Introduction to Evolutionary Dynamics
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Lecture - 32
Evolutionary dynamics when mutations are rapid - 2

Hi and welcome to the next lecture of the course Evolutionary Dynamics. And what will do today is continue our discussion of the regime where mutations are taking place very rapidly. What that employ does is for in the last lecture is- that coexistence of multiple genotypes each of which correspond to a different phenotype in the terms of the rate at which growth is taking place.

Coexisting in one tube and what that leads to is then eventual equilibrium dynamics associated with genotypes, where selection is continuously or removing genotypes which are growing at a slower rate where as the high rate of mutation is associated with this regime keeps cropping up these genotypes which are growing at rates which are faster than those existing.

And eventually these two forces selection and new mutations are going to establish themselves in a new equilibrium, and we are interested in that regime when that equilibrium is established what is the speed at which the mean fitness associated with the culture is increasing with time; that is the expression that we are interested in and what we are calling speed of evolution.

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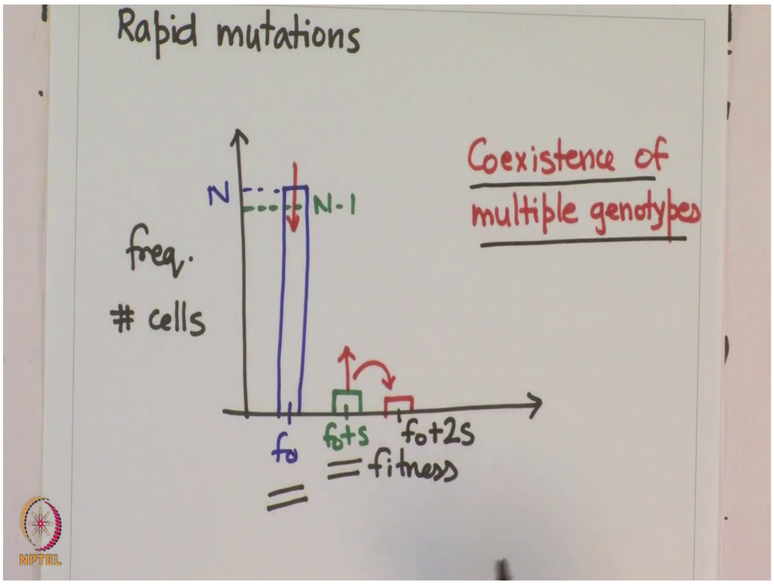

So, just to recap what this rapid mutation regime corresponds to is that we have we start of with an environment with whose carrying capacity is N and a t equal to 0 all individuals in this environment are at a fitness f naught. So, a t equal to 0 at f naught you have n individuals and as the experiment progresses new mutations will arise and eventually one of those beneficial mutations is going to get established in the population.

What that means, is that now you have f naught you have individuals at fitness f naught plus s, and consequently what that means is- individuals at fitness f naught have now come down. Once you have these two genotypes co existing in the population, selection would ensure that individuals correspond to this fitness increase in number and individuals corresponding to this fitness decrease in number. And while this is been eliminated and this is going towards fixation the mutation is are occurring at a frequency which is very high and what that results in is another beneficial mutation occurring in the environment, and now you have individuals which are present at fitness f naught plus 2 s.

And what that eventually results in is now coexistence of these three genotypes and the story keeps on repeating itself and you have newer genotypes arising while the older ones have been removed continuously by selection. And what this leads to is coexistence of multiple genotypes and if we let this picture play out in time you last in the last lecture we saw what is what is the equilibrium dynamics look like associated with the distribution of the number of individuals belonging to a particular genotype, and we sort of intuitively guessed the that picture looks like a normal distribution which is a shown here.

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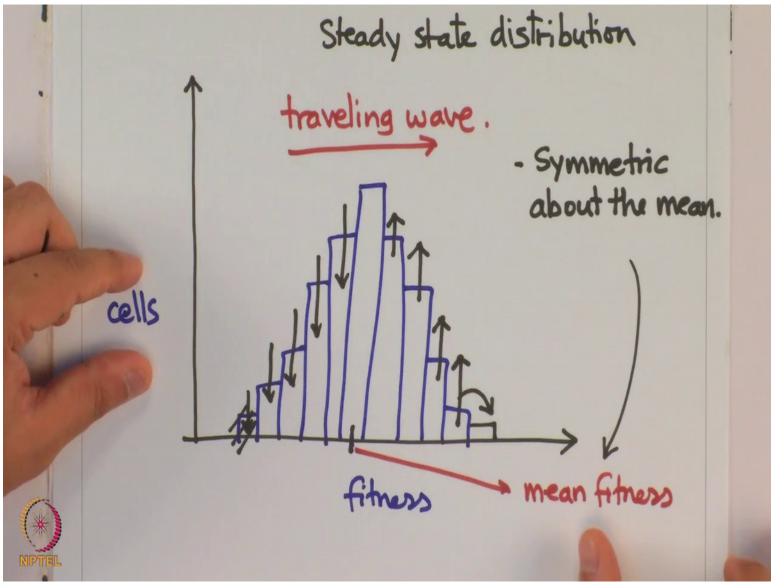

So, at steady state this distribution is going to acquire a shapes such as this where this is the leading edge leading edge which corresponds to the most fit individuals and this is the lagging edge which corresponds to the least fit individuals. And what we are going to assume here that this distribution is symmetric about the mean; what that means, is that if this is the this is the mean fitness associated with this distribution if on either side of this mean fitness the distribution is the same which means at symmetric about the mean, then the mean fitness is just equal to the fitness associated with the most frequent genotype in this distribution.

And now we have new mutations occurring which means this normal distribution is moving to the right as new mutations are occurring. In addition selection is attained and the frequency associated with those genotypes whose fitness is more than the mean will increase with time, and frequency of those genotypes whose fitness is less than mean will decrease with time.

So, at this particular certain this is what is happening to the picture new mutations are being generated hence the wave is moving to the right and as soon as you have one mutation that gets established here by that time, this genotype would have been totally eliminated from the environment and the travelling wave is looks identical at any instant of time and it is moving towards a right at a uniform speed. And it is this speed with which this traveling wave is moving is what we are interested in.

So, we developed the analytical expression associated with this travelling wave, and this lecture, and this development of this expression is perhaps going to be the most challenging analytical thing that we do in this course. So, this what follows is a little bit tricky, but it makes a lot of intuitive sense and reducing a couple of very (Refer Time: 05:32) in order to come up with an expression which gives us speed of evolution in this environment that we are talking about. So, how do we think about it?

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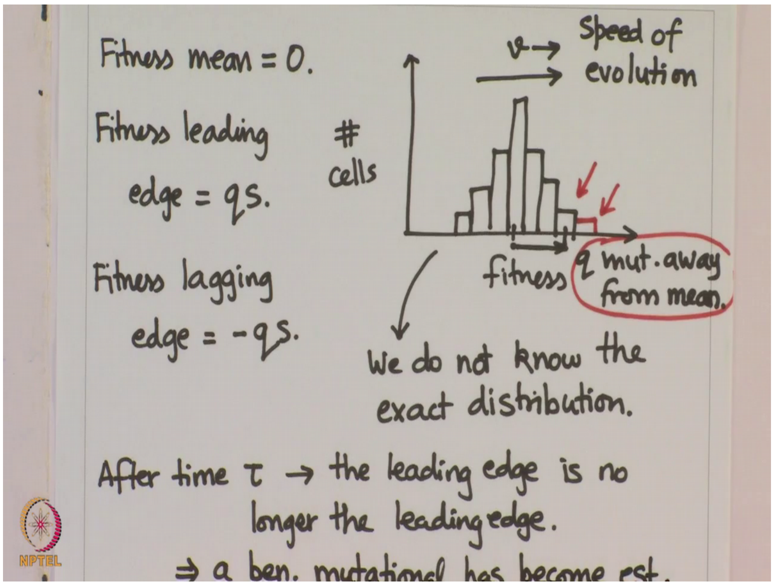

Fitness mean = 0.

Fitness leading edge = qs.

Fitness lagging edge = -qs.

We do not know the exact distribution.

After time τ → the leading edge is no longer the leading edge.

⇒ a ben. mutational has become est.

Let us revisit our normal distribution x axis represents fitness y axis represents number of cells, and at any given point in time once the steady state is established let us assume that this is the distribution this is what the distribution looks like. And this is moving to the right at speed v which is what we are referring to as this speed of evolution the rate at which mean fitness increases with time.

Now, what we are going to assume of course, a priori we do not know the exact distribution. So, we do not know the exact distribution at this steady state, but what we are going to assume is the fact that the leading edge is this is the fitness which corresponds to the mean associated with this distribution, what we are going to assume is that the leading edge is q mutations away from mean. So, the leading edge is q mutations away from the mean, and what that means, is that the fitness of the leading edge if fitness of mean I can normalize the fitness is here.

So, fitness of the mean let us say is equal to 0 that means, the fitness associated with the leading edge is equal to q times s because leading edge is q mutations away from the mean and each beneficial mutations confers a fitness advantage s to that particular individual this is one of assumptions hence the fitness of leading edge is q s if the fitness of mean is normalize to zero.

Similarly, fitness of the lagging edge; edges be equal to minus q s because the distribution is symmetric about the mean. So, the lagging edge is q s deleterious mutations or q s less beneficial mutations as compare to this mean, and hence it is fitness can be quantified as minus q s. Now this wave is moving towards the right at a constant speed. So, let us say after time tau the leading edge is no longer the leading edge, let tau be that time after which this leading edge is no longer than the leading edge, and will no longer be the leading edge when another beneficial mutation has become established in the population.

So, tau is the time it takes for this culture to have another beneficial mutation get established so that the leading edge is no longer the leading edge. So, the leading edge is no longer than the leading edge implies that a beneficial mutation has become established in the population. So, let tau be the time. So, what we are interested in now is will come up with an expression for this tau, in the sense of just looking at this leading edge.

The leading edge is the most fit is the set of most fit individual which are present in this environment and it is frequency is the numbers belonging to the genotype will keep on increasing with time because selection ensures that. And while they are numbers are increasing one of those individuals is eventually going to acquire a beneficial mutation and that beneficial mutation will have a fitness which is s units more than this current leading edge.

Now, this beneficial mutation that has occurred from one of the individuals in the leading edge may survive or may get lost because of tripped. Eventually one of those beneficial mutations will survive and get establish, and that is the time tau.

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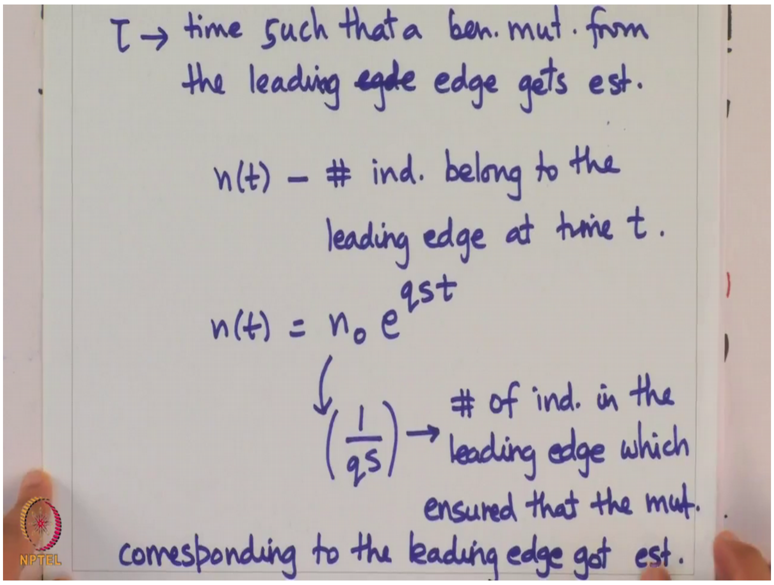

$\tau \rightarrow$ time such that a ben. mut. from the leading ~~egde~~ edge gets est.

$n(t)$ – # ind. belong to the leading edge at time t.

$$n(t) = n_0 e^{qst}$$

$\downarrow$

$\left(\frac{1}{qs}\right) \rightarrow$ # of ind. in the leading edge which ensured that the mut. corresponding to the leading edge got est.

That we are interested how much time does one beneficial mutation which is happening from the leading edge need to get established. So, that time is tau. So, how do we estimate this tau? So, again tau is the time such that a beneficial mutation from the leading edge gets established.

Let n t be the number of individuals which belong to the leading edge at time t. Now if n t is this number of individuals belonging to the leading as a time t how does n t vary with time is the next question we want to ask; and since if you look at our leading edge our leading edge is qs units fitter than the wild type that means, qs units fitter than the mean; that means, relative to the mean this is going to go at grow at a rate e to the power qs, because that is a relative advantage that this particular genotype has over the genotype corresponding to the mean fitness in the environment. So that means, nt varies as n naught e to the power q s t, but n naught is just equal to 1 upon qs because this is the number of individuals corresponding to this particular genotype such that the leading edge got established.

So, this ensures that this was the number of individuals in the leading edge which ensured that the mutation corresponding to the leading edge got established. So, this is a starting number of individuals that we have for this particular type, and because it is relative advantage over the mean fitness of the culture is qs that is the rate that it is going to provided.

Now, we are interested in the time when a population which is growing at this particular rate acquires one beneficial mutation and that one beneficial mutation is able to establish itself. Because when a mutation occurring in this particular genotype establishes itself that is the time which means that the leading edge is no longer the leading edge and another favorable mutation occurring out of this leading edge has become established and which and this new mutation has now become the leading edge.

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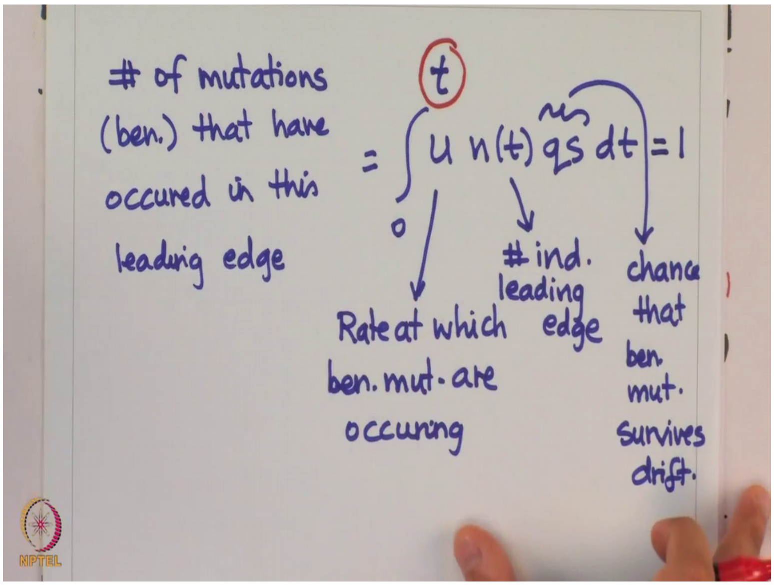

So, the number of mutations which are beneficial that have occurred in this leading edge is equal to u n tq s dt integrated from 0 to tau let us say t. What does this expression mean? U is the rate at which beneficial mutations are occurring, and t is the number of individuals in the leading edge and qs represents the chance that this beneficial mutation occurring out of this is going to survive drift; chance that beneficial mutation survives drift.

Remember, we have previously studied this test result that should a beneficial mutation which has a selection coefficient associated with that as s occurs in a medium, the chances that that beneficial mutations survive drift is equal to s. The probability associated with that mutation surviving draft is just equal to s which is the selection coefficient. In this case the beneficial mutation that has occurred is from the leading edge. So, the advantage that this beneficial mutation has over the mean is equal to qs and hence we say that the chance that is beneficial mutations survive draft is just equal to qs.

And then, because n t is changing with time we integrated from 0 to t and this is the total number of beneficial mutations that are occurring at the leading edge which also survived drift is given by this expression. But we are not interested in the number of mutations that are occurring in this leading edge what we are interested in how much time is needed before the first beneficial mutation that occurs from this leading edge gets established that is the quantity we are interested in.

In other words, what we are most interested in here is that for what value of time does the total number of beneficial mutations occurring in this leading edge equal to 1. That is because this would mean that one beneficial mutation has occurred and gotten established. So, we are interested in that time that corresponds to this relationship and that is what we are going to solve for which gives me my tau.

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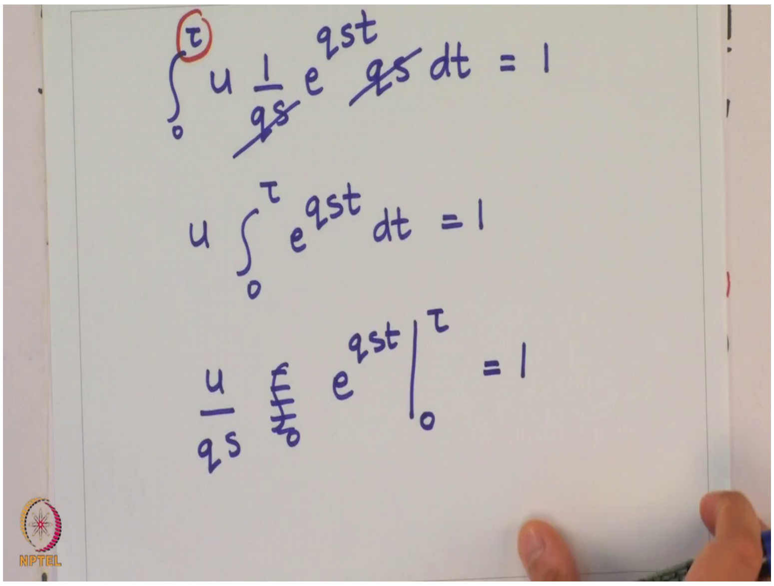

$$\int_0^{\tau} u \frac{1}{\cancel{qs}} e^{qst} \cancel{qs}\, dt = 1$$

$$u \int_0^{\tau} e^{qst}\, dt = 1$$

$$\frac{u}{qs}\; e^{qst}\Big|_0^{\tau} = 1$$

So, let us plug these expressions in and solve for solve for an expression for tau and so we have 0 to tau, u beneficial mutation rate n t is just one upon qs e to the power qs times qs times dt t here equal to 1.

Now, you may ask that the if a mutation occurring out of the leading edge has happened then it is relative fitness to the mean is q plus 1 has and not qs. So, why are we plugging qs here and we answer to that is because this leading edge mutation has becomes established and because we are assuming that the wave is moving continuously with time. What that means, because the wave is moving continuously with time and the leading edge mutation has become established what; that means, is that as soon as this mutation got established the mean also moved to the right by s units, and hence this new mutation which has gotten established now relative to the mean is qs units fitter than the mean of the culture at that particular instant.

So, we solve we are interested in solving this, what we are interested in is solving for this tau that time tau for which this relationship holds and this is qs gets cancelled u can be pulled out. So, we have u 0 to tau, e to the power qst dt equals 1, which gives me u qs 0 e to the power qst. Integral of e to the power qst is just equal to 1 by qs e to the power qst lower limit is 0 tau equals 1 which can be simplified as.

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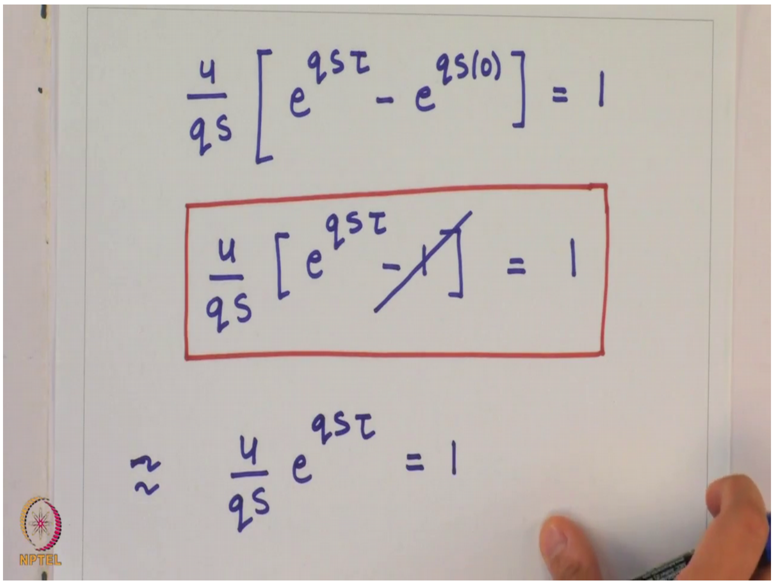

$$\frac{u}{qs}\left[e^{qs\tau} - e^{qs(0)}\right] = 1$$

$$\boxed{\frac{u}{qs}\left[e^{qs\tau} \cancel{-1}\right] = 1}$$

$$\approx \frac{u}{qs} e^{qs\tau} = 1$$

So, which can be simplified as u divided by qs e to the power qs tau minus e to the power qs into 0, which equals 1 which gives me u divided by qs e to the power of qs tau minus 1 which is equal to 1. Now have to solve this particular expression for a value of tau and that will give me the time it takes for a new beneficiary mutation to become established in the population, and to solve this it is relative be hard we can make a simplifying assumption that this minus one quantity is negligible one is negligible as compared to it is exponent of this number and hence we can just dropped is this is approximately equal to u by q s e to the power qs tau equal to 1.

And then it just simply take log of both sides and I get qs tau is equal to l n of qs by u or just equal to one upon qs l n of qs by u ok.

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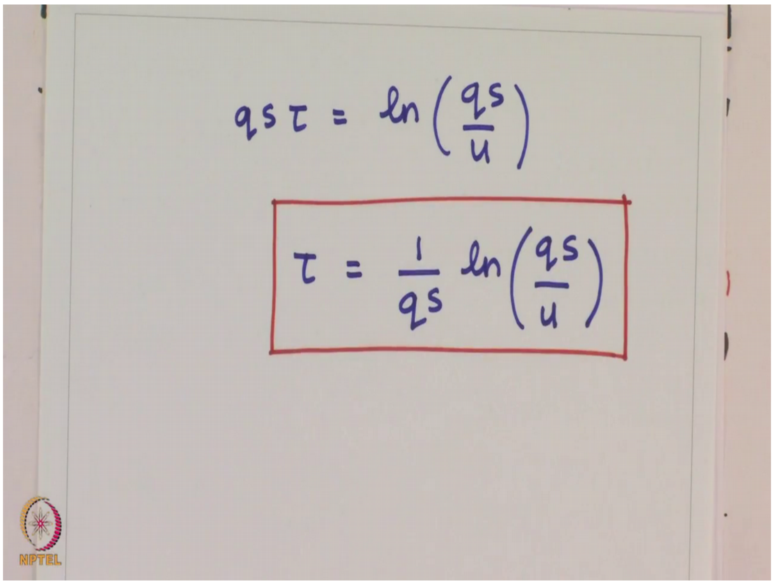

$$qs\tau = \ln\left(\frac{qs}{u}\right)$$

$$\boxed{\tau = \frac{1}{qs}\ln\left(\frac{qs}{u}\right)}$$

So, we derive an expression for this tau and remember what was tau? Tau is that when we have a steady state distribution of this frequencies associates with various genotypes in a culture, how long does it take for the entire wave that I have to move (Refer Time: 21:42) and the wave approach that problem is that I will calculate the time looking just at the leading edge, that how much time is needed for the next beneficial mutation to get established and that corresponds to the entire wave moving to the right by s units, and that is the expression of tau that we have now.

But if you look at it carefully remember that q is a variable which we have arbitrarily defined, which talks about the distribution of this traveling wave around the mean. We do not really have an idea of q will just said that the width of the traveling wave around the mean is defined by these q beneficial mutations which have occurred and we do not really have a hundle of what is value of qs. So, while we have an expression of tau that we have derived here, this expression of tau is in terms of q which we do not really have an idea of right now and which is somewhat arbitrarily defined as things done currently ok

So, that is one way of looking at now we will going to approach the same problem in a different way and try to drive another expression between tau and q. And the approach that we are going to take is we are going to revisit the standy the leading edge that we just looked at and eventually what is going to happen is as the movies was the wave is moving towards the right the frequency associated with this leading edge will keep on increasing.

And eventfully as the wave is moving to the right that leading edge after sometime will become the most frequent genotype in the in the culture.

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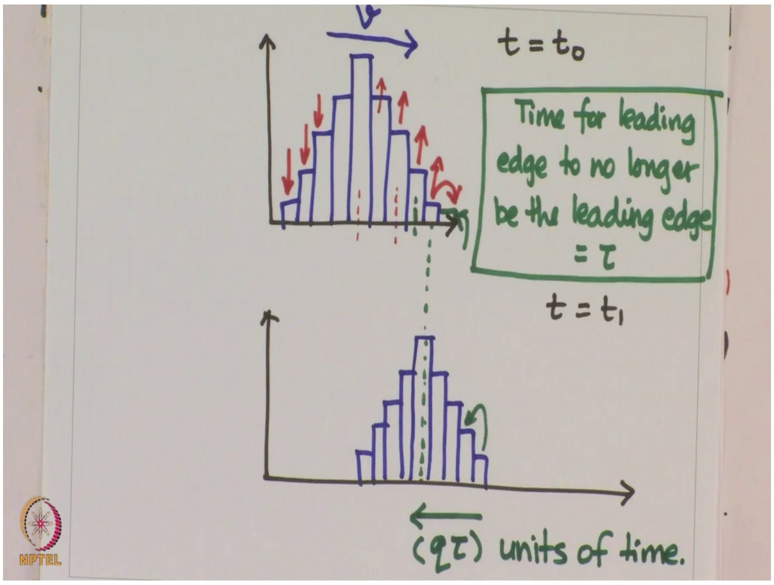

That we have and we are going to calculate the time associated with the leading edge becoming the most frequent genotype associated in the culture. So, just to clarify that graphically what; that means, is that let us imagine that any at any time t naught the distribution looks as the following will try and draw the symmetrically around the mean. So, this is the distribution at t equal to t naught.

And now, if you move forward in time let us say at t equal to t 1, of course, what is happening at this particular instant is that these genotypes are getting eliminated by selection and the frequency of these genotypes is increasing and they will be another genotype because of beneficial mutation at the leading edge, that is the pictures that we have at this particular instant.

So, all these frequencies are going to go up, but eventually when the move for when the mean for instance moves from here to here, then the fitness of this particular genotype will be less than the mean and hence it will start coming down because the mean is currently here. So, the fitness associated with this genotype will start to come down even though it is increasing at this particular instant when the mean is somewhere over here.

So, eventually every particular genotype will reach it is mean and then start to fall; and we are interested in that particular instant when the frequency associated with the leading edge at t equal to 0 which is this particular genotype when the frequency associated with this particular genotype is maximum at t equal to 0 this particular genotype was the leading edge at t equal to t one the same genotype is now the most frequently genotype in the culture and we are interested in that how much time has passed between these two distinct snapshots of the of the population that I have and one way to look at the approach that we are going to take is that since the wave is.

Our assumption is that this wave is moving at a constant speed v and we have already calculated that that time it takes for the leading edge to no longer be the leading edge is equal to tau. So, we going to use this result that time for leading edge to no longer be the leading edge is equal to tau. What that means, is that the leading edge is no longer the leading edge, but is now second in this distribution; that means, at in time tau the leading edge becomes the second one which means in time tau the distribution which was second to the leading edge will now become third to third when I am counting from the leading edge.

Similarly, every particular distribution has move moved s units back because of this leading edge being redefined by this new beneficial mutation that has occurred in the culture. So, in time tau everybody moves back one unit in terms of the number of beneficial mutation it is carrying with respect to the mean. If that is the case and it needs tau units of time to move back one step in this distribution, the number of unit that it is going to take for the leading edge to become the mean is going to be q such units and hence this transition will happen in q tau units of time ok.

So, it is a relatively straight forward logic what we are saying is that the leading edge becomes the second in distribution it is no longer the leading edge in time tau. What that means, is in that time tau the leading edge which was which was the first in terms of fitness has become second, the second one which was already existing has become third, the third has become forth and all of these transition happen in time tau. What that means, is that each of since each of these transitions takes tau times the leading edge will take q of these two intervals to become the most frequent genotype associated with this distribution.

And in the next lecture, we will use this logic to develop an expression for the time it takes for this leading edge to become mean and come up with another expression for tau. And hence, we will combine that with the expression of tau that we have just developed and solve them together to a eventually come up with an expression for speed of evolution.

Thank you.