Teaching Exponential Growth and Decay: Examples from Medicine

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A treatment of exponential growth and decay is sketched which does not require a previous course in calculus. Rate of change is introduced by considering compound interest and is determined graphically by using semilog paper. Examples of exponential growth and decay are given which will interest premedical students. These include bacterial growth, sterilization, survival in certain chronic diseases, clearance, and drug absorption.

INTRODUCTION

Introductory physics courses, particularly those for which calculus is not a prerequisite, often pay little or no attention to processes of exponential growth or decay. This is due in part to the fact that we think of this topic as requiring mathematical sophistication, and also because the only application which we often think of is radioactive decay.

Processes involving exponential growth and decay are widespread in the biological and medical sciences and are not always clearly understood by students in those areas. We have found it worthwhile to devote both lecture and laboratory time to exponential processes, in our courses taken by majors in premedicine, biology, medical technology, preveterinary medicine, food science, etc. Since these students have not had a prior course in calculus, the concept of a fractional growth or decay rate is developed in class. The graphical determination of the rate using semilog paper is then discussed. This paper describes the arguments used in lecture and presents some biological and medical examples which interest the student and display the utility of graphical analysis.

LECTURE TREATMENT

It is a matter of choice whether this material is introduced early in the course as part of a section on graphical analysis or whether it is taught the first time an exponentially decaying phenomenon is encountered. Compound interest is a familiar process in which growth occurs at a constant rate. Since it is familiar to most students, it forms a natural starting point for the discussion. Since this is a common way to introduce exponential growth, the argument will only be outlined. One first considers interest compounded annually and derives the equation

$$y = y_0(1+b)^t, \tag{1}$$

where b is the interest rate, t the number of years, and y_0 the initial amount. It is shown that taking logarithms of this equation transforms it to a linear equation. Plots on both Cartesian and semilog paper are discussed. The interest is then compounded N times per year, in which case

$$y = y_0[1+(b/N)]^{Nt} = y_0\{[1+(b/N)]^N\}^t. \tag{2}$$

It is then asserted that, as N becomes very large,

$$[1+(b/N)]^N \rightarrow e^b$$

so that

$$y = y_0(e^b)^t = y_0 e^{bt}. \tag{3}$$

The disadvantage of having to use tables of e^x is compared to the advantage of having the growth rate appear explicitly in the exponent. It is interesting to compare the growth rate of interest compounded annually with the exponential growth of "instant interest."

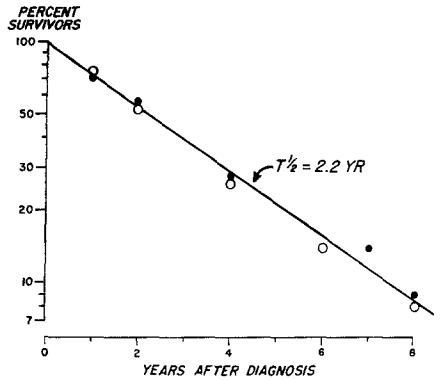

FIG. 1. Survival in treated and untreated disseminated breast cancer. Treatment appears to have no effect on survival, presumably because the cancer has already spread before treatment. ●, average of four treated series; ○, average of four untreated series. From Ref. 4, used with permission.

Negative values of b are considered, beginning with the argument that at the end of each time interval a fraction $(1-|b|)$ of the initial population remains.

The student is shown how to determine b from a semilog plot using the equation

$$\log_{10}(y_2/y_1) = (\log_{10}e)b(t_2-t_1)$$
$$= 0.4343b(t_2-t_1).$$

Half-life and doubling time are introduced as

$$T = 0.693/|b|.$$

We next point out that during a small interval Δt, the fractional change in y is $b\Delta t$, so that

$$\Delta y = by\Delta t,$$

which is another way of stating that the rate of increase or decrease is proportional to the amount present.

For the case of compound interest, the rate of change is constant and is known in advance. In most situations, however, we wish to determine whether or not the rate of change of some quantity may be proportional to the quantity. Such a proportionality may exist only for a limited period of time, or not at all. This may be tested by plotting the data on semilog paper. If b is constant, a straight line will result. If b is not constant, the line will curve. In that case, one may speak of $b(t)$ and determine an instantaneous value for b by drawing a tangent to the curve and applying to the tangent line the method described above for determining b. Thus, plotting data on semilog paper can be useful even if strictly exponential growth or decay does not exist in the problem at hand.

EXAMPLES

Examples from Physics

Examples from physics which can be discussed either in lecture or in homework problems include radioactive decay, RC circuits, damped harmonic motion, growth of a nuclear chain reaction, attenuation of sound, light, or neutrons, and the exponential atmosphere.

Miscellaneous Examples

First-order chemical kinetics is exponential. Although b usually depends on time, semilog paper plots are useful for analyzing problems involving such things as growth of population, energy consumption problems, and the value of investment stocks.

Bacterial Growth[1]

When bacteria are introduced into a new environment, they undergo a quiescent stage in which they adapt to their surroundings. Then they grow exponentially until they are limited by

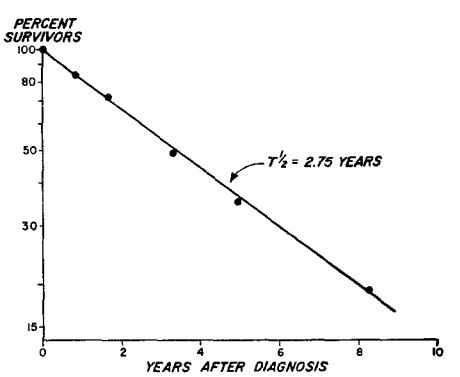

FIG. 2. Survival in chronic lymphatic leukemia. From Ref. 4, used with permission.

some factor such as availability of nutrients. A stationary phase follows, after which they die and the population decreases. Since the bacteria grow as well as divide, one has slightly different exponential curves for total cell mass and for total number of cells.

It is interesting to point out that antibiotics which are metabolized and incorporated into the bacteria are ineffective unless the bacteria are in the exponential growth phase.

Sterilization[2]

Various processes of sterilization (ultraviolet light, heat, and chemical agents) depend upon the chance operation of the destructive mechanism on the organism. In such cases the fraction of organisms surviving decays exponentially. In some cases the survival curve departs from exponential and levels off because certain organisms are resistant. These considerations are quite important in preparing a vaccine of killed or inactivated virus, such as the Salk type of poliovirus vaccine.[3]

Mortality Rates and Survival

In human mortality studies semilog paper is quite useful even if the decay (death) rate is not constant, because it is reasonable to assume that the total number of fatalities in a given period is proportional to the population at that time. This utility is not always appreciated by people working in the field.

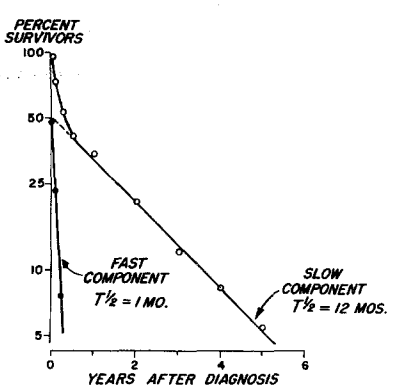

FIG. 3. Survival in portal cirrhosis, showing two half-lives. The time origin is discussed in the text. From Ref. 4, used with permission.

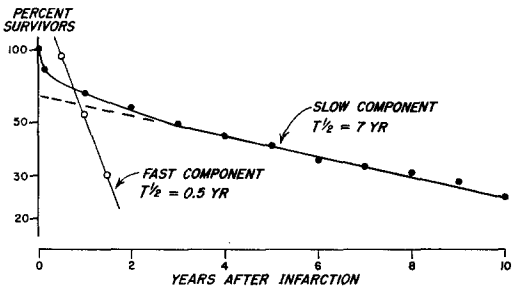

FIG. 4. Survival after myocardial infarction, showing two half-lives. From Ref. 4, used with permission.

Remarkably, it is found that for some diseases, the fraction surviving actually follows a straight line on semilog paper.[4] This implies that the death rate in such patients is independent of time. Some examples from Ref. 4 are shown in Figs. 1–4. In the first two cases, breast cancer and chronic lymphatic leukemia, the survival follows a simple exponential decay. In the other cases b is not independent of time; rather two mortality mechanisms seem to be operating. This results in a two component decay, as shown in Figs. 3 and 4. In this case, unlike those above, the choice of $t=0$ is important, or the fast component will be lost. In the case of portal cirrhosis, $t=0$ is the time of discovery of varicose veins in the esophagus. (These are a common finding in this disease, because blood from the alimentary canal passes through the portal vein and liver before returning to the heart. This path is shunted by small veins in the esophagus. Congestion of the liver can thus cause portal hypertension and hence esophageal varices.) The other example, in Fig. 4, is for a heart attack or myocardial infarction. Here the choice for $t=0$ is the initial infarct.

Further study of the patients surving a myocardial infarction showed an increase in the death rate in later years, as shown in Fig. 5. This is due to the increase in death rate from competing causes as the patients become older.

Another interesting example is the survival of patients diagnosed as having congestive heart failure. In this disease the heart is incapable of supplying sufficient blood to the tissues for normal metabolic needs. The causes are diverse, but the disease is characterized by enlargement of the heart and excessive accumulation of fluid,

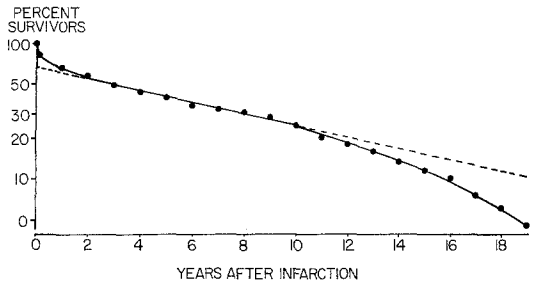

FIG. 5. Survival after myocardial infarction for a longer period of time, showing increasing death rate from other causes with advancing age. From Ref. 4, used with permission.

either in the lungs (pulmonary edema) or the extremities. A large scale study[5] of such patients was recently done as part of the Framingham study of cardiovascular diseases, which was begun in 1949. The fraction surviving can be calculated from the data in Ref. 5 and is given in Table I and plotted in Fig. 6. From these data, one can deduce[6] the mortality rates and half lives shown.

Clearance

In physiology situations often arise in which the rate of decrease of some substance is proportional to the concentration of the substance in a solvent; diluting the substance with more solvent lowers the rate of decrease. A typical example is the diffusive or active transport of a substance through a cell wall, as in the kidney. Let $N(t)$ represent the total quantity of the substance in the solvent at time t, $n(t)$ the concentration, and V the total volume of the solvent, which is assumed to remain constant. Then

$$\Delta N = -k(N/V)\,\Delta t = -kn\Delta t = -(k/V)N\Delta t.$$

The quantity k/V is equivalent to b in the discussion above and has the units of (1/time). The coefficient k, which thus has the units of (volume/time) is called the clearance. As with b, it is not necessary that k be independent of time. One can define an instantaneous clearance[7] as

$$k = -n^{-1}(\Delta N/\Delta t).$$

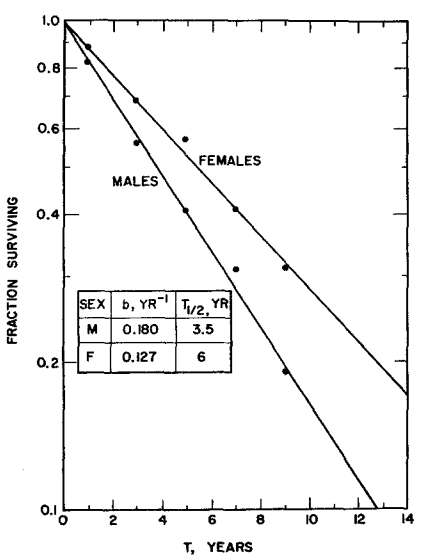

FIG. 6. Survival of patients with congestive heart failure.

TABLE I. Fraction of 81 males and 61 females surviving after diagnosis of congestive heart failure. The data are calculated from Table 4 of Ref. 5.

	Fraction surviving	
Years after diagnosis	Males	Females
1	0.795	0.860
3	0.548	0.680
5	0.385	0.567
7	0.293	0.397
9	0.181	0.309

Reference 7, incidentally, is very worthwhile for students going into the life sciences who have mastered elementary calculus. Chapter 6 has a good discussion of exponential growth and decay with many examples, including the fitting of curves by multiple exponentials and the dangers inherent therein.

Pharmacology

Exponential behavior can be expected whenever the rate of disappearance of some substance is limited by the amount of that substance and not by some other factor. For example the absorption of an intramuscular or subcutaneous injection by the bloodstream follows an exponential decay. It is

quite possible to have a chain of processes, which result in the decay product from one compartment feeding another. For a drug, for example, these processes may be absorption, combination with another compound, metabolic alteration, and excretion. If exponential loss occurs from each compartment, then the resulting equations[8] are precisely those for radioactive series decay.[9] While we have not discussed these in our classes, the buildup and subsequent decay of the daughter nucleus can be discussed qualitatively, or this material can be used for a term paper by an interested student.

Interesting examples of exponential behavior in drug interactions, reminiscent of the response of a capacitively coupled amplifier to a squarewave, may be found in the literature.[10]

Vasectomy

With the increasing popularity of ligation of the vas deferens as a means of sterilization among males, there has been interest in determining when the presence of spermatozoa after surgery is due to continued flushing out of those distal to the surgical site, and when it means that there has been recanalization of the vas. One study[11] shows an exponential decrease of the number of spermatozoa as a function of the specimen number. Approximately 35 percent of the spermatozoa were found to remain in the distal vas after each ejucalation.

SUMMARY

A line of argument has been presented for discussing exponential growth and decay with students who have not had calculus. The determination of the rate of change from the slope of a semilog plot is emphasized. Several examples from physiology and medicine have been included. These examples, which help maintain student interest, are by no means exhaustive, but are presented for the convenience of physics teachers who may find it difficult to obtain them.

ACKNOWLEDGMENTS

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[1] B. D. Davis, R. Dulbecco, H. N. Eisen, H. S. Ginsberg, and W. B. Wood, *Microbiology* (Harper and Row, New York, 1969), p. 142.

[2] Reference 1, p. 351.

[3] Reference 1, p. 1292.

[4] B. Zumoff, H. Hart, and L. Hellman, Ann. Intern. Med. **64,** 595 (1966).

[5] Patrick A. McKee *et al.*, New Eng. J. Med. **285,** 1441 (1971).

[6] R. K. Hobbie, New Eng. J. Med. **286,** 606 (1972).

[7] Douglas S. Riggs, *The Mathematical Approach to Physiological Problems* (M.I.T. Press, Cambridge, 1970).

[8] Reference 7, Chaps. 8 and 9.

[9] R. D. Evans, *The Atomic Nucleus* (McGraw-Hill, New York, 1955), Chap. 15.

[10] J. Koch-Weser and E. M. Sellers, New Eng. J. Med. **285,** 487 (1971).

[11] M. Freund and J. E. Davis, Fertility and Sterility **20,** 163 (1969).