Evolutionary Dynamics

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Lecture 41

Music. Music. Welcome back, everyone. Let us continue our discussion of mutations in a regime where tau weight is much bigger than tau fixation. We will wrap up our discussion, continuing from the last video, and then move to the other regime where tau weight is much shorter compared to tau fixation. So, the last thing we discussed in the previous lecture was the following: should a beneficial mutation occur here,

its fate is stochastic to begin with, but then it follows a deterministic trajectory. And what is the number of individuals that must be there in the chemostat of this genotype, which is carrying this beneficial mutation, beyond which the trajectory becomes deterministic? So, this is nc, beyond which the trajectory is deterministic and below which the trajectory is stochastic. And we said that this actually is a function of

If we compare the two genotypes, if this genotype has a fitness F naught and the green genotype—the mutant that comes up here—has a fitness F naught plus some delta F. Then, the selection coefficient associated with this mutation is F naught plus delta F (the fitness of the mutant) minus F naught (the fitness of the ancestor), divided by F naught (the fitness of the ancestor). F naught cancels, and we get delta F divided by F naught. So, this is the selection coefficient associated with the benefit that this mutation is conferring upon the population. Now, if that is the case, what we know from mathematical analysis of these systems is that mutations with larger s

become deterministic their trajectories become deterministic with fewer individuals. On the other hand, the converse is also true that mutations which confer a very small benefit, have a very small S associated with it, their trajectories become deterministic when there are relatively much larger number of individuals of that kind present in the population. So for instance, and this change happens, this number of individuals at which it's largely deterministic, number of individuals at which trajectory is deterministic nc can be simply approximated as 1 upon s. where s is the selection coefficient associated with the benefit that this mutation confers.

So, if you have a mutation whose s is 0.01, that means it only increases fitness by 1 percent, then the number of individuals beyond which trajectory is deterministic is 1 upon 0.01 which is 100. So, trajectory becomes deterministic in that case when the number of individuals cross 100. On the other hand, if you have a mutation with a very large benefit to have taken place which is 0.05, in this case trajectory becomes deterministic when number of individuals is 1.05 which is 20. So, in that case let us imagine that this mutation took place here. and this was 20, it would go like this.

So this mutation escaped from the sort of the clutches of drift much sooner as compared to a mutation whose benefit was smaller as compared to the purple one which happened here. So that's sort of the one regime that we wanted to discuss. Now let's go to the other regime. where tau wait is actually smaller. Tau weight is much smaller as compared to tau fix.

And discuss that in the two representations that we have been talking about, how does the picture that we have tried to paint change when the relative time constants of these two processes are switched? in their magnitude. So, in the first representation what is going to happen is that we have population at F naught and everybody is of fitness F naught. So, we start with an isogenic population. Now, tau weight is really small.

So, I do not have to wait for a mutation to come up for very long. So, this system transitions relatively soon to the following. This is n minus 1 and let us say this is 1. So, this beneficial mutation has occurred fairly rapidly and this beneficial mutation is at fitness F0 plus S0. And, what we are going to say here is that this mutation although it is at only one number of individual is carrying it, this is the mutation which is able to select which is able to escape the action of drift.

So, without any loss of generality we will say F naught is 1. So, all these fitnesses will become 1 plus s naught and now s naught is the selection coefficient because the denominator in the calculation of selection coefficient becomes 1. So, as time moves forward, this is going to increase in frequency, this is going to decrease in frequency. But remember that the time it takes for this mutation to reach fixation is very long as compared to time I have to wait for a newer mutation to come up. So, what is going to happen in this context is that as these numbers are increasing and

changing because the this genotype which is at fitness 1 this is decreasing with time so this is decreasing the next genotype the blue kind is increasing with time that's 1 plus s naught this is increasing with time and it needs tau fix amount of time to reach fixation However, there is a problem here that because tau fix is really long as compared to tau weight, even before this reaches n, what is going to happen is that another beneficial mutation is going to take place in this population and we will have a third genotype make its appearance whose fitness is 1 plus 2s naught. And this beneficial mutation also is able to escape drift because tau weight is associated with both the occurrence and ability of mutations to escape the action of drift. So, well before the blue genotype has reached fixation, another genotype has come into the picture which is carrying another mutation and is higher than the fitness associated with the blue genotype. So, if we carry this picture forward in a little bit of time, this may look something like this.

That the ancestral genotype is very close to extinction, which is at 1. The blue genotype is also going extinct because now there is a genotype which is of higher fitness than blue so eventually blue will also start to decrease in frequency this is that 1 plus s naught the red genotype has increased in frequency because it's of it has higher fitness so this is at 1 plus 2 s naught but while the red was increasing in frequency And because tau fixation is really long and tau weight is really small relatively, another beneficial mutation has happened and actually the population at this stage looks like this. This might be the state of the population.

So, and obviously this will be 1 plus 4 s naught, this will be 1 plus 3 s naught. I mean, in this representation, we have assumed that every beneficial mutation confers a benefit of s naught only. That is not strictly true because every beneficial mutation will confer a benefit associated with its own selection coefficient. But for the sake of simplicity, we are saying that every beneficial mutation confers the same benefit. So,

Now, let me ask you: if the system is in this particular state, we have these five frequency bars associated with the five genotypes that exist in the population. Which of these is increasing? So, let us say at this instant, the state of the system increases. It is as shown in the figure here. How will you calculate that at this instant? Because the picture is very dynamic—in a little bit of time, the black bar might go extinct, and another newer genotype, which has a fitness of 1 plus 5 S naught, might come up in the population. So, we are talking as of this moment, as of this snapshot. How will you find out which of the 5 genotypes is increasing in frequency and which is decreasing in frequency?

And I'll give you 10 seconds to think about this problem. So, in order to think about this, what we should do is go back to the lesson that we learned when we were discussing two competing genotypes in a chemostat. What we have—this number here—so, let us say the number of individuals of the black genotype is n1, the number of the blue genotype is n2, this is n3, n4, and n5 for the last one. So, We have the numbers associated with each one. We also know the fitness of each one.

So, if we are talking about the first genotype, let me list all five genotypes here. They are black, blue, red, green, and purple. So, at the instant of time that I have been asked to look at the system, the fitnesses of these—fitnesses will not change. This is 1, this is 1 plus S naught, this is 1 plus 2 S naught, 1 plus 3 S naught, and 1 plus 4 S naught. So, that is simple—that is just the fitness of each genotype.

But I also know the frequency of each genotype. The frequency of the first one is just N1 divided by N, N2; let me call it F1. Well, F is a bad choice because fitness—we have been using F for fitness. So, let us just let it remain as N1 by N. The second genotype is N2 by N. This is N3 by N, N4 by N, and N3. 5 by N. So that's the frequency.

And now we are going to compute the mean fitness of this mixture of 5 genotypes. This collective growth that I have taking place in the chemostat. What is the mean fitness of this genotype? Of this culture? So the mean fitness is going to be simply equal to

fitness of each genotype Fi multiplied by the frequency of each genotype, and I sum them over all genotypes that are there. So, in this case, it is going to be the first genotype's frequency is 1. I multiply that with its frequency. So, N1 upon N. plus the second genotype's fitness is 1 plus S0, and I multiply that with N2 by N, and so on and so forth.

This is for the third genotype, its fitness times its frequency N3 by N. Fourth is its fitness times N4 by N and last genotype is 1 plus 4so times N5 upon N. This quantity is F bar, mean fitness of the culture at this particular instant in time. Note that as time is moving forward, these numbers are going to change. The N1, N2 will change with time and as a result, the mean fitness will also keep changing with time. So, now if I want to ask the question that which of these 5 bars is decreasing and which of these 5 bars is increasing, I simply have to compare this number with the mean fitness.

If the fitness of the genotype is higher, then that genotype increases in frequency. But if the genotype's frequency, if a particular genotype's fitness is lower than the mean fitness, then that genotype decreases in frequency. So, I simply compare these two fitnesses. I will write this here that compare with F bar and for each genotype if fitness of a genotype is bigger than F bar then its frequency

going up as of that instant and if and conversely if the fitness of a genotype is less than the mean fitness then its frequency is going down as of that instant so in this case this will go down this will go up this will likely go up and so likely go down and this one is hard to tell because that depends on what is the mean fitness it looks like the mean fitness might be around here slightly so this might be going up slightly but very soon it will change so this is because this is a all a dynamic process so by looking at this we can tell the state of the system but remember that as this is going down so very soon this will go extinct But what will also happen is that this would have increased by that time and not just increased. Its increase would have led to another mutation happening and this system would have spread to this. And by the time this would have reduced maybe to this height.

So you will always have the same width of this fitness distribution that we have. On the left end, these will keep going extinct. And on the right, higher-fitness genotypes will keep coming. Higher-fitness genotypes will keep coming, and so on and so forth. So, this interplay between the left ones keeping getting extinct and the right ones keeping coming up will continue as we move forward in time.

So, that is the first representation that instead of only two bars, now if I take a look at this at any given point in time, I am seeing 5 to 6 genotypes coexisting with each other. But in the other case where tau weight was much bigger than tau fix, and in that case, more often than not, I was only seeing one genotype and only once in a while I would see two genotypes when one was being replaced by the other. So, that is the big change that has happened in this case. Now, let us look at the same thing in the other representation. In this representation, of course, the x-axis is now time, and the y-axis is the number of individuals, which goes from 0 to N, and this is t = 0.

The same ideas apply: now a beneficial mutation will take place. Its fate will be decided by drift—largely drift in the early phases—but then it will escape the clutches of drift and increase in frequency. So, let us say it is increasing in frequency. And there were these prior beneficial mutations also that took place, but they went extinct almost as soon as they came. But they're there, but we won't represent them going forward.

But we'll only focus on the ones that are able to escape the action of drift. So now, at the time when the numbers are here, if I draw this at this instant in time, Then what we are seeing is that I have n1 number of individuals which are of the blue genotype, and at this instant in time, I have n minus n1 individuals which are of the original genotype that I started with, represented by black circles. So, this picture is changing because, as I am moving forward in time, black is being replaced by blue. But what will happen here is that an individual which is carrying a blue mutation picks up another mutation which is beneficial.

And it escapes drift and starts to go up. So, as we move forward in time, this green genotype is increasing. But I also have this blue genotype which is going forward, and I also have the ancestor genotype coexisting. And all of this while, as all of this was going on, another mutation comes up where this is happening. So now, if I were to draw a picture of this at a given time, let me stretch this to the same time point, let me make this green. If I take a look at this particular instant in time and ask what is happening in the system—what are the different genotypes that are existing—then let us start from the beginning of the experiment and move forward to see how these mutations were taking place.

Originally, all genotypes were the same, and let us call this genotype as as we did in the last video, represented by this. As you can see, the number of these individuals was n when we started the experiment, but these are shrinking. At any given point in time, they're getting fewer and fewer. Eventually, they will go extinct.

So, this genotype will eventually go extinct. What happened here was that this following genotype emerged. which is carrying a blue mutation. And this, at any given point in time, the distance of this blue line to its neighboring line tells me the frequency of this genotype, which is carrying only this blue mutation. When we move a little bit forward, this happens.

At this point, one of the individuals that was already carrying a blue mutation picks up another mutation, which we'll represent by green here. So the blue mutation was already there, and now we also have this green mutation. Again, as we move forward in time, I can draw this line, and this is the number of individuals carrying both these mutations. Finally, one of these individuals that was carrying both these mutations picked up another mutation, which we will depict with red here.

So the first one was blue, the second one was green, and the third one is a red mutation. And this happened at this particular point in time. So now, at this time t_0, what we have is four genotypes coexisting. The original genotype has this many individuals; let us call it N_1. The number of individuals carrying only this blue mutation is N_2 at this stage.

The number of individuals carrying the blue and green mutation is N3. The number of individuals carrying all three mutations is N4. If we divide them by the total N, we get the respective frequencies of each kind. And so on and so forth. So, unlike the previous case, now we have this scenario where, for large parts of growth,

we actually have different genotypes growing and competing with each other. This idea that, at this instant in time, I have these four genotypes which are competing against each other—as compared to only two genotypes competing with each other in the previous case, where one mutant emerged and eliminated the ancestral. There was the original one and a new one, and the new one eliminated the original one—and that was it. In this case, I have these four genotypes, and more might emerge before any of them reaches fixation. This idea of competition between more than two genotypes is called clonal interference.

Alternatively, Alternatively, An interesting scenario could take place. Let us say the fitness of this genotype was F0. Let us call it 1, or let us say F0 was 1.

The fitness of this genotype was F0 plus S0. The fitness of this genotype was F0 plus 2S0 and fitness of this genotype was F0 plus let us say 3S0. Now, while we made this assumption in the previous representation that beneficial mutations will always confer a benefit of S naught only. So, even if there was an individual which picked up a mutation here, its fitness, because it is occurring in a background of fitness F naught equal to 1, its fitness will only be F naught plus S naught. But that assumption that we are making was unreasonable.

Beneficial mutations come in a range of benefits that they confer. So it's not impossible that there might be a scenario where one of the individuals here, let me pick up another color, one of the individual here picks up a great mutation. And by great mutation, we mean that fitness of this individual is F0 plus let's say 6S0. Which means the fitness of this guy is actually the highest in all the genotypes that exist in the chemostat at this moment. And as a result, this individual will start spreading in the population also.

So you might have a scenario where the picture actually looks like this. So, if I fast forward from T naught to this time now and ask what is happening here, this many number of individuals belong to this genotype, this many number of individuals belong to a genotype which carry the blue and the green mutation which is this, this many number of individuals belong carry only one mutation which is the black which is the blue one which is this and as you can see the blue is shrinking so it's going extinct and lastly this new individual that has come up has actually reached this many numbers and this type and what is the genotype of this individual that is simply Again, I'll give you five seconds to think about it. What is the genotype of this individual?

Remember that this individual acquired a mutation in this background. So it has nothing to do with blue, green, or red mutations. This individual has only one mutation, which happened to be a great mutation. And let's say this. So that's the genotype.

So as of this moment, it's these four mutations. Genotypes that are coexisting in the population. And this phenomenon of competition between mutations is called clonal interference. So, in the next video, we will start with some preliminary calculations to actually find out the two regimes that we discussed, depending on whether tau weight is greater than tau fix or the other way around. We will start with some calculations to ascertain which of these two regimes is a more realistic scenario when I conduct an evolution experiment in a lab setting.

We will continue that in the next video. Thank you.