Computational Systems Biology
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Lecture - 97
Robustness and Evolvability

In today's lecture we will review the very interesting concepts of robustness and evolvability, which almost sound contrary to one another. So robustness is the ability to resist change whereas evolvability is the ability to change and adapt. So how do these 2 seemingly conflicting properties coexist in biological systems. We will overview the concepts of parametric robustness, topological robustness and we will also look at what is evolvability.

Welcome back, let us today look at robustness and evolvability in biological systems. So in the previous class we studied a lot about how robustness is the common feature of biological systems and we ended on the note that robustness and evolvability are actually coexistent in biological systems which sounds somewhat counterintuitive, right, because robustness as we discussed yesterday is the ability to resist change.

Whereas evolvability is essentially the ability to take change, so evolvability is the ability to take on new functions, whereas robustness is the ability to preserve function and these 2 are somewhat surprisingly interrelated as we will see today.

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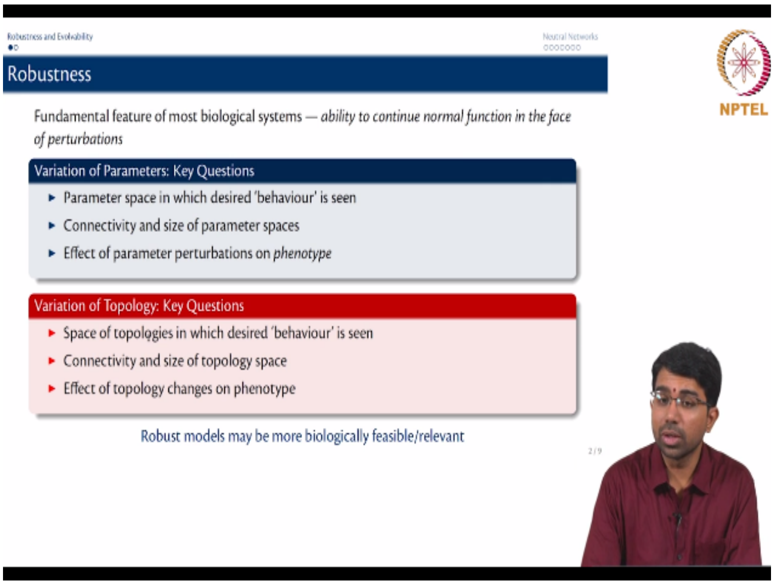

So robustness as we saw in the previous class is a fundamental feature of most biological systems and it is the ability to continue normal function in the face of perturbations and as we discussed earlier, it is the ability to continue a certain set of functions, not all functions. So you always have to define what are the features that are going to be robust and to what perturbations the robustness is expected.

And if you are looking at a model, you can typically ask 2 questions. If you have a model of a system and you want to examine its robustness there are 2 aspects that you can look at. First is the variation of parameters and the second is the variation of the topology itself. So if you have a model.

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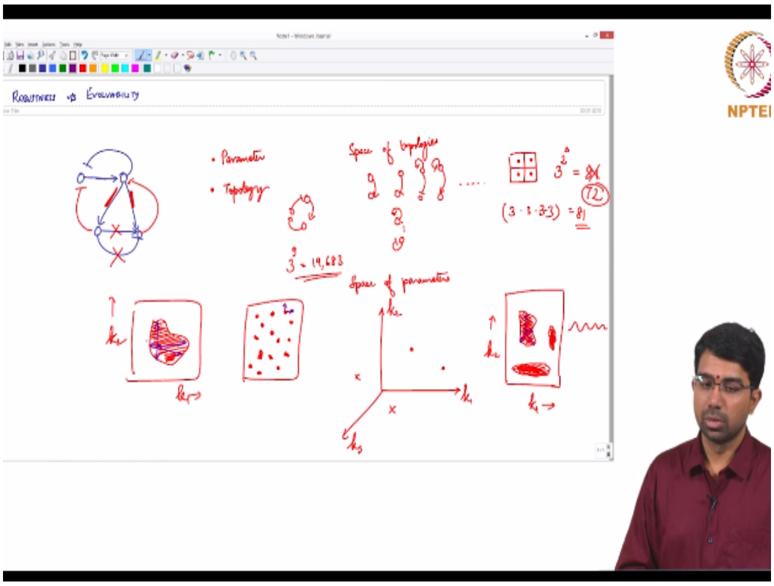

Let us say you have a model of this sort. So you can either think about varying the parameters, which should be all these interaction strengths or you can think about varying the topology itself, which is like having another edge, or not having this edge, not having this edge, having some other edge and so on. So you can think about robustness to parameters and topology. So how do we look at this.

So you can ask very similar questions in both cases. Firstly, what is the parameter space in which a desired behaviour is seen, like you know the system is viable, the system produces a behaviour very similar to the data that you have measured and so on, based on your fit parameters or what is the space of topologies in which the desired behaviour is seen. So you need to start imagining a little more here.

We are now going to talk about a space of topologies and of course the space of parameters. This is something you are all familiar with classes or even elsewhere. K1, K2, K3, this is the parameter space so any point here denotes a particular parameters set, like this, like this, like this and if we actually go back to the two-dimensional case which is easier to think about, we did look at some plots like this.

So this may be K1 and this might be K2 and these are regions where you observe the desired behaviour, let us say looking at oscillations. You observe very similar kind of oscillations for these parameters ranges, these parameter rangers and these parameter ranges. So we were thinking about how this could be a measure of robustness and so on. We thought that the whole overall area could be a measure of robustness things like that.

This was when we were talking about dynamic models, but now let us look at the space of topologies. So in the space of topologies we now let us consider this 2 node model, this is the topology, this is the topology, this is another topology and so on. So you have very many possible topologies. So for 2 nodes you can think of adjacency matrix, you have an adjacency matrix of size 2 * 2 and each element could potentially be 0 1 or -1.

So you have 3 to the 2 to the 2, possible topologies which is basically 81 topologies you will find that about 9 of these are disconnected, you know a topology like this. This is not a topology really right because there is no connection here. So this comes down to 72 if you carefully enumerate them. So how do we get this number again? you have 4 possible numbers to fill, each of them can take 3 values.

So 3 * 3 * 3, four times, so we are talking about 3 node topologies, we will have 3 to the 9 = a pretty large number. So you have a very large space of possible ways in which a bunch of components can be wired. If you have 3 components there are so many ways they can be wired. If you have 2 components there are so many ways or in fact so many ways in which they can be wired, but this is a space of possible topologies in which one can conduct a search.

We will come back to this in a few more slides when it will become more Apparent. So then I can ask the question what is the connectivity and size of the parameter spaces. So are my parameters spaces like this or alternatively are they like this. This you can see is quite disconnected right. So if I colour a little more you might be able to see that these 2 areas are somewhat equivalent, but this is heavily disconnected whereas this is somewhat connected.

Or you know a better scenario would be something like this. So you have K1 and K2, wherein the parameters you know the space is rather connected, right, so all 3 areas maybe the same actually. So whereas you know one is much more robust, this is not at all robust we might imagine, right, because if you slightly vary K1 or K2 you go out of the space, right. If you vary around this point you immediately go out.

But suppose you are here you can vary so much in this direction, so much in this direction, in any of the directions you can actually vary without losing function. Similarly, here you can vary a lot at this axis, a lot in this axis without losing function and the next thing you want to study is what is the effect of parameter perturbation on the phenotype or what is the effect of topology change on phenotype.

So this becomes very relevant from the perspective of synthetic biology as well, as we will see in the next class because if you want to design a system you want to design a system that is robust because biological systems have typically evolved to be robust, but now you want to design a system that is going to be pretty much robust, right. So how do you build a robust system.

So you want to look at a parameter set or a parameter point in parameter space where variation is not going to be too you know detrimental. Similarly, you want to look at a topology in the topology space such that the variation is again not going to be too detrimental and if you are even trying to model a system or predict some performance you can try to pick a robust model of all candidate models you come up with for a system.

If you have no other way to discriminate them like, suppose you have 10 models that fit the data identically well, right. You may want to pick the most robust of those because that is probably more biologically plausible. So this is the other implication the robustness has for modelling itself.

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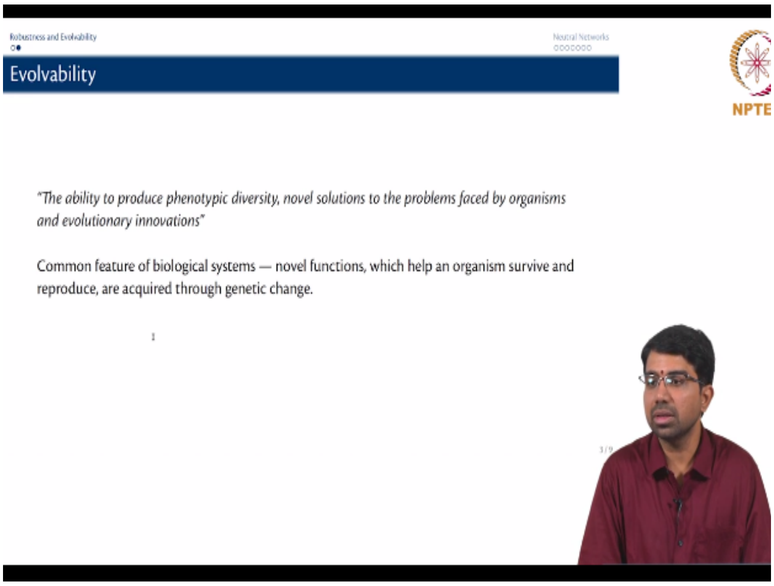

What is evolvability? Evolvability is the ability to produce phenotypic diversity, novel solutions to the problems faced by organism as well as evolutionary innovations, right, and this is the common feature of biological systems whereby novel functions which help in organism survive and reproduce are acquired though you know mutation or any other genetic change.

So how does this work or what implications do this have. Let us try to understand the concept of neutral networks, this is very central to our whole understanding of robustness and evolvability in biological systems.

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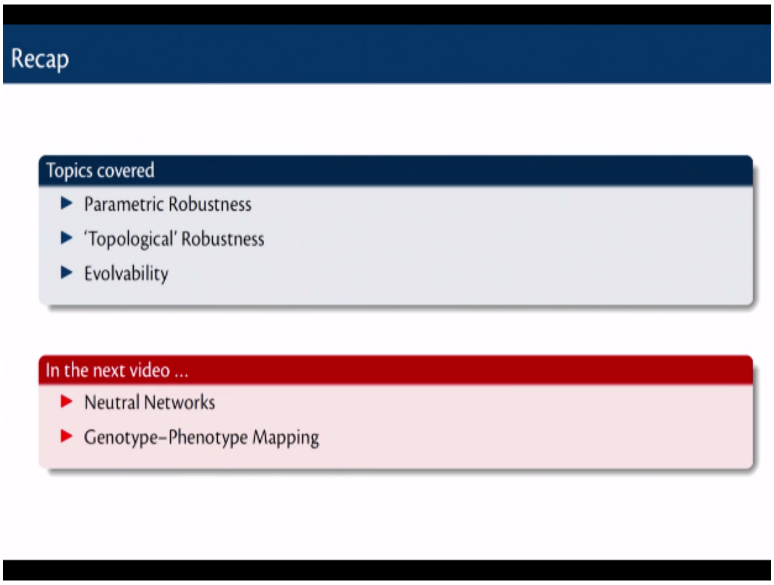

In today's lecture I introduced you to the very interesting concepts of robustness and evolvability. If still not reconciled how they can coexist we will do that in the next lecture.

We looked at parametric robustness, topological robustness and evolvability so far and in the next video I will introduce you to this very interesting concept of neutral networks and how we build these networks or study these networks building on a genotype-phenotype mapping.