Evolutionary Dynamics

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Lecture 36

Hi, welcome back, everyone. Let us continue our discussion of deriving these transition probabilities for the neutral case. So, in the last video, we derived expressions for p i to i minus 1 and p i to i—sorry, i plus 1—and now let us just do the transition probabilities for the other case, which is p i to i. And this can happen in two different ways, as we have been seeing.

So, this is P I to I where A both dies and is born, and in the other case, it is P I to I where B dies or is born. So, in this case, the probability of A being born is just equal to N minus I times RA divided by total fitness, which is N minus I RA plus I RB, times A dying, which is N minus I divided by N. And again, for the neutral case, we will plug that RA equals RB equals R naught, in which case R naught is going to cancel out, and this is going to simply reduce to N minus I squared divided by N squared, which is just N minus I by N whole squared. And in the other case, we have the probability of B being born, which is just I times RB divided by N minus I times RA plus I times RB, times I upon N. And again, when we do this substitution, in this case, we are going to simply get I squared divided by N squared, which is just I upon N whole squared.

So, from these transition probabilities, these two were done in the last video. If we combine these four, those of you who would like to complete this exercise can now, with this information, solve the system of linear equations that we derived and actually arrive at the probability of a new mutation reaching fixation. But the endpoint and the lesson that we want to take away from this is, To summarize this entire discussion of a neutral mutant arriving and calculating its probability of reaching fixation, the overall lesson that we see from here is that in this context, if I have N minus one individuals of the same fitness and a neutral variant arising, it's numbered at one, then the probability the probability that this individual reaches—the probability that the blue individual reaches fixation—is simply equal to one upon N. The other N minus one upon N times

The other n-1 upon n probability, thus this mutation is going to go extinct. These are the only two fates available to this mutation. So an overwhelming number of times, and you can see that when N is large, this number is going to be exceedingly small, and this number is going to be very close to one. So the most common fate of a neutral mutation in a context like this is going to be that it's going to be lost from the population, and only very rarely will it reach fixation. That's the intuition about the biological process that we want to see.

And again, to summarize that, you should also remember that we arrived at this result via three different ways. One was only by intuition—that one of them has to reach fixation, and it can be any one because they are all neutral variants. The other one was a comparison with the marbles-in-jar game. And the third one was this development of equations, which led us to the same result. So, there were different approaches that we used to understand this problem together.

And all of them led to this result: that the probability of a neutral variant reaching fixation is simply equal to 1 upon N. We want to now look, before we move to a non-neutral variant. So, again in this context, this change is taking place—sometimes reaching fixation, rarely reaching fixation, most of the time it is being eliminated. This evolutionary change is taking place in the absence of natural selection, and only chance events are dictating this. Before we go to the case where the blue mutant has a different fitness as compared to the black mutant, we want to just understand one more representation of how populations change.

So, dynamically, this process can be represented as follows. On the x-axis is time. And on the y-axis is population, which is n from 0. At the beginning of this experiment, so this is time, this is t equal to 0. At the beginning of this experiment, all individuals are the black genotype in the figure.

And there is no genetic diversity. At some time t naught... A mutation happens, and a blue individual comes into the picture in the chemostat. So, this is one blue individual that has come into the picture. So, this is simply one.

At this point, the number of individuals that are black is simply going from here to n minus 1. Now, as we move forward from here, there are different fates for this particular mutant. So, the mutant that we are discussing is still neutral. So, it doesn't have any advantage over the black individuals. This mutant can have one of several fates.

Maybe this mutant in the next one will increase, in which case the way we represent this is that it was at 1 and now it's gone to 2, which has basically meant that the number of black individuals has now reduced to n minus 2. Thereafter, chance events dictated that it went to 1, then it stayed at 1, and then maybe it went to 2, came back to 1, and eventually went extinct. So, this is the fate and trajectory of one particular mutant that could be in the population. It came, it fluctuated around a little bit, and then it eventually went extinct. Remember that going extinct was overwhelmingly favored in the analysis as compared to this mutant reaching fixation.

And then after a while, this mutant is gone. After a while, maybe another mutant will come up. So again, every mutant for the first time comes, and its count is one. This mutant, maybe as soon as it came, it went away. This was just washed off by the chemostat immediately after coming up.

So this didn't stay in the population at all. Maybe there will be another one that comes up, goes to 2, goes to 3, comes back to 2, goes to 2, and so on and so forth. It fluctuates around for a little bit longer, but eventually the fate is the same. Remember, for every n mutations that come up, n minus 1 have this fate: they will go extinct. And only one mutation will reach fixation.

So most mutations, when we say they will go extinct, will have dynamics such as the one shown here. Maybe they stick around a little bit, go extinct immediately, or maybe reach some densities, and so on and so forth. So this is going to be the most frequent fate of neutral mutations. Very, very rarely will we have this type of situation come into being, and in that case, the mutant's trajectory might look something like this. It fluctuates around, but chance just happens to favor this mutant.

And while the numbers are increasing and decreasing, on the whole, these numbers are increasing as time goes on. And so on and so forth. Remember that, again, natural selection is not favoring this mutant. This is all happening by chance events, as explained by the Moran process. And sometimes it may decline, but eventually, it will take some time and reach fixation.

When the population reaches this point, we say that every individual is carrying that particular mutation. At any point during this process, if we were to answer how many individuals are of the black type, that's the answer. And how many individuals are of the blue type? That's the answer. So this is I, the number of blue-type individuals in a population at that time, and this is N minus I. And as you can see, as this mutation from its arrival goes towards fixation, as it is increasing in frequency, I is increasing and N minus I is shrinking. N minus I is shrinking, and here it's almost gone. Then eventually, the black genotype goes extinct from the population. In this window, starting here to this point, there is coexistence of both genotypes.

both genotypes coexist. And if this neutral mutation happened at time t1 and fixation happened at t2, this time is the time to reach fixation. And so on and so forth. So this is another graphical representation that is commonly used to represent these evolutionary processes. And this is sometimes very useful in being able to see what was going on.

But as we have seen that for neutral mutations, it's hard because there is virtually 10 to the power 6 minus 1 cases of this and only 1 case of this. So, most often this is what's going to happen and we won't really see a mutation rise in frequency. So at this point, when there are I variants of B type and N minus I variants of A type, the frequency in the population, the frequency of the black individuals is simply equal to N minus I divided by N and the frequency of blue individuals is is just equal to i upon n. And that is something that is useful and we will keep using this as we move further in the course. Okay, that is enough discussion about neutral variants arriving in the population.

We will next move to the scenario where the mutant that has arisen is not neutral now. So, now we have a non-neutral variant. variant that arises in the population and this non-neutral variant we are only going to consider it is carrying a beneficial mutation. So, in the context of the chemostat picture that we have been making in this scenario we have these individuals which are RA and N minus I and we have this one individual

which is Rb, but this time, well, there are i such individuals; i could be equal to 1 when the mutation first happened, but this time we make it explicit that Ra is not equal to Rb. So, how do we analyze this? What we want to understand is that the fixation probability of a neutral mutation was 1 in a million for a population of size 1 million. If the population size was 1 billion, which it could easily be, then the fixation probability would be 1 in a billion for a neutral mutation, and so on and so forth. So, it is very rare for a neutral mutant to arise in a population of that size and reach fixation.

But by how much does the chance of a beneficial mutation arise—a beneficial mutation that has arisen in the population—how much is its chance to reach fixation? That is what we want to understand now. Again, this beneficial mutation, if selection was the only force acting, then because Rb is greater than Ra, it would simply be driven to fixation by natural selection. And there was no question about it. However, there is this chance because it is small in numbers; even the first mutant could just be washed away, and then it does not have any chance to spread in the population. So, what is the chance of fixation on the number line going from state 1 to n, but in this case now for a beneficial mutation?

It is this X1 that we are interested in. So, we will follow the same approach as we did last time, but the math associated with this is going to be slightly trickier, yet we will go all the way through. The last one was a simple exercise, and hence I left it to you to complete it. This one is a little more tricky, so we will do it together. This is n, this is 0.

Same idea of Moran process that from a state i, you can either go to i minus 1 or go to i plus 1 or remain at i. There is no other fourth option. In a Moran process, these are the only steps permissible. We will not compute probabilities just yet. But we will say that let the probability of transitioning from i to i plus 1 be equal to alpha i. Additionally, let the probability of transitioning from i to i minus 1 be equal to beta i. in which case the probability that the system remains at i is simply given by 1 minus alpha i minus beta i because all these three probabilities sum together have to equal to 1 that we have seen before and obviously i remaining on i can happen in two different ways but this expression accommodates both these probabilities.

of A dying A birth, which will keep you at I, or B dying B birth, which will also keep you at I. So that's true for any I that we have. Same idea as before, we also know what, let's also discuss what is alpha naught. So alpha i is the probability of transitioning from i to i plus 1. So alpha naught is the probability of transitioning from 0 to 1. That means transitioning from a state where there were no blue individuals to a state where there is one blue individual.

Since there is no blue individual and our assumption of no new mutations still holds, this probability is simply equal to zero. I hope everybody sees that that if the system is here, essentially what alpha zero is, is the chance of a forward jump at a given place. So alpha zero is the chance of this jump. But the chance of this jump is simply zero because if there are no blue individuals here to begin with, you can't have a birth process which gives rise to another blue one because you need a blue one for that birth event to take place. So this is simply equal to zero.

Similarly, let's look at what beta n is. Beta n is the chance, starting from n, of a backward jump. This is beta N. Now, this backward jump can happen if the birth that occurs is of type A and the death is of type B. At this point, in the current state of the system, there are N B-type individuals here. So, any one of them can die. So, this can happen.

$$\alpha_o = 0$$

$$\beta_N = 0$$

But for this backward jump to take place, an A individual has to give birth. But since the state of the system is N, the number of A individuals at this stage is equal to 0. And hence, if there is no A individual in the population to start with, you can't have an A individual giving birth. And as a result, this step cannot happen. And as a result, Bn is also equal to 0.

So these are sort of the general rules we have available to us. Now we'll formalize this a little bit more. Let's write the number line again. i, i plus 1, i minus 1, this is beta i, this is alpha i, and this is 1 minus alpha i minus beta i. Like last time, we defined a variable called xi, which is the probability that, starting from here, the system reaches this state.

So, xi is the probability that starting from i system reaches n. It can take however long as it wants, but eventually the system reaches there, that is the probability. So it's fixation probability of a mutant which has i individuals of its kind already present in the system. And again like last time for i equal to 1 this x1 this is the number we are most interested in because this is the probability that the system transitions from x i equal to 1 to i equal to n and that is the fixation probability of a new beneficial mutation that I am most interested in.

So like last time, one step of Moran process can be written like this. So if the system is at i, is at state i, then the probability it reaches n simply equal to Xi that is just the definition of Xi so that straightforward however all of this is exactly the same as last time however it cannot reach that stage in one jump so it in one jump of the Moran process It can only go from I to I plus 1 or I minus 1 or remain at I. Those are the only three options that are available to the system in one step of the Moran process. It can go from I to I plus 1 with probability alpha I or it can go from I to I minus 1 with probability beta I.

So it reaches i, i minus 1 with probability beta i. But then if it reaches here, then the probability that it reaches xn is no longer xi, it's xi minus 1. Or it can remain at i whose probability is 1 minus alpha i minus beta i. And this is then multiplied by XI because it remains at the state I. And if it remains here, what is the probability that it will reach N? It is just XI. Or it actually makes a forward jump in the Moran process, which happens with the probability alpha I.

And then, if it reaches here, then what? Then its current state is not I, it's I plus 1. And what is the probability that from I plus 1 it reaches N? That is simply equal to X I plus 1. So, we have slightly changed the representation of these terms for reasons that will become clear later. And this is the equation that I can write for i equal to 1, going all the way to n minus 1.

In addition, I also have the result that x naught, which is the probability that my system is here and it reaches N, that probability is obviously 0. We have discussed this enough times now. And what is the probability of Xn? That Xn probability is that the system is here. What is the probability that it will reach here?

Well, it is already here. So, the probability of that is simply equal to 1. This is Xn. So, Xn is equal to 1. So, again, I have the same system of equations that I have: n plus 1 equations.

$$x_N = 1$$

That has to be solved together to get x1, and this derivation is what we will do in the next video. Thank you.