

Miles Fore

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Summer 2008 Summer REU Project

There were two goals of this summer's REU project. First was to get me educated enough in differential equations to be able to solve problems involving differential equations, and second to actually solve (or model) some problems using what I had learned. I must admit that at the first of the summer I had only a vague idea of what this project would entail, and I had no idea what problems we would look at for the research part. I did, however, have faith that Professor Tucker would be able to guide me so that I would be able to learn something, get some work done, and overall do something worthwhile.

The first goal of this project was guided by Professor Tucker's differential equation notes (and also partly by the book *Differential Equations and Dynamical Systems*, author: Perko). During this time I would read the notes and try to work out some of the problems (exercises) in them. I would do this until I became sufficiently confused. I would then meet with Professor Tucker in the mornings for a couple of hours so he could "drag my sorry ass" through the material and help clarify the concepts. Here is a brief (very brief) outline of the material covered (and knowledge I gained from) in the notes:

The first part of the notes deals with linear systems. The main ideas addressed here are existence and uniqueness of solutions, and techniques for computing such solutions (Chapters 1-4). Chapter five then gives an analysis of the behavior of solutions to differential equations using just the equations. The linear equations part of the text is finished with some non-constant coefficient cases.

The next section of the notes concerns non-linear ordinary differential equations. Some of the big ideas in this section are existence and uniqueness, and perturbation (whether small changes in the initial data will result in small or big changes in the behavior of the system). This is important for real world applications, as measurements are never exact.

The first two sections of the notes dealt with initial value problems. The

third part of the notes involves boundary value problems. This section was mainly a preparation to look at Sturm-Liouville systems, and then to actually look at them.

Some time ago Professor Tucker was asked by some medical students if he would be able to make a mathematical model for them of something called a measured response. This was our goal for the research part of this summer's project.

It seems to me that when they asked him this they weren't able to say exactly what they meant by a measured response (I wasn't there), but rather gave examples of a measured response with hopes that a suitable model could be made of this behavior. Some of the examples they gave were of a blood clot forming, and macular degeneration. Let's look at the blood clot example first. Imagine a vein somewhere in the body being damaged, torn open. A blood clot forms to stop the blood from leaking out. If, however, too big of a clot forms and the vein is completely blocked off no blood can flow past the clot. Clearly the clot must not be too big nor too small. It is said to be a measured response to the injury. The other example given was that of macular degeneration. With macular degeneration little spots appear on the macula (on the back of the eye). The macula then begins to degenerate around the little spots, spreading outward. The interesting thing is that it stops, and the area of each of the damaged spots tends to be about the same. It's as if a seed is planted in the macula, and the body responds to it allowing it to grow only so far.

After thinking about these examples for some time Professor Tucker and I came up with some other examples that we believe exhibit a measured response (a still undefined term). Some of these examples are:

Population growth- Every environment has a carrying capacity- that is the size of the population seems to exhibit a response to the environment around.

An epidemic- Here a disease spreads in a population, it can be thought of the same way as a population growth.

A fire spreading- Again the same situation as the epidemic and population, but the "carrying capacity" is a result of the number of items that can be oxidized (burned).

To figure out what a measured response is we figured a good place to start would be to look at examples and try to find the essence of them. In this paper I will present models for a blood clot, macular degeneration, and population growth, as well as a brief analysis of each. I will start with the blood clot model first.

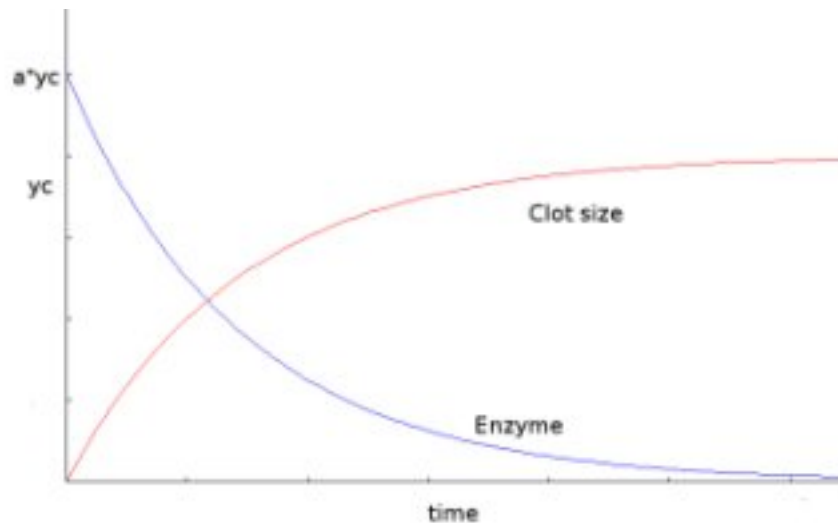
My understanding of how a blood clot forms is this: The cells that are damaged release an enzyme. This enzyme causes platelets to cover the damaged cells while they heal. I am assuming that the enzyme stays on the membrane of the cell. Otherwise it might be carried downstream by the blood, and the clot would not form over the wounded area. Let's call the amount of enzyme released at time t , $x(t)$, and the size of the blood clot at time t , $y(t)$. Also, let y_c be the size of the covering clot when the damaged cells are fully covered.

Then $x(t) = \alpha(y_c - y(t))$. That is the amount of enzyme exposed to blood at time t is equal to some constant multiplied by the amount of exposed damaged cells. In other words each cell releases a fixed amount of enzyme when damaged.

We will also assume $\dot{y}(t) = \beta x(t)$. That is the size of the clot grows proportional to the amount of enzyme present. Our system is then:

$$\begin{aligned}x(t) &= \alpha(y_c - y(t)) \\ \dot{y}(t) &= \beta x(t) \\ y(0) &= 0\end{aligned}$$

Then $\dot{y}(t) = \beta x(t) = \beta\alpha(y_c - y(t))$. Setting $K = \alpha\beta$ we have $\dot{y}(t) = K - \alpha\beta y(t) \Rightarrow \dot{y}(t) + \alpha\beta y(t) = K$. Solving the homogeneous equation $\dot{y}(t) + \alpha\beta y(t) = 0$ we get $y_h = c_1 e^{-\alpha\beta t}$. Also notice the particular equation $y_p(t) = y_c$. Thus $y(t) = c_1 e^{-\alpha\beta t} + y_c$. Using the initial data $y(0) = 0$ we get $0 = c_1 + y_c \Rightarrow c_1 = -y_c$. Therefore $y(t) = -y_c e^{-\alpha\beta t} + y_c = y_c(1 - e^{-\alpha\beta t})$. Substituting this into the $x(t)$ equation we get $x(t) = \alpha(y_c - y_c(1 - e^{-\alpha\beta t})) = \alpha y_c e^{-\alpha\beta t}$. A graph of the solutions looks like this:



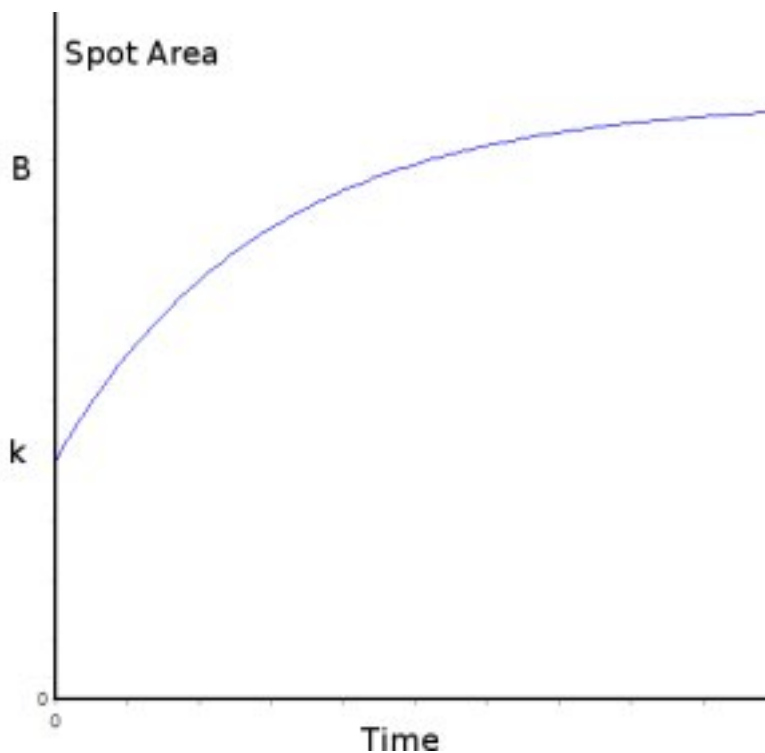
Notice that as $t \rightarrow \infty$ the size of the clot, $y(t)$, approach y_c , as it should, and the amount of exposed enzyme approaches 0, as would also be expected. Of course in real life these values actually achieve y_c and 0, respectively, but this model is based on the cells and enzymes being continuous- they are not. They are discrete things. Other than that it behaves as would be expected. One way to check this model would be to measure the amount of enzyme present, after an injury, at three equally spaced times: $t = 1, 2, 3$. Notice that according to the model $x(1)/x(2) = x(2)/x(3) = e^{\alpha\beta}$. If $x(1)/x(2) \neq x(2)/x(3)$ then the model isn't very good. If these measurements are made then $\alpha\beta$ can be computed. Then if there was a way to measure how many enzyme molecules are released when a cell is injured it would be easy to calculate β .

Possible uses of this model: If both α and β are known measuring the enzyme at anytime (and setting $t = 0$) would give an estimate of the size of the uncovered portion of the wound. Furthermore, if it is known about how long ago the injury occurred it would be possible to tell about how big the original wound was.

Now let's look at the macular degeneration case. This example was a little bit more difficult to model because we didn't know what causes it. To be honest, I only have a vague idea of the behavior it does display. We developed two models that describe the behavior of the macular degeneration as we understand that behavior. With this model I am assuming that the part

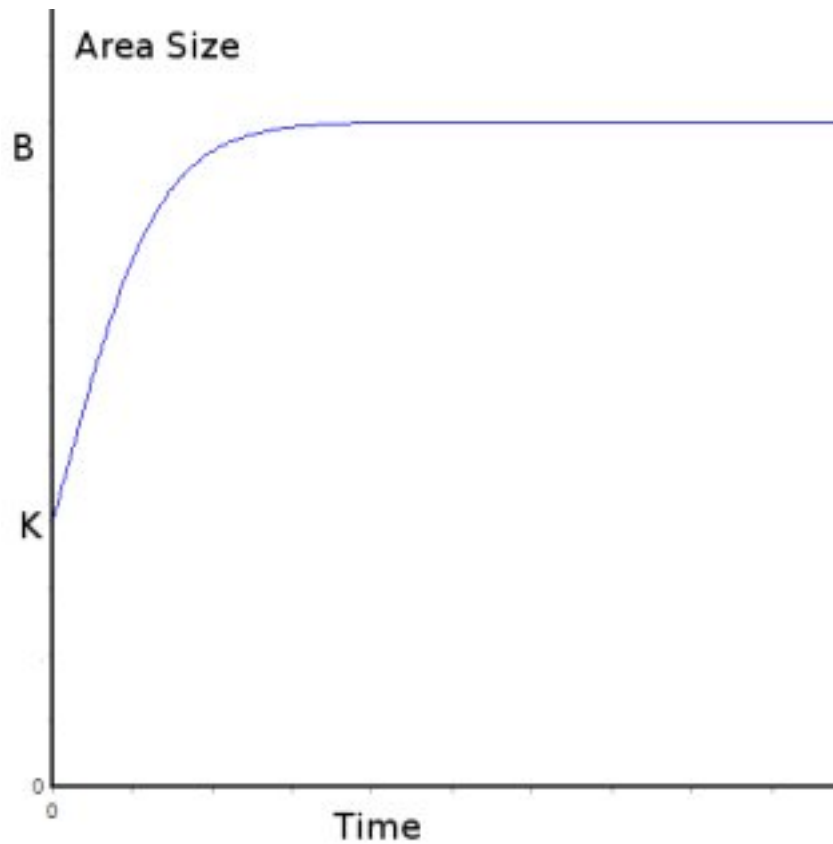
of the macula that deteriorates is where some sort of nerve ending is. That is why it stops. This may also explain why there is a scattering of spots- it may actually be do to a problem futher back from these endings where they come together. Anyway, that is the basic assumption of this model.

Here is the first model: $\dot{x}(t) = \alpha(\beta - x), x(0) = K$. Here x represents the area of the deteriorated spot, and t is the usual time variable. At time $t = 0$ there is the initial spot that appears, which is of size K . If we rearrange this equation we get $\dot{x} + \alpha x = \alpha\beta$. Clearly the solution to the homogeneous form of this equation is $x(t) = e^{-\alpha t}c$. Assuming a particular solution is of the constant form we find that $x_p(t) = \beta$. Thus the general solution is $x(t) = ce^{-\alpha t} + \beta$. Solving for c using the initial condition $x(0) = K$ we get $x(t) = (K - \beta)e^{-\alpha t} + \beta$. Here is a picture of that:



Notice it does what we wanted- to start out as a small amount and grow to a certain size. However, we can find another model which also does this:

$\dot{x}(t) = \alpha x(\beta - x), x(0) = K$. Solving this equation we find $x = \beta / ((\beta/K - 1)e^{-\alpha\beta t} + 1)$. Here is a picture showing the solution:



Notice that this model approaches the the maximum spot size faster. It should be easy to see that there are uncountably many models that do what we want. This begs a big question as to which model we should choose. Without knowing anything else about the thing we are modeling I believe it is best to choose the model that is computationally the simplest.

The last example I was going to present in this paper is that of population growth. This, however, has already been modeled fairly well. The equation being used is the Verhulst equation, also called the logistic growth equation. The equation the Verhulst came up with to model population growth is this: $\dot{p} = rp(1 - p/k), p(0) = p_0$. Here p represents the population at time t , r is the growth rate of the system, k is the carrying capacity, and p_0 is the initial population. The equation has been around for sometime and has the solution: $p(t) = (kp_0e^{rt})/(k + p_0(e^{rt} - 1))$.

In conclusion we really don't know anything. We do have a fuzzy idea of what a measured response is. It seems that a definite requirement is that the system have a stable equilibrium point (stable or asymptotically stable). One way to check this is to look at the Fréchet derivative at that point. If it has eigenvalues with negative real part then this is satisfied. If it has an eigenvalue with positive real part then it is not. If it has eigenvalues with real part 0 there is no definite answer, and the best way to go about it seems to be by using Liapunov functions. However, this requirement is definitely not sufficient, only necessary. We are, however, one step closer to finding the essence of the problems- if such a thing exists in these problems.