**Introduction to Evolutionary Dynamics**
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**Lecture – 03**
**Exponential growth models**

Hi and welcome to this part of the lecture. We are going to start with modelling the 3 most fundamental tenets of evolutionary biology. And while we are doing that we are going to be talking about microbial population in general. So, according to the theory of natural selection from what we have discussed already. We note that there are 3 aspects related to evolutionary dynamics. The first one is that there is reproduction, individuals reproduce and lead to progeny's, then in a crowded environment there is competition between these individuals. And because of mutations happening during the process of reproduction, there is variability in the progeny's produced in one generation to the another and these variations mean that individuals are differently adapted to survive in the particular environment that they are living in.

So, what going we are going to start with in understanding the mathematical formulation of evolutionary dynamics, is assume a microbial population the simplest case that we know. And for the sake of simplicity we are going to talk about the most common bacteria E-Coli, about which we know the most of all the bacteria that we know. And understand these 3 basic principles associated with evolution, reproduction selection and occurrence of mutations. So, if we are going to start and try and represent these 3 processes.

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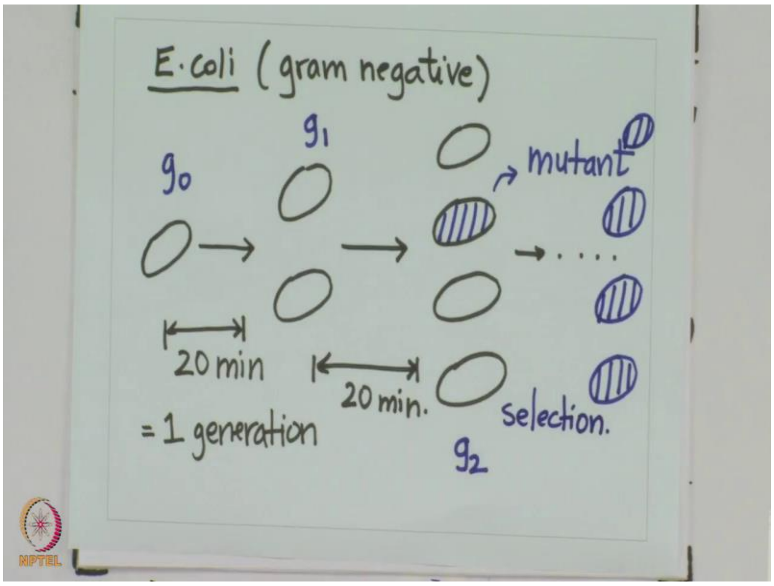


Imagine a single bacterial cell and we know that bacteria divide by fission. So, this single bacterial cell and for the sake of simplicity we are going to say this is E-Coli, which is a gram negative bacteria. So, and this divides by fission. So, when you grow E-Coli in an environment where nutrients are rich and the bacterium has all the nutrients available to it is for it is growth, the E-Coli bacterium divides every 20 minutes or so roughly.

So, we call that time a time of one generation. So, this is 20 minutes and this a important time in terms of evolutionary dynamics that this is equal to 1 generation. Upon completion of 20 minutes bacteria divides and we have 2 progenies, at the end of 40 minutes the 2 progenies, will themselves be ready for division and at the end of the time equal to 2 generations. We are going to end up with 4 bacteria and these processes will continue in the future provided the resources that are available to the bacterium are not constrained at any way. So, this generation is this time is 20 minutes this time is also. 20 minutes this is the dynamics of reproduction that is happening in growth of an E-Coli cell, but now we want to understand the other 2 facts associated with the evolutionary dynamical processes which are mutation and selection.

So, again let us go back to our go back to our cartoon, and let us imagine that one of the progenies which was produced in generation 2. So, this we call as generation 0 g 0, we call this as g 1 the first generation and we call these 4 as belonging to generation 2, g 2. Now let us assume that while the DNA was being replicated and the bacteria dividing from one to 2 the DNA replication was not particularly faithful in one of the cases and this particular cell has a mutation occurring in it. So, genetically these 3 are identical while as the fourth bacteria the shaded one in blue here is not identical and is carrying a mutation. This is the mutant whose DNA is not identical to the other 3. Now this mutation is likely to confer certain advantage or disadvantage to the bacteria depending on the precise nature of the mutation that has happened. The mutation may make the bacteria more fitter as in it might enable to enable the bacteria to grow faster in the environment in which we are doing this experiment, or the mutation might make the bacteria less well equipped to survive and multiply in the environment that it is being grown in.

There is also another class of mutations which are called neutral mutations, where the happening of this mutation does not in any way change the growth rate associated of that bacteria in this particular environment, but the point being that because of this mutation happening, there is a change in the rate at which this mutant bacteria is dividing compared to the other 3. And now if all 4 of them are competing for resources in a particular environment that is going to mean that the environment is going to preferentially select either the parent type. Or the mutant type and in case the mutation that has happened here is favourable in nature it allows the bacteria to grow better than the wild type then as we go forward in time this mutant is going to eliminate the original genotype that we started with, and we are going to end up with after a number of generations we are going to end up with bacteria which are all mutant genotypes. This; the mutant bacteria would have out competed the initial genotype that we started with.

So, that is we see here the 3 processes happening this is reproduction happening, this here represents mutation happening and once the mutation has happened we selection happening. So, in this in this initial part of the course we are going to talk about some very basic models which allow us to capture the dynamics of these 3 process. So, to start with we will first start with the most simplest models associated with reproduction of bacteria.

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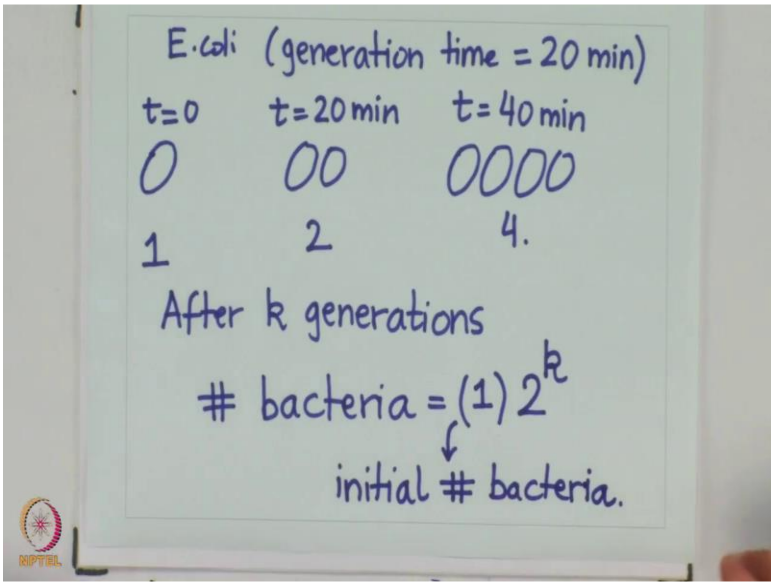


So, again we are going to assume E-Coli with generation time equal to 20 minutes. And if we assume that at t equal to 0, we start we start with one bacteria, at t equal to 20 minutes, we have 2 bacteria this is the number of bacteria, 1 2 t equal to 40 minutes we have 4 bacteria and so on and so forth. So, you can easily see a pattern developing here, that after k generations where each generation represents time it takes for the E-Coli bacterium to divide, which in this case is 20 minutes. The number of bacteria after k generations can be represented as one, which is the initial number of bacteria that we started with times 2 to the power k. One here represents the initial number of bacteria. This type of an equation is what is called the difference equation and we can re write this as; we can rewrite this as bacteria at the end of k generations is equal to 2 to the power k times N naught where N naught is the initial number of bacteria.

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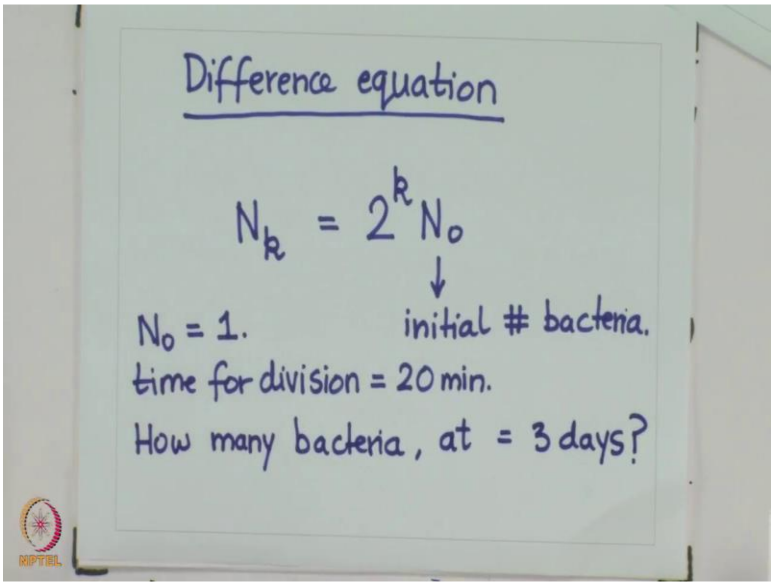


So, with this equation this is called the difference equation, let us try and do an example and calculate how many bacteria are we going to end up with starting with just one bacteria and if we allow for unconstrained growth for a time period of let us say 3 days. So, if we want to if you are given that N naught is equal to 1 and time for division is equal to 20 minutes, how many bacteria are we going to end up with are we going to end up with at t equal to 3 days. So, let us try and work through a simple example and just get an just get an estimate of what is the ball park order of magnitude number of bacteria that we are looking at for the simplest bacteria E-Coli that we know of when it is allowed to grow in conditions which are very favourable for growth the bacterium is dividing every 20 minutes for 3 days.

Let us try to work this through. So, we know that one generation is equal to 20 minutes.

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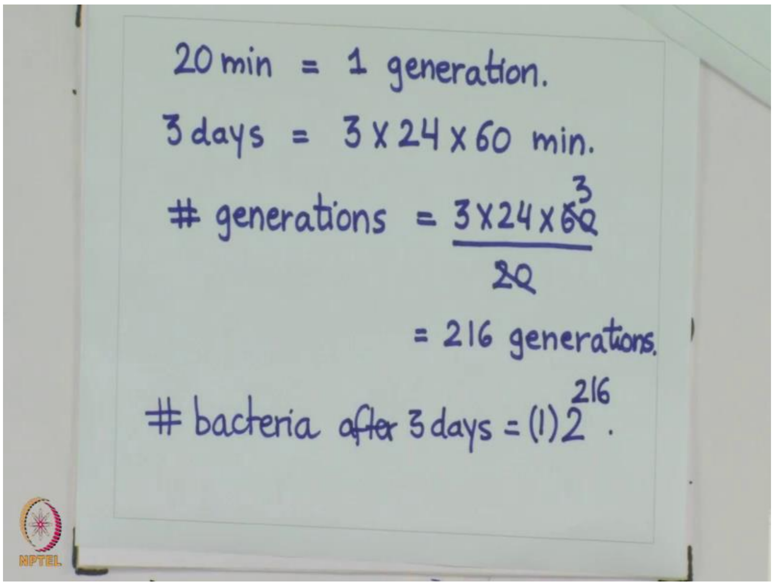


So, in 20 minutes we have one generation. And what we are interested in finding out is that how many generations pass in 3 days. So, 3 days is equal to number of days into number of hours in each day, into number of minutes in each hour this many minutes and now when we want to calculate the number of generations. This comes out to 3 into 24 into 60 this many minutes and we know one generation is equal to 20 minutes. So, we divide this by 20 and we get 216 generations. So, going back to our earlier result where we say that number of bacteria after k generations is just equal to 2 to the power k times N naught where N naught is the initial number of bacteria if we plug k is equal to 216 and N naught is equal to 1 we get the number of bacteria which are there after 3 days. So, number of bacteria at 3 days is equal to N naught which is one in to 2 to the power 216.

Now, this is a very large number or a small number we want to get a relative sense of the magnitude of this number. We will get to that in a second, but before we do that we want to talk about another way to capture the dynamics of growth of unconstrained growth in bacteria. And to do that we will use differential calculus.

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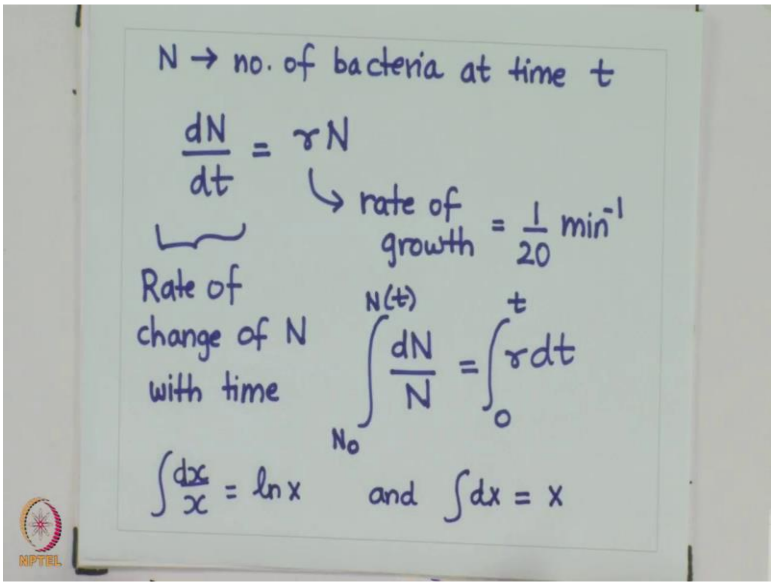


And we will say if N is the number of bacteria, at time t, dN by d t can be simply be written as r times N. Where dN by d t is the rate of change of N which is the number of bacteria with time and r is the rate of growth, which in our case we know that the bacterium divides every 20 minutes. So, the rate of growth is one division every 20 minutes. So, the rate of growth has unit is time inverse which is 1 by 20 minute inverse. So, this is a differential equation formulation of modelling bacterial growth. And now we can simply integrate this differential equation to get an analytical expression for getting and approximation of number of bacteria at time t, when we know we are starting with a particular number of bacteria N naught at t equal to 0.

So, again this is this is basic calculus from eleventh or twelfth standard what I am going to do is separate the variables and integrate the equation and arrive at the analytical form of the solution. If we try and do that we get dN upon N, I am bring N from here to the other side and I am bringing d t, to the other side equals r d t and now I have left hand side which is only dependent on N and the right hand side which is only dependent on t and when I integrate the 2 from time equal to 0 to time t equal to t and at t equal to 0 the number of bacteria that I started with was N naught at t equal to t the number of bacteria that I am going to end up with this N t. So, now, this the solution to this formulation invokes some remedy associated with how do we solve these equations. And what we know from calculus is that integral of d x upon x is equal to ln of x and integral of d x is just equal to x.

So, we are going to use these 2 results to integrate the left hand side and the right hand side of the equation. This is of the form my left hand side of the equation is of the form d x by d x. So, this is just the left hand side upon integration just becomes a ln of x and the right hand side is of the form integral d x because r here is a constant which does not change with time. So, it can be pulled out from the integral sign and integral of d t is just going to be t.

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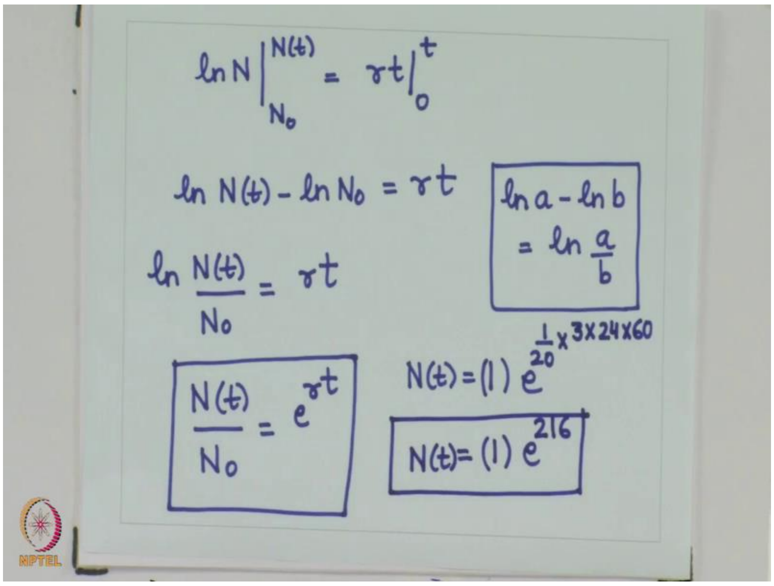


So, taking r solution forward, but we end up with is ln of N and the limit is for this r N naught at equal to 0 and t at equal to t is equal to r t, t equal to 0 and t equal to t. I apply the limit is in which doing after which I get ln of N t minus ln of N naught equals r t. And I am going to use a very basic result from logarithms which is that ln of a minus ln of b can be written as ln of a by b. So, I am going to use this result to write my left hand side as ln of N t divided by N naught is equal to r t and then I want to get rid of the log and to that I take the exponent of both sides which gives me the expression N t by N naught is equal to e to the power r t.

So, that is my answer to the E-Coli problem where I am trying to solve it using the differential calculus formulation. So, how does this compare the next thing, we want we are interested in is comparing that how does this answer compare with answer that we just derived from the difference equation. So, we want to, we want appropriate numbers for t which we know is 3 days is what we are interested in. We know r is equal to 1 by 20 and we know N naught is equal to 1, which is just a number of bacteria that we started with if we plug those in we get N t is equal to 1 which is N naught in to e to the power r is just 1 by 20 and t is just 3 days in to 24 hours in to 60 minutes per hour. This comes out to 1 into e to the power 216 N t. So, we have tried to solve the E-Coli growth equation using 2 different approaches here. And we seem to getting different answers depending upon which approaches that we are talking about. So, let us compare our 2 answers and try to understand; where is the difference coming from?

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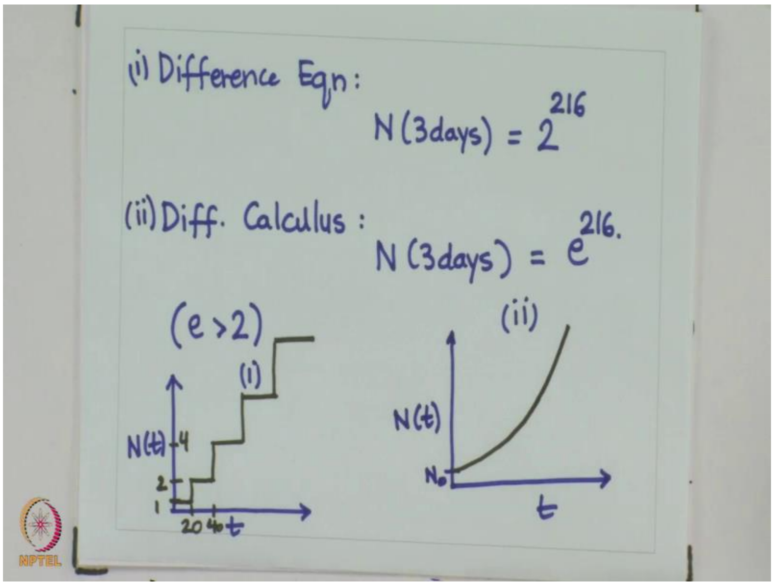


In the first approach in the difference equation approach, the number of bacteria at t equal to 3 days was 2 to the power 216. In the differential calculus approach, the number of bacteria after 3 days was equal to e the power 216. Now we know that e is more than 2 it is exact value is 2 approximately 2.3. So, the differential calculus answer is bigger than the answer that we are getting from the difference equation. Why is that? The case is what we want to understand first, because it is fundamental that we realize that we model growth as accurately as we can. And the reason for that is if we plot the number of bacteria in growth equation, from the first approach, this is time t and this is number of bacteria at time t. If we try and plot this how does this graph look like. And what it is going to look like is that at t equal to 0 I start with one bacteria. And it is it remains at one bacteria. At t equal to 20 minutes division takes place and the suddenly the number of bacteria goes up to 2. At t equal to 40 minutes the number of bacteria between 20 and 40 minutes stays at 2, and as we approach t equal to 40 at exactly t equal to 40 division takes place and the number of bacteria goes up to 4. And the same story keeps repeating itself over and over again every 20 minutes, which is the number of which is the amount of time which is equivalent to one generation in our problem. And we get the step like increase in number of bacteria as we keep going forward in time.

Essentially what we need to realize is, that in this formulation we are modelling growth as the very discreet event every single bacteria takes exactly 20 minutes to replicate it is doing the preparatory work producing all the proteins copying it is DNA for 20 minutes, and at sharp 20 minutes the bacteria divides and we get 2 progenies. So, growth is happening in very discreet steps like this, in the formulation associated with the difference equation.

In the second formulation; however, we have something different happening. When in the differential calculus formulation if we try and plot our solution t with N t, and observe the number of bacteria varying by time, and we start with N naught, the number of bacteria as we look forward in time increases in a very smooth manner like this. And the solution keeps going up and is approaches infinity if allowed to go for very long period of time. And the reason this solution is not discreet as compared to the difference equation is because in this formulation in the differential calculus formulation we have assumed there is an implicit assumption that the division time for bacteria is not 20 minutes exactly. In fact, 20 minutes division time only represents the average division time associated for bacterial growth. The actual division times for an individual bacteria are spread around the value of 20 minutes. Some bacteria end up multiplying for slightly faster that 20 minutes some bacteria end up multiplying slightly after 20 minutes, and 20 minutes is just an average representation of an average how long does it take for bacteria to divide.

What that results in is that you have some bacteria which replicates slightly ahead of 20 minutes which means you have increased your numbers before the generation time has actually arrived. And these bacteria which replicated ahead of the 20 minutes time would then in turn replicate again before the second generation time has happened. Which is 40 minutes and this cumulative affect leads to an answer which is bigger for differential calculus and the difference equation. So, you should ask this question to yourself at this point that which of the 2 approaches do you think is more represented at the biology of E-Coli division that we understand. And it is very inconceivable to imagine bacteria or any life forms for that instant to be to be respecting constraints such a division happens at that particular instant of 20 minutes only. There is bound to be variation in biology and some bacteria are going to by just natural variation in the process divide ahead of 20 minutes some bacteria are going to lag in divisions and divide after 20 slightly they are going to end up taking slightly more that 20 minutes.

So, that natural variation is a fundamental is a fundamental property associated with all bacterial species. And hence this; the differential calculus approach is very representative of what actually happens in in a growth process. And this answer although it is larger is a much more representative of what would E-Coli numbers be if allowed to grow unconstrained for 3 days.

We want to understand 1 or 2 more things associated with this one is what have been naught captured here.

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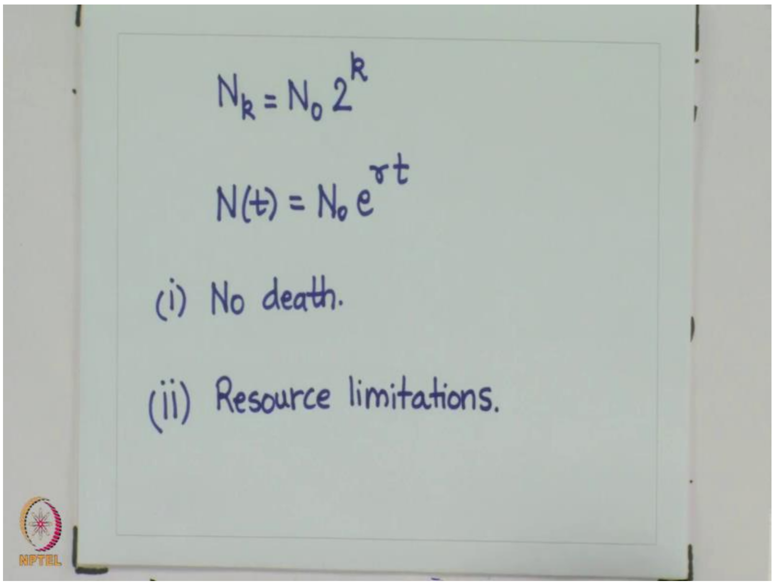


In this formulation of either N after k generations is equal to N to the power 0 2 to the power k where is k is the number of generations of the other formulation which set N t is equal to N naught in to e to the power r t, where r is the growth rate and t is the time for which growth has happened. We want to understand or a question that you should ask yourself at this point is that, what are the mechanisms of growth that we have not captured in these 2 formulations. So, what is it the first one that comes to mind is that there is not death in this model. In either of these 2 models we are not talking about death of bacteria at all. So, that is the first thing that we want to incorporate in our models as we move towards more realistic models of bacterial growth.

And the second thing is that we want to understand or that we want to incorporate in our model is that unconstrained growth for 3 days, we want understand how likely is it happening in real environments. In real environments constraints are very likely to set in very fast and competition for resources would mean that resources resource availability becomes a constraint and bacterial growth slows down because there are just not that many resources available to support growth for every single bacteria in the individual. So, there is no concept of resource limitation in either of these 2 models and both of them allow for unconstrained growth for as long as it takes both models allow for unconstrained growth for as long as the bacteria are allowed to grow, which clearly is not is not conversant with reality of these processes as we understand them. So, as we go forward in the next part of this lecture, we will talk about how to incorporate these 2 features in out model and develop it from there.

Thank you.