Evolutionary Dynamics

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Lecture 35

Hi, welcome back, everyone. In this video, we will complete our discussion of the probability of a neutral mutation, which does not confer any adaptive advantage, reaching fixation. Just to summarize the context in which we are discussing this, we have a chemostat in which there are two types of individuals. The black circles represent individuals that have a growth rate RA; the blue ones are growing at RB, and the state of the system is that there are i individuals of the blue type and N minus i individuals of the A type. We set this up in terms of transition probabilities when we looked at it from the context of this number line.

And in this number line, we saw that when the system is at state i, it is only allowed three possible transitions in one step of the Moran process: it can remain at i, it can go from i to i minus 1, or it can go from i to i plus 1. Each of these happens with different probabilities, whose expressions we calculated if the two different participating strains are growing at rates RA and RB. Then, we defined the important variable called xi, which tells me that if the system is at state i at any given point in time, xi is the probability that it will reach N. The particular xi I am interested in is computing the value of x1, which is the probability that, starting from here and with these three transitions allowed at the state, what is the probability that the system reaches N? Of course, that is not going to happen in one step.

It is going to happen in several steps. But over a sufficient amount of time, what is the probability that the system, starting from here, is able to reach the state N? And when we set up the equations to study the system, we ended up with these N plus 1 linear equations. These have to be solved simultaneously to arrive at the value of x1. x1 is the variable that I am most interested in, and the two x's I already know are x0 and x0.

x0 represents the case that when the system is here at this point there is no B individual. And hence, there is no question of starting the system at x equal to 0 and there being any chance of reaching x equal to i equal to n. If we start at i equal to 0, there is no b individual and hence you could never reach i equal to n. And as a result, x 0 is just 0. The probability of starting from here and reaching here is just 0. On the other hand, if the system is already here, then the probability of reaching here is 1 because you are already there. It is a certainty that you are there because by definition you are there.

And in between we have these N minus 1 equations. So, this is a total of N plus 1 equations, but two of those equations we know the answer. The N minus 1 equations give us x1 to xN minus 1. This is something that we do not know. And these have to be solved simultaneously to arrive at the answer.

$$x_0 = 0$$

$$x_N = 1$$

$$x_i = P(i \to i+1)x_{i+1} + P(i \to i)x_i + P(i \to i-1)x_{i-1}$$

These have to be simultaneous solution of these to give us the value of x1. Before we go there, we will use our intuition to see if we can arrive at the value of x1 just like that. So what we'll do in this case is go back to the marble example and ask the following question. that if I was playing the marbles in a jar game again, and this is the starting point, and I had marbles of N different colors starting out, then let us say this goes on, and I have in all N different colors. So, this is number of jars, and this is population numbers,

Going from zero to N, I know that eventually one of them—one of the colors—is going to take over the population. So, I know a few facts about how this game is going to end. I know that when this game is allowed to proceed for a sufficiently long time, one color will take over. Second, as a corollary to that, the other N minus one colors will get eliminated. Will get eliminated.

And because of the conditions that we set up when we were defining this game, we said that each marble had an equal chance of being drawn. Which, in the context of the game, could mean that the marbles have identical size, same shape, and identical weight. So, when I put my hand in the jar, there is no chance of me preferring one over the other. They all feel exactly the same to my hand. As a result of this, all marbles are equally likely to

be picked. And if I'm doing a random draw from this jar that contains N marbles, the chance that I'm going to pick any one particular one—let's say, in this case, the red one—the chance of this one being picked is simply 1 upon N. So the question is, given all of these, what is the chance what is the chance that the red marble replaces everything? And we have not set up any equation for this question. We are just going to use this intuition to And we'll see that in the case of the population that we discussed—or population of microbes that we discussed in a chemostat—our intuition leads us to the same result.

Now, the question here is, which color will win? And we're asking about the probability. What is the chance that red marbles will take over the entire population? So if there are N colors, if you think intuitively, there are N colors. Each is equally likely to win, the N colors at the start.

And at the start, I have no idea what's going to happen in the subsequent jars. So at this point, when I'm talking about jar number one, each color has the same chance to win, the same chance of winning. Let us call the chance that each color has as alpha. If that is the case, then color 1 has chance alpha, color 2 has chance alpha, color red has chance alpha, and so on and so forth. We go all the way down to color N, which has chance alpha.

So the total chance of all the colors winning is N times alpha. But this has to equal 1 because each color winning represents the sum total of all the possibilities that could happen in a game like that. Because we know in the marbles-in-a-jar game, one of the colors has to win. There is no other fate for the system. The game only stops when one of the colors takes over the entire population.

In case it has not at a particular time in the game, if one color has not taken over the entire population, that simply means that we have not given it sufficient time for one color to completely take over the population. So, N alpha has to be 1, which means alpha is equal to 1 upon n, which means each color has the same chance of taking over. each color has this much amount of chance of taking over. And since we are saying each color, red's chance is also 1 upon alpha and that is the answer. So, in the game that we discussed here, what we are saying is the chance that this individual is going to take over the entire population is 1 by N. The chance that this individual takes over is 1 by N. The chance that this individual takes over is 1 by N and so on and so forth.

So, every individual has an equal chance that is because they are equally fit, equally likely to be drawn from the population. Hence, each individual marble has an equal chance of taking over that population and that chance is equal to 1 upon N. And as we will see what we want to see is that this marbles in a jar context is absolutely no different from us trying to compute x1 for a neutral population. So in the context of the chemostat I am going to draw it in a way I am going to draw it in a way which is equivalent to the marbles in a jar game. So now I am talking of the neutral case.

where RA is equal to RB. RA was the fitness of the black individuals and RB was the fitness of blue individuals. In the neutral case when the mutation that led to arrival of the first blue individual This was a neutral mutation and fitness of these two genotypes is identical. So this is again population going from 0 to N. And at t equal to 0, at the start of the chemostat where I begin my analysis, there is one individual of the blue type.

The rest of the population is simply blue. And now I eventually know that the fate of the game is and I let time move forward. And in every step of the Moran process, one of these individuals So, let us say there is an individual here let us say this individual is does not reproduce and one of these individuals reproduces. So, this individual is washed away.

So, this is not represented in the next instant of time. So, this is at time t naught and this is at time t naught plus delta t. So, in this delta t time, one Moran process has taken place, which means one of these individuals has been washed away from the system and one of these individuals has reproduced. Now, it is possible that this individual was the one which did not reproduce and And our blue individual was the one which reproduced.

So, in this case, at t naught plus delta t, the representation of the population is going to be that I have two individuals of blue kind and n minus two individuals of the black kind and so on and so forth. And I will move forward in this scenario like this. Of course, it's more likely that one of the black individuals has replicated in the population and the system stays at one blue type and N minus one black type in the delta T time. So all those possibilities remain. But this is how the system is going to move forward.

But as you can see, eventually the fate of this system is going to be that one of these individuals is going to take over the population. And if we just remove this t naught plus delta t once from our analysis, if we go back to time t naught, we know that the fate of this game is the same as the fate of the marbles in a jar game where one of these individuals takes over the population. And that individual, because of this condition, that the fitnesses of the two genotypes are identical, could be any one of these individuals and as a result, let let that chance be equal to alpha so this individual has alpha chance of taking over this individual has alpha chance and this individual also has alpha chance and since there are n individuals and we know that one of them is going to take over the population we get n alpha is equal to 1 the same idea as we used in the marbles in a jar game and alpha is equal to 1 upon n and we get the same answer that we got for the marbles in a jar game.

So what that means is that starting from a number line context, if I'm at N, and this was zero, and I have one, two, three, i, i plus one, i minus 1 n minus 1. So, what this means is if I were to view the chemostat example on this number line again arrival of first mutation is the start point of the system is when I have one individual of the blue kind. So, the system is at this state and what is being what my analysis has shown is that the probability of going from here to here is simply x1 which was x1 that is equal to 1 upon N.

This was done more from the intuition that we have from this example, which was borrowed from the intuition that we have from the marbles in a jar example. However, if we solve these equations, these are not very hard to solve, but we won't spend the time to actually solve these equations. If we solve these equations correctly. and get an expression for x1 the answer that we are going to get from these equations is x1 is equal to 1 upon N in fact if we solve these equations xi is simply going to be equal to i upon N which is great because what that means is that if i plug i equal to 0 So, let us go back to the number line and do this there.

So, from the equations we get the analysis that xi is equal to i upon N. This is from our intuition and this is from the equations that we developed. We'll discuss just a bit more after we are through with this discussion about the equations. So what that means, if I plug I equal to 0, that means the system is here. then the probability that the system starting from this point reaches this point, that probability is i equal to 0, which is 0 upon N. So, there is zero chance of starting from here and reaching xN, which makes a lot of sense because there is no B-type individual in the population to start with. Hence, there is no question of B-type individuals taking over the population.

However, if I am at i equal to 1, which means I am here, the probability that the system will move from here to here is i is equal to 1. That means probability of taking over is 1 upon N. Similarly, if the system is here, the probability of taking over is 2 upon N. And so on and so forth. And if it is here, then the probability that this system will reach fixation in terms of the blue mutants taking over the population, that probability is n minus 1 upon N. So, as you can see that when I have only and of course, all of this is in a neutral case where RA is equal to RB. That is the case. These results hold for only neutral variants coming in the population.

What you what you should see is that the rightward movement, the chance that the population will reach the rightmost point is not uniform, is not constant everywhere. When I am at when I am at the leftmost, when I am at I equal to one. then the chance of reaching the rightmost point is only 1 upon N. That means n minus 1 upon N chance is there that I will not reach here. What will happen in this N minus 1 by N chance that the system will go here and this mutation is going to be lost from the population forever. It is only going to be once out of every n chances that this population makes it through and reaches fixation.

When there are two such individuals, the chance that these two individuals, the mutation that these two individuals are carrying reaches fixation becomes 2 out of N. But that still leaves the chance of N minus 2 upon n that these mutations will not reach fixation and in these N minus 2 out of N turns, this will reach 0 and the system will go extinct as far as these mutations that these individuals are carrying. So between the point 1 and 2, the chances of reaching the rightmost point and the chance of reaching the leftmost point, they are not equal. As we move towards the right, the probability that I will reach the rightmost point increases. And the probability that I will end up at 0 decreases which makes a lot of sense because if I have only one blue type individual which is neutral the chance that it is going to be lost are very high and the chance that this neutral individual is able to out compete everything when selection is not favoring it and only due to chance events it is able to reach fixation those chances are minuscule. What this also means is that neutral mutations, so x1 being equal to 1 by N also means another thing.

It means that neutral mutations because this entire discussion is when RA is equal to RB. Neutral mutations, when they happen, they have two fates. Either they reach fixation or they go extinct. they reach fixation with probability 1 upon N, whereas they go extinct with the probability N-1 upon N. Since n for microbial populations

is going to be a very large number. Even small microbial populations will be of the order of 10 to the power 6, 10 to the power 7. It can be much larger than this. Then you see that the probability that a neutral mutation is going to reach fixation is 1 into 10 power 6. That means for a population of size 10 power 6, for larger populations, it is going to be even smaller than that.

which means that a million, what this suggests to us is that a million neutral mutations need to happen before one of them reaches fixation. So out of 10 power six mutations that happened, only one reached fixation. and the remaining 10 power 6 minus 1 mutations so 10 power 6 happened one reached fixation the other 10 power 6 minus 1 mutations went extinct again on the number line this is when the mutation arose this is 0 this is N so a mutation arises the probability that it will reach here is N minus 1 upon N. So, if the population size is 1 million, which is 10 power 6, then 10 power 6 minus 1 mutations will end up here, and only one mutation will end up here.

And that is, which means a huge amount of diversity that is generated is lost because of the action of drift. And neutral mutations rarely will make it past and reach fixation as far as this context is concerned. So, if you are working out these equations, then and solving these equations to arrive at these probabilities, then you will need expressions for these P i i's and P i minus 1 and so on and so forth.

Let us quickly derive them for this neutral case so that should you be interested, you can derive these yourself. So, remember P i to i plus 1 let us do P i to i minus 1 this was basically A was birth and B was death. This equates to this we saw was equal to a birth meant n minus i times RA divided by N minus I times R A plus I times R B plus not plus that is the probability that A is going to be born. This has to be multiplied with that a B is going to die which is simply going to be i upon N.

And now, up until now, we had not made the assumption when we were deriving the expressions for these probabilities according to the Moran process. Now, we are going to plug in the fact that actually for the neutral variant, R_A is equal to R_B. So, if we keep these two constant, then simply this is going to become, let us say this is equal to R_naught, then this just becomes R_naught into N minus I divided by N minus i times R_naught plus i times R_naught into i by N. I can take R_naught common from the denominator and I get N minus i divided by N minus i plus i times i times N. These R_naught will cancel and these i's will cancel and I get an expression N minus i times i divided by N squared. That is the probability in the neutral case of transitioning from i to i minus 1.

Let us also do that transition probability from i to i plus 1. And this comes out to be; this was A death, B birth. And this comes out to be: B birth is just going to be equal to i times

R_B divided by N minus i, the total fitness of the entire population, which is just this times A death is just N minus i divided by N, and now I am going to substitute R_A equal to R_B equals R_naught, and using the same analysis as before, this is going to give me i times N minus i divided by N squared, which is the same expression as this. So, in the next video, we will close this video with these two derivations.

And in the next one, we will see what is the probability of transition from i to i, which can happen in two different ways. And then we will look at some graphical methods to examine what we have just derived. So, we will continue this discussion in the next video. .