
CALCULUS, 2016-17-Q1

Bioinformatics degree

Projects. List 1.

1. We consider the additional difficulties of modeling ibuprofen amounts in a patient, given that ibuprofen is slowly absorbed from the digestive system and relatively quickly eliminated from the body.

- (a) Plot a concentration curve for ibuprofen using the model $y = A e^{-kt}$. Assume a dose of 200mg and a rate constant of $k = 0.35$.
- (b) How long does it take for one-half of the drug to be eliminated? (Do this algebraically, not by trial and error.)
- (c) A more sophisticated drug clearance model takes account of the need for an oral dose to be absorbed by the digestive system. This model is

$$y(t) = \frac{A b}{b - k} (e^{-kt} - e^{-bt}),$$

where A is the amount of the dose, k is the clearance rate for the bloodstream, and b is the clearance rate for the digestive system. Normally, $b > k$. Use this model to plot a drug versus time curve for a 200-mg dose of ibuprofen, assuming $k = 0.35$ and $b = 0.46$.

- (d) Describe the important differences between the curves of part (1a) and part (1c). Consider qualitative features of the graphs as well as quantitative properties such as the peak value and the time at which the peak occurs.
- (e) We want to derive the law for the model (1c), including both the amount of drug in the digestive system, x , and the amount of drug in the bloodstream, y . Hence, the phase space is 2-dimensional. Notice that, initially, the whole dose A is in the digestive system. Explain first that the

$$x(t) = A e^{-bt},$$

and derive the law $\dot{x}(t) = -bx(t)$. Derive then that $\dot{y}(t) = -ky(t) + bx(t)$, so the complete model is

$$\begin{cases} \dot{x}(t) &= -b x(t), \\ \dot{y}(t) &= -k y(t) + b x(t). \end{cases}$$

Check that

$$x(t) = A e^{-bt}, \quad y(t) = \frac{A b}{b - k} (e^{-kt} - e^{-bt})$$

is the solution of the initial value problem with $x(0) = A, y(0) = 0$.

2. Medication regimens for multiple doses are designed so that the minimum level (just before a dose) is high enough to be therapeutic and the maximum level (just after a dose) is not high enough to be toxic. We explore this idea in this problem.
- (a) Suppose a person has been taking 650-mg doses of acetaminophen every 4 h for several days. This will result in a drug versus time curve that repeats over a period of 4 h. Let A be the unknown concentration immediately after taking a dose. Use the model for acetaminophen drug clearance, with $k = 0.3$, to obtain a formula for the amount of drug present after 4 h, immediately before the next dose.
 - (b) Use the result from part (2a) to obtain a formula for the amount present immediately after the next dose.
 - (c) Given that the concentration curve is periodic, the amount present immediately after that next dose (from part (1b)) must be A . Use this fact to calculate the value of A and to determine the minimum amount present during the 4-h period.
 - (d) Repeat parts (2a)(2c) with doses of B mg of a drug with rate constant k taken every T hours. [Keep in mind that we are using A to represent the amount in the system at time 0, which includes both the new dose and whatever is remaining of previous doses.]
 - (e) Prepare a drug versus time curve showing the amount of acetaminophen from parts (2a)(2c) over a 24-h period (note that we are assuming the patient has been taking the drug for several days already. The results would be more complicated if our study began with the very first dose).

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Projects. List 2.

3. Mathematics professor Tim Pennings reported on experiments he conducted with his dog Elvis. In each experiment, Pennings threw a tennis ball into a lake at an angle to the shoreline. Elvis ran along the shore toward the point closest to the ball, but he jumped into the water for the final swim before reaching that closest point. Pennings measured his dog's running and swimming speeds and used calculus to determine the optimal point for Elvis to switch from running to swimming so as to minimize the total time required to reach the ball. Repeated experiments showed that Elvis consistently chose a point near the optimal point, even though Pennings varied the distance and angle of the throw. In this project, we consider Pennings's optimization model along with an improved model that shows how a lot of careful thought put into the modeling can result in more meaningful answers.

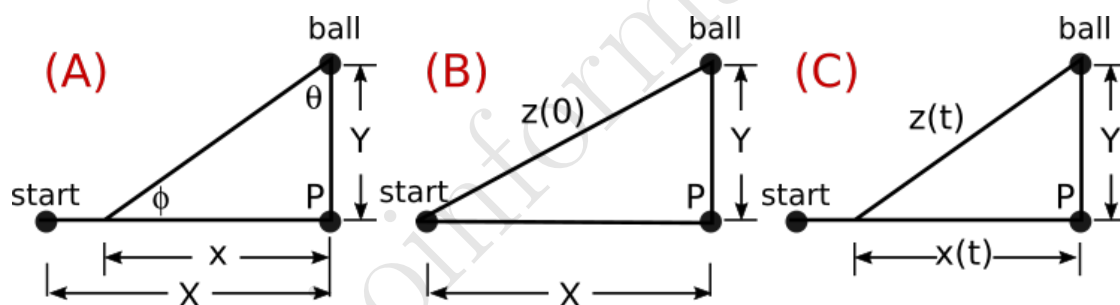


Figura 1: Graphics accompanying Project 1.

- (a) A dog owner standing near a lake with a straight shoreline throws a ball into the water, which lands Y meters away from the shore, see Figure 1(A). The dog begins to run with speed r along the shore toward the point P that is directly across from the ball's location. At a distance x from the point P , the dog jumps into the water and swims the remaining distance to the ball at speed $s < r$. Determine the total time $t(x)$ required for the dog to get to the ball. Assume that the distance between the start and the point P is X . [Note: Use the equation "distance = rate $\times$ time" to determine the times spent running and swimming.]
- (b) The function $t(x)$ from part (1a) contains parameters X, Y, r, s . Without loss of generality, we can assume $s < r = 1$, which removes the parameter r from the problem. The derivative dt/dx then contains only two parameters. Find the critical point x^* in terms of these two parameters.
- (c) Under what circumstances is this critical point the optimal solution? [Hint: Think about the range of possible x values.]

- (d) The distance x is only one of the variables that could be used to indicate the optimal jump point. One could also use either of the angles marked in the figure. While we would prefer the answer to be in terms of φ rather than θ , the calculations work better in terms of θ . Begin by writing down formulas for the swimming distance and the running distance in terms of θ rather than x , using the simplification $r = 1$. Then find the total time as a function $t(\theta)$.
- (e) The function $t(\theta)$ from part (1c) contains the same parameters as the original function $t(x)$, and the same parameter disappears in the computation of $dt/d\theta$. Find a simple trigonometric equation for the critical point θ^* in terms of the remaining parameters. This critical point is the optimal solution whenever the condition from part (1c) is met.
- (f) Note that θ and φ are complementary angles, meaning that the triangle containing them is a right triangle. What does this say about the relationship between the cosine of one of the angles and the sine of the other? Use this information to write the answer to part (1e) in the form $\cos \varphi^* = C$, where C depends on one or more of the parameters.
- (g) The model of parts (1a) and (1b) yields an answer for the optimal x , and the model of parts (1d)(1f) yields an answer for the optimal angle, either as θ or φ . Suppose you were going to design a robot dog to participate in a race from the starting point to the finishing point. Each of your answers carries with it an implication of the capabilities the robot would require. For example, the robot for part (1b) must be able to measure x as it moves, while the robot for part (1f) must be able to measure φ . We can assume that the speed s is built into the robot's program, so that it does not need to be measured. What must the robot for part (1b) be able to measure that the robot for part (f) does not need? The answer is of biological importance, because the capability of optimal behavior must be acquired by natural selection. The better model is the one that gives the simplest plausible explanation of behavior. Which of the two models is better in this sense?

Indeed, it is still difficult to see a connection between the mathematical solution and a mechanism for animal behavior. More recently, two French animal behavior specialists, Pierre Perruchet and Jorge Gallego, repeated Pennings's experiments, concluding that European dogs are as good as American dogs at consistently determining the optimal launch point. Their paper offers a more plausible explanation for the dogs' success that is based on related rates rather than optimization. This last part of the project explores their model.

- (h) Let $z(t)$ be the distance between the dog and the ball (see Figure 1(B-C)), and compute z' for the simplified case $r = 1$. [Hint: Let $x(t)$ be the distance along the shore between the dog and the point P . This distance is decreasing at the same rate that the distance of the dog from its initial location is increasing; however, this distance is easier to use in writing an equation to relate the distance z to known functions.]
- (i) Plot the rate of change of the distance between the dog and the ball as a function of the distance between the dog and the point P . Assuming that the dog wants to

get the ball as quickly as possible, why is it not a good idea for the dog to run all the way to the point P ? [Keep in mind that $x(t)$ is decreasing.]

- (j) Suppose the dog swims with speed $s < r = 1$. Determine the point x at which the dog should switch from running along the shore to swimming directly toward the ball, assuming that the immediate goal is to always progress as rapidly as possible. [Hint: What is the rate of change of z while the dog is swimming?]
- (k) Plot the optimal jump distance x as a function of the dog's swimming speed s for the case $Y = 1$. Examine the behavior of the graph near the extreme values $s = 0$ and $s = 1$ to verify that the result makes sense.
- (l) What must a dog be able to measure for the strategy suggested by the related rate solution to work? Is this a more or less plausible explanation of dog behavior than the strategy used in Project 1?

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Projects. List 3.

4. The development rate of many organisms shows an approximately linear dependence on temperature. Biologists measure the development of such organisms in terms of “degree-days”. These accumulate over time at a rate equal to the difference between the current temperature and a threshold temperature T_m . This temperature varies among species, as does the total number of degree-days required for full development.
- (a) Construct an integral to represent the total number of degree-days in t_1 days. This integral represents a function $F(t_1)$ that contains the parameter T_m and the function $T(t)$ in addition to the independent variable t_1 .
 - (b) In their study of the insect species *Thrips major*, David Stacey and Mark Fellowes determined that a total of 230 degree-days are required for development, with the threshold value $T_m = 7^\circ\text{C}$. Calculate the total amount of time needed for development of this species if the temperature is a constant 27°C .
 - (c) Suppose the temperature is a constant value T . Calculate the corresponding development time. Plot the development time as a function of T .
 - (d) Find data for mean daily temperature for the month of July in your area. Use this data set to estimate the number of days required for development of thrips born on June 30.
 - (e) How should the definition of the function $F(t_1)$ be modified if the function $T(t)$ can be less than T_m ? [Hint: Although the term “degree-day” reflects the connection with temperature data, we should think of degree-days as a measure of development rate rather than a record of temperature. Hence, the accumulation of degree-days should take into account the fact that development is not negative during periods when $T < T_m$.]
 - (f) Use the modified formula from (4e) to calculate the number of degree-days that accumulate in 1 day if the temperature is $T(t) = 14 + 14 \sin(2\pi t)$. [Hint: You can get a reasonably good estimate of the integral value by using either a right-hand or left-hand sum with 24 subdivisions, which corresponds to using hourly average temperatures rather than exact temperatures].
 - (g) Use the result from (4f) to calculate the development time for the temperature $T(t) = 14 + 14 \sin(2\pi t)$. Compare this result with the development time for a constant temperature of 14°C .