Evolutionary Dynamics

Supreet Saini

Chemical Engineering

Indian Institute of Technology Bombay

Week 12

Lecture 56

Thank you. Hi, welcome back, everyone. We are down to the last few videos of the course, and we will continue our discussion of some experiments that I think are interesting, innovative, and they have asked questions which are seemingly very difficult and tried to answer them through experiments whose ideas come across as very simple. And I think one of the things that I enjoy about working in a field like evolution is trying to answer deep questions about how evolutionary processes proceed. But doing them in a way where we are only doing simple experiments, thinking about creative ways of doing simple experiments to answer deep fundamental questions about evolution, is something that I enjoy a lot about this area of work.

So what we are going to do in this video is discuss one last experimental paper from LTEE. And interestingly, this paper came out well before the papers that we've discussed. So this is a paper from the mid-90s, from the early days of LTEE. But I think it was a really creative way to answer a particular question about evolutionary processes. So what the authors are asking is: evolution is dictated by three forces.

An evolutionary fate of a population is decided by one, selection, which is obvious. Suppose we are growing bacteria in an environment where there is an antibiotic around. So we are selecting for antibiotic-resistant bacteria. So the environment obviously dictates selection, and that's a big determinant of where an evolutionary trajectory will go. Alternatively,

Evolutionary processes are also influenced by drift—chance events. As we saw in the case of citrate utilization in the LTEE example, it was a very fortuitous mutation that enabled citrate utilization in only one line. So this is drift or chance events. And lastly, how does history... of a population determine its evolutionary trajectory?

To understand the role of history, let's explore it through an example. Suppose I am evolving E. coli in a flask—let's imagine I have two flasks. I set up identical experiments in these two flasks, just as Lenski did back in the day. And The environment in both flasks is low-glucose.

I subject these flasks to identical selection pressures and conditions. I allow growth for 24 hours. After that growth period, a 1:100 dilution takes place. There is shaking at a specific speed. Everything associated with these two flasks is identical.

Now, clearly beneficial mutations are going to take place, but neutral mutations will also take place. Mutations will fix just because of chance events. One of the ways in which neutral mutations can fix in a population is to imagine the following: we have an individual, here is its DNA, And as the process of evolution started, its DNA acquired a mutation. This mutation, however, was neutral in nature.

This was a neutral mutation, and by definition, because it is a neutral mutation, it does not confer any advantage to the individual carrying it. So there was no change in fitness, and as we have seen, as a neutral mutation, this has a chance of 1 in n to fix in a population, which in a large population is a really minuscule chance. Most likely, this mutation is just going to be removed from the population. However, because mutations occur randomly, maybe going a little bit forward, this individual or one of its progeny, before they were eliminated by selection, acquired this type of mutation.

So let us say this was the neutral mutation. And one of these individuals carrying this neutral mutation acquired a beneficial mutation, which conferred a really strong beneficial effect to this individual. So this individual now becomes the fittest in the population. If we think in terms of the traveling wave model, then maybe this individual... was here, but this individual picked up this beneficial mutation whose selection coefficient is really high. As a result, this jumps way ahead of the wave, and we have an individual with this level of fitness. Now, this individual may or may not survive, but if it survives drift, then its frequency will increase rapidly because the advantage it enjoys over the population mean fitness is huge.

As a result, this mutation will reach fixation. But because this neutral mutation happened to be in the individual which is carrying this great beneficial mutation, this neutral mutation also reaches fixation. And this is one mechanism also gets fixed in the population. And this is one mechanism via which Neutral mutations can easily fix in a population.

Neutral mutation fixing itself is going to be a very fortuitous event, but via this mechanism it can fix. So, when we are evolving this, let us go to the next slide. When we are evolving E. coli to flasks in glucose, then what might happen is that one of these flasks, the following mutation might happen. That here is the genome of the individual and on this genome is this gene called LacZ.

Now, lacZ if you remember is the gene which codes for the enzyme which is responsible for breakdown of lactose into its monosaccharides glucose and galactose. This reaction is facilitated by lacZ and if there was not any lacZ in the cell then this hydrolysis would not take place and the cell would not be able to grow on lactose as the carbon source. However, in the evolution experiment that I am conducting, the carbon source is glucose. So, having whether a cell has the gene for laxity or does not have gene for this enzyme, it does not really matter because it is growing on glucose and glucose utilization does not need lacZ. So, maybe in this line, the following mutation happens that this part of DNA which was carrying laxity

It was deleted. So, this entire region was deleted, and now this part, which encodes for lacZ, is no longer part of the genome. Now, this loss of lacZ—so, the lacZ gene was deleted from the genome. This loss of lacZ has absolutely no effect on the fitness of this individual because it's growing in an environment where the product of that gene was irrelevant.

And that product wasn't even being made because the lacZ gene is only transcribed and translated when lactose is present and glucose is absent. In this environment, in which I'm conducting this experiment, lactose is not present and glucose is present. So, the gene was not even being transcribed. So, the lacZ gene is deleted, and as a result—because it was a gene that was not being utilized in that environmental context at all—this is a neutral mutation. Now, via the mechanism that we discussed on the last slide, by some chance event, maybe a great beneficial mutation could happen here, and as a result of that,

this individual, whose lacZ gene has been lost and is carrying this great beneficial mutation for growth and survival in a glucose environment, reaches fixation. So, now there is no individual in this population that is able to grow on lactose, but that is irrelevant as far as growth on glucose is concerned, which is the medium in which I am conducting this evolution experiment. On the other hand, the same does not happen in the

other flask. And the individuals in this flask evolved and acquired mutations that made them grow better on glucose. But this deletion of lacZ did not take place here.

So at this point, you have the lacZ gene, which is still intact. And other beneficial mutations have occurred throughout the DNA of the organism. Now, let us say this evolution experiment was conducted for g number of generations. And at T equal to 0, both could grow on lactose. And from here on onwards, only one of them can grow on lactose and evolve to become better at growth on lactose, which is this individual. This individual cannot evolve on lactose as we move forward, and that is the result. If this was the starting point of my experiment, then the fact that this particular individual can grow on lactose and evolve to become better, and this individual cannot,

That is a product of the evolutionary history of these two individuals, where in its evolutionary history, one of these, the blue individual, lost the lacZ gene. And as a result, it cannot grow and evolve on lactose anymore. So the potentialities associated with an organism's evolutionary trajectories that could take place, that could be realized, are a function of its evolutionary history. So in this work, What Lenski and Travesano ask is, can we understand how much of evolution is taking place because of selection, how much is because of drift, and how much is because of history?

Can we design a simple experiment that allows us to mathematically differentiate a population's response into these three categories? And say something like, 80% is because of selection, 15% is because of chance, and 5% is because of history. Of course, I am making up these numbers, but that is the idea of quantification that the authors want to do. So, what is the simple experiment that allows us to do this quantification? Now, let us imagine that we have a trait.

Remember, this is in the context of the long-term evolution experiment. So, populations are being evolved in a low-glucose environment. And this is a paper that was published in 1995 by Travisano and Lenski in Science. So, the populations are being evolved in glucose, and there are 12 such populations. That is the design of the long-term evolution experiment.

So, now this population will have some trait which is—so let us call this as t equal to 0, t being the number of generations, and this let us be equal to t equal to t1. So, on the x-axis, we represent the ancestral trait at t equal to 0. What is this trait that I am representing? The trait could really be anything. The trait could be how well these 12 lines are growing on galactose.

How well are they doing on maltose or anything? It could even be how big the cells are. We know from evolution experiments such as LTEE and others that as cells become fitter, as cells become fitter, they increase in size. So, if this is true, then our expectation from the LTEE is that at t equal to zero, if cell size was this, then going forward so many tens of thousands of generations, the cells should be larger.

And that is indeed what we find from these experiments: faster-growing cells are larger in size. Anyway, that's a separate story altogether. It's a result that I find a bit counterintuitive, but that is how microbiology works. All right. So, ancestral trait.

And let's just worry about that. Maybe the trait that I'm looking at is just cell size. How big are the cells at the time of division? Maybe cell size at the time of division. So, this is the trait that I am looking at in the ancestral population.

And on the x-axis, I will plot the value of this trait for each of these 12 flasks. But because $x(t) = 0$, all of them are genetically identical. The trait value in all these 12 flasks is exactly the same because it is the same genotype. Hence, the ancestral trait value may be—so this is cell size, so let us say this is size 0. Now, on the y-axis, we evolve this for T1 number of generations and measure cell size for each of these 12 lines.

Now, the evolved cell size may or may not be the same. Because these individuals are going to pick up different mutations, these mutations may or may not have a different effect on the size of the cell that we are looking at. Remember that selection is not towards greater size. The selection is to improve fitness in how well a cell is able to grow in low glucose conditions. But there are these pleiotropic effects that when you change because the cell is such an interconnected system,

If you change one aspect of the cell's performance, it is bound to have ramifications on other aspects of cell's manifestations. And that is what we are looking at if we are looking at cell size. And that is why cell size will also change. Because although the selection was on faster growth rate in glucose, when we make mutations or when we make adjustments in the cell to grow fast on glucose, its ramifications on cell size will also take place. And because each cell is different, so let's say in line number 1, this is the mutation that you acquire which makes you grow better in glucose.

In this case, the ramifications on cell size will be something. Let's say this makes a delta S naught difference to cell size. However, in this line, if this is the cell, the mutation that happened obviously is going to be something different. the ramifications of this particular

mutation on cell size may or may not be the same. It may be delta S naught the same amount or it may be something else, delta S1.

And if the ramification is delta S naught in every one of these 12 lines, then it is unlikely that these changes are driven to the same extent by S1. Chance only means there must be some underlying necessity in how a cell functions—that when you improve the growth rate in glucose, cell size increases by delta S naught. However, if the cell size increase in every one of these lines is different, then what we can say is that cell size increase is not really linked with growth rate in glucose. In some lines, it's increasing by some amount; in some lines, it's increasing by another amount, and so on and so forth. So, anyway, let us go back to this experiment. This line here is simply the x equals y line. And on the y-axis, we plot the ancestral trait.

Not ancestral. Let me rewrite that. We plot the evolved trait. At t equal to t1. So, we will plot the values of the 12 evolved lines at some point in the future, which is t equal to t1.

Now, imagine this scenario: this is S0 because this is the x equal to y line; this point is also S0. Now, we said that faster-growing cells are larger in size. So, we expect that evolved lines have a cell size that is larger than the ancestral, which means the current size will be somewhere over here. Let us imagine that for line number 1, the cell size is this. The evolved line number 1 has a cell size of this.

Let us call it S1. Now, clearly S1 is bigger than S naught. So, in line number 1, cells have grown to be bigger, which is the null expectation. Now, that is fine. But now, when we do the same for line number S2, we find that line number S2 is also at the same point.

So, the exact same change has taken place in line S2 also, in line 2 also. So, this is line 1, line 2. And similarly, when we do this for all 12 lines, we find that all 12 lines have the same exact value of the evolved trait, the trait being cell size at T equal to T1. So, that's one possibility. Let's draw these possibilities on the next slide and then see what it tells us.

So, this is ancestral trait, evolved trait. One possibility is S naught. One possibility is that all 12 lines exhibit their point at the same value. So, all 12 lines have an evolved trait value which is S1, and because this is the x equal to y line, this is S naught.

What that means is that one, size has increased. Second, size has increased by same amount in all 12 lines. What that means is that there must have been a necessity for size to increase by the same amount when cells are adapting in glucose as the environment. If

there was chance associated with it, then we would see different responses for different lines. For example, an alternate response of the 12 lines could be the following.

S0 X equals Y. An alternate response could be that the 12 lines are present like this. And so on and so forth. So let's say maybe they are separated S1 to S12. Each has a different line.

Each has a different value. Now, what do we notice here? That one size has increased, that's the same. However, size has increased by different amounts in each line. So what we can say

is that it seems like there is a necessity to increase size because size has gone up in each one of the 12 lines. However, that increase doesn't have to be a strict number. There is a window associated with it where your increase in size could be anything, but it doesn't have to be an exact number like it was in this case. this one was driven, this change, if I saw the change being driven like this, then it was almost necessary for size to increase from S0 to S1. Here, it is not so strict.

The size can be increased by anything from S1 to S12. So, what we can conclude from this is that in this case, Evolution in cell size is driven by selection only because selection is very deterministic and that is why all 12 lines have the same exact value after evolution for T1 amount of generations. On the other hand, in this case, Selection did act because all 12 lines have increased from the ancestral value.

It's not like you can decrease your cell size value when you are evolving for faster growth in glucose. Increase has to be there. But that increase could be anything. There is a range in which the increase could happen. It doesn't have to be exact number like in this case.

As a result, cell size changes... is driven by selection, which means selection is the bit that increases has to happen, and chance, which depicts the scenario that this change is allowed. So the response in such a context will be A mixture of the effect of selection versus drift. Let's discuss the third case before we close this.

What do you think is happening here? This is S naught. This is also S naught. And let's say now in this case the response of the population is like this. Now, in some lines, the ancestral value has increased to this evolved value S1, but in other lines, the value of the trait in the evolved lines has actually decreased from S0 to S1'.

Some lines have exhibited an increase in the trait value. Other lines have exhibited a decrease. All of this has happened while all 12 lines have increased in growth rate in glucose. Because the experiment was conducted with that particular goal. As a result of this, we can say that

The mean change is actually 0. The average of these 12 lines. Some have increased. Some have decreased. And the average change is 0.

So selection doesn't change. Selection doesn't drive this at all. It doesn't drive this trait. What drives this trait is only chance. That is why, while you are selecting for increased growth rate in glucose, this trait could increase or decrease.

That is not necessarily a function or byproduct of increased growth rate in glucose. So now you can think of different traits and perform this experiment for the LTEE. Depending on what the data looks like—whether it's like this, this, or this—we can perform some arithmetic with these numbers and quantify what fraction of this. In this case, for instance, it is a result of selection and drift's action. So, we can perform some arithmetic analysis on these numbers and actually decouple the effect of how much evolutionary change is driven by selection and how much is driven by drift.

So, what we have discussed here allows us to decouple selection and drift. In the next video, we will understand how we bring history into this, because remember, that is the bigger question we started with: how do these three factors impact evolutionary change? We have looked at selection and drift. In the next video, we will discuss how history changes. How do we study the contribution of history in bringing about evolutionary change?

Thank you.