Evolutionary Dynamics

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Week 04

Lecture 18

Hi, welcome back to the next video. In this video, we'll talk about one more approach to modeling growth of bacterial cultures. So just by way of recap, we have done exponential growth which we found out that was extremely unrealistic because the numbers blew up very, very fast. In the last video, we talked about logistic growth which we found was extremely successful at capturing different facets of growth in a batch culture.

the near exponential growth, the slowing down phase, and finally growth approaching zero. This however, this was a very useful model But this was only appropriate for a batch culture. And we want to discuss one more model for capturing growth dynamics of bacterial species. And after that, we'll be armed with these three different models.

And depending on the context in which we are discussing results, we will be able to bring these models back into the system we are discussing and analyze what is going on. So the model that we are going to do today is going to be involved with capturing growth in a chemostat. Let me just describe a chemostat once again. This is what is called a chemostat. So this is a tank with volume capital V.

This is the volume of liquid that's present in the tank. This is stirred. And what that means, the stirring is important to define because what it means that the constituents of the tank are well mixed. which means that if I were to take small sections of this, if I were to analyze what are the concentrations in this cube here or in this cube here and so on and so forth, I might take a small volumetric sample from any part of this tank. Because this is well mixed, the concentrations of all constituents of this tank are exactly the same here.

And when I say that constituents of everything, all constituents have the same concentration, they would include all metabolites. So let's say growth is taking place on glucose. So glucose concentration is the same. Let's say acetate is a byproduct of the metabolism of the bacteria present here and it is being secreted into the media. So if I measure acetate concentration at different locations in this reactor, the acetate concentration is also the same.

If I look at the number of bacteria present per unit volume, in other words, if I measure the density of bacteria present at any part in this, at any location in this chemostat, that is also a constant. So any chemical concentration or even the concentration of organisms in this chemostat is constant. And that is the significance of saying that this is a stirred-tact reactor. In addition, what defines a chemostat is that it has an inlet and an outlet flow. V0, V0.

It has an inlet... and outlet inlet has flow of fresh media. So, this is unused resources. And it is important to note that it is only media. There are no bacteria that are present in the inlet stream.

So, this is just nutrients coming in. And this is happening at a rate V naught, let us say milliliters per hour. So, the units of these inlet streams are equal to volume per time. the unit of, this is just the tank capacity, so the units here is just volume. The unit here is volume per time.

And this is fresh media. At the opposite end, outlet is flow out of spent media which is also happening at the rate V naught and so also happening at rate V naught these two V naughts are exactly the same. which maintains the volume of the reactor at V because at any given point in time, in every given unit of time, V naught is being added to it and V naught is being taken away from it. So, the constant, the volume of the tank remains constant at capital V.

Now since this is stirred and concentration everywhere in this reactor are exactly the same, what is being taken out is what is present in the reactor. And where in the reactor doesn't matter because reactor is well mixed. So this is whatever is present. So bacteria are being removed. Unused resources are being removed.

spent metabolic waste is being removed and so on and so forth. And this hemostat settles into an equilibrium when the rate of removal of bacteria is exactly matched by the rate of generation of bacteria because of fresh nutrients coming in. So these fresh nutrients coming in provide resources for more growth to take place And in a unit amount of time, so let us say this is V0 ml per hour. So in this one hour, let us say N naught number of births take place.

This is the number of bacteria that are generated by division in this one hour. But in this one hour, I have also removed V naught amount of liquid from the reactor. And if this V naught amount contained N naught number of bacteria, that means that I added N naught number of individuals via growth supported by the fresh media that I added to the reactor. And this is exactly balanced by removal of N naught individuals from the reactor because of this exit stream that I have right here. So these two balance each other out and then the number remains constant.

So what this means here is that as a result of the balance between growth and exit—so balance between growth and exit—implies that the number of bacteria in that tank remains constant. And it remains constant, and that's sort of the key feature. So I hope this makes sense, and then we'll be able to move forward with this. I've been using the word 'chemostat tank' and 'reactor' interchangeably.

This is also called a continuous stirred tank reactor. It's a continuously stirred tank reactor—CSTR, continuous stirred tank tank reactor—or it's also referred to as a chemostat. So these two are used interchangeably, and that shouldn't throw you off. All right, so let's see.

Now let's take a scenario where we have a chemostat. The volume of the liquid is capital V. It has an inlet stream V_0 and an outlet stream V_0. But instead, the context that we want to look at this in is that it has a species A and a species B. And what we want to understand is that if we start this chemostat from a steady-state operation, so the total number is fixed—it's N—because growth is facilitated, exactly the same amount of growth takes place as is removed from the exiting V_0 stream.

And at the start at t equal to 0, when this is started, A and B are present in steady state and in some numbers. What we want to understand is how the number of individuals of species A and species B changes with time. So, to write this more formally, we say that at t equal to 0, N_A is the Let me say that again: at t equal to 0, N_A is the number of A-type individuals, N_B is the number of B-type individuals, and N_A plus N_B equals capital N, which is the total number of bacteria in the chemostat. So let me redraw that.

So we have the two species, A and B. And it's the total number of bacteria in the chemostat, but N is also the carrying capacity of the chemostat. So what this means is that we are starting at the steady state of the chemostat, where it couldn't possibly have any more individuals. It's completely occupied by A- and B-type bacteria that are occupying it. These numbers could be anything. And what we want to understand is how the numbers change

How do numbers, which means N_A and N_B, change with time as we move forward? And intuitively, we can have some ideas about it. We know that the chemostat is being occupied by A and B, and these two species are going to have their respective growth rates. Let us say this one is growing at rate R_A, and this one is growing at rate R_B. So, intuitively, we can say that if R_A is greater than R_B,

If this is the scenario that we are looking at, then as time moves forward, N A will increase and N B will decrease. Because this is growing faster than B, which means that A is going to grow faster. The number of individuals of type A is going to increase faster, and type B is going to increase slower. And to think a little more deeply about that, why that will happen is that imagine, Imagine that they are both being replaced at the same rate.

So the chance of who goes out is the same for either A or B, but if this is replicating faster compared to the B type, then A is adding to its number faster compared to B. However, they are both being washed away from the reactor at the same speed. So because of the virtue of its faster rate at which it is adding to its numbers, A is going to grow faster compared to B. And eventually, if we let this play out for a long time, all of the B types should be replaced by A type individuals, and eventually only A type will be left. Eventually, only A type will be left. And similarly, the opposite argument works as well: if Rb is greater than Ra, then as we move forward in time, B type individuals will replicate faster. They will outcompete the A type individuals, and eventually, B type will take over the chemostat.

On the other hand, if Ra is equal to Rb, both species are growing at exactly the same rates, then the numbers—the relative frequencies—should stay the same. But through this model, what we want to try and understand is to build a quantitative understanding of how much time it will take for a population of A to be 90% of the entire population present in the chemostat, or how much time it will take before there are only 10 individuals of type B left in the entire reactor, whose carrying capacity is, let's say, 10 to the power 11, and so on and so forth. It's this type of quantitative framework that we seek to develop. So to do that, let us redraw the chemostat. V naught exit at V naught capital V. This is A and this is B.

So, to develop that quantitative framework, let us take a look at this. So, for A-type individuals, their number is N_A. B-type individuals, their number is N_B. N_A plus N_B is capital N, which is also the carrying capacity of the chemostat. If that is true, then what we are going to do is define a quantity: the fraction of A-type individuals. So, the fraction of A-type individuals is simply going to be—let us call it X—is simply going to be N_A divided by N_A plus N_B. But since this is a constant, the carrying capacity is constant with time.

Let's call it some K. So this is just equal to N_A upon K. Similarly, we have the fraction of B-type individuals. And let's call it Y, and that's just equal to N_B divided by N_A plus N_B, which is equal to N_B upon K. And what we should note here is that X plus Y exactly sums up to one. That is always going to hold because There is no other third type of individual present in the population. A and B are all there is.

And the population size always remains at the carrying capacity. So, any increase in the number of A is going to come at the cost of the same amount of decrease that happens in the number of B-type individuals. And in this framework, instead of tracking actual numbers, we are going to track how the fractions of these two types of individuals change with time. So, we will not develop an equation for dN_A by dt. Instead, we will develop an equation for dX by dt.

So, we won't do this, but instead we will develop an equation like this. So, dx by dt will be comprised of two parts. The first part is what adds more a? So the first part is what adds more A-type individuals minus what removes A-type individuals. In this chemostat, the question we are trying to ask is that A-type individuals are being generated by growth and this growth is going to add to more A-type individuals.

However, A type individuals are also being removed from the chemostat by the exiting stream. And that is the second term that we are writing down here. So what adds is the answer to this is just growth. So that is easy to write that we will just say that is RA times X. This is the growth rate associated with A and X is a representative of how many A type individuals are already there in the chemostat. What removes A type individuals from this environment is simply the exit stream.

But it's not easy to say what is it, how many A type individuals are exiting per unit given amount of time because it's not just A type, B type individuals are also exiting. So to estimate this quantity, we'll make an assumption that rate of exit is proportional to frequency. What that means is that if A and B are present in 50-50 ratio inside the tank, then if I check this exiting stream that how many are A type and how many are B type, in the exit stream also, they'll be 50-50. However, if A is to be in the tank is 90 is to 10, then in the exit stream, I will also find them in a ratio 90 is to 10.

So whatever is present inside the reactor and is well mixed is going to be seen in the exiting stream associated with this reactor. And that's not a bad assumption at all to make. So what this tells me is that the exit is going to be proportional to X. The more A there is, the more of A is going to be washed away from the reactor. But this needs to be multiplied by a proportionality constant. So exit, if I write this as the rate of exit

of A, it's proportional to X, but I don't know what to multiply. What is the proportionality constant? So since I don't know that here, I will say the rate of exit of A is simply equal to phi times X. So I will just multiply this by phi and leave it at that, where phi is some proportionality constant, which I don't know, which as yet I do not know. So that gives me the first equation that I have to work with. And hopefully, this makes sense.

So similarly, let us rewrite the first equation again. We have dx by dt equals rax minus 5 times x. Similarly, we have the other equation for species B, which we can write as dy by dt equals rb times y minus phi times y. Now, remember phi is a proportionality constant that I know exists, but I do not know what it is. What we are going to do is sort of a mathematical trick here, which is that we are going to add these two equations. Add the two equations.

And what this tells me is the left-hand side becomes dx by dt plus dy by dt equals ra times x plus rb times y. Minus five times X plus Y. And now, we have to understand each of these three terms and what they actually represent. First, let's start with the easiest one: X plus Y. Remember, what is X? X is just the fraction of X, the fraction of A-type individuals. Y is just the fraction of B-type individuals.

And both these fractions, when added up, simply equal one. Because there is no other type of individual in the reactor. So X plus Y can be simply removed, and we just have one. Phi is something that we don't know, so we'll leave it at that. Let's move to the left-hand side.

Let's see what each of these two terms means. dx by dT means how x is changing with time, and dy by dt means how y is changing with time. But remember, we started with this assumption that this chemostat is operating at its steady state, which means that if I have A and B types of individuals and let's say they are at a 50-50 ratio, then as we move forward, these ratios will change. But they will always add up to one.

So if there is an increase in A type individual, it has to be matched by a decrease of the same quantity in the B type individuals. Or if B type individuals increase, that has to be matched by the exact same decrease in the A type individuals. So these two are not independent with each other. In fact, if x is increasing, y is decreasing at same rate. which means if this is positive, this is the exact opposite, that is, this is of the same magnitude but negative, or if x is decreasing, y is increasing at same rate.

What that means is, so let us say if dx by dt is increasing at 0.04 per time, if dx by dt is positive and is this value, what that implies is that dy by dt is simply equal to minus 0.04. add them together and we get 0 and so on and so forth. So, these two quantities actually because of the setup that we have when we add them together is equal to 0. So, what we get is phi is equal to RA times X plus RB times Y and now we come to this middle term and try and understand what this is. And this you should realize is the mean fitness or mean growth rate of the population.

$$\frac{dx}{dt} = x(r_A - \emptyset)$$

And

$$\frac{dy}{dt} = y(r_B - \emptyset)$$

What that means, if specie A is growing at, let's make a table to understand this better. Let's say this is RA, no, let's say this is R. So for A, let's say RA, growth rate of A is let's say 0.4 and growth rate of B is let's say 0.6. Then if the if any given point in time x is equal to 0.5 and y is equal to 0.5 which means the number of A type individuals is 50 percent number of B type individuals is 50 percent then the mean growth rate is simply equal to what is the growth rate of A which is 0.4. times how many A type individuals are there in the population, which is 0.5, plus what is the growth rate of B, which is 0.6, times how many B type individuals are there, which is 0.5. So this comes out to 0.2 plus 0.3, which is 0.5, which is the exact mean of these two because the population numbers were 50-50.

$$\emptyset = r_A x + r_B y$$

If, however, later on X becomes 0.1 and Y becomes 0.9, then phi becomes R A is 0.4 into 0.1 plus R B is 0.6 into 0.9. This equals 0.04 plus 0.54, which is 0.58. So, now, Because of the change in the fraction of individuals of each kind in the population, the mean growth rate has increased to much closer to the growth rate of pure B. And we will see some of the implications of this in the next video and continue further.

Thank you.