Computational Systems Biology
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Lecture – 49
Dynamic Modelling Recap

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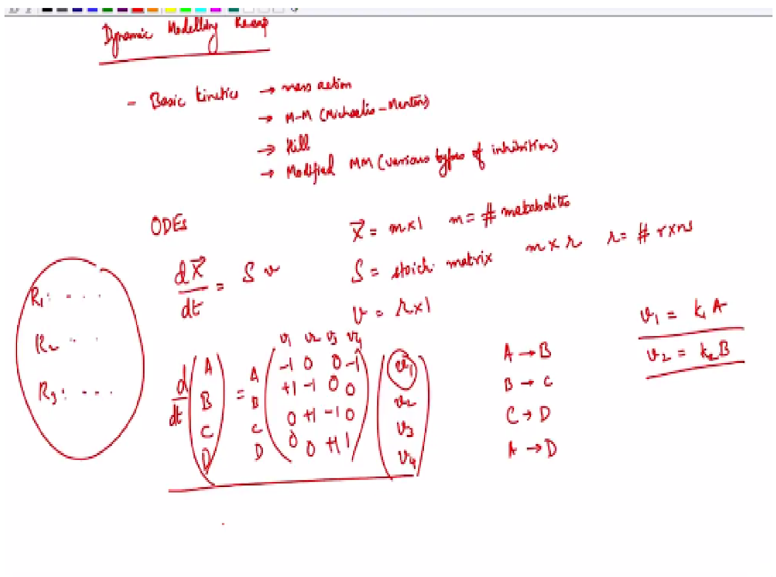

So, in today's video, I will do a sort of complete recap of all the concepts of dynamic modelling. Dynamic modelling recap; so where did we start with dynamic modelling? So, some simple basic kinetic models, Michaelis–Menten, we briefly look at Hill and various types of inhibition, right. So, essentially the logic was the same in all cases, draw sort of wiring diagram, figure out what are all the interactions, qualify every interactions with some kinetic equations.

And then assemble a bunch of equations; differential equations, so then ODE's, right, how did our ODE system look like? Right, where x is your m cross 1 vector m = number of metabolites, S; stoichiometric matrix which as negative coefficients for reactants in a reaction and positive stoichiometric coefficients of products in the same reaction, so this is an m cross n or let us say r matrix, where r = number of reactions and v is obviously going to be an n cross 1 vector or r cross 1 vector.

So, if you have all the reactions written down for any given system let us say you have R1, R2, R3 and so on with involving metabolites, let us say a simple example would be dA, B, C, D/ dt = some -1 +1 0 0 0 -1 +1 0 0 0-1 +1 -1 0 0 1 right * v1 v2 v3 v4, you have the same number of metabolites and reactions, so what are my reactions; if I were to reconstruct from here, A giving B, B giving C, C giving D and A giving D, is that clear, is from this matrix, right, so this matrix is essentially you have to think of it as AB, CD and v1, v2, v3, v4 where the v is correspond to every reaction; every given reaction.

R1; v1 is the rate of R1, v2 is the rate of R2 and so on. What is v1, what is that? dA/dt which is; so, k1 * A, v2, k2 * B, is something is reversible, then you have other things to worry about, so but this is literally or entire framework, this is all you need to know for dynamic modelling, right, you have a system of reactions, you write it out in this form, you then for each individual velocity, you can compute it in this fashion.

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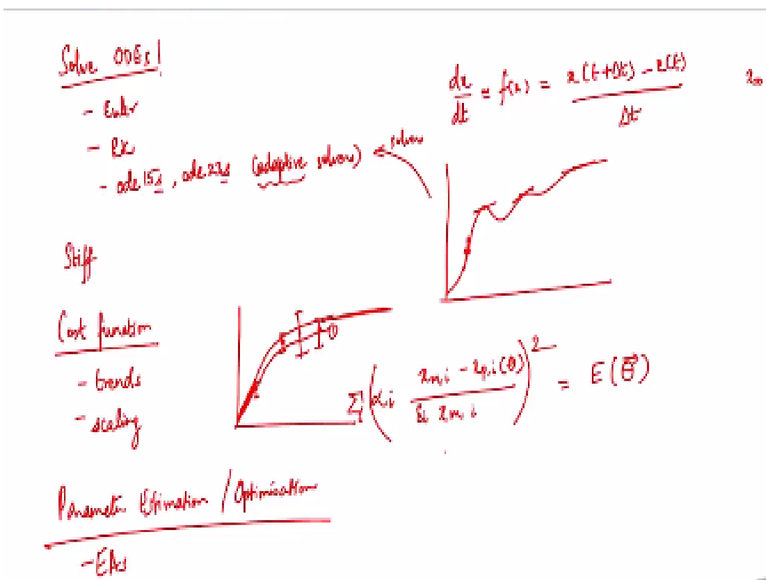

And you stick all these back into these equations; your differential equations and then solve the ODE's, how do you solve them? You have Euler methods, you have Runge Kutta methods or, what is adaptive; varying delta t, right, so all your methods basically use some f of x + delta t – f of x/ delta t and so on, right or rather we would say f of x dx/ dt = f of x = x of t + delta t – x of t/ delta t, you use this and the x0 value to predict x at different places.

So, you essentially have to reconstruct the curve based on the slopes known at different points, right, so for this you use several solvers and you also have to worry about stiff equations, which is what these solvers are good at taking care of, so stiff's equations typically involve you know several timescales, so you need to have, you know the varying delta t is to actually combat them and then we looked at cost function.

You basically said we have to worry about several things, first thing is; as one of you mentioned, trends in the data, I might be more interested in trends in the data rather than just the data and we said suppose, your data points are like this, I will not say that this is the best curve, all these curves, okay, both these curves are equally good, now may be the first one passes through the means or the second one passes more or less close to the standard deviations at least, right.

So, both of them captured the spread of the data, so we had to account for the varying standard deviation at different points. First thing is scaling, right, so we said we will do xmi – xpi of theta/ xmi, right, we said that may not be good enough, so different points may have different error bars, so you want to account for that and you may be less worried about the steady state than the initial action, so you may want to put something else to account for that as well.

And we will square this and sum across all the data points, this is your error cost function for any given parameter theta. How do you find these parameter sets; parameter estimation or optimisation, we will look at a battery of methods especially, focusing on evolutionary algorithms, right. So, this in some sense encapsulates dynamic modelling, there is actually another nice NPTEL course on dynamic modelling by Biplab Bose, which I think you can take a look at.

Because it paves specific attention to say modelling signalling networks, what are the; you know, how do you model positive feedback, negative feedback, those kinds of things in greater detail? Here, in this course, what we have essentially looked at is; there is you know a method to model the systems, you essentially set up these kinds of equation, apply the appropriate kind of kinetics for every given reaction.

And then directly go into parameter estimation and so on, so I have not gone into the depth of the math of modelling, these systems, so, if you look at a classic math bio course, you will also look at things like predator prey models, Lotka Volterra models, they are more classic models or you know classic dynamical systems course, we will look at bifurcation, phase plane analysis, things like that those are all the other things that you may want to study, if you want to look deeper into math modelling or dynamic modelling.

But I think for systems biology, these are the more important concepts that you need to worry about and typically, you will be doing a lot of parameter estimation, a biologist will come with; come to you with some data and some system and say, I want a model, so you will have to build a model using some of these concepts and then you will have to estimate parameters.

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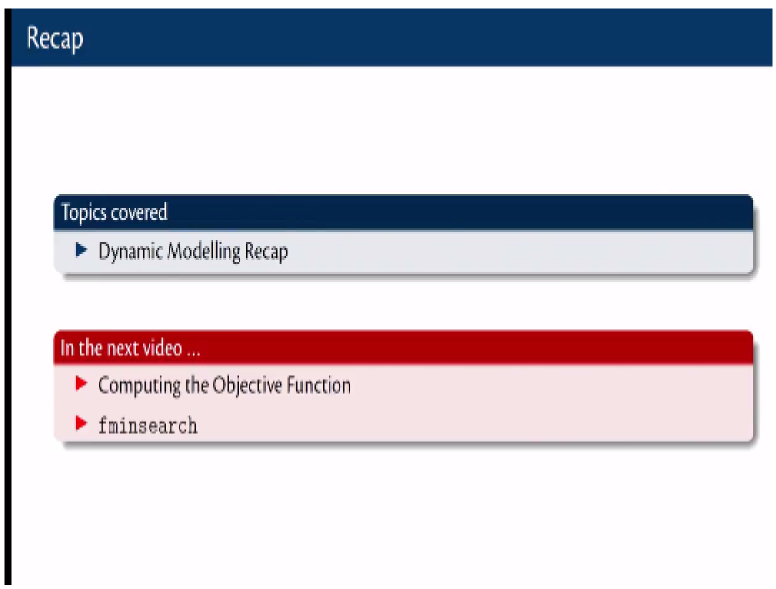

So, in today's video, I hope you had a good recap of dynamic modelling and there is a lot more to dynamic modelling than what we discussed in this course, I encourage you to go back and read about many of these things, I have also shared a lot of resources and papers that one can read. In the next video, we will switch over to a lab session where and we will use Matlab and try to you know compute the error for a given set of data, compute the objective function that you want to minimise essentially and also used is very classic Matlab optimiser known as fminsearch.