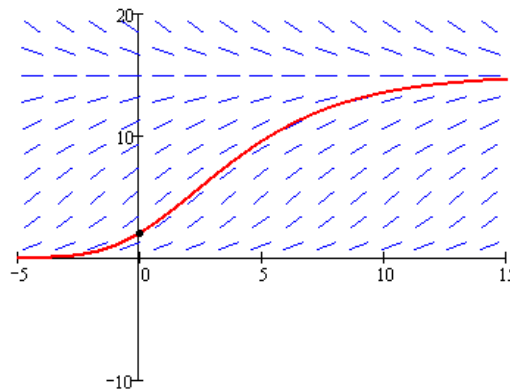


Observations on the growth of animal tumors indicate the size y of the tumor obeys the differential equation $\frac{dy}{dt} = -ky \ln\left(\frac{y}{b}\right)$ with k and b positive constants. This is known as the Gompertz growth law.

a) In this model of tumor growth, what is the range of y ? What does a slope field tell you about solutions to this equation?

It is always a good first step when considering differential equations to look at the slope field.

At right we see $\frac{dy}{dt} = -.3y \ln\left(\frac{y}{15}\right)$, but all others are similar. We see the point of inflection between 0 and 15 and the decreasing function for $y > 15$. This graph helps guide our investigation.



The maximum value appears to be limited to the value of b . I suppose we will see why in the ensuing work. The range appears to be $(0, b)$

b) When is the tumor growing most rapidly?

This is a standard, problem from calculus. The tumor is growing most rapidly when $\frac{dy}{dt}$ is at a maximum. So, we perform the classic optimization process on $\frac{dy}{dt}$ by setting the derivative of $\frac{dy}{dt}$ equal to zero. So,

$$\frac{d^2y}{dt^2} = \frac{-ky \left(\frac{dy}{dt}\right)}{b \left(\frac{y}{b}\right)} - k \left(\frac{dy}{dt}\right) \ln\left(\frac{y}{b}\right) = -k \left(\frac{dy}{dt}\right) \left(1 + \ln\left(\frac{y}{b}\right)\right) = 0.$$

Either $\frac{dy}{dt} = -ky \ln\left(\frac{y}{b}\right) = 0$ or $1 + \ln\left(\frac{y}{b}\right) = 0$. In the first case, $y = 0$ or $y = b$ are stable solutions and in the second case, $\ln\left(\frac{y}{b}\right) = -1$ so $y = \frac{b}{e}$. If y is not constant, then $y = \frac{b}{e}$ is the size at the maximum growth rate. Notice also that if $y > b$, then the function is strictly decreasing (we will use this fact later) and there is no maximum value. We need to find the value of t associated with $y = \frac{b}{e}$. To find t , we need to solve the equation, which is problem b).

c) Solve the differential equation with the initial condition $y(0) = y_0$.

If $\frac{dy}{dt} = -ky \ln\left(\frac{y}{b}\right)$, then $\int \frac{dy}{y \ln\left(\frac{y}{b}\right)} = \int -k dt$. The left side is a u -substitution with $u = \ln\left(\frac{y}{b}\right)$.

So, $\ln\left|\ln\left(\frac{y}{b}\right)\right| = -kt + c$ and $\left|\ln\left(\frac{y}{b}\right)\right| = Ae^{-kt}$. If $y < b$, then $\ln\left(\frac{y}{b}\right) = -Ae^{-kt}$. Exponentiating once again gives $y(t) = be^{-Ae^{-kt}}$. If $y(0) = y_0$, then $y_0 = be^{-A}$ which requires $A = -\ln\left(\frac{y_0}{b}\right)$ or

$A = \ln\left(\frac{b}{y_0}\right)$. So, $y(t) = be^{\ln\left(\frac{b}{y_0}\right)e^{-kt}}$ when $y < b$. If $y > b$, then $\ln\left(\frac{y}{b}\right) = Ae^{-kt}$ and

$y(t) = be^{\ln\left(\frac{y_0}{b}\right)e^{-kt}} = be^{e^{-kt \ln\left(\frac{y_0}{b}\right)}}$. In our problem, we need $y < b$, so $y(t) = be^{e^{-kt \ln\left(\frac{y_0}{b}\right)}}$ and we want

the t for which $y(t) = \frac{b}{e}$, we must solve the equation $\frac{b}{e} = be^{e^{-kt \ln\left(\frac{y_0}{b}\right)}}$.

This is a mess, but by persevering, we find $\frac{-1}{\ln\left(\frac{b}{y_0}\right)} = e^{-kt}$ and $t = -\left(\frac{1}{k}\right) \ln\left(\frac{-1}{\ln\left(\frac{b}{y_0}\right)}\right)$.

d) Find a relation between y_0 , k , and b so that the graph of y vs t has no point of inflection.

If there is not point of inflection, then we must have either $y = 0$ or $y = b$. If $y = 0$, then $b = 0$. If $y = b$, then $y_0 = b$. Also, if $y > b$, then $1 + \ln\left(\frac{y}{b}\right) \neq 0$, so there will be no point of inflection if $y > b$. As a real-world problem, our equation says that $y > b$ is not possible.

e) Find $\lim_{t \rightarrow \infty} y(t)$. What does this say about the growth of the tumor?

The limit $\lim_{t \rightarrow \infty} be^{\ln\left(\frac{b}{y_0}\right)e^{-kt}} = be^0 = b$. Indeed, as we had guessed earlier, the parameter b represents the maximum size of the tumor. Once it reaches this size, it cannot grow any more.

f) The Gompertz model is sometimes defined by the differential equation $\frac{dy}{dt} = me^{-ht}y$.

What is the relationship between k and b in the first model and m and h in this model?

If $\frac{dy}{dt} = me^{-ht}y$, then $\int \frac{dy}{y} = \int me^{-ht} dt$ so $\ln|y| = -\frac{m}{h}e^{-ht} + c$. Since $y > 0$, we have $y = Ae^{-\frac{m}{h}e^{-ht}}$

with $y_0 = Ae^{-\frac{m}{h}}$, so $y_0 e^{\left(\frac{m}{h}\right)} = A$. Then $y_2(t) = y_0 e^{\frac{m}{h}(e^{-ht} - 1)}$.

So, we are comparing $y_2(t) = y_0 e^{\frac{m}{h}(e^{-ht} - 1)}$ to $y_1(t) = be^{\ln\left(\frac{y_0}{b}\right)e^{-kt}}$. As $t \rightarrow \infty$ we have $b = y(0) e^{\frac{m}{h}}$.

The growth rate for the first equation is determined by k and the second by h .

f) It is easier to see the components of the equation in $\frac{dy}{dt} = -ky \ln\left(\frac{y}{b}\right)$. We see the stable values of $y = 0$ and $y = b$ immediately. With $\frac{dy}{dt} = me^{-ht} y$, we see the first but not the second. Pine View pointed out another important feature of the first model. If the tumor changes in size, then it is easy to change the value of y rather than have to recalculate the entire equation.

g) Which differential equation tells you more about the pattern of growth of the tumor?