Evolutionary Dynamics

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Lecture 38

Hi, welcome back everybody. In this video we will complete our derivation of fixation probability of an adaptive mutation which confers a benefit to the mutant that has arisen in the population. So in the last video, we had made quite a bit of progress towards deriving this expression through some cumbersome but simple math. The bookkeeping was a bit ugly, but the math itself wasn't very hard. And at the end of this exercise, we had come up with the expression for fixation probability of a beneficial mutation

the following expression 1 divided by 1 plus gamma 1 plus gamma 1 gamma 2 going all the way up to gamma 1 gamma 2 gamma n minus 1 so one thing you should realize so this is the fixation probability of for a mutation or this is also can be rewritten as probability that system currently at i equal to 1 will reach n. that the beneficial mutant that has arisen in the population will be able to outcompete the ancestor genotype that is present in the population of which there are N-1 individuals. It will be able to outcompete all of them and fix in the population. One thing that this expression immediately tells us that this expression is always less than 1.

Because the numerator is 1 and the denominator is 1 plus something. If I call all of this something. So fixation probability X1 it seems is equal to this which is always less than 1. So that means there is immediately a lesson to be learnt here. That we have been discussing natural selection and what natural selection tells us is that if any beneficial mutation comes up in the population, it will certainly reach fixation because it's going to get selected for and its progeny will be able to outcompete the progeny of the ancestral genotype that is already present in the population.

This expression, without working out the exact expression, immediately tells us that that is not going to be the case. X1 is less than 1. However, this obviously doesn't tell us by how much—how small is this quantity as compared to 1. Is it 0.99 or is it 0.01? And that is our goal in this lecture: we want to arrive at the precise expression which helps us quantify this fixation probability.

$$\gamma_i = r$$

So for that, obviously, all we need is these ratios gamma i, where gamma i was beta i upon alpha i. And if you recall, beta i upon alpha i was simply this ratio. If we are at stage i, and from there in one more step we can go to i plus 1, this probability was alpha i, or we can go to i minus 1, this probability was beta i, and we simply need the ratio of these two. Of course, the other possible outcome here is 1 minus alpha i minus beta i, and the two ends of the system are i equals n and i equals 0. So, we need an expression for gamma i. If we get that, we should be able to arrive at an expression for x1, and that is simply equal to beta i upon alpha i. Now, go back—let us take our minds back to the discussion of the Moran process, where we discussed beta i and alpha i. This is simply the probability beta i that the system is transitions from I to I minus one.

And alpha I is simply the probability that the system transitions from I to I plus 1. Transition from I to I minus 1 can only happen if the birth event is of an A-type individual and the death event is of a B-type individual, the mutant. This is the mutant that we have been discussing all along. And that is why the number of mutants in the population is going to reduce by 1.

Alternatively, I to I plus 1 transition will only take place if birth event is of B type and death event. is of A type. And hence, because of this, the number of blue type individuals in the population increases by 1 and goes from I to I plus 1. So, let us write down the expressions of these terms. The probability that birth of A type individual is simply going to be

The combined fitness of all the A type individuals divided by total fitness of all individuals in the population. So, the birth term probability is simply going to be N-I times RA divided by N-I times RA plus I times RB. The death, the probability of death of a mutant type is simply going to be proportional to the number of mutant individuals that exist in the population at the time, which is simply going to be i upon n. So, these two multiplied together give me an expression for the numerator in the numerator here is simply this. The denominator, we can write that by using the same logic that now we are saying that birth has to be of a B type individual whose probability is going to be the combined fitness of all B type individuals divided by total fitness of the entire population. In which case that is going to be I times RB divided by N minus IB.

times RA plus I times RB. And that has to be coupled with the fact that a death has to be of a A individual which is simply going to be proportional to the number of A type individuals in the population. which will be n minus i upon n. And this gives me the complete expression that I need for beta i divided by alpha i, which is gamma i. We can simplify this a little bit if you carefully look at this. And we can see that this n and this n can cancel each other.

So this goes. We can see that this i and this i can cancel each other. So this goes. We can also see that this n minus 1 can be canceled with this n minus 1. So all of this goes.

And we should be able to see that the denominator here was the total fitness of the population. And the denominator here is also the total fitness of the population. These two are identical. So this denominator cancels with this denominator. And eventually, we are left with a very simple expression for gamma I, which is equal to R A divided by R B.

And somewhat fortuitously for us, this value of gamma I—so this is gamma I—this value of gamma I is not dependent on I. Whether I is 1, 2, or 3, it does not matter. Gamma I, for every value of I, the value of gamma I is a constant, which is simply R A by R B. So, You should note here that R A is the fitness of the ancestor genotype, and R B is the fitness of the mutant genotype. Because we started this discussion with the assumption that the mutant we are going to be discussing will be an adaptive mutant, which has come up and actually has a higher fitness than that of the ancestral genotype.

We know that RB by definition is greater than RA. As a result of this, gamma I is actually less than 1. So, now the pieces are falling together. We have all gamma i's, whether it be gamma 1 or gamma 2, with the same value RA by RB. So, all I have to do now is go back to the expression for x1 and plug those in when I do that. So, x1 is simply equal to 1 divided by 1 plus gamma 1 plus gamma 1 gamma 2 plus gamma 1 gamma 2 gamma 3, going all the way to gamma 1 gamma 2 gamma n minus 1.

So, in the denominator, there are n terms starting with 1 and ending with gamma 1 to gamma n minus 1 all multiplied together. And each gamma i is simply equal to RA divided by RB. And we can write this as simply as 1 upon R. where R is the relative fitness of B as compared to A. Another way to see this is I can write this ratio as one upon RB by RA, and this ratio of RB by RA is what I'm calling R. So, then this x1 becomes 1 divided by 1 plus 1 by r plus 1 by r times 1 by r plus 1 by r times 1 by r times 1 by r, going all the way up to 1 by r times 1 by r times 1 by r, n minus 1 term n minus 1 times. I hope everybody is able to see that the denominator is a geometric progression.

Geometric progression with A as the first term. The first term of the geometric progression in our case is just this, which is one. And the common ratio between successive terms is simply equal to 1 upon r. So, this summation applies the formula of geometric progression, and in this entire expansion, in this entire series of geometric progression, there are a total of n terms. First term as 1, common ratio as 1 by r, and there are n terms.

So, that allows simply substituting the formula of geometric progression, I get this expression as 1 minus the common ratio to the power of the number of terms, divided by the common ratio minus 1. That is just the summation formula that I have applied in the denominator here for a geometric progression. Please look it up in any reference book if you are not familiar with geometric progression or have forgotten the formula for the sum. So this goes in the numerator, and then x1 comes out to be 1 upon r minus 1. divided by 1 upon r raised to the power n minus 1.

Remember that r was simply equal to, it is the common ratio. Let us take a look at what we called r. r was defined as rb upon ra. So, this is Rb upon Ra, and n is the population size. Since Rb is greater than Ra,

Since this is the case, what that means is that R is greater than 1 because the numerator is RB, which is a bigger number than RA. So that is greater than 1. So what that means is that 1 by R is a number which is less than 1. and 1 by r to the power n, where n is the population size, so another positive number. So this ratio, if I were to highlight this here, this ratio is less than one, and this ratio also is less than one.

So, when I subtract one from both, it turns out that the numerator will be negative, and the denominator will be negative too. But that is okay. But I can write this as, to make both positive, I can write this as x1 as 1 minus 1 upon r and the denominator as 1 minus 1 upon r to the power n. And I can do that because I have multiplied the numerator and denominator by minus 1. So, I have switched the terms. Now, we are almost there, except for the fact that we can simplify this a little bit more.

1 by r is a number which is less than 1 because r is greater than 1. And n is a number which is very large for a microbial population, let us say, of the order of 10 to the power 6. That is at the very least; it can be much bigger than that also. So, I have a number which is less than 1, and I raise it to the power of 10 to the power 6; this number will be very close to 0. For example, if you imagine that if I have 0.9, 0.9 squared is only 0.81, which is less than 0.9 to the power 1.

And if I do 0.9 to the power 3, that is going to be less than 0.1. And every subsequent time I multiply it by 0.9, the number keeps on decreasing. And here I am multiplying a number which is less than 1. 10 to the power 6 times. So, this is going to be a really small number, and I am just going to ignore it.

This number is a really small number. So, x1 is approximately equal to 1 upon 1 minus r. Okay. Okay, we are almost there. So, x1 is approximately equal to 1 minus 1 upon r, where r is equal to rb divided by ra. So, if I substitute that here, x1 is equal to 1 minus 1 upon rb by ra,

This can be written as 1 minus RA divided by RB, which can be written as RB minus RA divided by RB. Now, without any loss of generality, let us normalize everything with respect to RA and let us assume that RA is equal to 1 and RB is equal to 1 plus S, where S is the selection coefficient associated with the beneficial mutation that arose when a blue individual was born when existing black individual divided and a progeny had acquired a mutation. So, let us we are saying that the fitness of this guy is 1 and the fitness of this guy is 1 plus S. So, this is 1 plus S minus S minus 1 divided by 1 plus S. These ones cancel and we get S upon 1 plus S. This is the fixation probability associated with a beneficial mutation.

$$x_1 = \frac{s}{s+1}$$

So, we have finally arrived at the fixation probability of a beneficial mutation and it simply says that X1 is equal to S upon 1 plus S. So, now what we are saying is that if we have a population size N and we have a beneficial mutant that arises in the population, It's present at 1. The probability that this beneficial mutation will be able to out-compete the existing N- individuals of lower fitness and reach fixation, this probability X1 is simply equal to S upon 1 plus S. S is the relative advantage that it enjoys over the ancestral population. So let's plug in some numbers. In the E. coli evolution experiment, we saw what sort of effect did those five beneficial mutations had.

We saw that after the occurrence of these five beneficial mutations, fitness had increased by 35%. So by 0.35. That means Each mutation conferred a benefit of about 0.07. That was the S. Let's assume that each one of those conferred equal benefit.

So the S associated with each of these mutations was 0.07, which means for a mutation like that, the X1, this is approximate, is going to be 0.07 divided by 1 plus 0.07 X1. which is just equal to 0.07 divided by 1.07, which is approximately equal to 0.07. Because S is a small number usually as compared to 1, because as you can see, a single beneficial mutation only provides a benefit of about 5-6%, so S will typically be 0.04, 0.05, and so on. Whereas 1 is several times bigger than that, it is usually safe to assume that X1 is almost equal to S. Which means that When a beneficial mutation occurs, it only has a chance proportional to the fractional benefit—the relative advantage that it provides—of reaching fixation.

All other times, it's going to go extinct. So if we are talking about a beneficial mutation that confers an advantage of 5%, what that means is that if this mutation occurred 20 times in the population, 19 times it will go extinct, and only one time will it go to fixation. So, in other words, if all beneficial mutations were providing this amount of benefit, 20 beneficial mutations would need to occur in a population for one of them to go to fixation. Still, we see this is much better compared to what we saw with neutral mutations, where we saw that 10 to the power of 6 mutations needed to happen for one of them to go to fixation.

Almost a million mutations needed to happen for one of them to reach fixation under neutral evolution. This is adaptive evolution, where the mutation that occurs provides a fitness advantage to the population. Hence, you need far fewer mutations to happen before one of them has a chance to outcompete and reach fixation. But even then, we see that for typical values of the selection coefficients that beneficial mutations provide, most mutations—an overwhelming majority—still go extinct due to the action of drift. Only a very small fraction are able to reach fixation.

In other words, we can also think of this in the following way. Natural selection, when a mutation happens—when a mutation first occurs—the system is right here. The system is right here. And at this time, There is a tussle between what will happen to this mutation—between natural selection and drift.

Natural selection's effect will be that it increases the mutation. It selects for the fitter type of individual, which will take it toward fixation and toward the end. So this is natural selection. Drift doesn't really care. Drift doesn't care where the system goes.

It's happy to take the system in this direction or in that direction. Drift doesn't really care one way or the other. Despite the action. So this is the action of drift or chance events. Despite the action of natural selection and drift being associated like this, what we are seeing is that for a beneficial mutation that confers a benefit of, let's say, 5%, the numbers tell us that this mutation is actually going to end up at fixation.

For every mutation that ends up here, there are going to be 19 mutations that end up going extinct. And you might wonder why that is happening, despite natural selection acting in one particular direction and drift not caring which direction it acts on. That is because of the location of this point. Because starting a game from this point, The action of drift, even if 50% of the time drift takes a step in this direction, as soon as you reach this particular point, the game is over because the one individual carrying that beneficial mutation is gone.

So even if it was a 50-50 chance, the 50% that took a step in this direction are immediately removed from the population. For the 50 percent that took a step in this direction, they are still vulnerable because 50 percent of them will take another step in this direction, and 50 percent of them will take another step in that direction, and then they will go extinct. So when numbers are small, Drift and chance events do these things, which lead to a surprising outcome: you need 20 beneficial mutations with S equal to 0.05 to happen so that one goes to fixation, one fixes, and the other 19 just go extinct. And we will continue this discussion in the next video, where we do some more analysis on a system such as this.

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