Introduction to Evolutionary Dynamics

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Lecture – 27
Representing microbial evolution

Hi and welcome to the next lecture of the course, and in the last time we had discussed this evolutionary dynamics of a mutation associated with an experiment that we might be doing.

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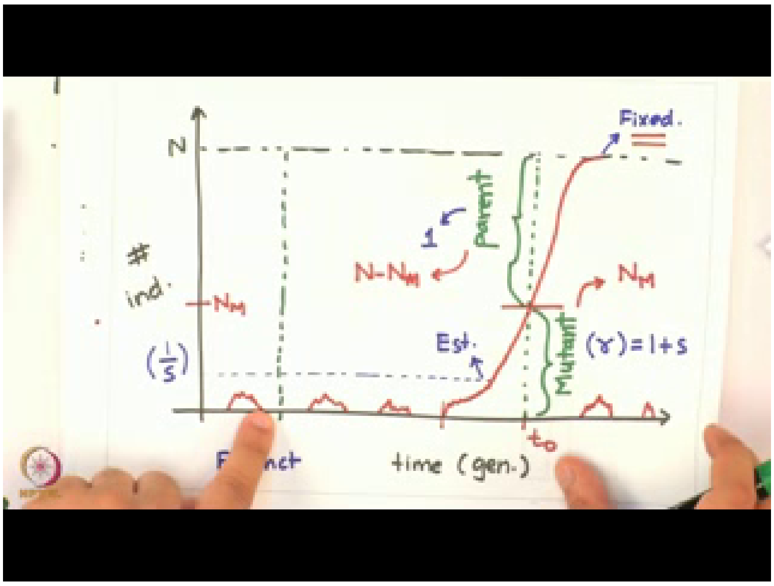

So, all these events in the first representation x axis represents time which is measured in number of generations and the y axis is associated with number of individuals and at various times during the experiment we are going to have these beneficial mutations which arise the numbers go up, but randomness or genetic drift ensures that most mutations are lost and they go extent as we progress in time. However, once in a while we will have a mutation whose numbers associated with individuals carrying that particular genotype will divide and exceed a number equal to 1 by s, where s is measured as one plus s gives me the fitness of the mutant r whereas, the rest of the population has a fitness associated with it equal to 1.

If the numbers associated with the mutant exceeds 1 by s that is when we say that the mutation has become establishment. Beyond establishment randomness does not play a role in deciding the fate of the mutation, and because randomness does not play a fate in this region now we have a mutant population which is fitter than wild type, and now selection effect is going to be very dominant over the stochastic effects and selection ensures that the mutant is able to eliminate the wild type from the population completely.

Eventually when all N individuals belonging to the population belong to the mutants genotype, that is when you say that this particular mutation which happened at this time has become fixed in the environment that we are talking about. At any particular time during the process if this is the time if I want to draw a vertical line here that gives me the composition of the composition of the individuals of the population at that particular time in the environment. So, at this time t naught if I draw the line that line intersects the curve associated with the mutant population at this point. So, what this tells me is that reading this of from here from 0 to Nm that is the number of mutant individuals that I have in the population at this particular time and from N to Nm, N from Nm to N that is the number of individuals associated with the parent genotype.

So, at this particular instant t naught I have Nm number of individuals which are of mutant genotype and N minus Nm number of individuals which are which belong to the parent genotype and of course, as we progress further in time eventually another mutation will happen, which will become established in the population and then its numbers will grow as well and it will become fixed as well and that keeps on happening as I keep moving forward in time a in this representation.

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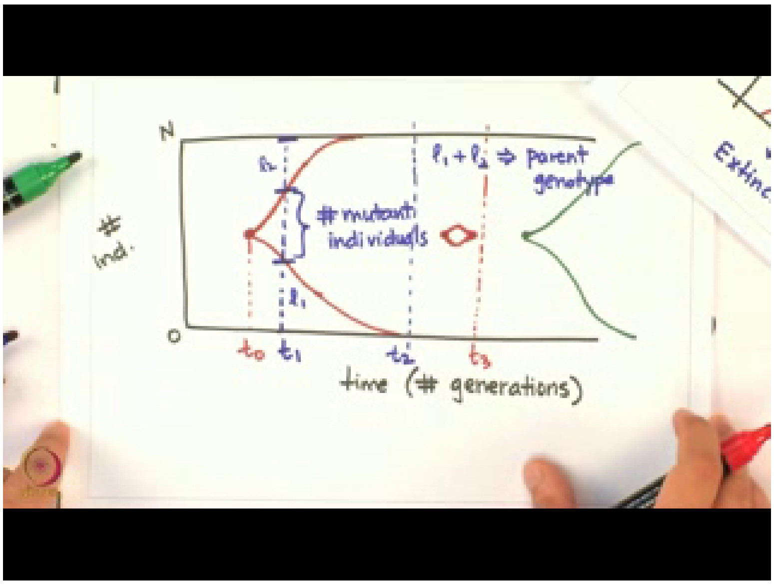

Another representation is as following, again in this one on the x axis I represent time which is again measured in number of generations and in the y axis is number of individuals which again 0 to N and I am not interested in regions beyond N because they do not correspond to the environment that I am talking about. In this representation what happens is that a mutation might occur at t time t equal to t 0. So, at this time i have this one individual which belongs to a mutant genotype and all others are the parent genotype. And as I move forward in time, suppose this mutation is able to establish itself and go to fixation its relative fraction in the population will keep on increasing.

So, starting from this one individual the mutation is spreading in the population and at any given time t 1 if I were to draw this vertical line at t 1 this corresponds to this width corresponds to number of mutant individuals, and these two lines l 1 from this point to this point and l 2 which is this point to this point l 1 plus l 2 correspond to parent genotype. So, at any point I had draw vertical line and because the mutation population arose from this particular individual which is now spreading in the population, and at any given point t 1 if I draw this vertical line the number of individuals between the spread give me the number of mutant individuals that are present in the population at that particular instant, anything outside this spread is the parent genotype that I started with.

So, this mutation if it is fitter than the wild type will keep on spreading and eventually something like this will happen and again what has happened here is that if I draw a line at t equal to t 2, everything is encompassed by this spread of the mutation and hence what that what this represents is that the mutation has gone to fixation all individuals in the population are carrying this mutation now there is no individual which is the original genotype of the parent that I started with ok.

And again this fate might repeat itself as I go to a forward time a mutation might happen in one of the individuals and that mutation now spreads through the population like this and so on and so forth it keeps on happening as I move forward in time what happens to these mutations. So, what you should try and do here is draw a parallel between this mutation which got established and went to fixation with this mutation which happened here and its numbers increased and it went to fixation. So, how do we represent these mutations which happened, but their numbers could not establish themselves and they went to extension, those mutations are represented like in this representation are represented like this. So, at this particular time point this mutation has become fixed and now another mutation arises in one of the individuals. So, this marks that point where that mutation occurred.

But because the mutation could not get established its numbers increased slightly, but then went back to 0, this represents what is happening to this mutation where it happened as one individual, it numbers oscillated a little bit, but their numbers never grew so much that the mutation established itself and eventually the numbers di term and the mutation went extent. The same is happening here the mutation happened with one individual and the numbers fluctuated grew a little bit, but eventually the population collapsed and then at t equal to t 3, no such individuals carrying this particular mutation were left in the population they were just eliminated via genetic drift.

So, this is another representation that you might have to represent an evolutionary experiment. In another variant of this we will come back to that lets talk about the third particular representation. The third one is a different in the sense that so far in our representations we are being using the x axis to represent time. In the third representation we do not represent time, but instead we represent fitness there and see how the fitness is spread across individuals in a particular environment.

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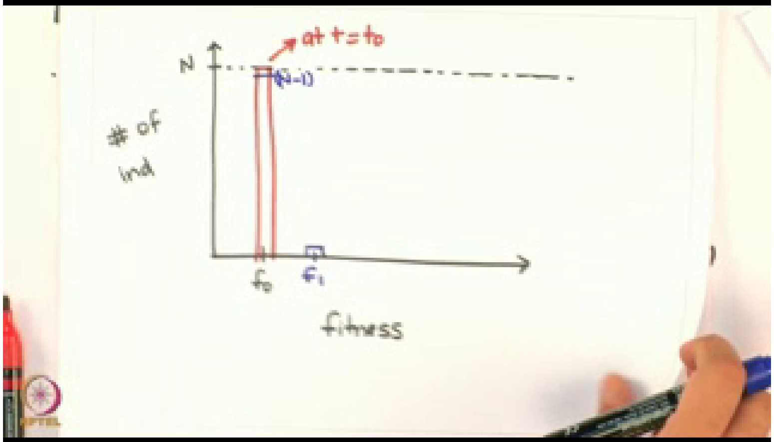

So, in this third representation we have fitness on the x axis and number of individuals on the y axis. Now what this means is let us say this is f naught and this is N which is maximum number of individuals in the population. What is means is that at t equal to 0 when I start the experiment I am starting with the genetically identical population which means all cells are at the same or carrying the same genetic material, and hence have the same fitness f naught associated with them.

So, in this representation at t equal to 0 all the cells in the population are present at fitness equal to f naught. So, this is like a population frequency histogram and the question that we ask is that at t equal to 0, how many cells are present at f naught fitness, but at t equal to 0 we are just starting there is no genetic variability in the environment. So, everybody is present at f naught and hence this is my population distribution at t equal to 0 t 0. What will happen as I let the let this an evolutionary experiment play forward in time to the fitness. Eventually a beneficial mutation will happen. So, I will get a case where I have one individual at fitness f 1 and N minus 1 individuals at fitness f naught. So, that number comes down by one and I have one individual which is at a fitness f 1 where f 1 is more than f naught and again. So, what we have been discussing so far same forces come into play this individual that has arisen which is at fitness f 1 might increase in numbers, but it will be subject to random affects while its numbers do not cross this threshold of establishment, and more often than not this mutation will just go extinct.

So, in this case if this mutation goes extinct because of genetic drift at t equal to t 2

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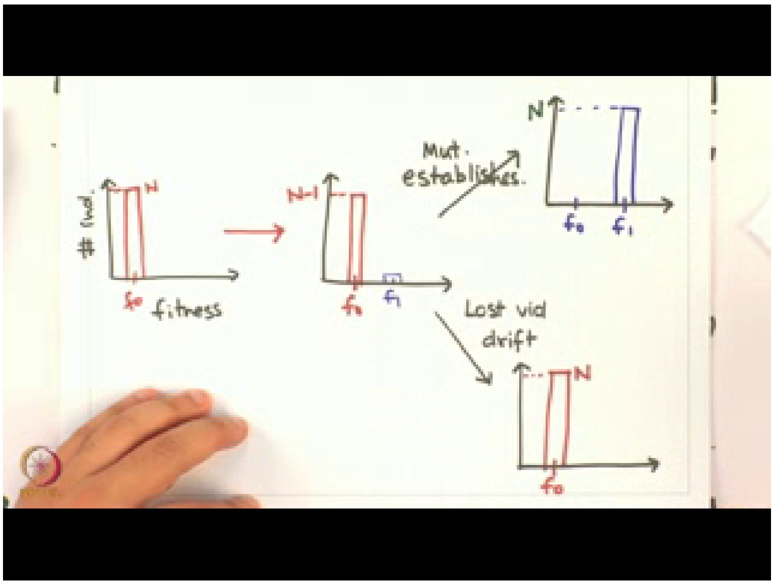

So, I may just redraw that you draw that smaller this is fitness, this is number of individuals and at t equal to t naught we saw that everyone in the population is at fitness f naught. Now as an we forward in time at t equal to t 1 I might have a case where this is N a first beneficial mutation happens; that means, the number of individuals which are present at f naught come down to N minus 1. So, I have one mutant individual present in the population and that mutant is present at a fitness equal to f 1 where f 1 is more than f naught.

Now, stochastic effects are going to come into picture exactly what we have been discussing so far and this fate of the mutation is going to be dependent on the first on the inter play between these stochastic effects and selection effect. Because of stochastic effects this mutation might get lost and we have genetic drift taking place and that mutation get lost forever. However, selection fevers this advantage this mutant individual and wants what want its frequency to increase in the population.

So, depending on whether this mutations survives or not does not survive, our representation changes. Let us draw the case where this mutation is able to establish itself and hence the mutation goes to fixation if that is the case then. So, this is the case when mutation establishes which means it will later go out to fixation and when it goes to fixation because f 1 is more than f naught, f 1 individuals will eliminate all f naught individuals from the population and after fixation I will have my entire population move to fitness f 1 and no individuals at fitness f naught ok.

On the other hand if this mutation is lost vid drift, then because this mutation is lost all individuals are going to belong to this particular genotype because all individuals which were carrying this beneficial mutation have been lost from the population, which means that all individuals are going to belong to fitness f naught this is equal to N. And again you should instead of draw these three representations yourselves and trying compare them to and see and convince yourself how the represent the same scenario. So, let us take a look at these two representations that we have the first in the third.

This point here represents the fact that a beneficial mutation happened which in the third representation is represented at this point where this beneficial mutation has arisen and is at fitness f 1 which is more than f naught. Now this particular mutation does not survive and it goes extinct hence at if I were to look at this time point, all individuals in my population are of parent genotype because a number of mutant individuals has gone to zero right

So, all individuals are belonging to the parent genotype that I started with, which is exactly the same in this representation where this mutation was lost vid drift all individuals in the population are belonging to the parent genotype which has a fitness equal to f naught. So, that mutant got lost and we have a situation where the numbers of the individuals belonging to parent genotype in top from N minus 1 to N again and hence we have N individuals at f naught which is exactly the same as this scenario. On the other hand if the mutation is able to establish itself, it quickly goes to fixation and all individuals at this particular point belong to the mutant genotype and none of the individuals belong to the parent genotype that we started with which is exactly what is represented here that the mutation establishes and from there of there on it goes to fixation and you have N individuals which now belong to a genotype f 1 and 0 individuals which belong to genotype f naught.

So, these are all identical representations they just represent different facets associated with it, in two of the representations you have time versus number of individuals. So, if that is the quantity that you are interested in you plot your data that way, but on the other hand the third one has fitness against number of individuals. So, if you are interested in looking at the frequency distribution of fitness in the population at any given point in time that is the representation that you will be interested in.

So, before we go ahead I just want to spend a few minutes talking about how in lab would you actually do an evolutionary experiment associated with a microbial population there are two standard ways to do this the first one.

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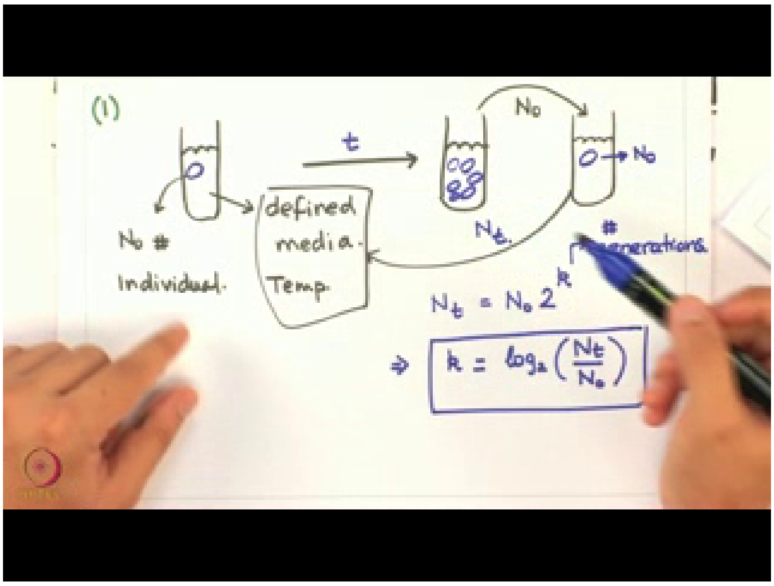

In the first one what you do is you take a test tube and you give it a media which is completely defined. By defined media what you are doing is you are making the environment associated with the experiment constant it does not change with time every time you do this experiment you use the same exact media. So, that the environment in which the cells are growing does not change with time and your studying evolution of this population in this particular environment. So, you fixed that aspect of it by defining the media, how much carbon and any of the other nutrients associated with growth you exactly quantify how much of each nutrient do you add to the media.

Once you define that you also define the physical aspects of both such as what is the temperature at what shaking are you went to do this experiment and so, on and so forth. So, define every aspect associated with growth, then you add N naught number of individuals. So, at t equal to 0 you add N naught number of individuals to this environment, and you let this media grow you let growths take place in this environment and after you wait a while your numbers will go to N to the N let say Nt is the number of experiments if you let growth happen for time equal to t. And one of the important variables that we have seen keeps arising in our representation is time is measured in number of generations.

So, if your number is changing from N naught to nt, accounted you are very interested in is how many generations have happened between these two time points.

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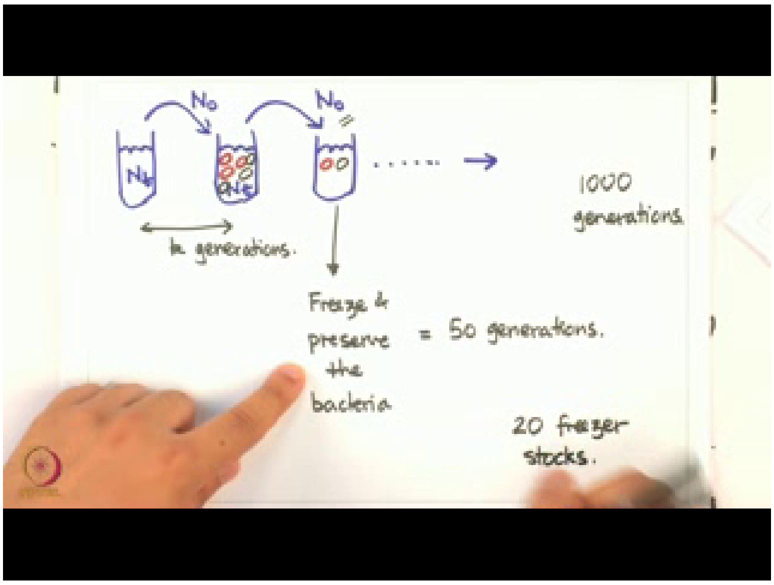

And the way did that you would calculate something that we did at the very beginning of the course you can simply represent that Nt is equal to N naught into 2 to the power k where k is the number of generations for which growth has taken place. Now you also did something at the beginning of the course which told us that this relationship is not exact, but for the time that we are interested in the difference between this representation and that differential calculation differential calculus representation that we have done earlier in the course, is not going to be very different and hence this is a good enough approximate approximation for what we are trying to find out now.

And you can just manipulate this a little bit and get k is equal to log 2 Nt divided by N naught. So, you get number of generations that the bacterium goes through via division in this time t, and what you do after time t in this type of evolutionary experiments is that you prepare an identical tube to what you started with. So, this tube here has the exact same conditions as what you started with for the first tube, and you out of these Nt individuals you randomly select N naught individuals, and transfer to the new tube to the new tube ok.

So, you have in reality what you. So this is N naught number of individuals who are randomly selected from this Nt. So, in reality what is happening is that it is as if you are repeating this whole process again where you are going from N naught to Nt numbers in time t in the same environment and you let this happen over and over again; and what is going to happen in this experiment this experiment can be simply represented by you have tube number one growth take place number goes up to Nt, you transfer N naught to tube number 2 growth take place and it goes to Nt again you transfer N naught and so on and so forth this can go far as long as you plan your evolutionary experiment to continue.

Every single transfer is equivalent to k number of generations associated with the experiment, and the idea is that during one of the transfers while these N naught are going up to Nt, you are going to have this one mutant that arises in the population and while this growth is happening this mutation this mutant increases in number. So, you have at any point in this experiment at the end of growth in this tube when you have Nt number of bacteria, you going to have some mutant individuals and we are going to have some individuals which belong to the genotype associated with the previous tube.

And now when you transfer N naught the mutant individuals may or may not get transferred depending on the numbers associated with their frequency, and hence you have genetic drift coming into picture and the mutants genotype being lost if none of the N naught individuals being transferred contains this red genotype. So, that is genetic drift coming into being.

But on the other hand if you do end up transferring a red and a original genotype equally in this tube. Now our because red is fitter than black it is going to quickly spread through the population, and the mutation in as we say in our representation becomes established in the population hence spread through and eventually all cells will in this environment as we go forward in time through the next few tubes will become red. So, the mutation grow become fixed and any subsequent mutation that happens in the environment will happen in the genotype which is associated with the red colored bacteria had.

So, that is the first type of evolutionary experiments that you do in lab and you have k generations take place in every transfer that you have.

So, evolutionary experiment could last from upto few tens, few hundreds, few thousands any number of generations depending on what exactly is at that you are going look at. What also happens during this evolutionary experiments is that periodically what you would do is you would take a sample from this tube and freeze and preserve the bacteria. So, let us say you are doing this every 50 generations, what that happens what that means, is that while you are doing these kth k generations every transfer and let say k is equal to 10 which is very representative number, and let us say you have this transfer take place every morning. So that means, every fifth morning you have fifty generations that have happened and after that you take a sample from your tube and you freeze the bacteria in your big freezer and you keep doing that every fifth morning of the evolutionary experiment that you are doing.

So, in all if you had a 1000 generations in your experiment, and you are taking this sample of your from your evolutionary experiment every 50 generations you would have 20 freezer stocks through the course of your evolutionary experiment, and this is important because now in addition to just comparing what you started with and what is it that you got after a 1000 generations that is the eventual goal that you want to study that I started with this particular genotype, I let growth happen for 1000 generations in this particular environment which was chemically and physically completely defined by me.

So, what did a growth of a 1000 generations made this bacteria do in terms of adapting to that particular environment and selecting for changes which help it survive in this particular environment. So, you typically compare the genotype that you ended with and the genotype that you started with and trying design out the logic which tells you about the mutation that happened in the process. But what making these freezer stock every fifth they do, they give you little snapshots into the trajectory of evolution as it happened. So, now, in addition to just comparing the starting and the ending genotype you can also compare that how did this transition from the starting to the last genotype happened because you have data about the intermediates steps that the bacterial population took towards going to going towards that end genotype.

So, for instants from if from going from the starting point to the end genotype ten mutations had become fixed in the bacterial, then you can find out that was there any order in which those ten mutations got fixed in the population. Did mutation this did this particular mutation have to happen first in order for the subsequent mutations to get fixed and you can answer questions like this with an experiment like this.

So, we will stop here for this lecture and at the beginning of the next lecture we will start with the second way you can do an evolutionary experiment in lab and continue our discussion forward then.

Thank you.