Physics of Biological Systems
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Lecture - 61
Condition for destabilization in pattern formation

So, now, what I want to do is that I want to see that if I introduce now diffusion. If I now say that these neighboring cells can all talk to each other by diffusing from one cell to the next, can I destabilize the steady state?

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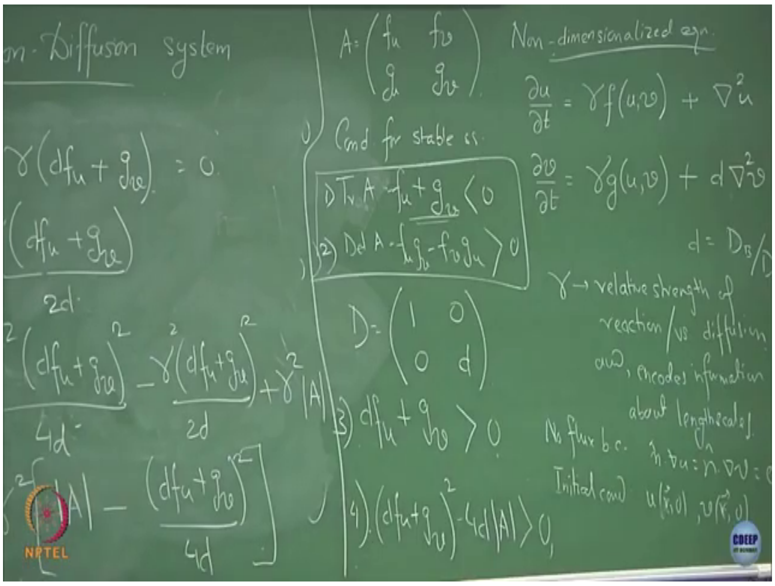

Is there some choice of this f f g d whatever such that I can destabilize this previously stable steady state.

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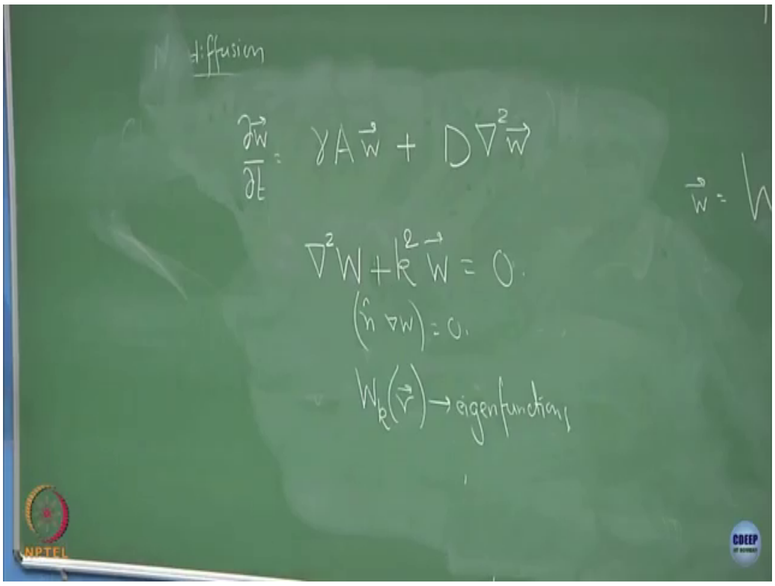

So, again so, if I now again write that equation in the matrix form. So, what I have is del w del t right is gamma times A the stability matrix times w. A being whatever it was; plus let me write down since I have writing it in matrix form plus let me write down a diffusion matrix times Laplacian w. And what is this diffusion matrix then? The diffusion matrix is simply 1 0 0 small d right.

So, for the u part of this, remember this is a vector equation it has u component and v component for the u component you will just get Laplacian of u, 1 into Laplacian of u, for the v component you will get small d into Laplacian of v which will recover give you back those equations. So, I will just written it in a matrix form nothing else.

So, what I want to do is I want to look at this diffusion driven instability if I can generate a diffusion driven instability of this homogenous steady state that I have written down. So, what do I do, I can start off by saying that let me define these space, let me just define the spatial eigen value problem which is equal to some k square times w. So, let me just write down (Refer Time: 02:22) with the same boundary conditions that n dot grad w is equal to 0. So, let me define. So, what am I doing basically I just to summarize. So, I want to solve this equation, what is the standard thing to do, maybe I do a separation of variables right.

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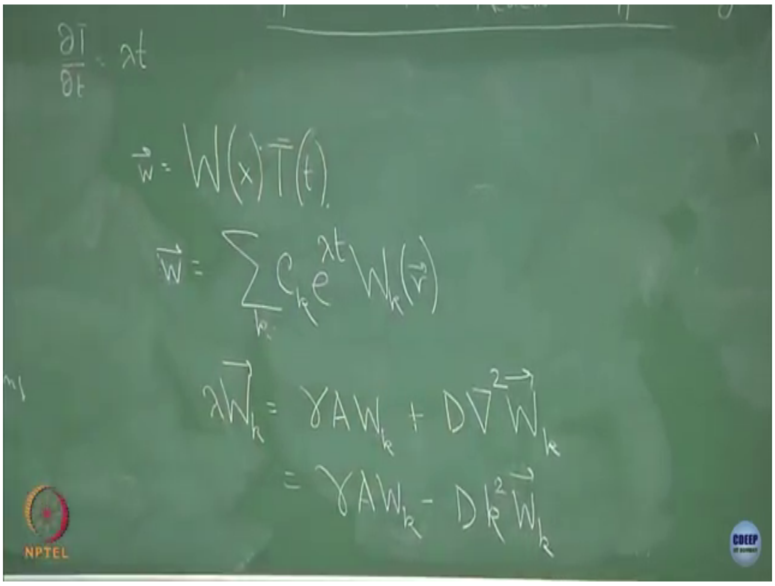

So, let me say that I will write this let me say this is a small w, I will write this as some capital W of space times some capital T of time right. I will plug it over here and I will plug it into this equation then I will get one term which depends only on the time terms, I will get one term which depends only on the space terms right, what will the space term will look like? It look like something as Laplacian of this capital W is equal to some k squared times this w.

So, you can find out the eigen, let us say that W k are the eigen vectors of this equation. So, let me say I get W k r are the eigen functions of this equation, satisfying this boundary condition, whatever is the boundary condition that I can written down. And then for this actual w that I am interested in, you can construct a general let me write a small w; you can construct a general solution by doing a linear superposition of all of these eigen functions right.

So, I can do a linear superposition of this W k of r the time part will we look like e to the power of some lambda t times some coefficients C k summed over all wave vectors k right. Is this clear? You do a separation of variables, you get a set of basis functions from the expansion from the equation of the spatial part which are these W k; which obey whatever boundary conditions that you have which means that you will have some allowed wave vectors right. For example, if you are doing in 1 d, your eigen functions would be some costs let us say n pi x by l or sin n pi x by l right and you allowed wave vectors would be n pi over l right for various value pi.

The time part, the time equation will look like something like del t del t is equal to some lambda t right. If you if you use this separation of variables, which will have some solution like e to the power of lambda t. The general solution you construct by doing a linear superposition of all of these allowed solutions and then you have to find out these coefficients the C k's my matching whatever initial condition is given right this ur comma 0 and v r comma 0.

So, now I take this I take this general solution and I put it back into this equation that I want to solve del w del t. So, what does this give me del w del t. So, the left hand side will del t will bring me down a lambda, a lambda times a W right. On the right hand side I have this lambda times this is the capital W. So, we can let us make it clear, left hand side and the right hand side I have gamma times the stability matrix times this W of k plus D. So, I really you get this with the summation.

So, if this holds true for every value of k, then you know that the your original differential equation is going to be satisfied ok. What is this Laplacian of this capital W k? That is nothing but minus k square w; because that is how this is defined right this is the. So, I can just write this is gamma times A times W k minus D k square W k ok. Because, Laplacian of W k is k square of W k, these are the eigen functions of this equation. So, I just use that ok.

So, now, what I need to do, because I want to now evaluate these lambdas because, these will now tell me that in the presence of diffusion; how does this how do perturbations from the steady state behave right. So, again I will solves the characteristic equation when the characteristic equation in this case is.

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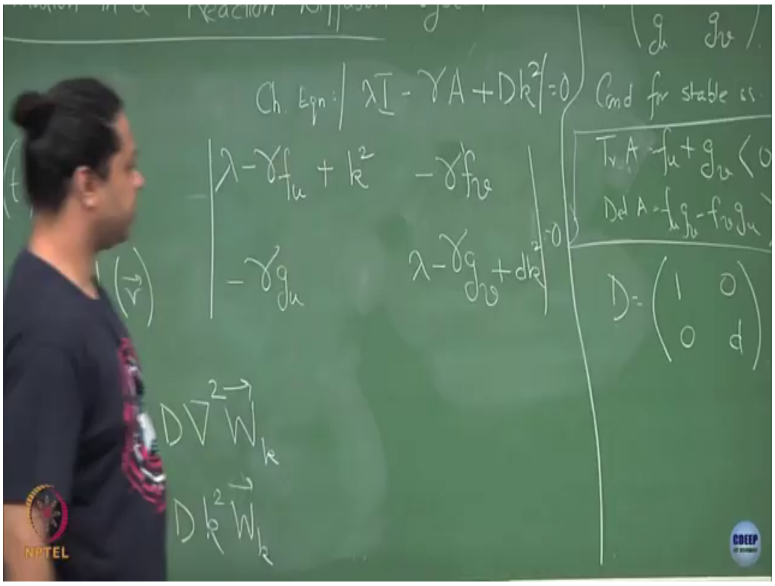

So, again the characteristic equation in this case is lambda times I, the identity matrix minus gamma times A, the stability matrix; plus D times k square, this is equal to 0. Yeah Lambda times I minus gamma times A plus D times k square ok. So, now, I can write this down, I know what all of this is. So, this is lambda minus gamma f u plus D k square, so plus k square then, here is minus gamma f v then, 0 minus gamma g u and lambda minus gamma g v plus small d k square is equal to 0, separate of this column ok.

So, this is now my two new equation that I have to solve. I know what is my A, I know what is my D, I know what is the identity matrix I can just write this down. And again I now need to solve it for lambda.

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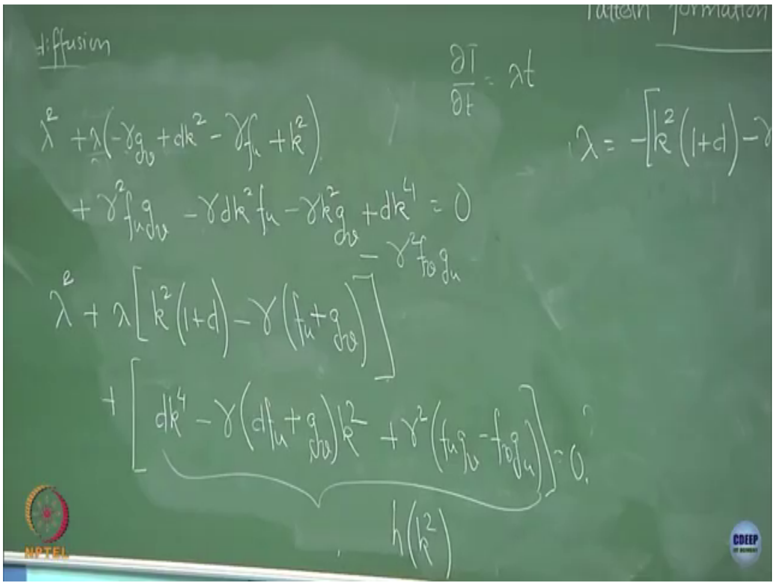

So, let me write this down. So, this gives me lambda square that is the first term plus lambda into minus gamma g v plus d k square right? Lambda square minus lambda comma gv it is dk square minus, lambda gamma minus gamma f u plus k square. And then what else have I missed plus gamma square fu g v, gamma square f u g v minus gamma d k square f u, minus gamma k square g v plus d k to the power of 4.

So, let me just reorganize this, so let me write it a little better lambda square plus lambda into k square 1 plus d minus gamma f u plus g v ok.

Student: (Refer Time: 11:51).

I have missed one term ok. So, right I have not written the last (Refer Time: 11:56) So, what is that? Minus gamma square f v, g u alright. So, plus something which is let me say d k to the power of 4; minus gamma what gamma tends to, I have gamma k square minus gamma d fu plus g v into k square right and then this and that. So, plus gamma square f ug v minus fv gu. It is a horribly complicated well not horrible.

So, its slightly complicated equation, but provided I have done everything correctly this is what you get. So, this is the equation for lambda again a quadratic equation, but at least its a quadratic equation. So, I can just solve it.

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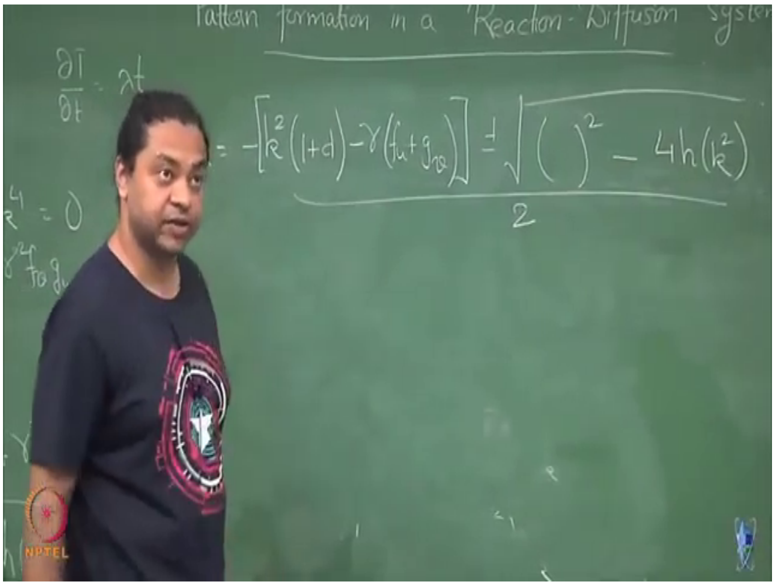

So, lambda is equal to minus of this thing, minus of k square 1 plus d minus gamma into fu plus g v, plus or minus this whole thing square. So, I am not writing it out again, minus 4 h of k square it just to save me writing this let me call this entire thing as h, h is a function of k square divided by 2 (Refer Time: 14:06) divided by 2. So, what I know is that in the absence of diffusion, the lambdas are less than 0 or at least the real parts of lambdas are less than 0. Absence of diffusion basically means that k square is equal to 0 right.

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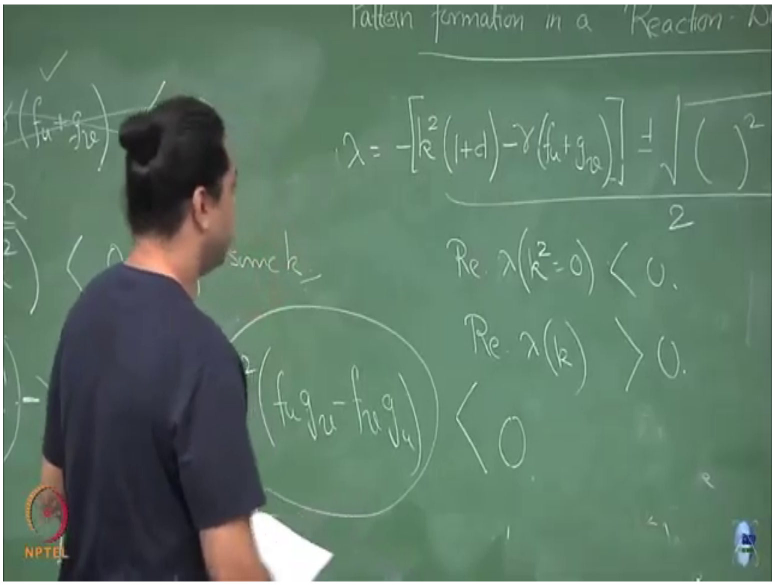

So, I know that the real parts of lambdas lambda act k square equal to 0, these are less than 0. So, because it is a stable steady state; what I want to find out is that, is there any value of this wave number k; such that this real part of lambda as a function of k this becomes greater than 0 right. If I can make this eigen value positive at least one of these eigen values positive, then I can destabilize what was previously a stable steady state and I have this possibility of patterns arising ok.

So, how can I do this? So, maybe let me see I can have this quantity itself whatever is in the bracket, if this was positive right then this will come with a negative sign, so then I would have at least one positive root right. So, I could say that well what is the if I want this thing that real part of lambda is greater than 0.

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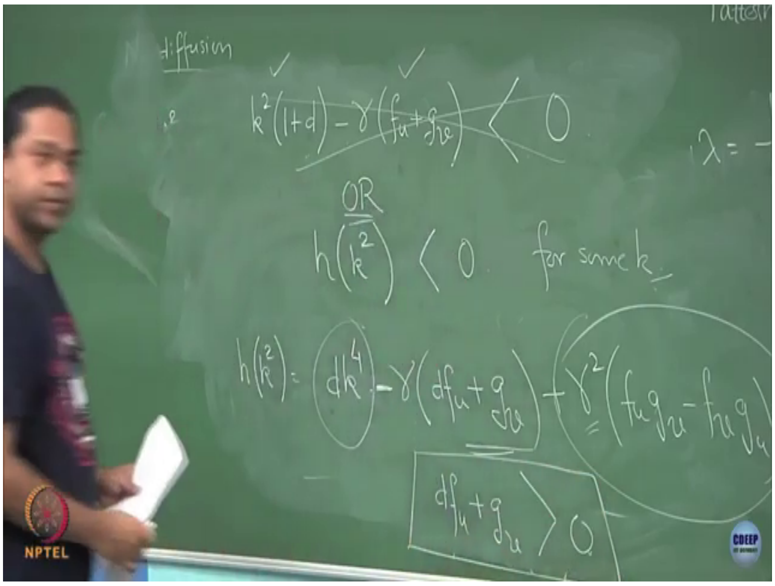

If this thing k square into 1 plus d minus gamma into fu plus g v, if this thing was greater than 0, then I can have this that real part of lambda is less than greater than 0. Or I have another possibility which is that if even if this was positive, if let us say this was positive, but h of k square is a negative quantity then this negative negative would become positive. I would in this negative term I would get something which was ultimately negative right. So, another possibility is that this h of k square this term is less than 0 those and or. So, let us look at these possibilities, let us look at this first one, k square is the wave vector yes.

Student: (Refer Time: 16:59).

Which one?

Student: (Refer Time: 17:00).

Is what do I want?

Student: (Refer Time: 17:13).

Yes it is; thank you that should be less than 0. So, if this is what I want, remember k square is the wave vector, so that is positive. d is the ratio of the diffusion coefficients so, that is positive. So, this is a positive thing f u plus gv, I know is negative because that was a condition of my stable steady state; which means that minus of our negative quantity is always positive. So, this is positive, this is positive therefore, this cannot be true, this can never be negative ok. So, this condition extract out of these two possibilities this first one is never possible. So, all I am left with is this term that h of k square is less than 0. For some k for some for some k, it need not be for all wave vectors, but at least for some k this should be less than 0 ok.

Student: (Refer Time: 18:18).

Yes.

Student: (Refer Time: 18:21).

Provided you have a stable steady state for the reaction diffusion evaluations. If you did not and yes of course, I mean if this was if this was positive, then in general yes, but then you would not even see a stable steady state even in the absence of diffusion.

Student: (Refer Time: 18:43).

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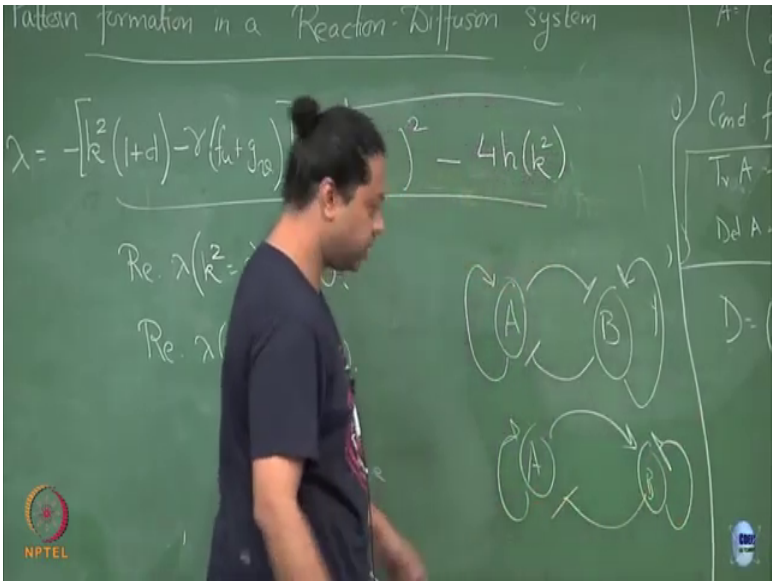

Yes, because for example, if I had an equation, if I had a chemical reaction like this I have two species A and B, let us say they both up regulate themselves and they mutually down regulate each other ok. So, neither is a clear activator or inhibitor right remember last day we were talking about a pattern in the equation that I saw in that we looked at where A activated itself and activated B; whereas, B auto inhibitor itself and inhibited A right. But if I think of something like this, where each species activates itself and mutually, they mutually repress each other. Then fu which is like del f del a is positive f g v which is del f del v that is also positive.

So, therefore, this would not be true and this is a very common pattern you will see in lot of in lot of genetic networks when you talk about transcription factors mutually interacting this is a very common motif that you come across. I mean; simplified, no motif is just two chemical reactions, but roughly guesses such motifs are possible ok.

So, what is h of k square? I have rubbed it off sorry, let me write down once more what is h of k square? So, h of k square is dk to the power of 4 minus gamma small d fu plus gv plus gamma square into fu g v minus f v gu ok. So, this was my hk square and I need this to be less than 0 in order to have some wave vector where this lambdas are positive so, in order to destabilize the system ok.

So, now let us look at this dk to the power of 4 is always positive ok. So, this term is always positive. f u gv minus fv g u, I have said needs to be positive in order for it to have a stable steady state; gamma square is positive. So, therefore, this term is also necessarily always positive. So, the only way you can have and this comes with a negative sign remember. So, the only way you can have this to be less than 0 is if this term is greater than 0 right. So, that the negative sign will make it less than 0.

So, the only possibility is if d fu plus gv this is greater than 0. The only way you can make hk square less than 0 is if this term d fu plus gv that is a positive term. Now let us think about what that means.

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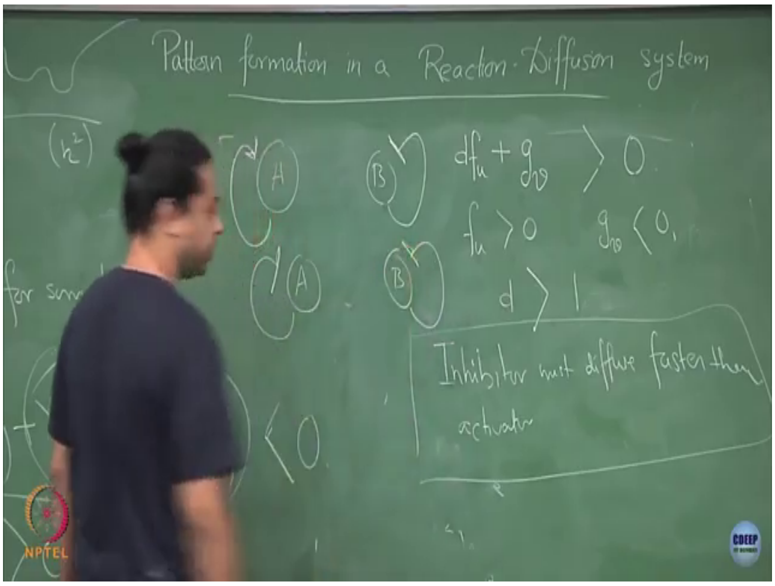

So, I have this condition now d fu plus gv is greater than 0. Can you have fu and gv, both to be of the same sign? Yes, you know. Can you have a fu and g v both to be of the same sign? No right, because then you would violate this condition f u plus gv less than 0.

So, let us say let us let me say that let us say f u greater, let us say f u is positive and let us say that g v is negative, I could take the other way also. If f u is positive and g v is negative, then d must be, then d must be greater than 1. In order for you to have this equality this inequality being satisfied, which means that remember what was d? d was the ratio of the second species to the first fu greater than 0, again if I draw my speck, if I draw my reaction that I have f u greater than 0 means A activates itself, g v less than 0 means B inhibits itself. So, A is my activator and B is my inhibitor.

So, which says that and this ratio being greater than 1 says that, whatever is my inhibiting species that my inhibitor must diffuse faster than the activator, faster than the activator. If I had reversed this if I had said that f u was less than 0 and g v was greater than 0 then I would have the less than 1 which again physically would mean the same thing that whichever was the inhibitor species that then in that case in this case B is the inhibitor if I took the other assumption then A would be the inhibitor and A, what this would say is that A would then need to diffuse faster. So, this inhibitor must always diffuse faster than the activator that continues to hold true.

So, let me write this condition here as well. The df u plus g v that is greater than 0. So, this was 1, this was 2, this is 3, but ok, is there anything else? Even if I had said that this is greater than 0, I need this to be greater than 0 in order for this h of k square to be negative. So, it is a necessary condition, it is not sufficient right because to get what to be sufficient this term dfu must overcome this and this the contribute the positive contributions of this and this. So, this is a necessary condition, but in order for it to be sufficient condition, so let me get rid of this is anyway this condition does not matter.

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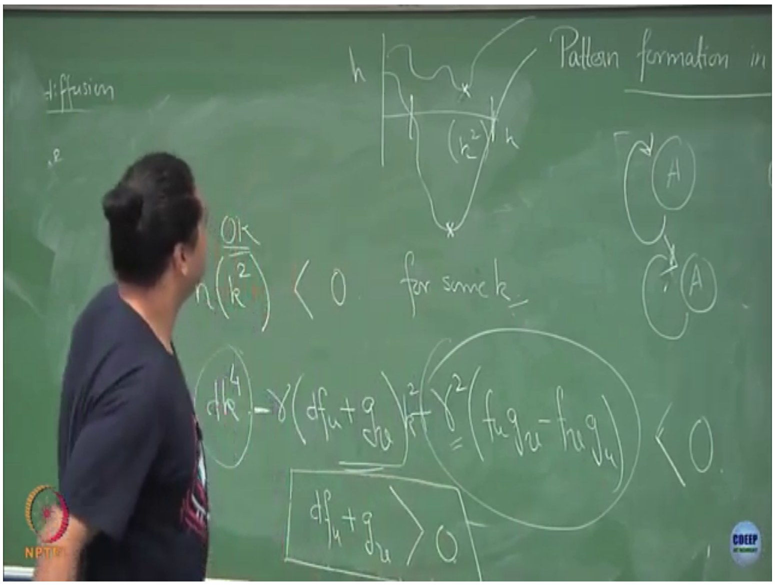

What I need to say is that let us say that I have this h let us say I plotted this h as a function of k square right. Some arbitrary whatever depending on whatever is some curve h of k square. What I need is that at least? Yes.

Student: (Refer Time: 25:45).

Yes.

Student: (Refer Time: 25:48).

The first condition is still satisfied.

Student: (Refer Time: 25:55).

But let us say that both are negative right. Can you ever get f a positive number into a negative plus another negative number giving greater than 0?

Student: So, in that case we will not (Refer Time: 26:10).

Will you cannot destabilize the steady state. So, that is what we are looking for right. So, in that case you cannot destabilized (Refer Time: 26:21). So, a think like this A B which is I think what you are saying that both sort of repress themselves; it can be a valid chemical reaction, but it will never have a pattern in this sense ok. In order to have a pattern, you need this that if one is activating itself the other needs to repress needs to repress itself. So, that is what 1 and 3 together imply ok. So, coming back to this so I need this hk square to be less than 0 for some value of k at least.

So, what I can say is that ok, this is a necessary condition for it to be sufficient what I can look at is I can look at the minimum point of this h curve ok, wherever this h of k square has a minimum and if at the minimum point, let us say this is my minimum point. If at the minimum point the value is less than 0 then I am guaranteed that at least one k exists where I have this h of k square less than 0 ok. There might be more. So, the curve might look something like this; in which case this whole range of ks are ks that will destabilize the steady state. But at least if I have one then at least I am guaranteed that I have one wave vector that will destabilize yes.

Student: (Refer Time: 27:43).

k square, the middle term has a k square thank you.

Student: (Refer Time: 27:54).

Student: (Refer Time: 27:57)

Yes.

Student: (Refer Time: 28:00)

Yes, I should not draw a random graph is that what you are saying.

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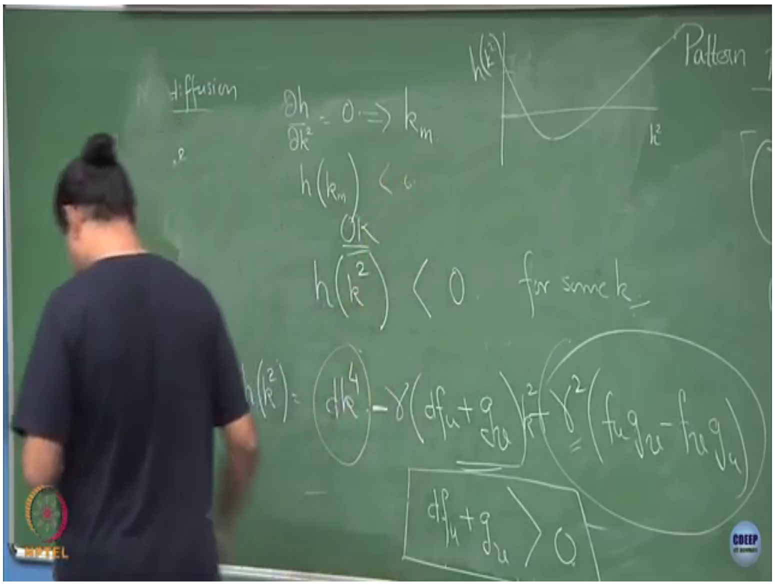

I can draw a nice graph draw something like this, yeah should not draw a completely random graphs ok. So, then what I want to do is that, in order to have a sufficient condition that this h of k square is less than 0 what I will find out is that I will find out the minimum of this hk square curve. So, I will do del h, del k square equal to 0 and find out so this solve this, this will give me some value km where this curve h of k square has a minimum, I will find out the value of h at this km point and see whether that is less than 0 or not ok.

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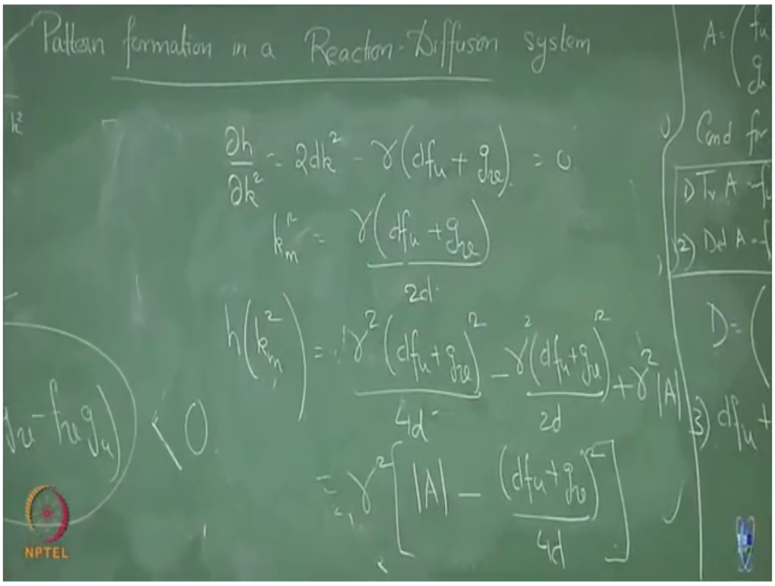

So, del h del k square. So, del h del k square is 2 d k square minus gamma d fu plus gv is equal to 0, which means that; this k m square is equal to gamma into d f u plus g v divided by 2 d. And the value of h at this point the value of h at this k m square, the value of h at this wave vector at this minimum wave vector is d into k to the power of 4. So, gamma square into dfu plus gv whole square by 4 d square minus gamma into, that means; write it straight of there is gamma square d fu plus gv whole square by 2 d and plus gamma square this is just a determinant. So, if you just write determinant of a what do I have this is actually the same term. This d and so this is 4 d and that is 2 d so minus 4d.

So, this is I can just write gamma square determinant of A minus d fu plus g v whole square by 4 d. So, this is the value of this h this quantity h at this minimum point ok. So, what this, so for this to be negative what this means then is that, this term must be greater than this determinant of A obviously.

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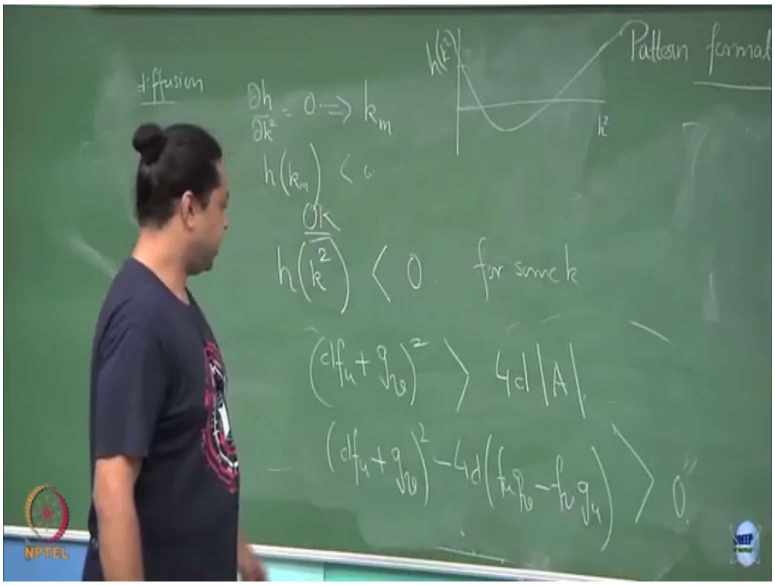

So, for this to be negative, what it means is that d fu plus g v right whole square must be greater than 4 d into determinant of A. Or if another way is if is write down d fu plus g v whole square minus 4 d into f u g v minus fv gu, that has to be greater than 0 ok.

If this condition is also satisfied, then at least I am guaranteed to have one wave vector at least one it can be more. I am guaranteed to have at least one wave vector for which you can destabilized this stable steady state and of course, the critical wave vector will come when you equate this to 0 right.

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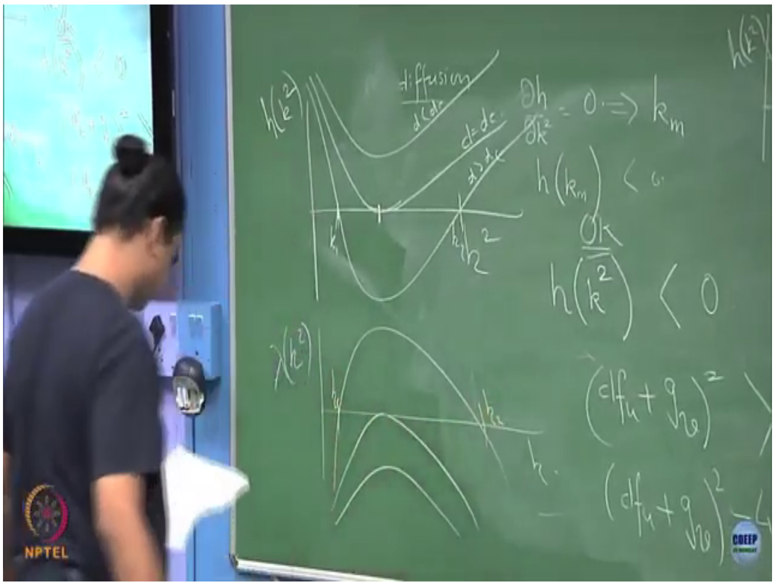

So, basically if I think about this h of k square plot. So, if I think about this h of k squared plot, h of k square versus k square plot, some h looks like this for some parameter values. Let me say I am just tuning the diffusion coefficient for example, then at some value it will just hit the axis and then for some values axis like this ok. So, this is let us say some critical ratio of the diffusions, this is some d greater than d c this is some d less than dc.

So, act the critical whatever, parameter let us say the diffusion ratio of diffusion coefficients, you have this one single wave vector that will destabilize the steady state. If you increase this ratio even more you have this whole spread of wave vectors from this k 1 to this k 2 for which this stable steady state will become destabilized. So, correspondingly if you were to plot this lambda; the actual eigen value, you would get something like this and then something like this and then something like this. At the critical point there would be 1, 1 wave vector for which this lambda is positive for just positive and then there will be a range of wave vectors k one vector k 2 ok.

So, this is the fourth condition that I now have for pattern formation which is that whatever I wrote down. So, d fu plus g v whole square minus 4 d into the determinant of A, that must be greater than 0. So, provided so, these two conditions 1 and 2 are required to say that you have. In fact, a stable steady state even in the absence of diffusion. Conditions 3 and 4 are what is required for this diffusion in order to destabilize this steady state and give rise to some spatially extended patterns.

So, these four conditions and this is quite generic I have not recourse to any particular form of f and g or whatever. So, you can take any chemical kinetics that you wish and think about whether you can destabilize the steady state.

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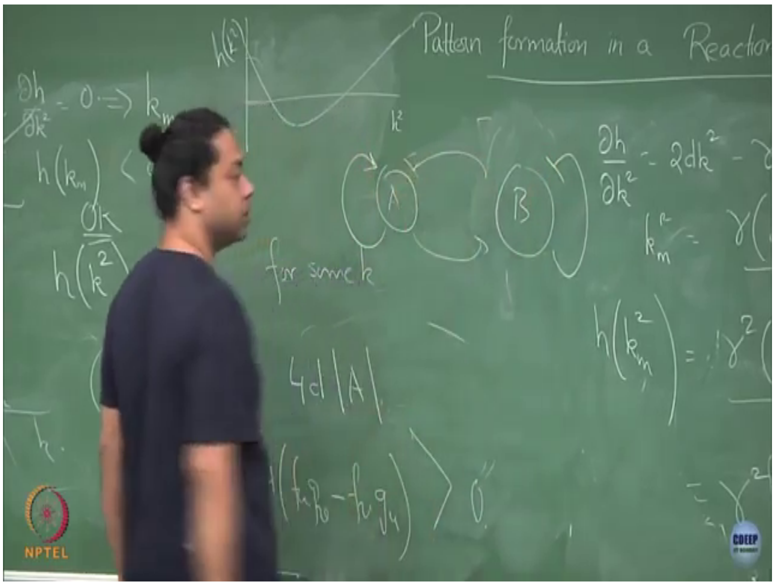

What this says is that in order to form a pattern, at least by this sort of a reaction diffusion mechanism; you need to have one of the species which is an activator and another species which is an inhibitor and then something about here.

So, you can try to construct patterns and see that what sort of chemical networks even without going into the rates and so on. What sort of chemical, what patterns of these chemical reactions will can give rise in principle to pattern information through this reaction diffusion mechanism. For example, like he said if both of these were inhibiting auto inhibiting then you would never have a pattern.