Introduction to Dynamical Models in Biology

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Lecture 16
Modeling Molecular Processes - 1

Hello. Welcome to module 4 of third week of our course. In the last lecture, we started discussion on modeling large molecular networks in similar processes. For suppose an example cell signaling, cell cycle control, something like that and if you remember, we discussed certain key issues there. First of all, this large network is made up of large number of molecular processes which are many a times very difficult to model.

Then we discuss that there are something called network motif or sub network made up of multiple but few in number, molecules and the handful of molecular processes, may be 2, 3, 4 of them. So each of this network motif has a particular architecture as well as they have particular types of dynamical properties and functions. For example, we discussed about positive feedback, negative feedback, we discussed about incoherent feed forward. Then we said that these processes, these motifs can be broken down again into elementary processes.

Each of the motif actually made up of elementary processes like transcription, translation, ligand binding to receptor, enzymatic reaction in a single step or something like that. So at the base of all the molecular processes, there are these elementary processes so if I have to create a mathematical (fo) model for a large molecular network in controlling certain (bio) biological process, I have to know how to write down the ordinary differential equation for each of these elementary processes so that I can club them together to create a larger model. So in this lecture, we will start discussing about that.

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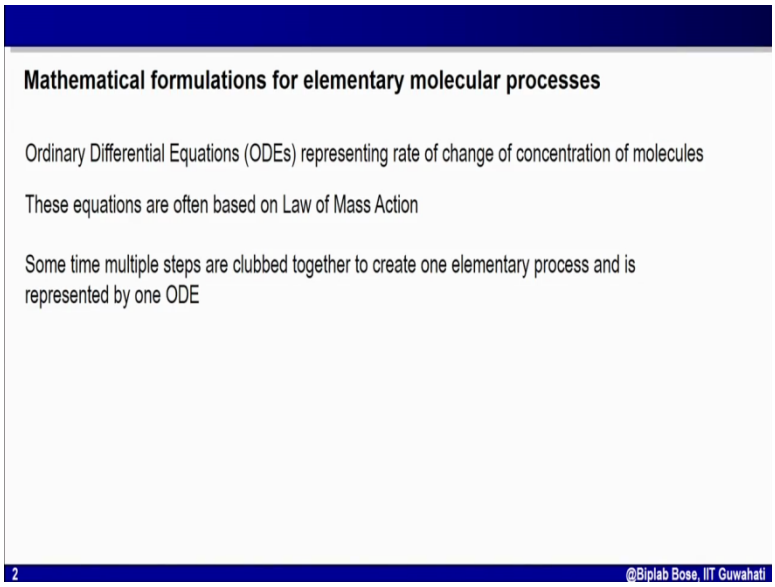

So before we jump into, we have to remember that there are certain particular key issues in this. So let us look into the key issues in mathematical formulation for elementary molecular processes. The first and foremost issue is that, we will use ordinary differential equation for our model. As you remember ordinary differential equation will represent the a differential will be there, a derivative will be there so that will represent rate of change of concentration of molecules in this case.

In many case, it may be number, change in, rate of change in number of molecules but usually it is concentration of molecules usually in molar term. Secondly this ordinary (eq) differential equation will be often based on law of mass action, that you have studied in the school level and we have discussed earlier in the course also. Many a times, the equation may not be exactly following the law of mass action but it may be inspired from law of mass action and similar to that because the processes may be not exactly same where are like elementary reactions where law of mass action is valid but we can get inspired from law of mass action and create a ordinary differential equation and I will discuss those issues in time.

Another key issue that we have to remember is that many a times, a process may have multiple steps but we club them together because of 2 reasons, first obviously it reduces my mathematical problem, secondly many a times we are not sure about how many such processes are involved

and what they are mechanistically for example, if I talk of transcriptional control of (trans) of a particular gene expression, so a transcription factor comes and bind on the DNA and the promoter region then it triggers formation of a complex with other molecules and then ultimately the polymerase comes and start transcribing the mRNA.

Now surely if you look at it from a mechanistic point of view, this is the multi-step process involving multiple molecules but most of the time, we are not clear about how many such steps are involved and what all others molecules are there. You may know only the few key transcription factor and polymerase involved in the process. So I may club all these processes and consider only 1 single ODE representing the rate of change of the mRNA concentration and represent the whole process of transcriptional control by that transcription factor by simply that ODE. So this type of reduction in the problem is done very frequently and we have to keep that in mind.

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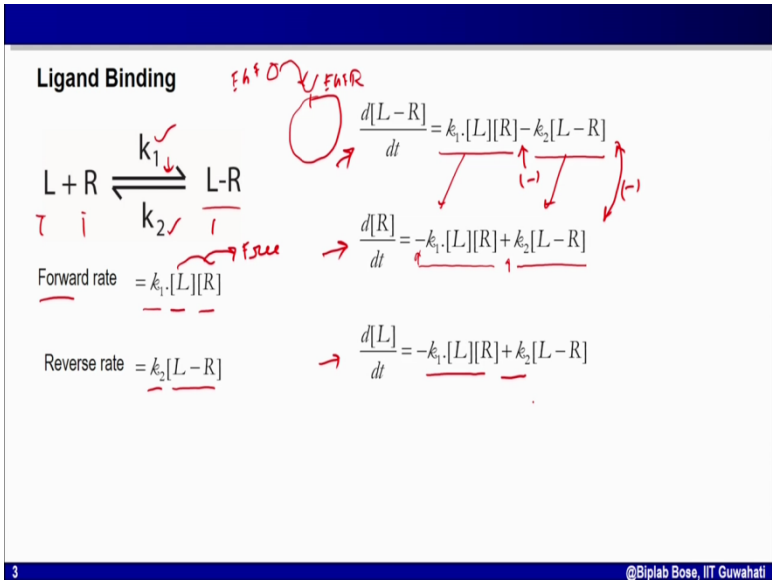

So let us start with these key issues in mind, let us start creating ordinary differential equation based model for simple elementary processes. We will start with ligand binding and it is a very common thing. It's very common to have cell surface on which you may have your receptor and a ligand like a growth factor comes and bind so this receptor may be EGFR, EGF receptor and your ligand may be EGF so ligand binds to a receptor and forms a receptor ligand complex, LR.

Remember this is a binding process. It's not actually a chemical reaction because there is no um molecular bond, covalent bond formation or (cro) or no covalent bond is broken here. Binding of a ligand with a receptor is through non covalent interaction like hydrogen bonds, electrostatic interaction or something like that so it is actually a process rather than a chemical reaction.

And it is not, does not involve any covalent bond formation, this process is reversible so you will have ligand bonding through the receptor forming the complex and in the next moment, it will break down again to give rise to the free ligand and free receptor. So it is the reversible, the way I have shown here by double arrow and the rate constant for the forward one is suppose K1 and the backward reaction or the reverse reaction, the rate constant is K2.

So let us write down what will be the forward rate. So using the law of mass action, I can consider, see remember stoichiometry here is 1 and 1 forming 1 molecule of the complex so using the (rate) or law of mass action, I can write forward rate is equal to K1, that is the rate constant into $L*R$. There is the concentration because that's why I have used square brackets and I will advise you to use that and these concentrations are usually in molar unit and remember L and R, these are free molecules so these are concentration of free ligand and free receptor.

Similarly using the same law of mass action, I can write the reverse rate will be K2, K2 is the rate constant for the reverse reaction and again in square bracket, LR is the concentration of the complex formed. So now these are forward and reverse rates. Using this I can write down the ODE representing change in concentration of the complex LR so that is $\frac{d[L-R]}{dt}=¿$ first term, this is coming this forward reaction, that is $K1*L*R$, this is how it is formed and minus the backward (rea) reaction because reverse reaction because by this process, this reverse reaction, the concentration of the complex is decreasing, that's why I have a minus sign here so that is as I know is $K2*LR.$

Now what will be a differential equation for rate of change of free R so that will be $\frac{d[R]}{dt}$ so obviously the free R is getting reduced by the forward reaction, that's why we have a minus sign here and that is $-K1*[L]*[R]+K2*[L-R]$ because when $[L-R]$ is breaking down it is forming free R so it is the positive sign here so you can see 2 are (equi) equal except there is

(mine) multiplication by a negative sign actually. So this has become negative and this has become positive, as a stoichiometry of this reaction, I have shown here is 1 is to 1, 1 ligand is binding to 1 receptor so the ODE for the ligand will be also exactly same as that of the receptor.

So $\frac{d[L]}{dt}$ is representing the rate of change of concentration of free ligand and that will be same as that for the free receptor that is $-K1*[L]*[R]$ because by forward reaction, the free L is getting (exe) used up $+K2*[L-R]$, the concentration of complex because by this reverse process, free ligand is formed. So what I have done, I have written down the ODE, 3 ODE's for for the free ligand and free receptor and also for the complex [L-R].

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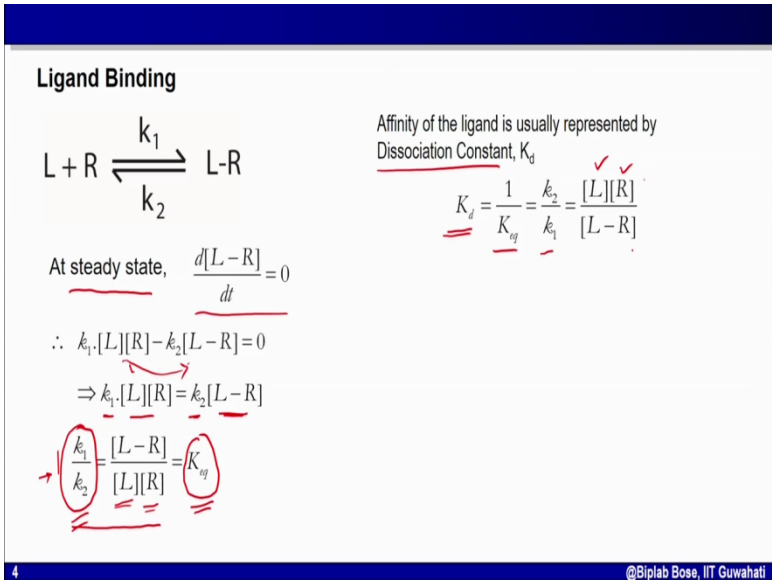

So now let us look into certain particular issue which is typical to uh ligand receptor binding. Let us look into the steady state of the system so at steady state if you remember, the rate of the process should become zero so I can write $\frac{d[R]}{dt}=0$ so if DLRDT by the ordinary differential equation that's just I have written in the last slide, I can write $K1*[L]*[R]-K2*[L-R]=0$ because that is equal to $\frac{d[L-R]}{dt}$ so if this is equal to 0, I can rearrange these terms and I can write $K1*[L]*[R]=K2*[L-R]$, this is the complex concentration of the complex.

So now take out this constant term in one side and the variable term on the other side so what I get, I get $\frac{K1}{K2}=[L-R]/[L][R]$. This ratio of K1 and K2 is called equilibrium constant in biological literature. Remember I started by saying I am considering a steady state, I have not said equilibrium but in literature, this steady state is actually called equilibrium, if you remember, we have discussed this issue earlier and usually we try to avoid use equilibrium because equilibrium may mean thermodynamic equilibrium also and that may sometimes be confusing but in this case, they are same and equivalent.

So I have K equilibrium which is a ratio of K1 and K2 and that is equal to [L-R] that is a concentration of (co) complex divided by concentration of free receptor and free ligand. Now in biological, biology literature, this K equilibrium is actually is not discussed or measured. Usually biologist measure dissociation constant and the affinity of a ligand is described in terms of dissociation constant. If you look into textbook, you will find, uh affinity of a antigen for a for a antibody for a antigen is (co) discussed in terms of its dissociation constant.

So what is a dissociation constant, let us look into it. The dissociation constant K_d is nothing but inverse of K_{eq} . $1/K_{eq}$ so if $K_{eq}=\frac{K1}{K2}$ then K_d will be $\frac{K2}{K1}$ and as we know here, K_{eq} is ratio of complex of the complex formed between receptor and ligand divided by that concentration of free ligand and free receptor then K_d is [L][R], L is the free ligand, R is the concentration of the free receptor divided by the concentration of the complex. So what we have done, discussed till now is how to write down the ODE for ligand, receptor and the complex (forma) complex formed by binding of the ligand and receptor.

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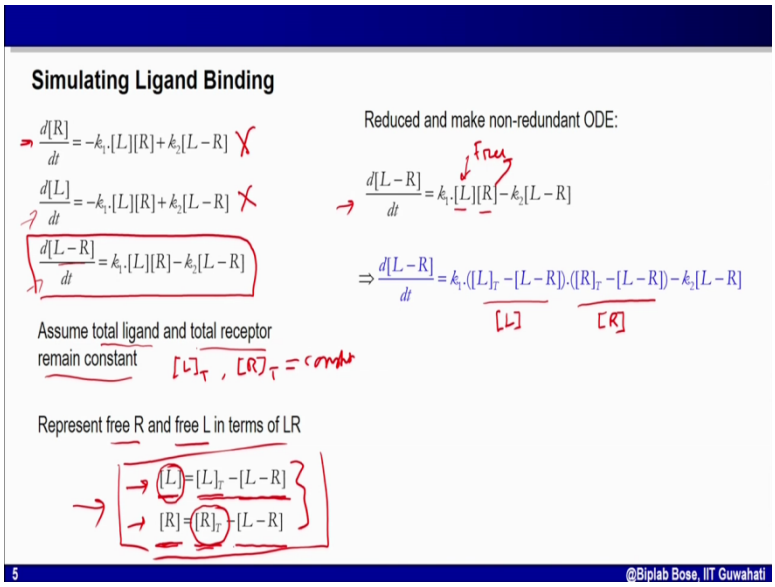

So suppose now I want to simulate this system numerically obviously ultimately you can use Jsim to stimulate this one so I have ODE's. One representing the rate of change free R, the other representing rate of change of free L, the other one is for [L-R]. And we are interested mostly in how much complex is formed in particular time point so I have to create a model, mathematical model for that, I will do some basic corrections here. For example, to reduce this system further, what I can do, I can assume that a total ligand and total receptor remain constant. For example, I will consider that total concentration of ligand is LT and total concentration of reception is RT and they are all constant and that's quite a valid assumption because when you do a antigen and (bi) antibody binding assay, actually you have a fixed amount of antigen which is allowed to bind with the fixed amount of antibodies.

So so total amount of antigen and total (anti) (concen) uh concentration of antibody is fixed. When you have a cells growing in a plate and you give suppose insulin from outside and insulin will go and bind to the insulin receptor present on cells so for a short duration of time, you can easily consider that the total number of receptor and the total amount of insulin given remain constant but you have to remember, with time, concentration of insulin will also get degraded because it is degrading. Receptors will also (ge) will also get processed and degraded so number of receptor will also change but for a short period of time, I can consider the number of total

ligand molecules and the number of total receptor molecules remain same so their concentration is always constant for that period of time.

So if I have assumed that these 2 things are constant then I can represent free R and free L in terms of these equations, (math) algebraic equation given here. So concentration of free L will be equal to nothing but total concentration of the ligand minus the concentration of the complex because that complex has sequestered some amount of ligand so the concentration of the complex should be deducted from the total concentration of the (liga) ligand, that will give me free (co) concentration of free ligand. Similarly concentration of free receptor should be equal to concentration of the total receptor, all receptor minus concentration of the complex because that complex also has receptor in it, so once you have these conservation rules then what I can do.

See here in this case, L can be (re) replaced by this thing, $[¿¿T]-[L-R]$. $[¿¿T]^{L}_{¿}$ is a constant so I don't require a differential equation for $[¿¿T]^{L}_{¿}$. R which is, for which you have a differential equation here as $d\frac{[R]}{dt}$, R can be replaced by $[¿¿T]-[L-R]$. Again $[¿¿T]^{R}_{¿}$ is constant so I don't require a ordinary differential equation for $[¿¿T]^{R}_{¿}$ so I am left with 1 dependant variable that is $[L-R]$, that is a concentration of ligand. That means I don't require these ordinary differential equations representing the rate of change of (recept) free receptor, I don't require the ordinary differential equation for L because I have considered L in terms of a constant that is $[¿¿T]^{L}_{¿}$. and $[L-R]$. What I require is only the ordinary differential equation for $[L-R]$ because at any moment, if I can calculate the amount of $[L-R]$ then I can easily calculate amount of free ligand and free receptor by these 2 algebraic relationship.

So from 3 ODE, I have reduced to only 1 ODE so let us see how far I can change this only 1 ODE that I have to deal with so I am left with only 1 ODE that is representing the rate of change in concentration of the complex $[L-R]$ so $\frac{d[L-R]}{dt}=K1*[L]*[R]-K2*[L-R]$. Now L is free ligand. R is also free (li) receptor so if I use these algebraic relation, I can replace these L and R by these algebraic relations. That's what I have done. So the equation after replacement of free L and R will be $\underset{K1*¿}{\overset{L}{[¿¿T]-[L-R]}}$, this is nothing but $[R]*R_T-[L-R]$, this is nothing but $[R]-K2*[L-R]$ as it is.

So what I have done, I have started with 3 ODE, I have assumed a conservation of both receptor and ligand, that helped to reduce number of ODE from 3 to 1 which is a non redundant ODE. So now I want to simulate it and I will discuss now the code of stimulating this in Jsim and I will advise you to try this in Jsim. Yourself and you can follow the code exactly here.

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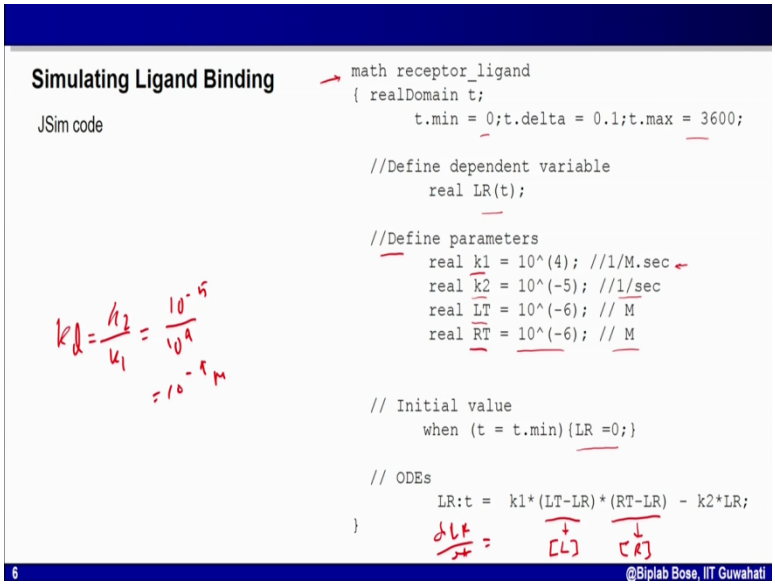

So the code is given here. If you remember it should start with the tag math so it's a math receptor model, you can put any other name there in place of receptor model and you have to decide the initial time point that is 0, maximum time point I have taken 3600 because I am

configuring the time scale may be in second so 3600 so $60*60$ so there is 1 hour. Then I have only 1 ODE so I have only 1 dependant variable that is LR concentration of free (lai) uh (comP) concentration of the complex form between L and R and that is a dependant variable on t, that's why LR (t).

Then you have to define the parameters, so the first parameter is K1 that is the forward rate constant, it is 10^4 and I have annotated saying that unit is $\frac{1}{molar.sec}$. The second parameter is K2, that is I have taken as 10^{-5}. It is, unit is actually $1/sec$. Remember these units are written in annotation, that means Jsim will not consider this unit so the whole calculation is based on consideration that everything is unitless but I have written them in annotation so that we can remember what is the unit we are using.

So if you look into it, the K_d in this particular ligand receptor case is nothing but $\frac{K2}{K1}$, it is nothing but 1 $\frac{10^{-5}}{10^4}$. So this is 10^{-9} molar so a nanomolar affinity for ligand and receptor are considered. I have considered micromolar considered micromolar concentration for ligand and receptor both so LT is the total amount of ligand. Remember we are assuming the total amount of ligand remain constant so that's why LT ligand total is equal to 10^{-6}. In annotation, I have written down that is molar unit so it is actually micromolar, 10^{-6} whereas RT is a total concentration of receptor so that also is considered as 10^{-6} molar, unit is written in annotation, unit will not be considered during calculation.

The initial value for LR is obviously 0 because at the time equal to 0, there is no complex formation so $LR=0$. Then comes writing the ODE, following the equation that we discussed just now in the last slide, LR: T which means essentially $\frac{dLR}{dt}$ is equal to so this is nothing but $\frac{dLR}{dt}=K1*¿-LR$) so this is nothing but $L*(RT-LR)$ that is nothing but $R-K2*LR$ so this is the reverse, last part is the reverse reaction. So that's all. So just 1 ODE and I have all

this parameter K1 and K2 and LT and RT, these are the constant term and I can I am ready to simulate so I will advise you to write down this code Jsim and simulate it.

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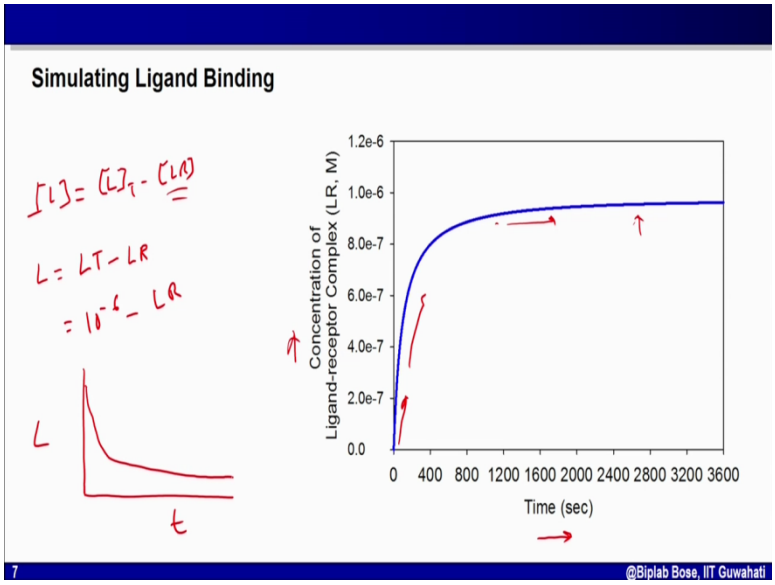

I have already simulated it and you can see the result here so here, what I have plotted, I have plotted time, I have written in second scale and obviously on the vertical axis, you have the concentration of LR, the complex in molar unit. As we can see, with increase in time, it reaches, slowly increases (sa) sharply and then reaches the saturation. This is a typical ligand receptor binding curve that you get repeatedly in most of the ligand receptor system and interestingly you can see here by much before 1 hour, that is 3600 seconds, actually the system has reached a steady state or equilibrium so suppose you are doing an experiment, using real experiment using an antigen antibody interaction involving the affinity of nanomolar then actually the reaction is over.

The complex formation is over. The steady state is reached by 1 hour and you can then further process the experiment. I can also plot the concentration of free ligand like this because free ligand is nothing, concentration of free ligand is nothing but $[L]_T t - [LR]$ so that I can do in case of Jsim simulation, Jsim will give me the LR concentration that's what plotted here so I can plot L as free L is nothing but $[L]_T$ there is the total concentration which I activate constant minus LR. Right? That is the concentration of the complex so I have taken $[L]_T$ as

$10^{-6} - LR$ at any time point so you can plot that and if you plot L versus time, L versus time, you will see just reverse of this complex plot, I will get a something similar to like this. You can try this one.

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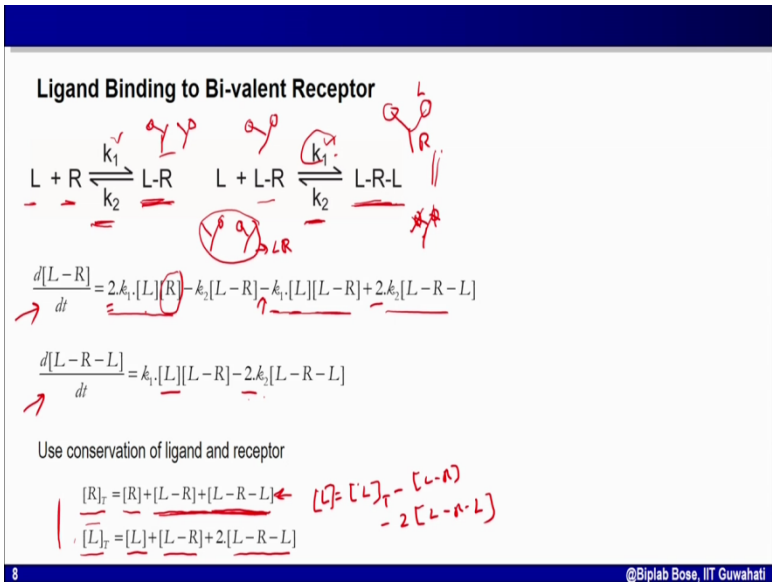

So what I have discussed till now is actually binding of a ligand to a receptor. For example, insulin going and binding the insulin receptor or suppose EGF going to bind EGFR or something like that but many a times, actually receptor can have 2 hands. So I receptor will be called bivalent, for example antibody. If you remember, the antibody is a Y shaped molecule so you have identical 2 hands in a antibody and the same (antig) one antigen molecule can bind here and another molecule can be bind here so 2 ligands can bind to 1 receptor. You can have opposite where the ligand has 2 hands and it goes and bind to a 1 receptor and another receptor side by side, so this type of complex situation complicated situation can arise so let us look 1 example where I have monovalent ligand but the receptor is bi-valent.

So what we are doing here is actually I have this type of thing where 1 ligand can bind here, other ligand can bind here so these circles are ligand, R is the Y shifting is the receptor. So I can break down this whole process into 2 steps. 1 ligand binding to receptor to form ligand receptor complex so this can be like this, ligand is bound here or it can be like this two (configura)

configuration are possible right. So both of them are actually LR, both of them are complex where there is only 1 molecule of ligand and 1 molecule of receptor.

Then once they are formed then the second ligand can come and give rise to the final complex where the both the hands of the receptor are catching the binding the ligand. So that is L binding to [L-R] to give rise to [L-R-L]. All these binding processes are noncovalent interactions. So they all are reversible, that's what I have shown here and here and what I have done here, to for simplify the process, I have considered that the forward rate constant for this reaction, that is the first ligand binding is K1 and it is same for the second ligand binding also.

Here also K1. So similarly, I have simplified the whole thing by considering that [L-R], the reverse rate constant from [L-R] to L and R is K2 and the same rate constant is there for dissociation of [L-R-L] so this K2, this K2, this K1, this K1 are same so this uh in reality, they may be different but for simplification and discussion here in the class, I have considered them as same thing. So now if I have to make, write down the ODE's, what I will do, so obviously, I can write a ODE for L, I can write down a ODE for R. I should write down ODE for [L-R] that is 1 ligand, 1 receptor complex and also I have to write down ODE for [L-R-L], the final complex so 5 ODE (shou) sorry, 4 ODE's should be there.

Now if you remember in the last example, I have considered, conservation of L, total ligand and total receptor, similar conservation can be assumed here and therefore, we are left with only 1 variable [L-R] and the other uh dependant variable [L-R-L]. So let us look into the ordinary differential equation that will represent rate of change of concentration of [L-R], the first complex where 1 ligand is bound do 1 receptor. That is given here. That would be equal to the rate of formation of this complex that is $K1*[L]*[R]$, L is concentration of free ligand, R is concentration of free receptor and it is multiplied with K1.

Now see, I have multiplied this whole thing with K2 because as you have seen here, ligand can come and bind here also to give a product and it can bind to the other arm also, both of them are actually nothing but [L-R] for us mathematically so that means 2 processes can give rise to [L-R]

so that means I have a double variant so I have $2*K1*\begin{matrix}L\\ ¿\\ R\end{matrix}$. Minus K2LR is representing the reversal of breaking down of [L-R] to L and R. So that's why the minus sign is there. Now remember, [L-R] is also getting used up in formation of the second complex where another ligand come and binds so that rate is represented by K1*[L], that is the concentration of free ligand into concentration of the first complex [L-R].

So this process, this process is actually using of [L-R], that's why I have a minus sign here plus this [L-R-L] is breaking down. Now, [L-R-L] is nothing but like this. Now it can breakdown where this one will break first or it can also breakdown from here so I have 2 processes by which I can get back [L-R] from [L-R-L] . That's why I have 2 here so it will be $2*K2*[L-R-L]$ that is the concentration of the second and final complex. Now look into the ODE for the second complex $\frac{d[L-R-L]}{dt}=K1*[L]*[L-R].$ That is the forward rate, this one by which the [L-R-L] is formed minus again $2*K2*[L-R-L]$ as explained just now because I have 2 arms, both are occupied by the ligand, first this ligand can break and also at the same time, in another molecule, this ligand can break so there are 2 paths by which I can get back back to 1 ligand state so that's why I have 2 here.

So this example shows that when you are writing down the ODEs, you have to be very careful about stoichiometry, at the same time, you have to look for all the processes involved here. Although this graphical representation show both reverse and forward processes, it is not clear directly from this diagram that the complex can be formed, [L-R] complex can be formed by 2 way as well as [L-R-L] can be broken down in 2 way. That you have to imagine and incorporate into your ODE. So if I have written down this ODE and if I assume that total amount of ligand and total amount of receptor remain constant, I can have some conservation rules that algebraically represented here. That is total amount of receptor in the system is equal to free R (con) concentration, there is a concentration of free receptor plus concentration of free ligand plus the concentration of the second complex that is [L-R-L] .

So I can represent this R here by this relationship. So I don't require a separate ODE for R because $R=R_T-¿$ this whole thing. Similarly I am considering total ligand L_T is equal to constant which is nothing but summation of free ligand plus LR that is the first complex because it has 1 copy of the ligand plus 2* [L-R-m], remember [L-R-m] is the final complex where 2 ligands are bound, that means 1 complex molecule will have ligand so the total concentration of ligand consumed by this is nothing but 2 into concentration of this complex that is 2 into [L-R-L].

So that is the conservation rule so I can replace this L anywhere else using L will be equal to concentration of L will be equal to nothing but $L_T-[L-R]-2*[L-R-L]$ So I don't require a separate ODE for L so I have only ODE for [L-R]and [L-R-L], these 2 are the dependant variable in my system. All other things are represented in terms of these 2 dependant variables and now I can again use Jsim to simulate it considering certain numerical value for K1, K2 and r_T and L_T . Till now what I have discussed the about uh only about the ligand receptor interaction and obviously this is the elementary process as we have discussed earlier. Another elementary uh process is process is formation of a molecule and breakdown of a molecule.

If you remember all these molecular processes are actually nothing but molecules interacting with each other involving reaction and physical processes. So molecules are produced and at the same time, if a molecule is produced, after some time, it will also get degraded, distracted so production of molecules and their degradation are elementary processes. Protein will be produced by translation and protein will be degraded, mRNA will be produced by transcription and mRNA will get degraded. Lipids will be produced by metabolic pathways and eventually, lipids will be broken down so production and degradation are basic elementary processes. That happens in most of the large network that we will deal with.

Now how should we write down ODE representing production of a molecule or breakdown of molecule or degradation of a molecule. Remember production of a molecule can be a very complicated process. For example I have discussed few minutes back about production of uh (sorr) the production transcription of a molecule so in a transcription of mRNA in is multiple steps are involved are there. For example, few transcription factor has to come first bind to the

promoter then a large complex is formed. That complex incorporate the polymerase then polymerase start transcribing.

So a transcription is a multi step process, translation is a multi step process and if you remember, we sometimes club them down into 1 single step and write a simple ODE for that so it is many a times advantageous that we don't look into each of this mechanistic complexity and reduce the whole process into a simple 1 step process. So that type of (as) thing I will try to discuss today for production and degradation. Although the production of the molecule, there is a protein or a lipid or a mRNA or DNA is multi step, I will consider them a single step simple process for degradation and production. Remember we can do this assumption for make this simplification as long as there is no compulsion on us that we have to assume a mechanistic complicated process here.

There will be cases where we have to explicitly understand how transcription is controlled by a transcription factor, for modeling those processes, we may have to write a complicated ODE but for other, we will always try to write down a simplest ODE possible.

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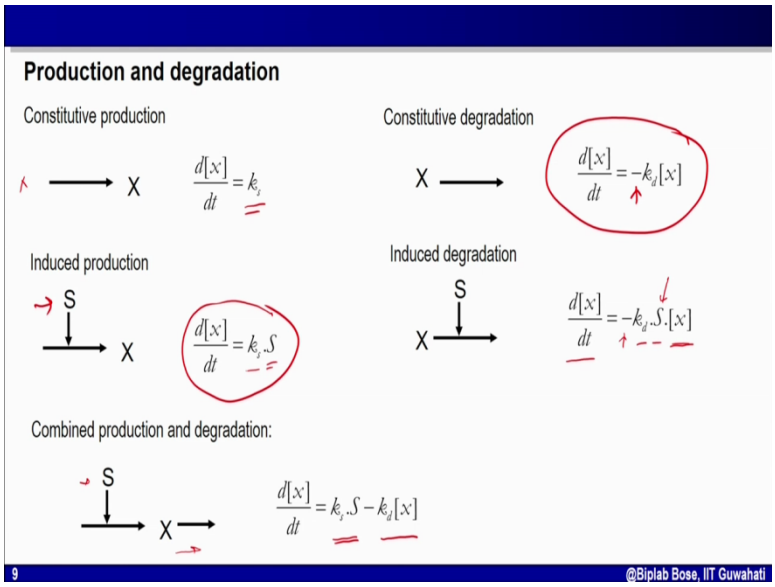

So let us look into the simplest one. Constitutive production of a molecule. Say for a protein. For constitutive production, we mean the cell is producing that molecule without any external queue or any (in) external induction so it is continuously produced. So there are certain molecules which are (conti) constitutively produced in cell because they are required continuously. For example, enzymes involved in your glucose metabolism. As long as the cell has to survive, it has to metabolize sugar so those enzymes required for the sugar metabolism (ha) have to be in a high concentration in the cell so they are produced almost constitutively continuously so that's what I have shown that X is produced and there is nothing.

It is it may be coming from transcription, translation, that's why I have not written anything here, nothing is here so X is produced so what can be the simplest ODE representing this rate of change of X, (conc) concentration of X in this case. The simplest can be like this. $\frac{dX}{dt}$ that is rate of change of concentration of X is equal to a particular rate constant, K_S, K synthesis. As I said, I can (as) put a complicated ODE here representing the mechanistic details of the mechanism by which X is produced but as long as I do not have compulsion to do that, I will try to put this type of, use this type of simplest ODEs. Now suppose the production of X is not

constitutive but a signal S come and tell the cell that you have to produce X so it a inducing thing.

For example, you may be growing bacteria having plasmid carrying a gene of interest under the control of Lac Operon you may add ITPG from outside to induce the Lac Operon for production of the gene, gene product. So in this case, IPTG is the signal given to bacteria that it has to produce the gene product so I have represented graphically here. S is the signal that comes and it tells the cell to produce X so what again be the simplest way to representing the dynamics here, it will be $\frac{dX}{dt}$ that is the rate of change of X concentration is = K_S * S because when S = 0, there is no production so is it is simple multiplication of K_S, that is the rate constant for synthesis into S, that is the signal intensity.

Here signal intensity can be nanomolar molar term or in other unit, accordingly that you have to change the unit of K_S also. If your molecule is produced, it will get degraded, that's obvious so again degradation can be controlled by many mechanism. For example protein degradation are many a times controlled by complicated mechanism but we will not consider that for here but unless and until we have a compulsion to consider, it's always wiser to consider a simple degradation.

Just the way I have shown here, X is getting degraded and the simplest ODE I can think of using the law of mass action is a first order ODE where $\frac{dX}{dt} = -K_d * X$ will be equal to minus KD into X, K_D is the rate constant for the degradation, X is the concentration of the molecule present at time and minus sign I have given because by this degradation, the concentration of X is decreasing so that's why you have minus sign here. That you have to be very particular about. Now degradation can be also induced. Sometimes a a signal generated within the cell or from outside can go and tell the cell that you have to degrade a particular molecule so in that case, what type of ODE I will write?

Taking the Q from the induced production I can write in this case for induced degradation $\frac{dX}{dt} = -K_d * S * [X]$ So K_d is the rate constant for the degradation, S is the signal for (deg) uh

degradation, X is the in a square bracket is the concentration of X free uh at that time so minus sign has been given again because by this process the concentration of X is decreasing. Now note that when S = 0, when S = 0, this rate will be 0 obviously because we have assumed that S is inducing the degradation of X in absence of S, there is no degradation of X.

So now let us club this degradation and production together. So suppose I have a small process where X is induced, production of X is induced by signal S and it gets constitutively degraded so what will be my ODE for X so combining this equation and this equation, I can write,

$\frac{dX}{dt} = K_s * S - K_d * X$, that is a degradation term.

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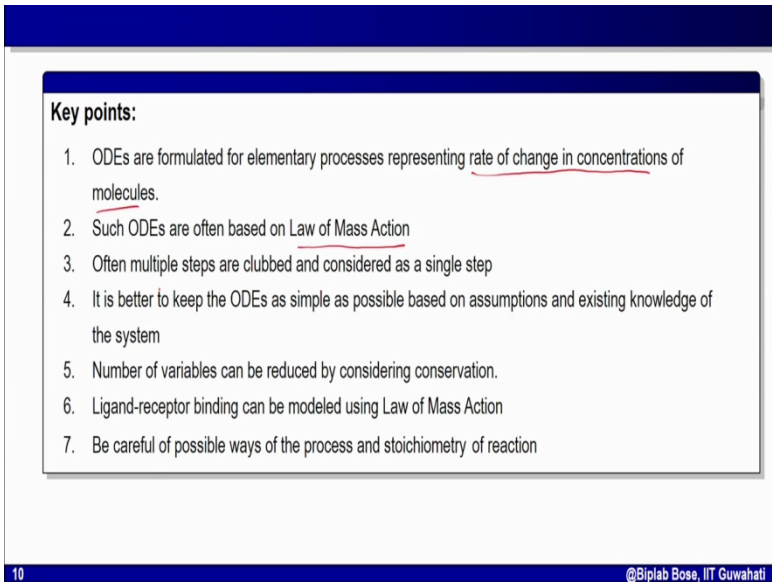

So let now jot down what we have discussed in this module. We have discussed that we want to create ODE based ODEs for elementary processes that will represent rate of change of concentration of molecules involving this elementary processes. Many of ODEs will be based on law of mass action. Many a cases, actually they are not elementary reaction but still we get inspired by law of mass action and try to use similar type of equations. Another interesting and crucial issue that we have to keep in mind that many a times, multiple steps are involved in the process but we club them together and we consider them a single step.

Now 1 thing I will always advise to you is that try to keep the ordinary differential equation that you like to represent a process as simple as possible, make assumptions, look into literature, discuss with the biologist who is doing the experiment to know what is the bare minimum thing that I have to include and try to discard the other. Unless and until you have a requirement to make it complicated, do not write a complicated ODE. So it is better to keep ODEs as simple as possible. Whenever possible, we will try to use conservation rule.

The way we have did in we have done in case of ligand receptor. I have considered total amount of ligand and total amount of receptor as constant throughout the process and in many case, in other biological processes also, you can assume this type of conservation where the total amount of particular type of molecule does not change with time. So if you can configure conservation, number of ordinary differential equation in your model will reduce so reduce number of variable by considering conservation. We have discussed ligand receptor binding in system and we have written down ODE using law of mass action, we have tried to reduce the number of ODEs there and ultimately I have discussed about the Jsim model for this particular system.

Please try to simulate that using Jsim, using the code, if you require, you can change the parameter value or the model code. One important thing that we discussed while discussing a bivalent receptor and that everybody should keep in mind is that many a times, the graphical representation hides the stoichiometry or the multiple way a particular process so when you are writing down the ODE keep in mind the stoichiometry involved in these processes, stoichiometry of the molecules involved in the processes and the number of processes which are there and giving rise to or removing a particular molecule. That’s all for this video. Thank you for watching.