Physics of Biological Systems
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Lecture - 59
Reaction diffusion and spatial pattern

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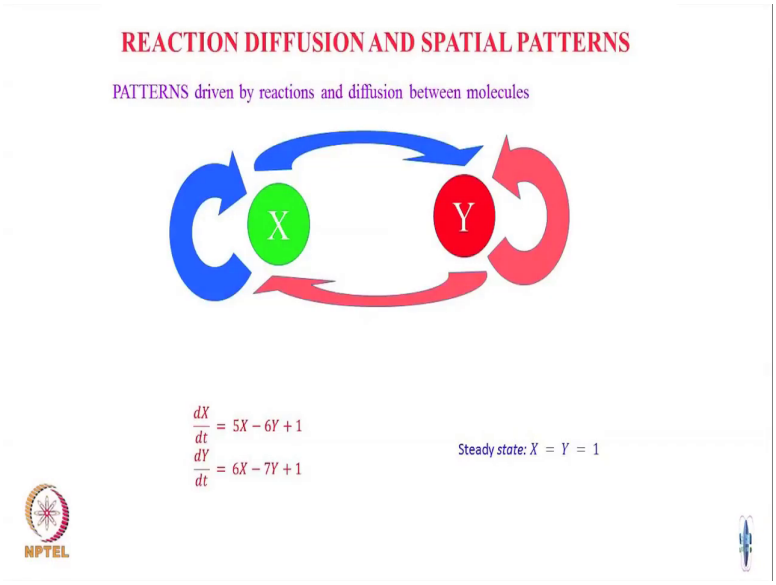

So, the idea is this that we have talked about chemical kinetics. So, let us say these are two species X and Y and they have some sort of interactions amongst themselves. So, for example, let us say that X up regulates itself Y up regulates itself. So, there is some maybe up maybe some is a down regulation some is a up regulation.

So, there is some sort of cross talk between this X and Y and let us see you know what how to write down these k on's and k off's and whatever. So, you have written down a chemical kinetics equation. This is very this is a toy model of course; this is a toy model which was

actually proposed by Turing himself, it is just to illustrate the point. So, let us say these are my chemical kinetics ok.

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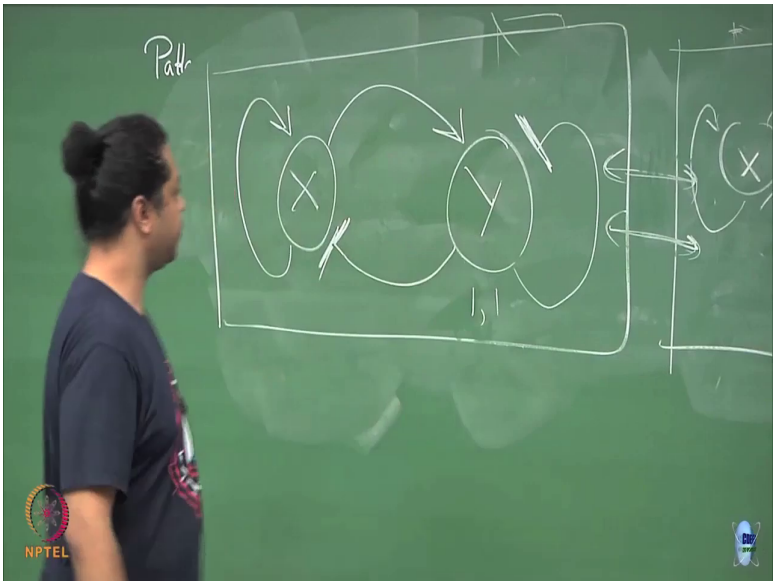

So, basically what it says is that, so if this two species X and Y and I have 5 X minus 6 Y, so the more of X I have the more of X I produce. So, X up regulates itself let me point write that by an arrow, the mode of X I have the mode of Y also I produce say X up regulates Y ok. Then the more of Y I have the less of X and the less of Y itself.

So, Y down regulates itself which I let me draw by this sort of an arrow and Y down regulates X as well ok. So, X in some sense is an activator it activates itself it activates Y, Y is an inhibitor it represent itself and it represents X. So, that is the basic chemical kinetics that I have and I have written down an equation like this to correspond to this chemical guidance.

So, I can say that well given this sort of a chemical kinetics. So, what is the steady state? What will be in steady state? What will be the concentrations of X and Y? So, you can solve dX dt equal to 0 dY dt equal to 0 and get the steady state of this model. And because its chosen in such a simple way that the steady state is just X equal to Y equal to 1.

If you put 1 1 both of these will just cancel out, because a steady state of this sort of very simple kinetics is that X equal to Y equal to 1. So, now this is simple enough. So, now, the idea is this that I have this sort of I have this reaction. But, now let me say that I have this reaction is going on in every cell. So, let us say this is one cell where this reaction is going on.

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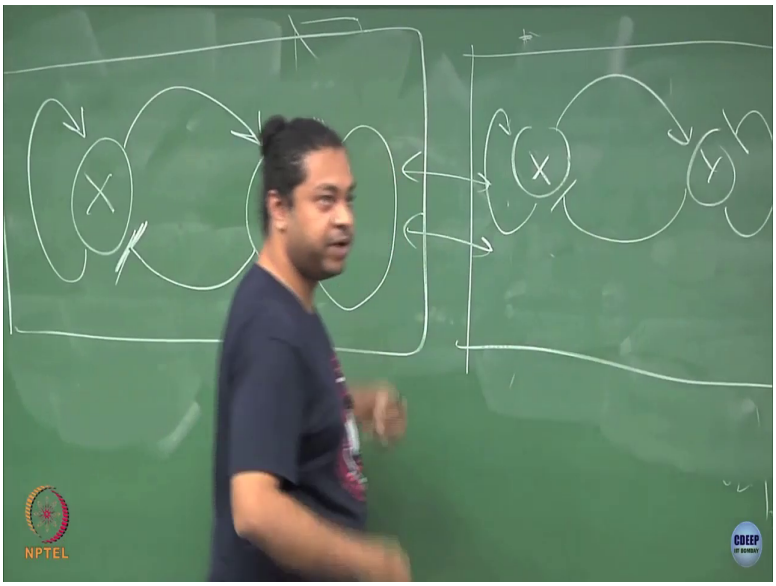

I have a neighboring cell where the same reaction is going on X Y up regulation, up regulation, down regulation, down regulation. And these X and Y they can diffuse between cell to cell. So, there is exchange between these cells. So, what was purely a chemical kinetics

model the moment I build in space that I have multiple cells these concentrate these different molecules can now diffuse from cell to cell, so, I bring in some sort of motion as well.

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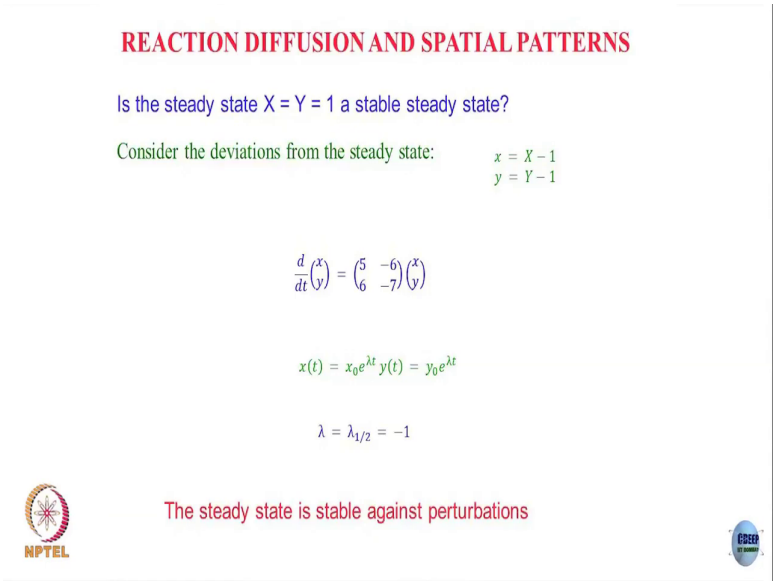

And I could now ask that well I have again jumped the run. So, before I do that this is also a trivial check that the steady state that I got you just check that whether it is a stable steady state or unstable steady state. So, you the you do the standard sort of analysis you consider deviations from the steady state. So, small x is that is X minus 1 small y is Y minus 1 you write down.

So, these are my perturbation away from the steady state you write down the how do these perturbations evolve in time. So, you get these 2 cross 2 matrix we find out the eigen values. If the eigen values are positive the perturbations will grow in time, if the eigen values are negative the perturbations will die away in time standard linear stability analysis.

So, you find out in this case again the matrix is chosen such a simple way that these eigen values it is a degenerate. So, both eigen values is the same its minus 1 which means that this steady state is a stable steady state. If you were looking at this inside a single cell and you perturb the concentrations away from this 1 1 steady state. It would come back very quickly to that steady state its stable against perturbations ok.

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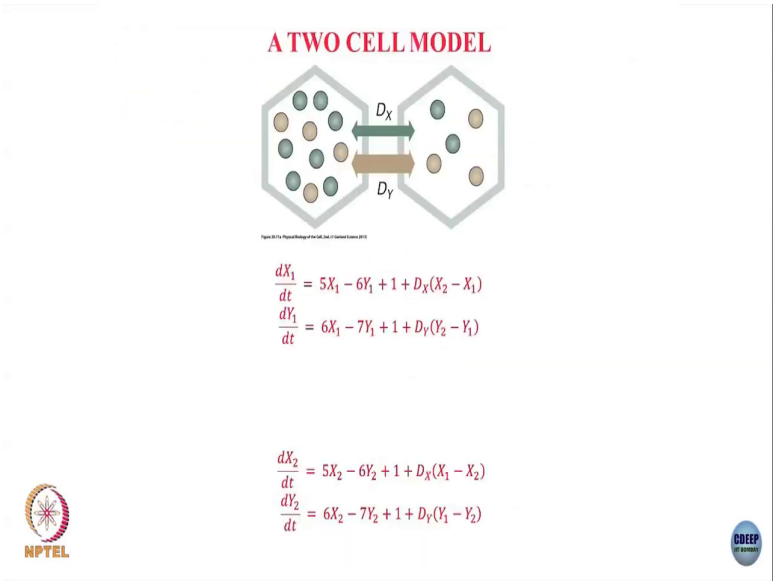

So, now what I want to do is that you want to couple these, so you introduce space use let us start with a single simple two cell model actually there are only two cells and they are coupled to each other. The two species can then hop between these two neighboring cells with some sort of a diffusion coefficient dX and dY. So, in addition to this chemical kinetics I introduced this diffusion and the idea is this that when there was no crosstalk I know that one it was 1 1 over here and was 1 1 over here ok.

So, I might naively assume that even when there is crosstalk ultimately what diffusion wants to do is that it wants to get rid off any sort of in homogeneities right one smoothen away any fluctuations. So, I am naively I might assume that it will remain at 1 1 throughout provided right. So, if these were already in steady state just by because of the fact that I have coupled them should not change anything maybe it will remain at 1 1 2 throughout. What Turing did was that he realized that this is not necessarily the case?

What was a steady state in the absence of diffusion? Once you introduce diffusion you can make that steady state unstable, so that is what it will try to show in this simple model. So, now, I have two cells, so let me say that the concentration in cell 1 I write as X 1 and Y 1 and the concentration in cell 2 I write as X 2 and Y 2. It is the same kinetics 5 X minus 6 Y plus 1, 5 X minus 6 minus 2 except now I have a diffusion light term.

It is not really diffusion because it is this two cell but whatever the diffusion like term it wants to sort of erase out any in homogeneities. If one is greater than the other it will flow from the greater side to the lesser side with some sort of a diffusion coefficient, X for this X species Y for this Y species. So, the one I have these two cells I now have coupled these I now have these equations. And now, I want to ask that whether does this state 1 1 continue to remain stable against perturbations.

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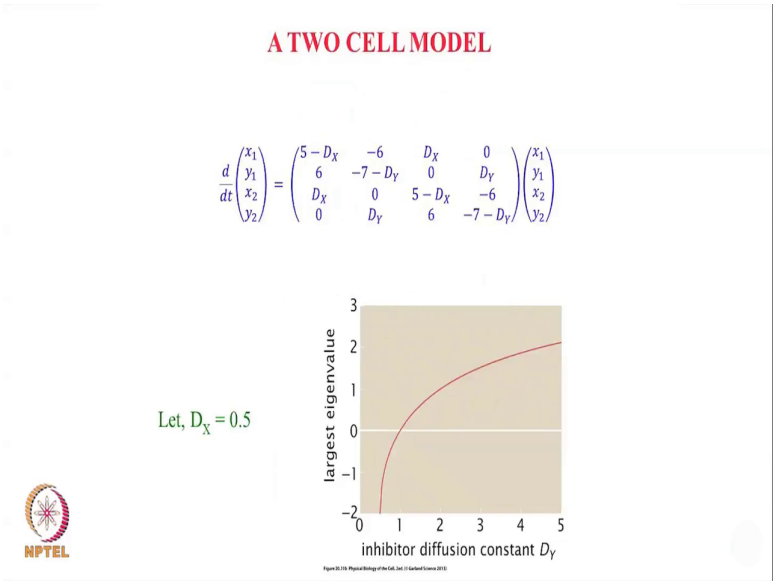

So, again you define your sort of perturbation, so these small x is are again X capital X minus 1s and you are. So, now, you because you have 4 species X 1, Y 1, X 2, Y 2 you have a 4 plus 4 matrix. So, I am not doing the I am as if it is simple in (Refer Time 06:50) other and then ask that what are the eigen values and so on of this. So, you can do this numerically, so you need some values of D X and D Y to find out the eigen values.

So, let us say I choose D X equal to half completely random is anyway a toy I just want to illustrate the idea and then you vary your D Y. So, remember my X is the activator in this sort of a scenario Y is the inhibitor. So, for the activator I have chosen half, for the inhibitor I will choose I will bear with that and I will plot the largest eigen value of this matrix.

So, what it shows is that there is a range of values of D Y, so let us say D y which is greater than roughly 1. Where this largest eigen value becomes positive right which means that you

have now destabilized this steady state this 1 1 steady state. You have now destabilized it against perturbation simply by introducing a differential diffusion.

You cannot do it if the diffusion coefficients are exactly the same, but if the inhibited diffusion constant is actually greater than this activator diffusion constant. If its lower also it does will not happen, but if it is greater than this activator diffusion constant then you will have a regime where this 1 1 state will become unstable ok.

So, this was sort of Turing's main idea that you can take a steady state which is steady in the absence of any coupling. And once you couple it to various cells or basically you introduce space you introduce diffusion, you can make this stable steady state unstable with respect to perturbations.

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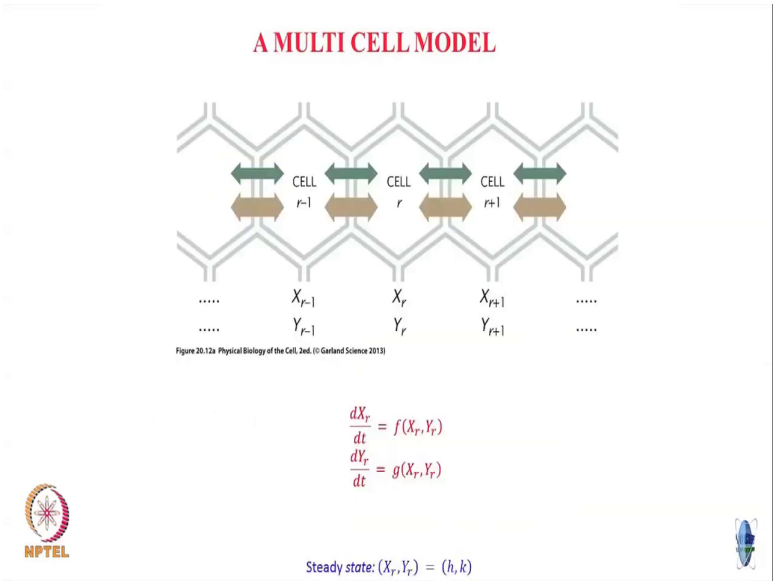

You can now extend this, so you can now say that well of course, there are many many cells. For example, in the circular or whatever organism that you thinking of there are many many cells like this and there is the diffusion between diffusion of this X and Y between these many cells ok. And of course, you can write any chemical kinetics whatever is the appropriate chemical kinetics that you have between this X and Y f and g are this 5 X minus 6 Y and 6 X minus 7 Y. So, I have just written generically in this case some f and g this was my chemical kinetics and it is some steady state h and k X Y equal to h k.

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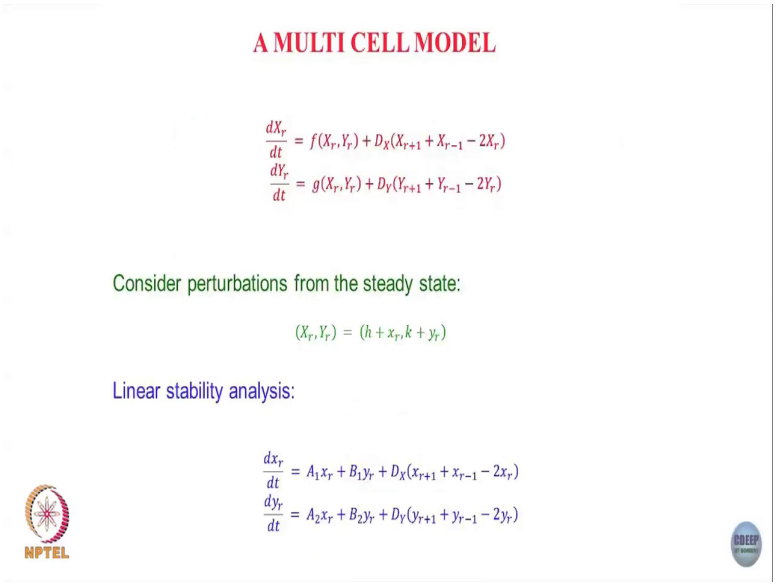

So, again I can look at perturbations away from this steady state and look at how to describe those perturbations. So, once I introduce the diffusion coefficient again because this is a discrete sort of a model I write a discrete d 2 c D X d 2 X D X 2 in some sense X r plus 1 plus X r minus 1 minus 2 X r. If you were writing in continuum this is just t times del 2 c del X 2. And you consider perturbations away from this steady state and you see what happens to these

perturbations. So, you do again a standard linear stability analysis this A 1 B 1 are just this the partial derivatives of f and g at the steady state.

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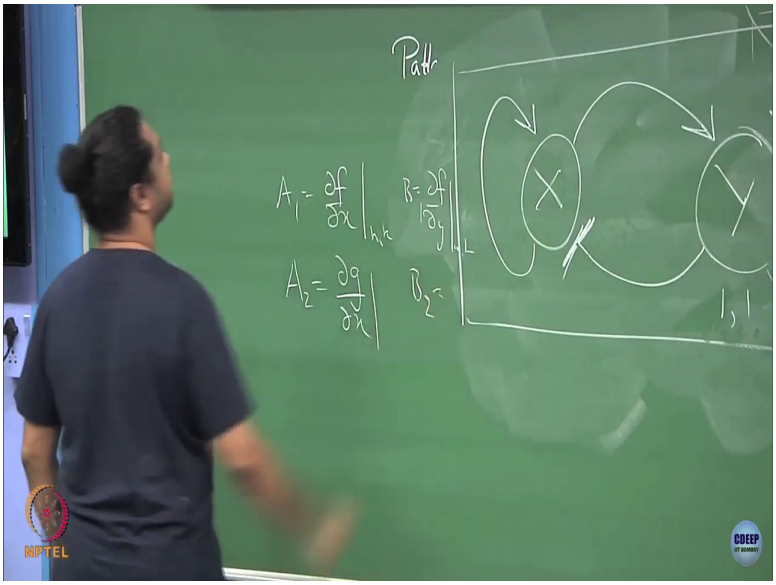

So, A is like del f del x at h k B is del f del y at h k and so on. What else do I have A B A 1, B 1, A 2, B 2, A 1, B 1, A 2 is del g del x so on right ok.

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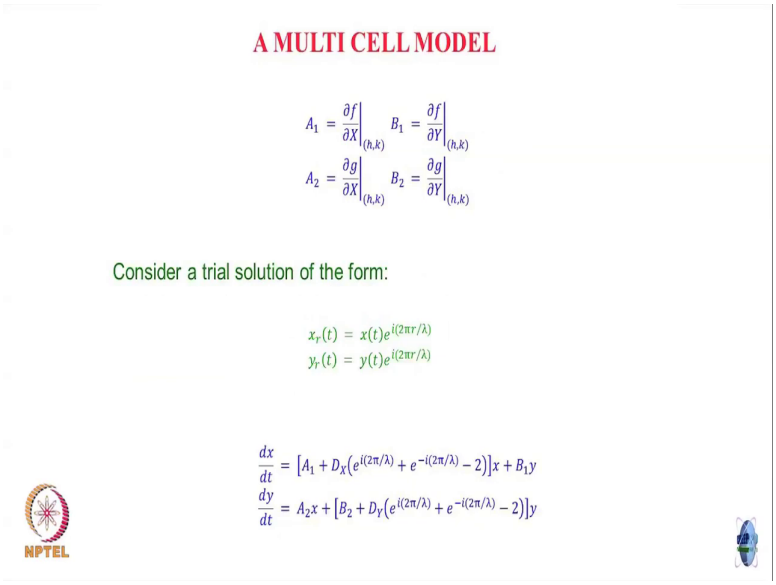

So, you do a linear stability analysis I have already this here also. So, you do A 1, B 1, A 2, B 2 are just the partial derivatives of these chemical kinetics terms around the steady state ok. And then again I consider this sort of trial solutions and I find out what are these eigen values lambda, so this is what this D X dt and DY dt gives me.

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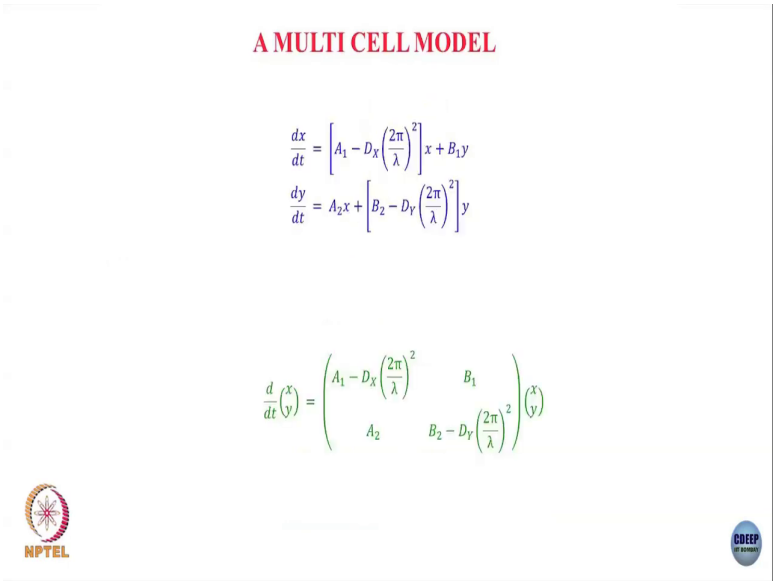

Typically if I, so what I have done instead of just said that lambda is large and expanded these exponentials and I get some sort of an equation. So, I will do this concretely for some values of f and g I just want to show the main idea now. So, you look at how these perturbations grow with time and you can find out the eigen values. So, again you write it in a matrix form and you find out the eigen values of this matrix and again you for some particular choice of this A 1, A 2, B 1, B 2.

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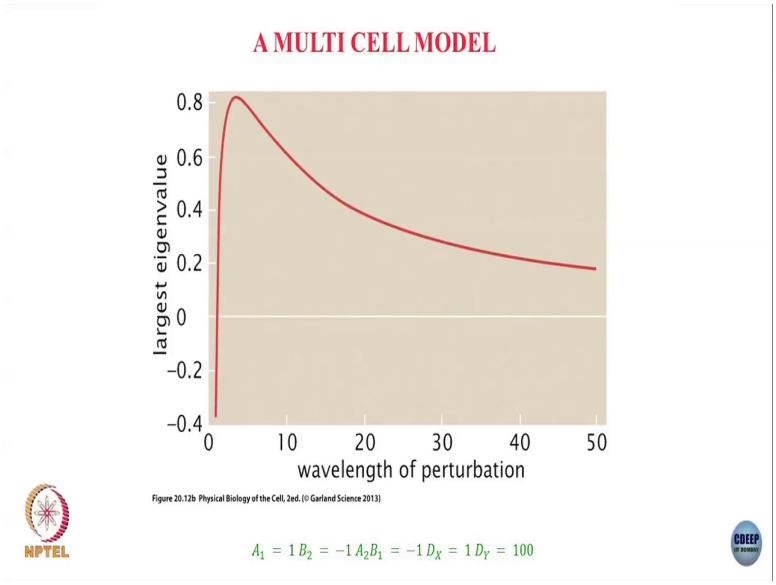

So, this is plotted for some particular choice of A 1, A 2, B 1, B 2 and again X is activator why is the inhibitor. So, I have taken the diffusion coefficient of Y to be much higher than the diffusion coefficient of the X. And again you will see that the largest eigen value there is some regime where the largest eigen value is positive which means that you will have the steady state becoming unstable.

Not only that you will have some the perturbation that will grow that will grow with some characteristic wavelength. And you can find out that characteristic wavelength as well and there is some particular wavelength which has the highest eigen value which means that if you waited long enough this eigen value would be the eigen.

This wavelength would be the wavelength that you would see in your in the steady state in the infinite time limit all other wavelengths would sort of die out. So, small times we would see

solutions which were combination of all these eigen values which had all these wavelengths which had positive eigen values. If you waited long enough only this one would survive and that is the dominant wavelength that you can see.

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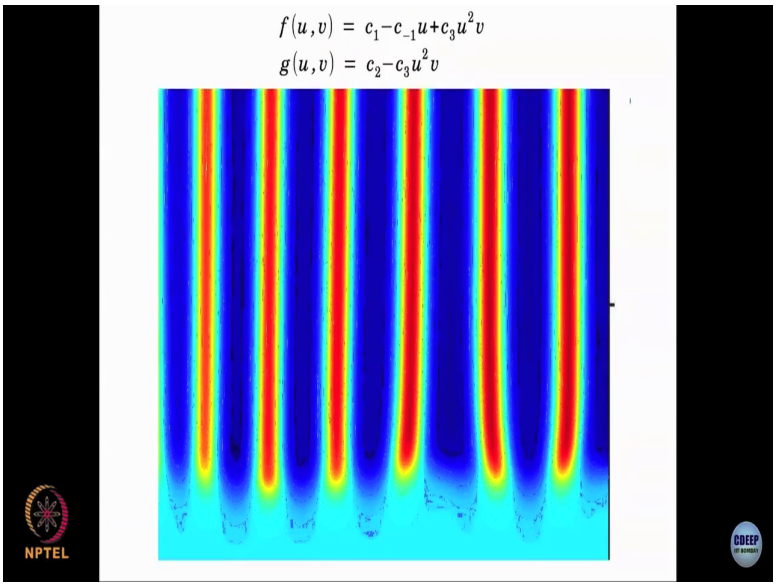

So, that is basically the idea. If you now, so if you now see a particular choice of this f and g. So, here is one particular model it is called the Schnakenberg kinetics. So, you put some sort of chemical kinetics between f and g you start initially from an uniform steady state and what you. So, this axis is sort of time, this axis is space. So, you start off with initially everything well mixed and then as time goes on you will see you will get patterns.

So, red let us say I am plotting one of the species, so red is the highest concentration blue is the lowest concentration, so you will get some sort of patterns that are emerging. The starting

from an initial well mix tape depending on that whatever particular chemical kinetics that you choose you will get some sort of that.

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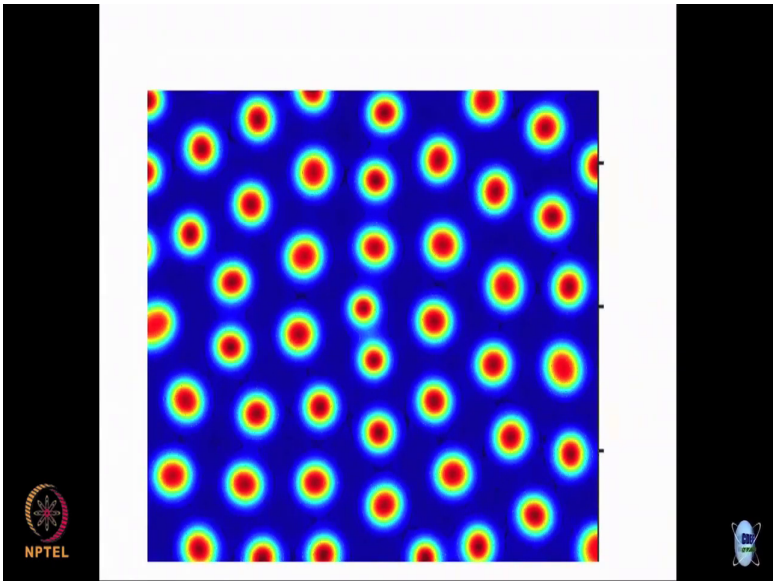

This is the 1 d example you can do this similar business for example in 2 d. Again for the similar sort of kinetics the same kinetics is differ Schnakenberg, except now I have two dimensional space. So, this is X and this is Y and then in certain limits for certain parameter values of these diffusion coefficients you will see that you will get maybe the spot like patterns ok.

So, in these regions intensity is very high in between in this blue regions intensity is very low. And again these forms spontaneously ok, so you start from the steady state which was steady state of this uncoupled models. And then that is you give a small perturbation the steady state

is unstable against perturbations and you get some sort of wave length which is maybe the distance between these spots and so on.

You get some dominant wave length in the large time limit which will slowly emerge. So, this was basically Turing's idea that is how do you get this large scale pattern formation starting from spontaneously in some sense starting from this sort of chemical kinetics and adding in diffusion.

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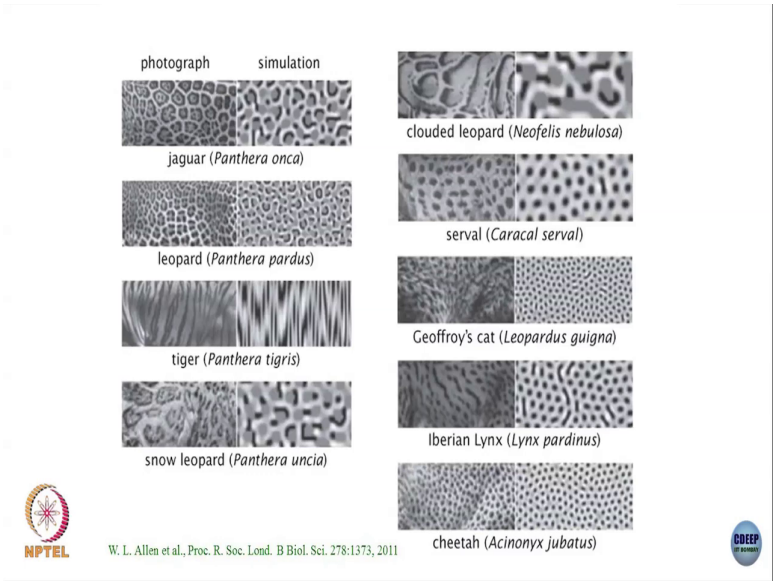

So, what Turing wanted to do was to sort of Turing with thinking about these various patterns that occur in nature like zebra stripes and various animals and so on. It turns out that this is not a very good model maybe for these sort of things because if you think about. If you say that well I have a tiger and I have to form the spot stripes of a tiger and some chemicals are diffusing and so on. You could ask that what is the time scale it would take given the size of

the tiger and it turns out diffusion is not a good mechanism for that. The diffusive time scales are too small.

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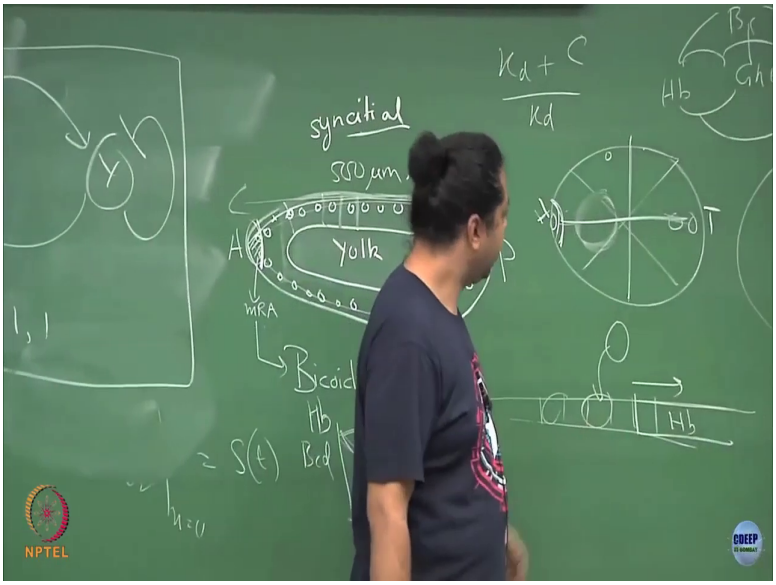

But on the lines scales of embryo and so on, so for in the context of this development these processes are actually important. So, what happens in part of this animal coat patterning and so on is slightly different, it is not really this sort of a thing. But, in the context of this development of embryos and so on, where these length scales are some tens or hundreds of microns maybe not very large.

The initials are a patterning that happens like this hunchback or whatever, you can think in terms of these sort of reaction diffusion systems, so I think I will stop here. So, what I will do is that I will take this generic, so you can ask that well will I always get a pattern right, so what are the conditions.

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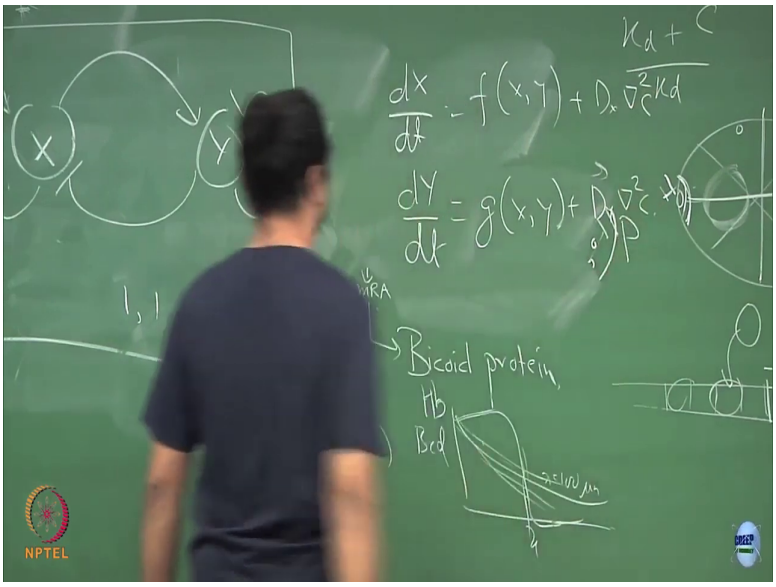

So, given chemical kinetics some given some dX dt and dY dt equal to some f and some g of X comma Y, X comma Y plus some D X D Y right. When will I what I have shown is that it is possible to form these sort of orders. So, I have chosen the parameters such that you see this nice sort of spots or stripes or whatever coming out.

It is not true that whatever d X d Y or whatever rate constraints you choose in your chemical kinetics you will always see order. So, there are some constraints on that and that one can work out very nicely mathematically analytically you can show very nicely that when you will get nice order like this that emerges. So, that I leave for next class because I do not want to brake in the middle.

So, what I will do is the generic theory of these sort of reaction diffusion systems and try to answer the question that what conditions must this f and g and this D X and D Y satisfy. In

order to destabilize the steady state and form some sort of a pattern. So, that is what I will do next class. I have this code for this Schnakenberg kinetics in mat lab. I can upload that on moodle and you can play around with it and check that when these patterns come and when do they not come so on.

So, let me stop here and then we will continue on Tuesday.