Calculus in Biology

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In the recent developments in biological sciences, complicated problems arose which necessitate the application of calculus. Calculus is often used in the quantitative analysis of biological problems.

Calculus in biology did not start in this decade only. It may be traced back in 1798 when Thomas Malthus published *An essay on the Principle of Population as it Affects the Future Improvement of Society* where he warned of the impending disaster awaiting an Earth whose agricultural capacity could no longer support its population. His theory made a great impact in the study of populations. Stirred by such theory, biologists began to seek the help of mathematicians to transform biological problems into mathematical problems.

Some years later the *logistic equation* was used by the likes of Verhulst (1840) to model world-population growth and Pearl (1920) to describe various forms of biological growth. Likewise, Lotka (an American biophysicist) and Volterra (an Italian mathematician) came up in 1925 with the famous Lotka-Volterra predator-prey population model.

These mathematical models that described biological phenomena need various ideas of calculus. Hence, calculus became a tool in solving not only physics, chemistry and engineering problems but biological problems as well.

Calculus has placed biology in a different perspective, far more complicated yet interesting.

The examples below are some of the practical applications of calculus in biology. These problems do not require any in-depth knowledge of biology but these will show how the basic ideas of calculus, e.g., the limit concept, differentiation and integration, are used in biology.

The following problems and solutions are selected from the books of Stancl [1], Gentry [2], and Cullen [3].

Hollings's functional response curve. Suppose we are studying the feeding habits of a predator (e.g., a fox). How does the number y of prey (e.g., rabbits) eaten over a prescribed period of time depend upon the density x of the prey? Surely as x increases, that is, as the prey become more abundant, $y = f(x)$ increases. Since the predator can consume only a certain number of prey, it should be the case that $f(x_1) \approx f(x_2)$ for large values of x_1 and x_2. The curve relating y and x should possess a horizontal asymptote. In 1959 Hollings discovered a rational function that works well in describing the feeding habits of invertebrate predators and some fish:

$$y = \frac{ax}{1 + abx}, \quad \text{for } x \geq 0.$$

Evaluating the limit as x tends to positive infinity, we find the horizon-tal asymptote to be

$$\lim_{x \to +\infty} \frac{ax}{1 + abx} = \frac{1}{b}.$$

Thus, the line $y = \frac{1}{b}$ is a horizontal asymptote.

The curve, called ***Hollings' functional response curve***, is shown below:

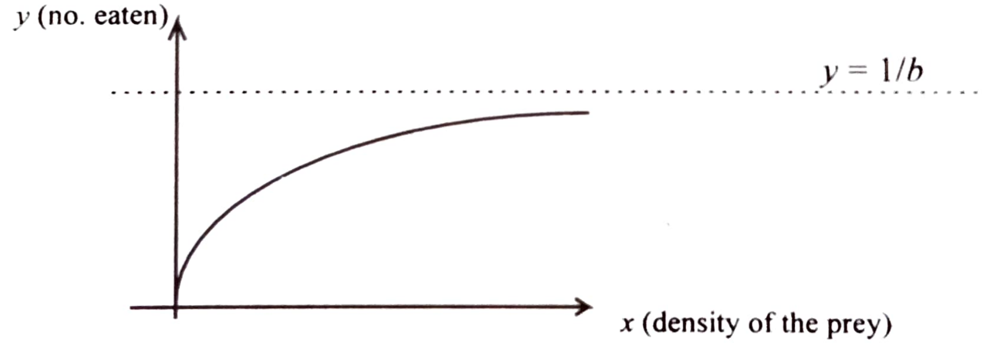

Figure 1

The residues of a drug in the body. A drug is administered every 4 hours in doses of 2 mg.. The drug is neutralized at an exponential rate with rate constant $k = -0.5$. Not all of the drug is neutralized before the next dose is administered. Denote by $A(t)$ the amount of drug in a patient's system at time t (in hours). Then

$$A(t) = A_0 e^{-0.5t}.$$

To determine the drug leftover from the first dose, we compute

$$\lim_{t \to 4^-} A(t) = \lim_{t \to 4^-} 2e^{-0.5t} = \frac{2}{e^2}.$$

Therefore, the drug leftover from the first dose is $2/e^2$. To compute for $A(t)$ over the next time interval [4,8), the drug leftover in the first dose must be included. Hence for the given intervals, we have the corresponding $A(t)$:

for [0,4): $A = 2e^{-0.5t}$, the leftover is $2/e^2$;

for [4,8): $A = (2+2/e^2)e^{-0.5t}$, the leftover is $2/e^2 + 2/e^4$;

for [8,12): $A = (2 + 2/e^2 + 2/e^4)e^{-0.5t}$, the leftover is $2/e^2 + 2/e^4 + 2/e^6$.

In general, for any time $t \in [4n, 4(n+1)]$, A is given by the formula

$$A_n(t) = (2 + R_{n-1})e^{-0.5t},$$

where R_{n-1} is the leftover of the preceding time interval.

Now, we will determine the residual amount of drug in the patient's system at the end of the nth dosage period.

The residue is simply the leftover of the drug. Hence, for the first dosage, that is, $n = 1$, the residue is $R_1 = 2/e^2$ (this is the leftover after the first dose) When

$$n = 2,\ R_2 = 2/e^2 + 2/e^4;$$

$$n = 3,\ R_3 = 2/e^2 + 2/e^4 + 2/e^6;$$

$$n = 4,\ R_4 = 2/e^2 + 2/e^4 + 2/e^6 + 2/e^8.$$

In general, the residue for the nth interval is

$$R_n = \lim_{t \to 4^-} A_n = \sum_{i=0}^{n} 2e^{-2i} .$$

The Michaelis-Menten relation. Special proteins known as ***enzymes*** act as catalysts for a wide variety of chemical reactions in living things. The term ***substrate*** refers to the substance that is being acted upon. In 1913, Mihealis and Menten devised the formula (see below) relating the initial speed V with which the reaction begins to the original amount of sub-strate x:

$$V = \frac{ax}{x+b} .$$

(Typical units are moles/liter for x and moles/liter/second for V.) This equation has been verified experimentally for a variety of enzyme-controlled reactions. There also exist theoretical derivations of the equations. When x is very large, $V \approx a$. We can show this by taking the limit of V as x tends to infinity:

$$\lim_{x \to +\infty} \frac{ax}{x+b} = a.$$

Thus, the line $V = a$ is a horizontal asymptote.

Bites from a poisonous snake. If a person bitten by a poisonous snake receives an immediate shot of antivenum, then t seconds after the shot is given there will be

$$y = \frac{0.5t + 2000}{2t + 3} \text{ ppm}$$

of poison in the victim's blood.

To find the concentration of poison in the blood as time passes by, we take the limit of y at infinity, $\lim_{t \to +\infty} y = 1/4$. Eventually, the concentration of poison in the blood decreases toward 0.25 ppm as time goes by.

The instantaneous rate of growth of a tumor. A tumor is estimated to have a total mass of $6\times10^{-3}t^2$ gm., t days after its discovery. How fast is the tumor growing on the 8th day?

Let $f(t) = 6\times10^{-3}t^2$. Then the instantaneous rate of growth on the 8th day is

$$f'(8) = 12\times10^{-3}(8) = 96\times10^{-3}\text{ gm./day.}$$

Forest fires. The number of forest fires in a particular region can be expressed as function of the number of days x since the last measurable rainfall. However, the fires fall into two categories:

(a) those caused by nature (i.e., lightning), and

(b) those attributable to man.

Let

$N(x)$ = the number of fires due to natural causes,

$M(x)$ = the number of fires caused by man,

$F(x) = N(x) + M(x)$, the total number of fires, and

$R(x) = M(x)/F(x)$, the proportion of fires that are caused by man.

The rate of change of the relative number of man-related fires is

$$R'(x) = D_x[M(x)/F(x)].$$

If we substitute $M'(x) + N'(x)$ for $F'(x)$, then

$$R'(x) = \frac{N(x)M'(x) - M(x)N'(x)}{(M(x) + N(x))^2}.$$

If $N(x) = (0.1)(x - 1)$, $M(x) = (0.4)x^2$ and $F(x) = 0.4x^2 + 0.1x - 0.1$ then the rate of change in the proportion of man-related fires is

$$R'(x) = \frac{(0.04)(x^2 - 2x)}{(0.4x^2 + 0.1x - 0.1)^2}.$$

Glucose metabolism. To test for diabetes, a patient is subjected to a large quantity of sugar. The amount of glucose in the patient's urine is then measured over an interval $[0,T]$. If the amount of glucose is given by $g(t) = 10 - 0.6t^2$, where t denotes hours, at what rate is the patient metabolizing the sugar two hours after the test begins? Since $g'(2) = -2.4$, then the patient is metabolizing at a decreasing rate of -2.4 units/hour.

The size of the human eye pupil. The size of a human eye pupil is related to the amount of light incident to the retina of the eye. The equation describing this relationship is

$$A(l) = \frac{40l^{-0.4} + 23.7}{l^{-0.4} + 3.95},$$

where A is the area of the pupil and l is the quantity of visible radiant energy per unit of time incident on the retina of the eye.

The rate of change in the pupil area corresponding to a change in light intensity is given by

$$A'(l) = \frac{-53.72l^{-1.4}}{(l^{-0.4} + 3.95)^2}.$$

A parasite model. ***Parasites*** are animals or organisms that live on or in another organism called ***host***. Parasites can either be helpful or harmful to their host. (Ruminant animals such as sheeps are dependent on parasites to complete their digestive process). Parasites are frequently employed to biologically control pests. One such parasite destroys the eggs of a spider. If the number of spiders in an area is H and the relative number of parasites is P, then the number H is a function of P:

$$H(P) = M(1 - 2P^3),$$

where M is the maximum host population. However, this parasite can only reproduce when the temperature is between 24 and 30 ^0C. Consequently, the relative number of parasites is a function of the temperature t. Assume that

$$P(t) = (t - 24)(30 - t)/9,$$

Then, although the spider population is not sensitive to the temperature
t, its population size H is affected by the temperature. This can be described by the following composition equation

$$\hat{H}(t) = H \circ P(t) = H(P(t)), \text{ for } t \in [24,30].$$

If the temperature is 28 ^0C, is the spider population increasing or decreasing, and at what rate? To answer this, we need to evaluate the derivative $\hat{H}'(28)$ at $t = 28$.

By composition of functions,

$$\hat{H}(t) = M(1-2[(t - 24)(30 - t)/9]^3).$$

Then the derivative of $\hat{H}(t)$ is

$$\hat{H}'(t) = M(-2/9^3)(3)[(t - 24)(30 - t)]^2 [-2t + 54].$$

From the equation above, we have $\hat{H}'(28) = (256/243)M \approx 1.053M$, where $M > 0$. This means that the spider population is increasing at the rate of $1.053M$ spiders per ^0C.

Poiseuille's Law. One of the contributing factors in the accumulation of lipid (fat) deposits inside the blood vessels is the fact that the flow of blood near the vessel walls is much slower than the flow of blood at the center of the vessel. Due to the slower flow rate near the walls, the lipid molecules have a greater chance of becoming attached to the vessel walls. This eventually leads to a heart attack.

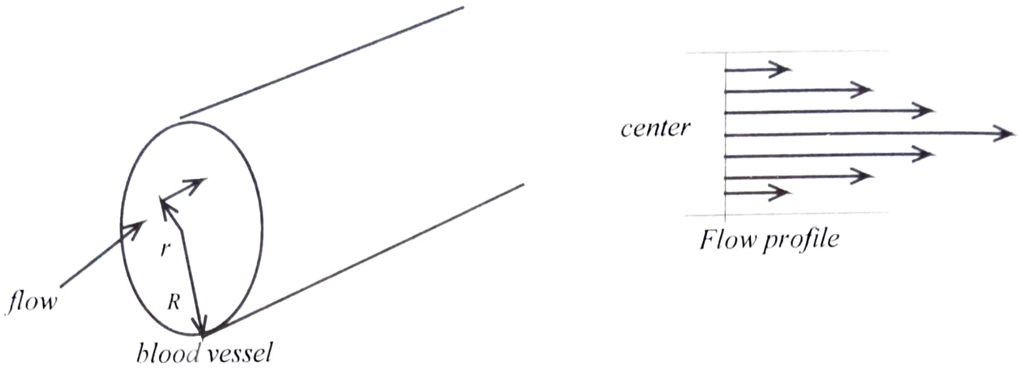

Figure 2

The French physician Poiseuille discovered the relationship that describes the velocity V of blood flow as a function of the distance, r, from the center of a blood vessel. It is now known as Poiseuille's Law:

$$V = \frac{\rho}{4\lambda\eta}(R^2 - r^2),$$

where

V = velocity of blood flow,

R = radius of the blood vessel,

r = distance from the center,

and the numbers ρ, λ, and η are physical constants corresponding to pressure, length, and viscosity.

The outer radius of a blood vessel can be changed by administering drugs, which either constrict the vessel (R decreases) or dilate the vessel (R increases). Aspirin dilates blood vessels. Assume that an individual "took 2 aspirins on a doctor's orders" and as a result, the radius R of her or his blood arteries increased in size at a rate of

$$\frac{dR}{dt} = 2\times 10^{-4} \text{ cm./min..}$$

At what rate would the velocity of the blood flow be changing? The answer is obtained by computing the derivative of V using the Chain Rule:

$$\frac{dV}{dt} = \frac{dV}{dR}\frac{dR}{dt}.$$

Since $\frac{dV}{dR} = 2\left(\frac{\rho}{4\lambda\eta}\right)R$, the rate of change in V is

$$\frac{dV}{dt} = 2\left(\frac{\rho}{4\lambda\eta}\right)R(2\times10^{-4})\text{cm./min..}$$

If $R = 0.02$ cm. and $\left(\frac{\rho}{4\lambda\eta}\right) = 1$, then $\frac{dV}{dt} = 8\times10^{-6}$ cm./min.. Note that the rate of change of the velocity does not depend on the distance r from the center of the vessel.

Gazelle population. The size of a gazelle herd is a function of the amount of the edible grasses within its grazing territory. The amount of grass is estimated by sampling techniques to be x tons. The size of the gazelle herd is assumed to be

$$g(x) = \begin{cases} 0, & \text{if } x < m, \\ (x-m)^2 - (x-m) + 2, & \text{if } x \geq m, \end{cases}$$

where m is the minimum amount of grass necessary to sustain a pair of gazelles.

But the amount x of grass is a function of the total rainfall r over the grazing region. Assume that

$$x(r) = 40r - r^2.$$

Then the size of the gazelle herd is a function of the rainfall

$$\hat{g}(r) = (g \circ x)(r) = g(x(r)).$$

The formula for the gazelle population as a function of rainfall is

$$\hat{g}(r) = \begin{cases} 0, & \text{if } 40r - r^2 < m \\ (40r - r^2 - m)^2 - (40r - r^2 - m) + 2, & \text{if } 40r - r^2 \geq m \end{cases}.$$

If $m = 10$, the rate of change of the herd size due to a change in rainfall is

$$\frac{d\hat{g}(r)}{dr} = 2(40r - r^2 - 10)(40 - 2r) - 40 + 2r.$$

Basal metabolism. This term is used to describe the normal chemical activity in an organism not subject to stress - for instance, a plant growing under ideal conditions or an animal resting over a period of time.

The metabolic rate of an animal will vary in response to environmental changes (temperature, humidity, air quality) and changes in physical activity. As air temperature fluctuates on a daily basis, the ***basal metabolic rate*** (BMR) of an animal will vary over a ***diurnal cycle***; the BMR increases at night to compensate for the lower temperature and decreases during the day

Metabolic rates are expressed in several equivalent ways - as a measure of heat produced in kilocalories per unit (kcal/hr), as a measure of oxygen consumption per unit of body weight (cm.^{3} O_2/g.), and as a measure of carbon dioxide expelled per unit of time (cm.^{3} CO_2/hr.) . In all cases, the total basal metabolism BM over a period is obtained as the integral of the basal metabolic rate over the time interval

$$\text{BM} = \int_{t_1}^{t_2} \text{BMR}(t)\,dt.$$

Suppose the BMR is given by the following function:

$$\text{BMR}(t) = -(0.15)\cos\left(\frac{\pi t}{24}\right) + 0.3 \text{ kcal./hr..}$$

Consequently, the BM value for a one-day period would be

$$\text{BM} = \int_0^{24}\left[-(0.15)\cos\left(\frac{\pi t}{24}\right) + 0.3\right]dt = 7.2 \text{ kcal./day.}$$

This would correspond to the BM of a mouse, whereas the value for an adult human would be approximately 2000 kcal./day.

Cardiac output. In measuring cardiac output, one method, known as the ***dye-dilution method***, is performed as follows. A fixed amount of a dye is injected into a vein or the right side of the heart. This dye then is circulated with the blood through the heart to the lungs, back to the heart, and into the arterial system. At a peripheral artery, the blood is continuously monitored for the presence of the dye for 30 seconds from the time of injection. The concentration of dye passing the monitored artery is then plotted as a function, $c(t)$, of time. (After about 15 seconds, recirculation of the dye occurs and care in monitoring of the blood circulation must be exercised.) The cardiac output is defined to be the volume of blood pumped per minute. This is obtained as the ratio of the amount of dye injected to the average concentration monitored over the 30-second period, multiplied by two, so that it corresponds to one minute:

$$\text{Cardiac output} = \frac{2[M_g \text{ of injected dye}]}{\frac{1}{30}\int_0^{30} c(t)dt}. \tag{8.1}$$

The dye-dilution method is used in experiments in basic physiology laboratories. The integral,

$$\int_0^{30} c(t)dt,$$

is estimated by drawing a continuous curve through dye-concentration values which are plotted on standard graph paper over a 30-second interval. The integral is then approximated by counting the squares of the graph paper under the curve. This corresponds to interpreting the integral as an area.

Assume that in an experiment in which 5 mg. of dye was injected at time $t = 0$, the concentration curve was found to be

$$c(t) = 0, \quad \text{if} \quad 0 \le t \le 3 \quad \text{or} \quad 18 \le t \le 30, \text{ and}$$

$$c(t) = (t^3 - 40t^2 + 453t - 1026)10^{-3}, \quad \text{if} \quad 3 \le t \le 18.$$

Note that $c(t)$ is in mg./100 ml.. No dye passes the observation artery for three seconds, and then a large quantity of dye passes. After 18 seconds, all measurable amounts of dye has passed. To compute the cardiac output determined by this experiment, we evaluate the average

$$A = \frac{1}{30}\int_0^{30} c(t)dt\,.$$

Since

$$\int_0^3 c(t)dt = 0$$

and

$$\int_{18}^{30} c(t)dt = 0,$$

the average A is given by

$$A = \frac{10^{-3}}{30}\int_3^{18}[t^3 - 40t^2 + 453t - 1026]dt.$$

Substituting the value of A in equation (8.1), we obtain the cardiac output for this experiment, which is approximately 6.275 liters/min..

Measuring abundance in the sea. Shown below (Figure 3) is a water column, a typical 1×1 meter square column extending from the ocean surface to the ocean floor.

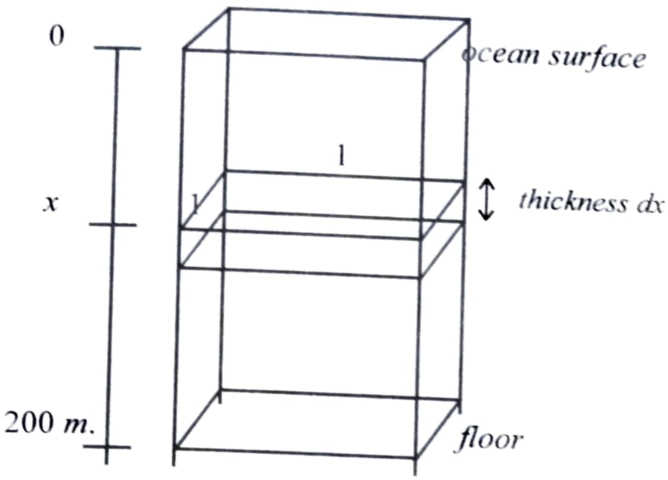

Figure 3. A water column

It is impossible to measure directly the total amount of, say, sardines in the column. By taking water samples, however, we can measure the concentration or density at various depths. Let $f(x)$ = density(in no./m.^{3}) at depth x. We may imagine that the water column consists of an extremely large number of their square layers, each of height dx, piled on one another. The number of organisms in a typical layer is

$$f(x)\ (\text{no./m.}^3)\times 1^2\ dx\ (\text{m.}^3) = f(x)\ dx.$$

The integral adds all those term from $x = 0$ to $x = 200$ to obtain $\int_0^{200} f(x)dx$, the total number of organisms in the water column.

Suppose that the density of sardines (no. of fish/m.^{3}) is given by

$$f(x) = .005x(75-x)\text{, where } 0 \le x \le 75.$$

We can determine the total number of sardines in the water column by computing

$$\int_0^{75} .005x(75-x)dx = 351.56.$$

Hence, the total number of sardines in the water column is about 352. The density of the sardines is the largest at the depth 37.5 m.. This can be seen by noting that $f(0) = f(75) = 0$ and $f'(x) = 0$ when $x = 37.5$ m..

Suppose that a fisherman is trawling sardines. His net has an opening that is 10 m. wide and 10 m. deep. It is lowered down between depths 32.5 and 42.5 m. in an attempt to capture the most fish. If the normal trawling speed is 20 m./min., how many sardines could be caught in 15 min.?

Between the depths 32.5 and 42.5 m. in a 1 m.^{2} water column, the number of sardines is

$$\int_{32.5}^{42.5} .005x(75-x)dx \approx 69.9 .$$

Hence, if the net moves through 1 m., it can capture 10(69.9) = 699 sardines. Over a 15 minute period, the net is moved through 20(15) = 300 m.. Hence, in theory, it would contact 300(699) = 209,700 sardines. However, since the escape rate is probably quite high, we would expect to capture only a small percentage of this number.

The examples presented here shows the importance of calculus in biology.

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