Evolutionary Dynamics

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Lecture 39

Hi everyone, welcome to the next video. So today, what we will try to do with the fixation probabilities that we discussed in the last video—when a mutation's fate is being decided purely under the action of drift or when it is being decided under the combined action of drift and selection—we derive these relationships for different probabilities. And today, we will discuss two different regimes under which mutations can occur. And we will try to get a sense of what is actually happening in a flask or in a chemostat when a microbial population is evolving. So, if we go back to the chemostat example.

We have a genetically identical population. Let us represent that by these black circles, and in this population, we have a blue mutant individual that arises. And what we have been deriving so far tells us that the fixation probability of this mutant—if it is a neutral variant— The fixation probability is simply equal to the probability that the blue individual reaches fixation, which is 1 divided by N, where N is the population size. Alternatively, in the neutral case, since the fitness of the blue individual is exactly the same as the fitness of the black individual, selection is not doing anything. Selection has no way to distinguish between blue and black individuals, and it is only chance or drift that decides the fate.

On the other hand, if this mutation is beneficial—so if the blue mutation is not neutral but is in fact beneficial—then its fate is determined by the combined action of selection and drift. And what we saw in that case is that the probability that it reaches fixation is approximately equal to s, where s is the selection coefficient. associated with the mutation that has occurred. And the precise definition of this was (fitness minus fitness) divided by fitness. Let me just do this.

So, the precise definition of the selection coefficient was It can be represented like this: the fitness of the selection coefficient associated with this particular mutant, in case it is a beneficial mutation, is simply equal to the fitness of the blue individual minus the fitness of the ancestral population. So, the numerator here represents the benefit that the mutation confers. And the denominator is simply the fitness of the ancestor. So, the selection coefficient is the fractional advantage that a mutation confers to a population.

So, we discussed these two cases. So, now we know that the fates of the populations are going to be decided by these two fates. Of course, there is the third possibility that the mutation can be deleterious, but that is a case we need not worry about because selection will just eliminate it. One way to think about the effect of a deleterious mutation could be that, even if a deleterious mutation is able to survive the action of drift and increase to higher frequencies, then selection will start acting, and it will try—selection will try—to get rid of those variants because they are lower in fitness. So, even if they were to

$$s = \frac{f_{evolved} - f_{ancestor}}{f_{ancestor}}$$

escape the action of drift and not be eliminated early on, and their numbers increase in frequency, even then, selection will not let them rise too much in frequency—too much in the population. All right, so given this, now let us take a look at how mutations are actually happening in a chemostat or a flask. And we can think of this as two different possibilities that could be occurring inside a flask. Let us discuss these possibilities. So, we are going to use two representations, and now, in three or four videos' time, we are going to move toward experiments, and the rest of the course is going to be just discussing evolution experiments and the lessons we learned. And these two representations are useful in the context of—these are also the representations that we will see in papers when we are discussing results from experimental evolution.

So, in the first one, let us say x-axis represents fitness and y-axis represents numbers of individuals. So, let us imagine a population in a chemostat which at t equal to 0, all individuals are identical. all n individuals population size is N and the fitness of each individual is F naught. So, if I were to represent This population in a graph like this, I would identify the point F0 here and the total population size in this chemostat is N and hence the state of the population at this particular moment looks like this.

That there are N individuals with fitness F0 and there are no other individuals with any other fitness level because this is an isogenic population. And the chemostat will continue to operate like this while divisions are happening, cells are dividing, newer individuals with F naught are coming in, some individuals are being washed away and so on and so forth until a beneficial variant arises whose fitness is no longer F naught but it is F naught plus s. So, this mutant is carrying a beneficial mutation which has increased its frequency by some amount s. At that point, when this mutation has happened, then this is no longer an appropriate representation of what is happening in the chemostat. And hence, the representation in that case will change to at F naught and at F naught plus s. Let us say this is N. Now, this is represented by the following that there are N minus 1 individuals of fitness F naught and there is 1 individual of fitness F naught plus s.

So, this graph is now going to represent the state of the system as of the moment when that beneficial mutation occurs. So, from here the system has transitioned to this particular state. So, now what is going to happen? Now, let us take a look back at the chemostat and see what is going to happen. Either this individual is going to increase in frequency.

Or this individual is going to be lost from the population because of the action of drift. There might be a chance event that this individual couldn't replicate and was washed away from the system and hence green individuals are lost. So now this can be represented the fate of this mutation can be represented as two alternate ways. In one case, the mutation is lost from the system, in which case this graph just becomes same as what we started with, that the mutation was lost and now I am back to a state where there are n individuals at fitness F naught. So, this is the scenario where mutation lost from system.

because of drift and actually as we saw in the last video that the most common fate of a beneficial mutation is going to be this that it's going to be lost by the action of drift and it's not going to be able to increase in frequency because of that on the other hand if the mutation is able to survive the action of drift then what is going to happen is that as we move forward in time there are more number of green individuals and now the chance that all these green individuals are going to be washed away from the reactor from the chemostat is extremely small. So, the green mutation is not going to get lost because of action of drift. So, the relative role of drift in dictating the fate of the green mutation decreases as the number of individuals carrying that mutation increases. Now, there are sufficiently large number of green individuals here that drift is no longer going to be the significant player.

It is going to be selection which is going to dictate the fate. As a result of that in this scenario the frequency associated with F naught plus S will increase because you know selection is acting and the more fit individuals are going to get selected for and hence increase in frequency and conversely the less fit individuals are going to decrease in frequency. So, this relative change will take place once the mutation has survived the action of drift. So, in this graph, I have f naught and f naught plus s, n is somewhere here and what this graph will look like at this stage now is that this would have reduced a lot from n and this would have increased a lot from its starting point, but this is still coming down and this is still going up. So, this relative change in frequency is taking place and this is at some time point T after the mutation was able to survive drift.

Remember that this is the more common fate of a beneficial mutation. And if we let sufficient time pass, then what is going to happen is that the F0 genotype, the ancestral genotype, is going to get completely eliminated from the population, and F0S will be the only genotype that survives in the chemostat. So, the future fate of this chemostat might look something like this. That there are only these green individuals left in the chemostat is because the green individuals, being of higher fitness, were able to completely eliminate the ancestral genotype. This fate is going to be represented by the following change in the graph that I have: F0 and F0 plus s. This is fitness.

And this is numbers. And now there are zero individuals which are at F naught. And this is N. And there are N individuals which are at fitness F naught plus s. And this has represented a cycle where a mutation occurred, a beneficial mutation occurred. So this was the—let me use a different color.

This was the event that a beneficial mutation occurred. This was the case that the same beneficial mutation survived drift and thereafter increased in frequency. So this was step one, step two. Alternatively, we can go from step one to here, which is the more common fate, but this just brings us back to this particular point, and we start over again. And the third step is that, as a continued increase in frequency of the beneficial mutation, the beneficial mutation reaches fixation.

And it's not as if the process of evolution halts at this point. This process continues as we move forward. And now the population in the population, we are waiting for an event like this to take place, that this happens now, where everyone, all the green individuals, all the green individuals in the population change. R at fitness F naught plus s. And now we are waiting for an event to take place where a newer individual comes into being whose fitness is F naught plus 2s. So, the newer individual is going to be here.

this is f naught plus 2s, this has to be changed then, this frequency of the ancestral genotype reduces slightly from n and it comes to n minus 1 and the frequency of the new genotype, the new beneficial genotype that has come in the population is equal to 1. So, in some sense the same process keeps on repeating itself over and over again. This is one view of how evolutionary change could be taking place. One thing that we want to note is that there are two time constants associated with it. So, let me just on a fresh slide quickly sketch these again.

So, I started with this and this changes to a new benefit mutation. the beneficial mutation starts to increase in frequency and then it reaches fixation. See, these are the four steps. So, this is occurrence of beneficial mutation. This is surviving drift.

and increasing in frequency and lastly this is reaching fixation and in the case in in case that this mutation does not survive drift then you go back here and this was mutation lost because of drift And this is how change will take place. Now, we want to understand the two time constants which are associated with this particular process. The first time constant in all of these graphs, obviously, this x axis is fitness and y axis is simply number of individuals. So, the first constant first time constant is this one which is the time associated with occurrence of a beneficial mutation which survives drift.

Let us call this time as tau occurrence. So, this is the time that I have to wait on an average for a beneficial mutation to occur and it be able to survive drift. Because remember that for this event to happen, two things need to happen. One is that there is waiting time associated for a beneficial mutation to occur in the population. And second is that beneficial mutation will more often than not be lost because of drift.

And hence, after occurrence, I have to wait for this beneficial mutation to survive drift. So, even within this, there are two things that we are looking at. First is occurrence of a beneficial mutation. And secondly, that beneficial mutation has to survive the action of drift. These two things need to happen because more often than not, beneficial mutation will occur and I go back to the state because it is lost due to drift.

It will occur again, and I will go back because it is lost due to drift. Last time, we saw in the numbers we were doing that, actually, with reasonable values of s found in experiments, 20 beneficial mutations need to happen for one of them to survive the action of drift. So, this tau occurrence represents the combined waiting time associated with the happening of the mutation and then its surviving drift. The second time constant associated with this process is what happens thereafter, which is the time it takes for a mutation Not just any mutation, but a mutation that has survived drift to reach fixation.

Let us call this time tau fix. So, these are the two time constants that we have in the process. Time of occurrence and surviving drift, and thereafter, once it has survived drift, the time to reach fixation. Now, in the picture that we have sort of painted here, we have made an assumption that tau occurrence is much longer than tau fixation, and we will see how that is true.

So, let us discuss the first case where tau occurrence is much bigger than tau fix. What does this regime actually mean? What this means is that if I start with a population and the population is at F naught n individuals, then because tau occurrence is much greater than tau fixation, tau occurrence can also be thought of as tau wait, the waiting time associated with a beneficial mutation occurring and surviving drift. So, this can also be called the waiting time.

Associated with a beneficial mutation to occur and survive drift. How long do I have to wait for these processes to occur? In the regime that we are discussing here, tau occurrence is much bigger compared to tau fixation. What that means is that I have to wait a really long time before a beneficial mutation can occur which is able to survive drift. So, I am waiting, and then eventually what will happen is that this beneficial mutation will occur, and as a result, the picture looks like this.

This is N minus 1 individuals at F naught and 1 individual at F naught plus S. And then, because by definition this mutation has been able to survive drift, the numbers of the ancestral genotype will start to go down, and the number of this mutant genotype will start to go up. So, this change will begin to happen. And the time it takes for this to reach the following state, F0 plus S, that time is tau fix. This time is tau occurrence.

So, in the first regime, what we are saying is that tau occurrence is much bigger and tau fix is much smaller. So, as a result, if you imagine this population, the fate of this population in a chemostat is going to be the following. That you have an isogenic population; all individuals are of the same genotype. Eventually, one of them will acquire a beneficial mutation, and this beneficial mutation will survive drift. But that has taken a long time because that is the meaning of tau occurrence being very high.

Once this new beneficial mutation has occurred, tau fix is relatively small. As a result, this new beneficial mutation will go toward fixation really fast, and we will reach this third stage where fixation has happened fairly quickly. After this, we are back to square one because now we are waiting for the next beneficial mutation. Waiting for the next beneficial mutation. Which is going to be dictated by tau weight, but we know that tau weight is actually very long.

So, again, we have to wait a long time for this beneficial mutation to take place. So, there are these two processes playing side by side in this process of fixation of mutations. One is occurrence, and the other is reaching fixation once occurrence has happened. So, in this particular regime, occurrence takes longer, and hence the picture that we are painting is like this. Now, the question I want to end this video with is the following: if I am operating in a regime like this.

So, these cells are growing, and this is the regime that I am operating in. Tau occurrence is much more than tau fix. Then, if I look at the system at an instant of time, an instant of time, How many genotypes do I see? That is the question.

And what you should realize at this moment is that the answer to this under this regime should be 1. Because in this regime, tau occurrence is really long. So, you have to wait a long time for a beneficial mutation to occur and survive drift. That means most of the time the system is spending in this particular state where we are just waiting for this mutation to come and the system to reach this stage.

Most of the time the system is spending is in this particular state of just waiting. Once the wait is over and I reach this particular state, then the transition from here to here is fairly rapid because tau fix is much smaller. As a result, this transition is much faster. And suppose, just to give it sort of made-up numbers, maybe I was waiting 10 hours for this beneficial mutation to arise and survive drift. Then maybe this fixation only happened in 15 minutes.

So, if I take a snapshot of this system at a particular time, chances are that the system will be stuck in this state because this is fairly rapid. As a result, when I take a snapshot of this chemostat, I will only see one genotype at a time more often than not. Occasionally, it is possible that I will see two genotypes while this is going to fixation and that one is going to extinction. In that case, the answer will be two for very few instances of time. But the most frequent answer that you will see in this regime is only one.

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