basically you can interpret this K m, this Michaelis constant as the concentration of the substrate at which you get half maximal rate. So, if K m was equal to, if S is equal to K m; then you get a half over here 1 by 1 plus 1 which will give you a V max by 2. So, a way of interpreting this Michaelis constant is that it is the concentration of the substrate at which you get half maximal rate of this product formation, ok.

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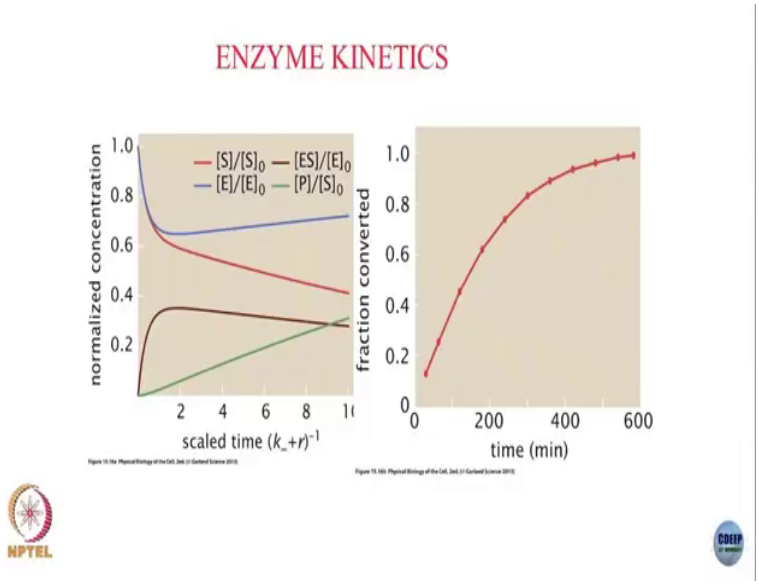


So, if you look at, so if you now solve this equation and if you look at what it gives; this is basically the rate of formation of this product as a function of. So, this is the rate of formation of this P is a function of time and wait this is the fraction converted. So, this is P by S. So, let me first look at this, these are these various normalized concentrations. So, S divided by S naught E S divided by E naught E by E naught and E by s naught. So, these are all scaled by these concentrations of the initial times.

So, this is what it looks like. If you look at this enzyme substrate complex which is where we made this Quasi Steady State approximation it is sort of varies of course; but it varies that are slow rate compared to these others, which is why we make this sort of a Quasi Steady State approximation. So, this is valid not in this sort of regime this approximation that we have made. And this d P d t grows something like this.

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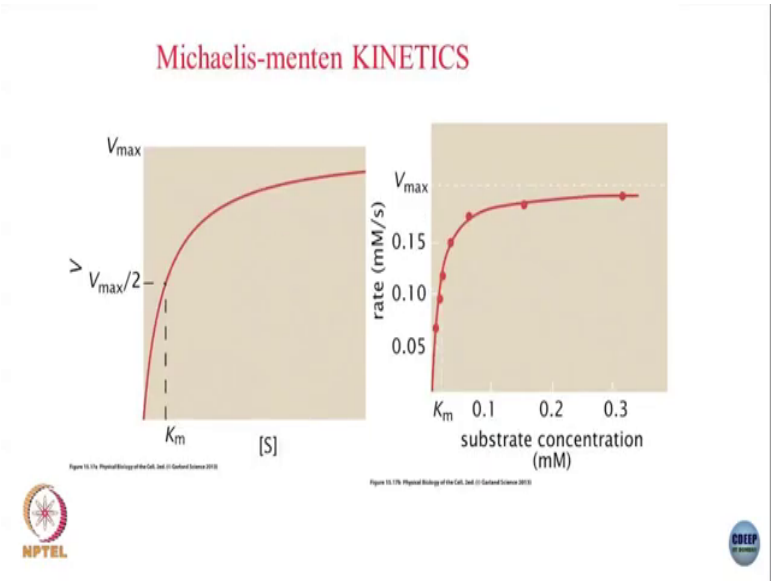


So, at the max, so this is scaled by this V max and if I look at this, so this is this d P d t again as a function of this substrate. So, that is product as a function of time, this is actually d P d t as a function of this substrate concentration. So, the maximum rate possible is V max which is what I have. And at this half maximal rate, so wherever it becomes half that gives me the appropriate value of K m. So, wherever it is 0.5 that gives me the appropriate value of K m, ok. So, if V max is whatever around 0.16, then around 0.08 over here is where my K m would

be that line has not come. So, the corresponding value of K m for whatever this reaction is some I do not know 0.01 milli Molar.

You could of course, solve this full set of equations explicitly, which is how one gets these curves. I just wanted to cast this product formation equation, the rate at which you get the product in this form; because this is often a form, this Michaelis Menten form is often something that you see referred to in various equations that this rate of product formation goes. So, this is again like this still function life of a behavior, it is S by 1 plus S with some pre factor which is the maximum rate of formation of product, ok.

I think I will stop here for today. What I will do is that I will use this language of rate equations. So, this is sort of very generic, you can use it in biological systems; but also in any sort of chemical equation chemical reaction that you were interested in. But what I will do is that, I will use explicitly this sort of a framework to look at cytoskeleton polymerization of microtubules and of actin starting from the next class.