Computational Systems Biology
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Lecture - 96
Robustness in Biological Systems: Trade-offs

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In today's lecture, we will continue with robustness in biological systems and particularly study what are all the trade-offs involved in robustness. So there is robustness on one hand, fragility on the other hand and you know these systems are all parts of a complex biological system. So how do robustness, fragility and complexity go hand in hand, we will also look at this concept called highly optimized tolerance.

And I will also try to introduce you to the concepts of evolvability and how it strangely coexists with robustness.

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So what are the trade-offs that we need to consider while looking at robustness?

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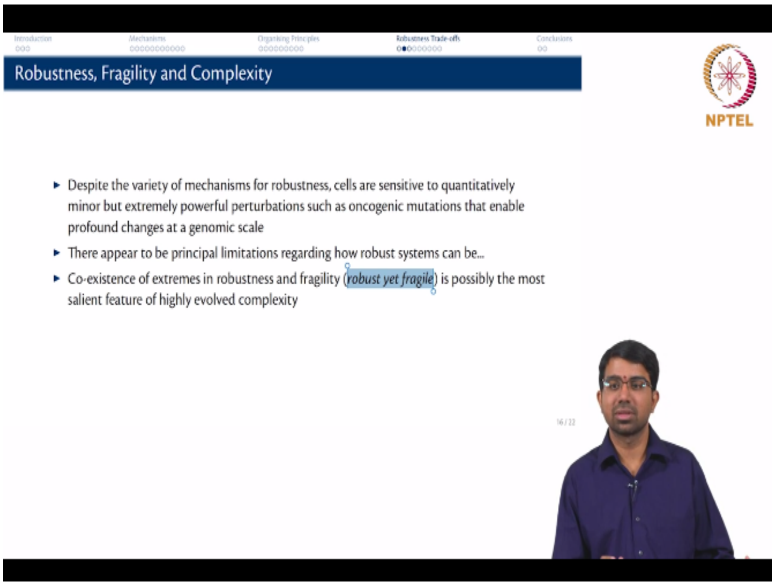

So despite the various mechanisms that we talked about for robustness, cells are sensitive to quantitatively minor but extremely powerful changes such as you know same mutations and so on like oncogenic mutations still a mutation right. We have mutations going on all the time in the body but certain so where an oncogene gets mutated cancer sets in and so on right and it seems that there are principle limitations on how robust a system can be.

There is some quality that needs to be concerned in some sense right and this is kind of pointed towards by the co-existence of extremes in robustness and fragility right and this happens in highly evolved complex systems right. So it is very robust yet fragile. Classic examples, scale free network, it is very robust but potentially fragile. I can knock out 5 nodes and destroy the network.

I would not be able to do that in the random network. You can argue the random network is not very connected to begin with but you know a scale free network can just collapse spectacularly right.

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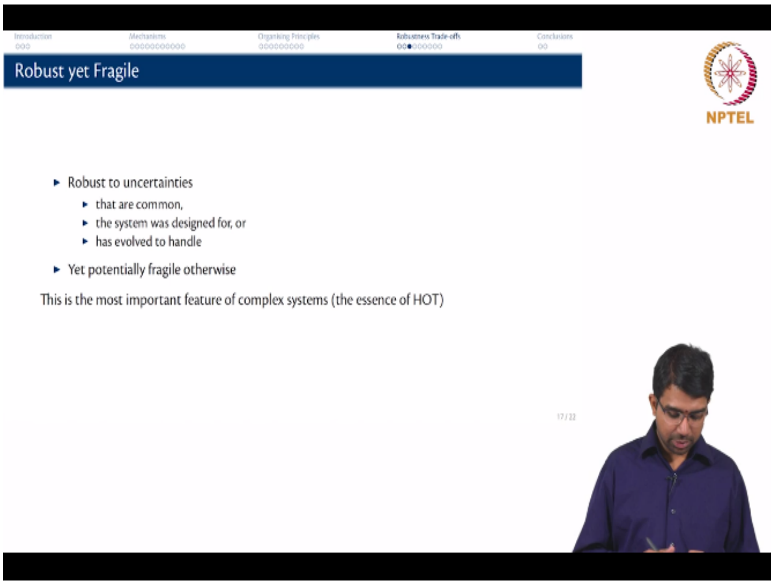

So what is the characteristic of these robust yet fragile systems? They are robust yet fragile systems. They are robust to uncertainties that have been anticipated or you know common or evolved for and so on but very in fragile otherwise like a targeted attack. So this is called highly optimized tolerance right.

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So what is highly optimized tolerance?

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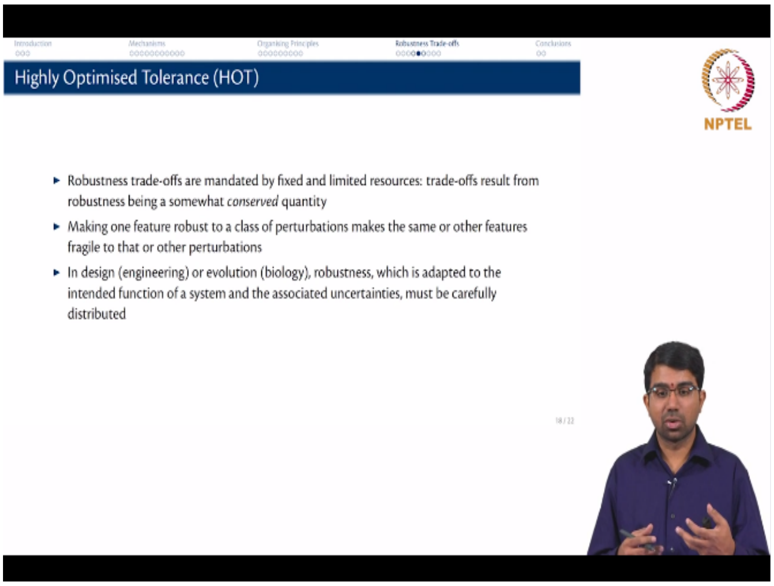

So robustness trade-offs are mandated by fixed and limited resources and trade-offs result from robustness being somewhat conserved right. There is only total so much robustness that a system can have and how it is distributed across definite aspects of the system. So if you make one feature very robust to a class of perturbations, it could make the same feature or some other features very fragile to the same or different class of perturbations right.

Again you can recall the example of scale free networks wherein you know you made the network very robust to node failure but only random node failure. When you have targeted node attack or targeted failure, it does not hold. So in both engineering and evolution robustness adapted to the internet function of a system and the associated uncertainties must be carefully distributed right.

So we talked about how robustness can be distributed right. You have distributed redundancy and so on so you need to make sure that the core of the system is sufficiently guarded, sufficiently controlled, sufficiently there is redundancy in the core as well and so on.

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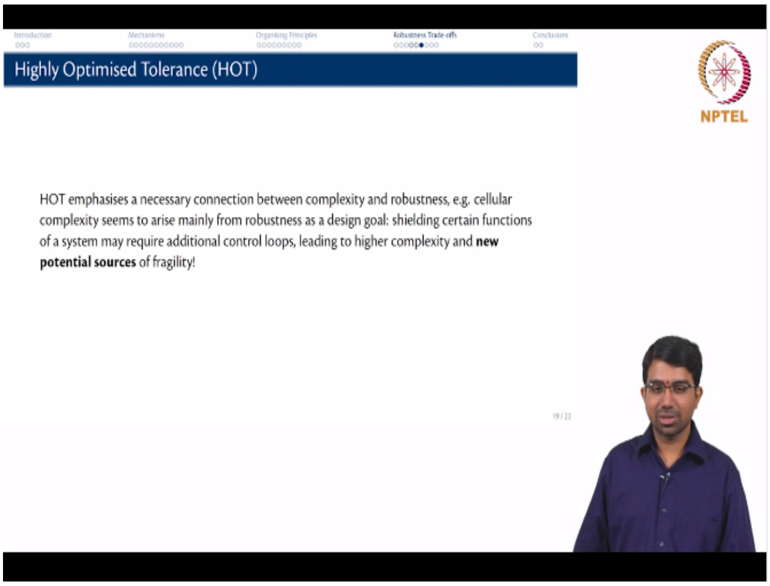

So highly optimized tolerance emphasizes a necessary connection between also complexity and robustness and cellular complexity seems to arise mainly from robustness as a design goal right, you could have a very simple system that performs a same function right with maybe half the number of genes but if you look at say E. coli, it is just remarkably robust right.

You can delete 30% of the genes in E. coli or even more without making an effect right but there is a cost, there is always a cost right so there is probably you know more the size is bigger so the organism requires more ATP to survive and so on and so forth. So this is always a trade-off somewhere here. So you know if you want to shield certain functions, you want to insulate something you want more loops, more regulation, more complexity, more sources of fragility right.

So we have more complexity, more additional components, so failure in those components also becomes a potential source of fragility right.

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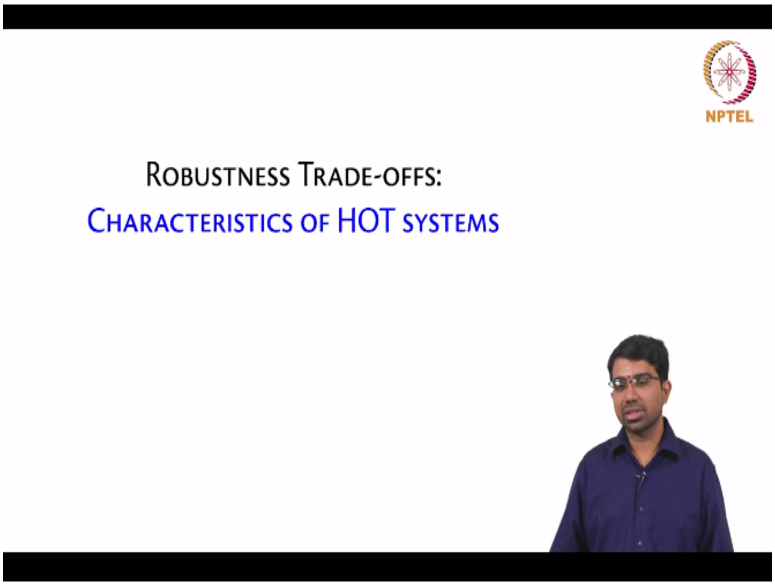

So these trade-offs are a classic characteristic of these highly optimized tolerance systems.

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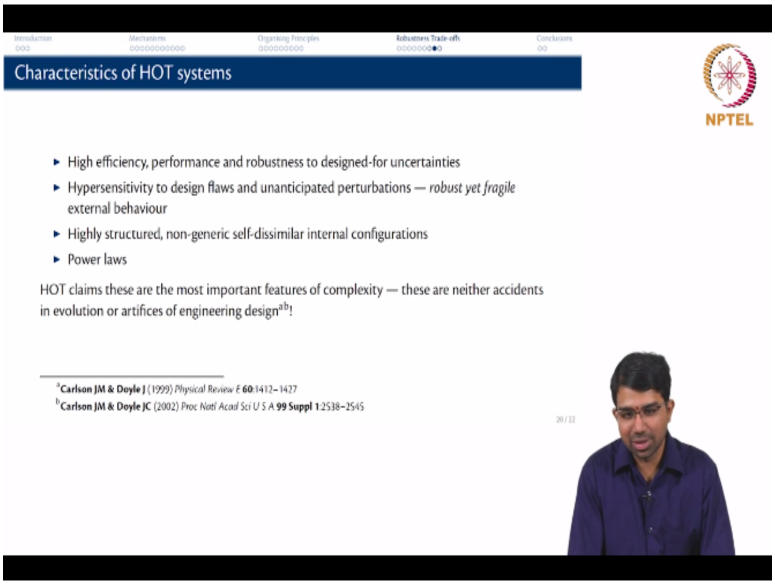

So they are highly efficient and very high performance and robustness to uncertainties that have been accounted for or evolved for. Yet hypersensitive to what they call design flaws or unanticipated perturbations so you have robust yet fragile behaviour and typically you have highly structured, non-generic, self-dissimilar internal configurations right. So there is a lot of diversity in the internal configuration where all your robustness is distributed and typically ends up with power laws.

So the highly optimized tolerance theory claims that these are the most important features of complexity and neither accidents and evolution or artifacts of engineering design.

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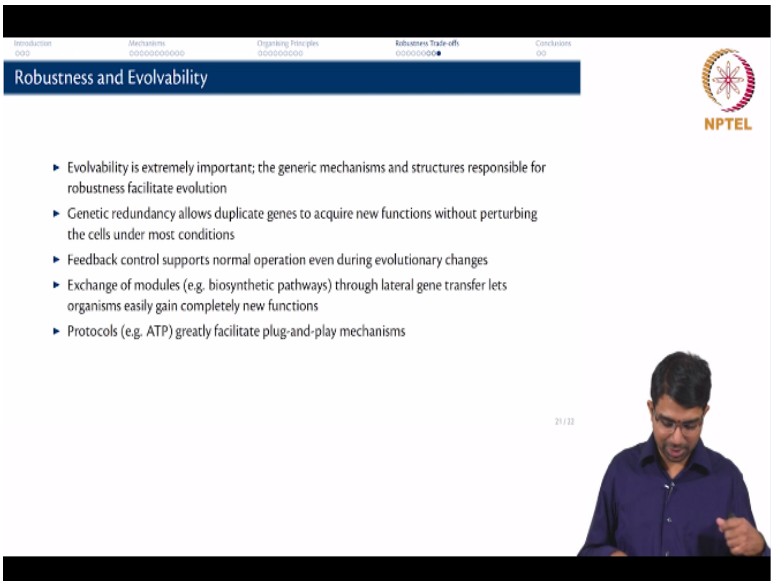

How do we now reason with evolvability right, so evolvability is extremely important? What is evolvability? It is the ability to generate change whereas robustness is the ability to resist change or ability to not change right and it turns out that in biological systems as we will also see in the next class, the generic mechanisms and structures responsible for robustness also nicely facilitate evolution right.

Because we had like a conserved core and a very flexible you know fan, it turns out that this exact structure actually obviously we have seen that it facilitates robustness, it also helps evolvability because you have a lot of latitude to vary in these fans. The core is conserved but it is a small part so say 70% of the systems is open to variation which can be beneficially used right.

So for example genetic redundancy or gene duplication allows genes to acquire new functions without sacrificing cellular function. I have a gene, it has now duplicated, I have two genes performing the same function, so there is no selection pressure on in fact the either of the genes. One of the genes is free to evolve as long as it leaves behind the other for performing that critical function right.

And feedback control supports normal operation even during these changes and perturbations and you can also have you can import modules, lot of time you see antibiotic resistance you know these clusters are taken by horizontal gene transfer or lateral gene transfer. These are available to a cell in the environment of wherever it just picks these, integrates them into the existing cellular machinery right.

And you have the same protocol across cells right or across pathways or across systems.

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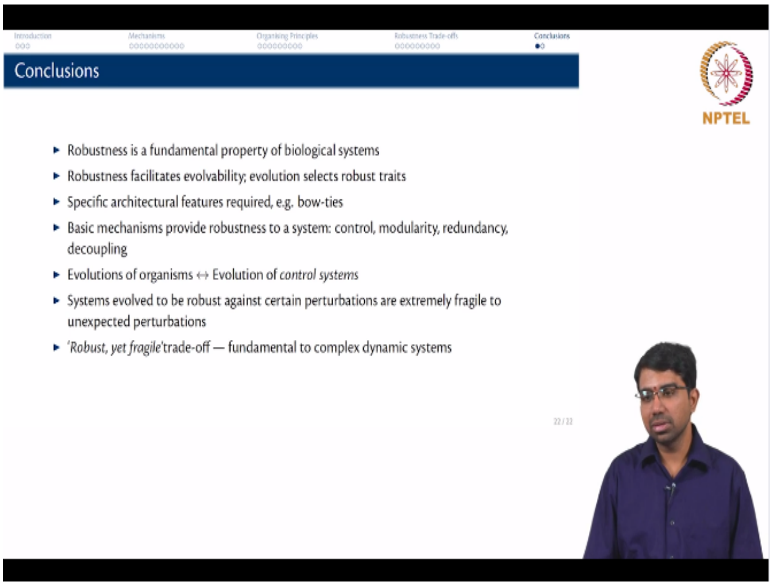

So to conclude robustness is the fundamental property of merely all biological systems, it facilitates evolvability and in fact evolution selects for robust traits right. We will see how these nice seemingly contradictory concepts are very well aligned with one another and there are specific architectural features that are required like bow-ties or power laws and so on and the basic mechanisms that we saw are control absolutely important, modularity, redundancy and decoupling.

And you can think of the evolution of organisms is actually evolution of control systems right. So can you better evolve control systems right, so because an organism cannot evolve an isolation, the entire control system as a whole evolves and the one catch with many of these systems like our scale free networks is that if they are robust under certain perturbations, they are extremely fragile to certain other perturbations right.

And this sort of trade-off of robust yet fragile is seemingly fundamental to most complex systems and particularly also to biological systems.

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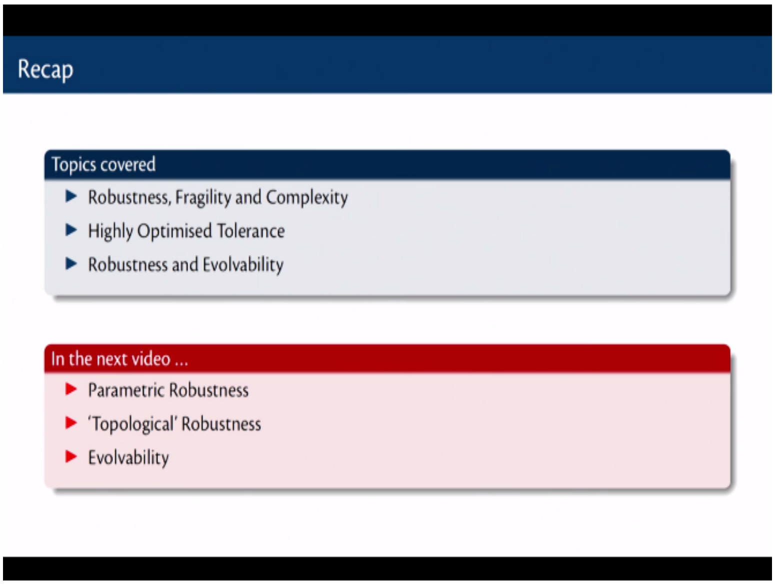

In today's lecture, we looked at the concepts of robustness, fragility and complexity and how they are all interrelated and complexity is one key factor underlying biological systems and you know how robust they are and how fragile they are depending upon a lot of interesting factors and we also looked at this concept of highly optimized tolerance and you know how power laws are rampant in biological systems.

And I briefly introduced you to the concept of robustness and evolvability which brings me nicely to the next video wherein we will focus a little more on how do we systematically study the relationships between robustness and evolvability in biological systems. We will start with the study of parametric robustness, so what happens when you change a particular parameter, how robust is the system and topological robustness which is what happens when you start rewiring a system and how robustness and evolvability are intertwined.