Evolutionary Dynamics

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Week 9

Lecture 43

Thank you. Hi, welcome back, everyone. So, we were trying to get estimates of tau weight and tau fix, and we were able to estimate tau weight in the last video at the end of the last video, where we said that tau weight is actually much less than one generation. These taus are time, but they are being measured in number of generations. So, what that tells us is that in every generation, multiple beneficial mutations arise, and each one of these is able to outcompete drift and get established in the population. For instance, in one of the calculations we did, we saw that tau weight—that is, the wait time for one beneficial mutation to arise and escape drift—was actually 0.05.

What that means is that in one generation, this is 0.05 generations. That means in one generation, not one, not two, but 20 beneficial mutations are able to arise, and each one of these is able to escape drift for a population size of 10 to the power of 8. Of course, the number of beneficial mutations occurring is much, much larger in this one-generation timeframe. But out of all those occurring, we know that only about one in 20 or 25 survive drift. But despite that, 20 of them are able to survive drift.

And hence, it's easy to see that these beneficial mutations will be competing against each other, trying to increase their frequency as we move forward in time. The approach that we take to get a measure of tau fix will be slightly different. And to get an estimate of—so this is to estimate tau fix. We do not want very exact measures, but we are interested in order-of-magnitude comparisons between tau fix and tau weight. And how we will do this is we will simply ask a question: if this is the genotype at fitness 1 and this is a genotype at fitness 1 plus S naught, then how long does it take for this genotype to reach population size n and this genotype to go to 0?

That's all we will ask. And let's see that how does this fixation, how is this fixation time compared to tau weight that we've just been talking about. So how do we start with this?

Remember that this mutation, when it occurred, its fate was decided by drift But we said that once the numbers associated with this mutation reached 1 upon S0, then more or less drift was not relevant and its future trajectory was decided only by selection.

So what we'll see, so this was able to escape drift. when numbers reach 1 by S naught. So, we will assume that we are starting this calculation only when this mutation has been able to escape drift because beneficial mutations were occurring before this also, but they were not able to escape drift. So, we only start when a mutation has escaped drift. So, our N naught, which is number of mutant

types at t equal to 0 is simply 1 upon S naught. Now, this particular genotype holds an advantage of S naught over the ancestral genotype. And that advantage is quantified by this. So this number, its numbers are going to increase exponentially. And the exponent associated with that is going to be the advantage that it holds over the other genotype.

So this is going to increase. So this is at equal to zero. But as we move forward in time, moving forward in time, As we move forward in time, its numbers increase as e to the power s naught t, where s naught is the advantage that it has over the ancestral genotype. What that means is that its numbers are going to increase as n naught e to the power s naught t. So, if I want to find the number of individuals of this mutant genotype at any particular time t, I simply plug that here and that gives me n t which is number of mutant individuals.

at any time t. But what I'm interested in is tau fixation, that how long does it take for this mutant numbers to start from 1 by s naught and reach n which is the size of the population. So, what I am interested in solving this is n equals 1 by s naught e to the power s naught t. This is because the number of mutant individuals is equal to the entire population and this is time it takes for that to happen. And this time that it takes for this fixation to happen because the mutant is getting fixed in the population, this time is simply equal to tau fix.

So, we solve for tau fix here and we simply get e to the power s naught tau fix is equal to n times s naught and we take log of both sides and we get s naught tau fix. equals ln of n s naught and which gives me tau fix is equal to ln of n s naught divided by s naught. So, the exercises associated with this week. We will plug in some numbers for tau fix and tau weight and what we will find out that for microbial populations of any reasonable size, tau weight is much less as compared to tau fix. What that means that regime 1 is practically impossible to achieve in a microbial population.

So for all practical purposes, a microbial population will be operating in regime 2 that we are discussing where multiple mutations coexist and are competing amongst themselves and which we last time wrote is called clonal interference. So we'll spend a little bit of time trying to understand this clonal interference. And this treatment is slightly mathematical. This is as mathematical as we are going to get. And very soon after this, we'll transition to only understanding experiments.

So I hope you pay a little more attention to the analysis that's coming up next. So in this regime, So now we have shown that it's regime 2 which dictates how populations behave in a microbial context when they are adapting. So what that means is that any given point in time, I will get a distribution like this where all these genotypes coexist at a given instant in time. This is fitness.

And this is number of individuals. Now, if you look at this a little more carefully, what's happening is that this distribution, which looks like a normal distribution, it may not be a normal distribution, but it doesn't change the principles of what we are saying. On the right edge. Obviously, this is the fittest genotype. So, let us call the mean as 1.

This is 1 plus S naught, and we might have any number of bars representing these different genotypes. Let us say this is called the leading edge of the distribution. And let us say this is K mutations better than the mean, better than the population mean. What that means is that this is the population mean, and if the population mean has a fitness of 1, we can always normalize fitness to the mean of the population and call the mean 1. So, in this analysis, the mean fitness of the population will remain at 1. And shown here is K equal to 4.

This is 1 plus S naught. This is 1 plus 2 S naught, 3 S naught, and 4 S naught. But it may be 6 S naught or 7 S naught, and so on and so forth. So what we are saying is that the leading edge is K beneficial mutations away from the population mean. So the fitness of this genotype here is 1 plus K times S naught.

K in this cartoon happens to be 4. We also assume—this is under the assumption—that all beneficial mutations confer the same benefit S naught. The selection coefficient associated with every beneficial mutation confers benefit S naught. Under these two assumptions, What is going to happen is that—let us look at this genotype, for instance.

As these cells are dividing, it is not as if that beneficial mutations are not occurring in these individuals. They are occurring. But as a beneficial mutation occurs, it is going to land up in this genotype pool because this is 1 plus S naught, this is 1 plus 2 S naught. So, that individual is going to land up here. But there are already so many individuals present in this next bar that adding one is not going to make any difference from the context of the numbers that we are dealing with in a microbial population.

Hence, the beneficial mutations occurring in either in any of these lagging in any of these lagging genotypes that is not going to dictate how evolution is going to take place. The only place where beneficial mutations are going to dictate the fate of the population is when they are occurring in the leading edge. This because when a beneficial mutation occurs in a leading edge, you get a new edge. And that is the change that happens because there was no one here. Now, this mutation, this new leading edge that has occurred, it may go extinct because of drift, in which case we are back to square 1, our leading edge is again the leading edge.

Or it may get established in the population, in which case this begins to increase in frequency and we have a new leading edge. I hope that makes sense to everybody. So evolutionary trajectory of this microbial population is decided by the leading edge where beneficial mutations are occurring. Now you may rightfully ask that is the following scenario not possible that you have this population here and one individual picks up a great mutation which lands here and if this mutation gets established in the population if this mutant is able to escape drift then it will start to increase in frequency and the dynamics completely changes and yes that is possible although relatively rare. So, people have done theoretical and experimental work to sort of observe these kind of jumps in actual microbial populations.

But for the purpose of this discussion in this course, we will stick with only jumps that confer a benefit of S0 being allowed in this setting. So, The first point we notice is that all these beneficial mutations are happening, but they're not relevant as far as driving evolutionary change is concerned. They are only bringing about a minuscule change in the frequency of genotypes, and it doesn't really matter. At the other end, we have what is called the lagging edge.

These are going down in frequency because, as of this moment, in this population, this is the least fit genotype. And remember the result that we derived. That in a population, if you have several genotypes which have different fitnesses, then how do we decide which genotype increases in frequency and which genotype decreases in frequency? And the simple result that we observed was that any genotype whose fitness is greater than the population mean fitness will increase in frequency in that instant, and any genotype whose fitness is less than the population mean fitness will decrease in frequency. So, as of this moment, this genotype here is the least fit genotype in the population. So, the population mean fitness will be somewhere around here. So this is way less fit than the population mean. So this one is going extinct.

So these two dynamics are being played out at the two extremes, extreme ends of this distribution. And at steady state, when the population has been adapting and newer mutations are coming up at some rate, the older genotypes are going extinct at some rate, a balance will be established between the two. And eventually, we are looking at this in a scenario where The time for a new leading edge to get established is to get established is the same as time for lagging edge to go extinct.

And let's call this time as tau. So this is at steady state what happens in this population. So this is what I am looking at right now but after tau time what will happen is that a new leading edge will come up here. This old leading edge would have increased in numbers and maybe it would have gone to these numbers. This would have increased in numbers and maybe would have gone to this number.

this would have increased, this would have increased, this would start to decrease, this would definitely go down, this would go down and this genotype would also go down and come to this number and the lagging edge in the previous window, this goes extinct. So, what you should do? See that at this point is that it is as if the entire distribution has been moved forward by one S naught unit. Let us draw this again a little more formally and see what we are trying to say. So, at a given point in time, the distribution looks like this.

This is at time t naught and what we want to see what happens at time t naught plus tau. This is fitness and let us say this is 1, this is plus s naught, this is plus 2s naught, 3s naught, 4s naught and this is ks naught. K happens to be five, but it could be anything. And same idea there. Let me draw these down because we want to study what was there earlier and then what happens.

Okay, we are done. So now, and this is obviously number of individuals. Now, what we are saying is that at time t naught, some of these bars are increasing in frequency, those who have a fitness higher than population mean, and some of these bars are decreasing in frequency, and these are bars which have fitness less than the population mean. So, this is going on. However, so this is going to bring some change in the shape of this distribution as we move forward in time.

After tau time, this bar will go extinct. This will be completely eliminated by the population. That is the first qualitative change that takes place that in the new distribution, this bar is gone. This one reduces, this one is reducing and in tau time it reaches to this height which I will draw here and this genotype now becomes in the next time step new lagging edge. The old lagging edge went extinct in tau time and this the next to the lagging edge genotype that reduced in frequency to become the current lagging edge.

This one was reducing and it came to this level. So this one becomes the new neighbor of the lagging edge and so on and so forth. So all of this is going on. This genotype increases in frequency and in tau time reaches this. So this is the population mean fitness now.

So we can normalize, we can have a new normalization and we will say this is 1. And the most important bit is that in this tau time we have a new leading edge which has come into the picture. which happened because a mutational event took place here and a new beneficial mutant arose and escaped drift. As a result of this, we have a new leading edge at the beneficial end of this distribution. While that was happening, the original leading edge is increasing in frequency because its fitness is definitely more than that of population mean.

This increases to this level. So, it is now not the leading edge but actually neighbor of leading edge. This genotype's frequency is also increasing. So this increases a little bit more in frequency and so on and so forth. So the new distribution now looks like the following.

This is the new distribution after time tau. So What is happening here is that it's almost like, in time tau, the entire distribution has moved one step to the right. The population mean was right here. And it's like every bar that we have in the graph above has shifted by S naught units to the right, and we get the bottom picture.

So, we can view this evolution in this clonal interference regime, where all these genotypes are competing with each other, in this prism of the distribution moving to the right. So, in time tau, all bars in the distribution represented here move one unit to the right. The shape of the distribution doesn't change at all, but only that the distribution has moved to the right. That is the picture that this type of analysis paints for us. What that means is that evolution, in this context where you have multiple genotypes coexisting, multiple genotypes,

Evolution in this type of framework can be looked at as a traveling wave. There is no change in the shape of the wave taking place. It is almost like this is just a wave of constant shape, which is moving one unit to the right every tau time. So, this just continuously moves to the right. And the question that we want to ask is: how fast is this wave moving?

This question also has another meaning, which we can ask as: how fast is adaptation taking place? How fast is adaptation taking place? And adaptation, in this case, is simply an increase in the fitness of the population. And if you look at this picture in a slightly intuitive way, the answer is actually really simple. What we are saying is that every tau time, every tau time unit, the population moves to the right.

By how much? Everyone moves to the right by S naught units. So, everyone moves to the right by S naught amount. So, the question is: what is the increase in fitness of the mean population? The increase in the mean population will also be S naught.

So, this is the increase in the mean population. I hope everybody sees that. For instance, think of this as an exam in your class that took place: somebody got 20 out of 100, somebody got 30, somebody got 90, and so on and so forth. Now, what is the average score? Maybe the average score in the exam was 50.

But now, if everybody's score is increased by five points. So, somebody who had 20 now has 25. Somebody who had 30 now has 35. Somebody who had 90 now has 95, and so on and so forth. Everybody's score went up by five.

So, what is the new average? If the old average was 50 and we simply added five to everyone's score, the new average of the class is going to be 55. It's the same idea here: everybody had a fitness. We added S0 fitness to everybody in the population. So, by how much did the mean fitness of the population increase?

By the amount that was added to everyone's fitness. By the amount that was added to everyone's score in the exam that took place. But this S0 increase in fitness took place in time tau. So, how fast is this wave moving? It is simply equal to S naught divided by tau. S naught is by how much it moved to the right, and tau is how long it took to move to the right.

And in the next video, we will do some math and find out if we can derive expressions to estimate the value of tau. We will continue with this in the next video. Thank you.