**Evolutionary Dynamics**

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**Week 8**

**Lecture 40**

Hi, welcome back, everyone. Let us continue our discussion of the two regimes that we discussed in the previous video. So, the regime that we first started with was tau weight or tau occurrence much greater than tau fixation. And in this regime, we saw that this point of tau weight is much longer, and tau fix

is relatively shorter. As a result, when I take a snapshot of this picture, I am much more likely to find the system in this particular state as compared to where two genotypes are coexisting, where this is going to fixation and this is being eliminated, because this process happens relatively faster compared to the occurrence of mutation. So, that is the first regime that we want to talk about, and that is sort of the snapshot of this regime. There is one more representation of this regime that we should look at because the literature that we read will introduce us to this representation, which is the following. That in this particular representation, we have on the x-axis time.

So, remember that we are representing exactly this process but in a different way. Both these are popular representations, and that is why we want to understand what they are actually telling us about the process. So, in this case, this is plotted against time, and on the y-axis is the number of individuals. What you should realize here is that in the first representation, let us call this A and let us call this B. In the A representation, there is no mention of time in the graphical representation that we are doing. So, graphs have fitness versus number.

And they do not have a representation of time on them. On the other hand, in the second one, the graph is between time and the number of individuals, and there is no mention of fitness per se, although it does make an appearance, as we will see in just a little bit. So, the population size in the chemostat is from 0 to N, and at t equal to 0, this point is t equal

to 0. The entire population is an isogenic population. So, we start with an isogenic population.

All individuals have a fitness of F naught. Now, we move forward in time. So, on this graph, we move from this point forward in time, and this time is associated with tau weight because now the population is waiting for a beneficial mutation to occur. And what is going to happen is that at some point, a beneficial mutation is going to take place. And this point represents the fact that there is one individual which is carrying this beneficial mutation, and the remaining N minus 1 are carrying the ancestral genotype.

Now, as we move forward in time, maybe this individual will divide again, and its numbers will increase to 2. And what that means is at this instant of time, I have two individuals of this blue genotype, which is of higher fitness, and N minus two individuals, which are of lower fitness. Also, the way to read these graphs is that at any given point in time, if I want to find the composition of the population—how many individuals are there of a particular genotype—what I do is draw this vertical line here. From 0 to N, and this vertical line at any given point in time represents the number of blue individuals, the number of blue individuals. And everything from there to N, which is the size of the system in terms of the carrying capacity of the chemostat, everything from this point to N is the number of black individuals present in the population.

So, if I were to draw that graph here, this graph simply tells me that all individuals here are of the black type. And there is no diversity available in the population. So, that is how I can measure the relative frequency of the two genotypes, which at this point for black individuals is (n minus 1) upon n, and for blue individuals, that is simply equal to 1 upon n. But remember that the most likely fate of a beneficial mutation is that it will go extinct from the system. So, the fate of this population can be represented simply as this.

So, a beneficial mutation came, fluctuated around a bit, and then went extinct. This is the process which, in the first representation, was depicted by this beneficial mutation occurring but then lost due to drift, resulting in the system going back to the state we started with. The same is happening here. Initially, it was all N individuals, and after the beneficial mutation went extinct, I am back to the state where all N individuals in the system are of the ancestral genotype, represented by black circles here. So, the system went back to the state it was in prior to the occurrence of this blue beneficial mutation.

And since, on average, we saw that 19 beneficial mutations occur and are lost, and out of 20, only one survives. This will keep happening. So, this fate will keep happening. Some will persist a little longer but eventually go extinct. Some might immediately go extinct.

And so on and so forth. So, in this representation, we have all this information that can be read if we have that detailed information available from the experiment. Eventually, though, what will happen is that finally there will be some beneficial mutation that occurs which is able to survive drift. Which roughly will be 1 in 20. So, its numbers go up and down because fate is decided by selection and drift, but its selection is weaker as compared to the strength of drift when numbers are small, but eventually it escapes drift and increases in numbers.

Once it increases beyond a certain threshold, Once it increases beyond a certain threshold, now the fate of this population is no longer dictated by drift to the extent that it was when numbers were small. Now onwards, the fate of this mutation is going to be decided primarily by selection. So, this happens when its numbers in the chemostat have gone up to a sufficient degree that It's unlikely that all of them, all these individuals carrying this beneficial mutation, are going to be eliminated by selection only.

If it was one or two, then it's quite possible that these individuals might be lost because of drift. But now there are so many that it is unlikely that all of them will be lost by the action of drift without giving selection a chance to increase their frequency. So, what that means is that here onwards this increases in frequency more or less deterministically, exactly as the exponential, exactly as the two-compete equation for two competing genotypes in a chemostat that we derived several videos ago, exactly in accordance with those rules, and this will increase in frequency and eventually reach fixation. And now this process will repeat itself over and over again, and hence we get adaptive change taking place. At this point, once this has reached fixation, if I were to draw a vertical line, so at this point, the frequency of this genotype is n upon n, which means it's just 1.

That means this genotype has reached fixation. On the other hand, if I were to ask at this point what the frequency of this genotype is at this point, that is now 0 upon n, which means this genotype has become extinct. Extinct. So, 1 has reached fixation, and the ancestral genotype has become extinct. So, now in the representation that we have done here, you should note a couple of things.

One is that the time it took for a beneficial mutation to arise before it survived the action of drift is this tau wait. Several other beneficial mutations occurred prior to the one that

eventually escaped the action of drift, but all these were lost. Tau wait is associated not just with the occurrence of a beneficial mutation but with its occurrence and ability to survive drift, which happened at this point. So, this was tau wait. From there on, it reached fixation.

So, let us call this time in the experiment t1, and it reached fixation here. So, let us call this time t2. So, in how we have drawn this picture, what we see is that tau wait is equal to t1, and tau fix is equal to t2 minus t1, which is this window of time. And as we can see in how we have drawn this, tau fix is actually much smaller compared to tau wait. So, going back to the question that we ended the last video on: if we were to take a snapshot of this picture, if we were to take a snapshot of this chemostat at any given point in time, what would we see?

So, if we took a snapshot here, there is no mutation; snapshot here, no mutation; snapshot here, no mutation. If we take a snapshot here, I will get one individual out of N which is carrying this beneficial mutation. But such low frequencies are really hard to detect because, remember, the N that we are working with is in hundreds of millions, billions, or even hundreds of billions. And detecting one individual is really hard in those settings. So I won't even detect this mutant until it increases to a certain frequency.

So I won't detect it. It's only around here. That when I start taking this snapshot, I will see that, oh, this population actually does not have just one genotype; it has two genotypes. So, in this window, I will see two genotypes, but the rest of the time, I am actually only seeing one genotype in this entire chemostat, and the time associated with where I saw the mutation go to fixation. So,

If we draw this for t2, but if we draw this picture for a much longer time, this graph will begin to look as follows. So now we don't want to draw it for only t2 but for a much longer time. This is t = 0, and this is the number of individuals, which is 0 to N. And now what we will see is that, over a much longer time frame, this is what we are going to see. A mutation came, escaped the action of drift, and reached fixation. Then we have to wait a really long time for a new mutation to come, which was able to escape the action of drift. And then this mutation came.

This mutation also had its fate, and then it was able to reach fixation. And this process keeps repeating itself. Newer mutations keep occurring and go to fixation, and so on and so forth. This process will keep repeating itself. In each one of these, as you will see, let me just fix this.

In each one of these, as you will see, the time associated with waiting. So, if you look between red and blue, the time associated with waiting where it escapes drift may be somewhere here. This is tau wait. And this, when it reaches fixation, this is tau fix. And as we can see, in each one of these three mutations that fix in the population, tau fix is much smaller compared to tau wait.

We want to discuss two other things. Let us compare the ancestral genotype that we started with. We will compare this with what we end up with. So, let us say this was the ancestral genotype that we started with. I should also mention that I have not shown in this figure, but what is constantly happening is that beneficial mutations are coming and going extinct because of the action of drift.

So, that is constantly happening. In this figure, we are only showing beneficial mutations that were able to escape the action of drift. All these little mounds here show beneficial mutations that appeared but were quickly lost by the action of drift. So, the first point we want to make is that when we start this experiment, let's say this orange circle represents the genotype of the ancestor. Now, as we move forward to the first mutation, it has happened that in the genome of this individual, one red mutation has taken place somewhere.

In this little window, Prior to the occurrence of this red mutation, every individual in the population had this genome. When the mutation occurred, until it reached fixation, in this window, the coexistence of both these genomes took place. And from here onward, let's call this time T1, where the first mutation reaches fixation. And from here onward,

every individual from T1 onward—let me write T1 again—from T1 onward, every individual in the population is carrying only this genotype. So, here everyone is carrying this genotype. So, we started with this genotype, and it went extinct at T1. So, any change that happens after the red mutation reaches fixation is going to take place in this background now and not the ancestral background. At this time, from T1 to this time, it is only this genotype that exists.

From here, let us call this T2 now. The genotype that exists in the population is the red one; obviously, everybody was carrying it. But now, another blue mutation has happened, so in this window of time, these two genotypes are coexisting: this one and this genotype, which is carrying two mutations. Up until time T2, from time T2 to time T3, in this entire window, the only genotype that exists is just this genotype, which is carrying both these mutations. This particular genotype went extinct at T2.

Remember that this mutation did not go extinct, but there is no individual left in the population which is carrying only this mutation. Every individual in the population is carrying the red mutation in conjunction with the blue mutation that has occurred. And finally, this process continues, and at T3, a new genotype makes an appearance in the population, where we have three mutations in that genome. We have the red one from the first mutation that survived drift, and then the blue one. But now, a green mutation has also taken place.

And eventually, beyond this time T4, only this genotype exists. So, as we will see, as an evolution experiment proceeds forward, as the evolution experiment proceeds forward in time, we keep accumulating more genotypes on previous genotypes that have reached fixation, like here—like the red mutation reached fixation—and hence newer mutations are going to occur on that background itself, and this is how genomic change will drive itself forward. That is sort of the first point that we want to make: that this is how we can view adaptive change, the genetic changes associated with adaptation. This is how we should be viewing this process. All of this, remember, is still in the regime where we have tau weight much greater than tau fix. The second thing we want to ask is the following: in this context

Now, let us zoom in a little bit and talk about a smaller time scale that what is happening is that beneficial mutations are coming, but going extinct, coming, going extinct. And eventually one is able to escape the action of drift and then selection, more or less selection dictates its fate, which means what we are saying. So, again, this is time. and this is number of individuals going from 0 to n. So, what we are saying that there seems to be a threshold here and if the mutant numbers are below this. So, let us call this some nc n-critical

And n-critical, what it is doing, if number of mutants is less than nc, that means these are scenarios where number of mutants are less than nc, then fate of mutation is is largely dictated by drift and you should all be able to guess by this time that this should be dictated by drift. As we can see here that we saw that because of the action of drift, even this fit genotype went to extinction. Same here. Mutant came, which was actually beneficial, but it still went extinct because of the action of drift.

Selection would never permit it. But it seems like there is a critical number NC that if the number of mutants go beyond NC, then in that case, the fate of the mutation is, is now

largely dictated by selection. Selection operates via precise mathematical laws. We derived all those equations.

So, this trajectory is a smooth trajectory, a smooth deterministic trajectory. We can write equations for them, get the exact profile, and every time we do an experiment, we will get the same precise trajectory. However, for mutations whose action is decided by drift, these are driven by chance events. A lot of noise drives these processes. And as a result, these trajectories are stochastic.

In this diagram, we have pictures of three beneficial mutations occurring. Let us imagine that the ancestral genotype we started with had a fitness of F0, and this beneficial mutation conferred a mutation F0 plus S0. This one also conferred the same benefit, and this one also conferred the exact same benefit. However, we see that the fate of all three is a unique trajectory. This one never went up to very high numbers; it went extinct the fastest. This one was able to increase the numbers a little bit more, and this one was able to escape the action of drift and go to selection. So, despite conferring the exact same benefit, these mutations have different adaptive trajectories.

And that is because of the stochastic nature of how drift treats these mutations, which confer the same benefit. So, the second point we want to note is to ask the following question: what is the number of individuals of a particular genotype beyond which the fate of a mutation is decided by drift or decided by selection, and drift can be ignored thereafter. As we can see in this trajectory, from some point onwards, this trajectory is relatively smooth, obeying mathematical laws.

And this is the deterministic trajectory. This here is the stochastic bit. And people have worked this out mathematically. And what is believed is that if you have a beneficial mutation—so for a beneficial mutation, with selection coefficient s, s-naught, then the trajectory is largely deterministic if its numbers are bigger than 1 by s-naught.

What that means is that if you have a beneficial mutation occurring which only provides a very small benefit, in that case, in order to go beyond the action of drift—in order for that mutation's fate to be decided by selection—you need a larger number of individuals. However, if you have a beneficial mutation that confers a lot of benefit, In that case, you only need a few individuals, and then selection can take over and drive that mutation to fixation. So, this This number—beyond which a mutation's fate is decided by selection and it has escaped the clutches of drift—that number is a function of what the selection coefficient is: how much benefit is this mutation conferring upon the population? And

that decides what the critical number of individuals is that allows us to make the assumption that trajectories are largely deterministic thereafter.

And we will continue this theme in the next video. Thank you.