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The Use of a Small, Desk Top Analogue Computer In Nuclear Medicine Education

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INTRODUCTION

The behavior of a biological system can be described in terms of one or several discrete variables. If the interrelationship among these variables is given as a mathematical expression, the knowledge of any one provides information about the remaining variables in any given situation.

The resulting equation describing the biological (or physical) system may be simple or of considerable complexity. The more complex equations are often more readily "solved" by labor saving devices called computers. In utilizing an analogue computer, and in setting up its program, an electrical system is constructed in such a way that its behavior resembles the system under study and "solutions to the equations that describe the system under study are represented by varying voltages taken from the computer" (1).

For instance, the charge and discharge of a capacitor can represent the filling and emptying of a physiological space within the body, the entrance or exit of air from the lungs, or the decay of a radioactive isotope. The magnitude of the quantities which represent the units in each of these is the voltage of the capacitor at a given time. It is important to note, though, that the decision as to whether the analogy is appropriate must be made by the experimenter on the basis of observations on the biological system.

As early as 1954 Fossier and Rosen (2) designed a small, portable, desk size analogue computer which engineers could use as easily and rapidly as a desk calculator. The desk type analogue computer has turned out to be a valuable tool in engineering, and many applications to the biomedical field are possible. Examples have been furnished by Clynes (3), Stacy (4), Hiltz (5), and Chance (6), from the fields of cardiovascular physiology, pulmonary physiology, neurophysiology, and biochemistry.

Many of the problems concerning the decay and physiological interactions of radioactive isotopes in nuclear medicine are particularly suited to analogue

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techniques, because the same basic mathematical laws govern both isotopic decay and the discharge of a capacitor through a resistor. Differential equations governing radioactive decay can be solved on an analogue computer with almost the same ease as multiplication on a slide rule.

The student of nuclear medicine acquires soon a familiarity with differential equations and their use in explaining the physics and physiology of radioactive isotopes. The solutions of these equations, as algebraic functions of time, are somewhat more difficult, but the log-log slide rule, one of the first analogue computers, has been most helpful. A typical problem is illustrated below for which the calculation of a complete solution, even with the slide rule, is a task of considerable complexity.

The analogue method is easily mastered by anyone with the appropriate background in the basic mathematics of nuclear medicine. When used with a suitable readout device, such as a cathode ray oscilloscope, X-Y plotter, or a recording milliameter, the curve describing the change of the isotope with time may be presented in a dynamic fashion. One of the most important lessons which the analogue computer demonstrates to the student is that the interaction of the radioactive isotope with the biological organism is governed by precise mathematico-physical laws. Furthermore, the knowledge of any process is advanced when it may be defined in the precise language of mathematics. In biology, this is necessarily an inductive method, and hence the necessity for a quasi "trial and error" method, in determining the appropriate model.

PRACTICAL DETAILS

The computer employed by the author was constructed from a commercially available kit,[1] which cost less than $200 (Fig. 1). It is well suited for student

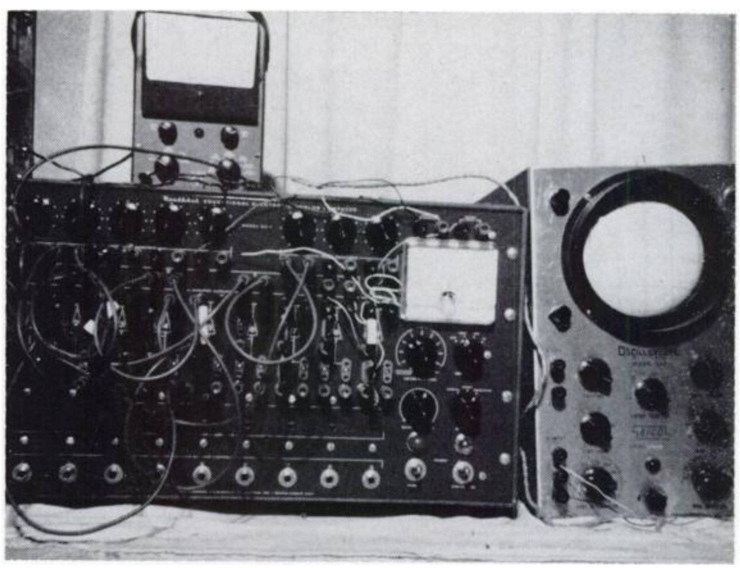

Fig. 1: Computer and read out oscilloscope.

[1]Model EC-1 available from the Heath Company, Benton Harbor, Michigan

use and operation and is capable of solving linear differential equations of the first order. (The order of the differential equation is limited by the number of operational relays in this particular device.) At a somewhat greater expense, commercial models, such as the Donner Model 3400, are available for the more sophisticated user who requires greater accuracy.

The following analogue solutions illustrate a few of the many in nuclear medicine which may be solved by the analogue type computer. For the purpose of generality, I have omitted specific numerical values for the hypothetical isotopes. In addition, the factors for converting machine time to real time have been omitted for the same reason. Such practical "set-ups" are readily obtained from any of the texts in the field. (See Chapter 2 in Korn (7) or the Donner Tech Notes (1).)

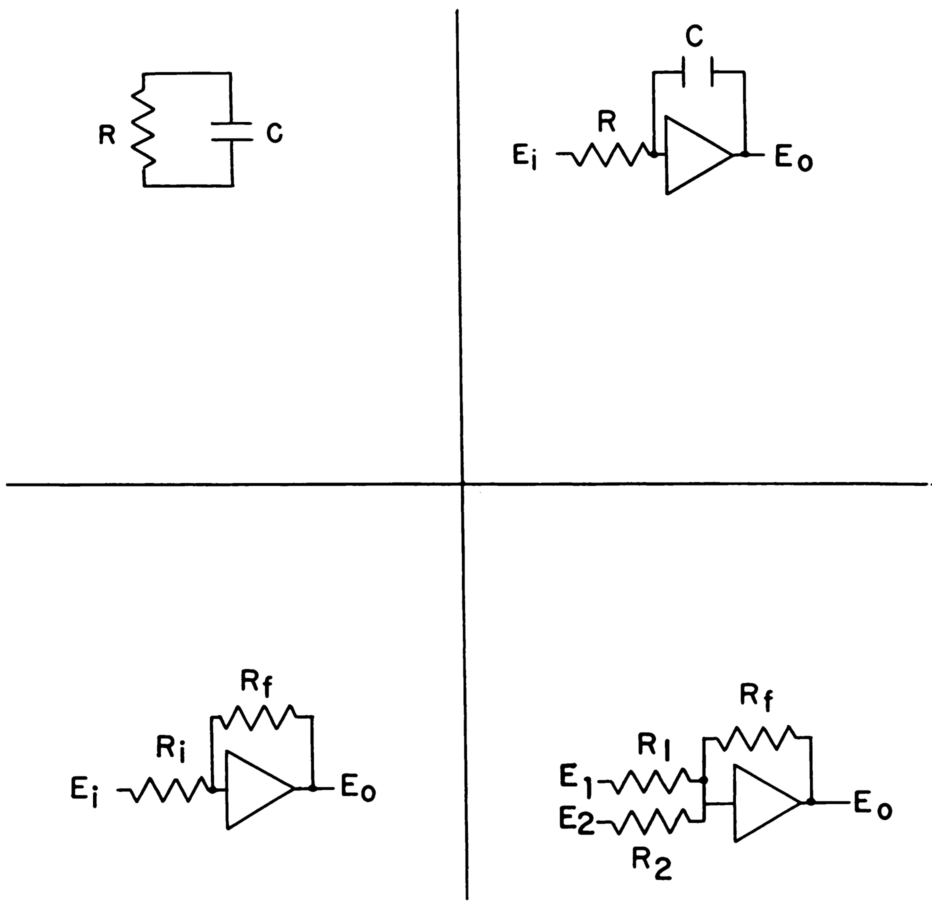

Fig. 1a: A resistance-capacitance (R-C) network.
Fig. 1b: An operational amplifier, symbolized by a triangle lying on its side, employed as an integrator.
Fig. 1c: Use of an operation amplifier to multiply by a constant, $\frac{R_f}{R_i}$.
Fig. 1d: The use of an operational amplifier for addition.

THE ELECTRICAL ANALOGUE OF RADIOACTIVE DECAY

Though radioactive decay and the discharge of a capacitor through a resistor are analogous and are described by similar mathematical expressions, the practical considerations of accuracy, reproducibility, and versatility of application limit the use of simple passive networks in analogue computation.

In a RC network (Fig. 1a) the current through the capacitor is proportional to the derivative of the voltage

$$I = -C\frac{dE}{dT} .$$

I and E are the instaneous current and voltage, respectively, and C is the capacitance. Since

$$I = \frac{E}{R} ,$$

the expression representing the voltage across the resistor is

$$\frac{E}{R} = -C\frac{dE}{dt}$$

If the capacitor is charged to a voltage Eo, and then allowed to discharge through the resistor R, the above relationship becomes

$$E = -RC\frac{dE}{dt}$$

with the minus sign being inserted because the voltage across the capacitor is decreasing. The solution of this equation, a function of time, is

$$E = E_o e^{-t/RC} .$$

By recording the voltage across the resistor at various times, and plotting the values obtained on graph paper, a curve results which is identical in appearance to that obtained by "plotting" this equation as an analytical expression using F_0, R, and C as parameters, and t as the independent variable. The RC network, employed in this manner, "solves" the differential equation, and as the solution represents an integration, under the conditions of the problem, the circuit is considered to be an integrating network. If Q, representing quantity of radioactive material is substituted for E, and 1/RC is replaced by λ

$$Q = Q_o e^{-\lambda t}$$

the familiar equation for radioactive decay results.

In order to avoid the inaccuracies introduced by power consumption in passive networks, the modern analogue computer employs a high grain amplifier, most often d-c, symbolized by a triangle lying on its side (Fig. 1b). Input voltages are represented by lines directed toward the base of the triangle, and output voltages are shown to appear at the apex. The introduction of feedback results in a very high input impedance so that almost no current flows in the input circuit. Since the current is negligible, no power losses are present.

Detailed circuit analyses, available in Korn (7), show that if a capacitor, C, connects the input and output of the amplifier, the equation governing the operation of the amplifier in Figure 1b is

$$E_o = -\frac{1}{RC}\int E_i dt \cdot$$

Replacing the capacitor by a resistor, R_f, multiples by a constant $\frac{R_f}{R_i}$ (Fig. 1c)

$$E_o = -\frac{R_f}{R_i}E_i$$

or if voltages E_1 and E_2 are inserted, the output voltage is equal to the negative of the sum of the input voltages, provided $R_f = R_1 = R_2$ (Fig. 1d)

$$E_o = -\left(\frac{R_f}{R_1}E_1 + \frac{R_f}{R_2}E_2\right)$$

To solve the differential equations which occur in the mathematical formulation of isotope problems, the operational amplifiers are set up to perform one of the fundamental operations described above, and are then interconnected so their behavior represents the equation to be solved. The following examples will illustrate this procedure.

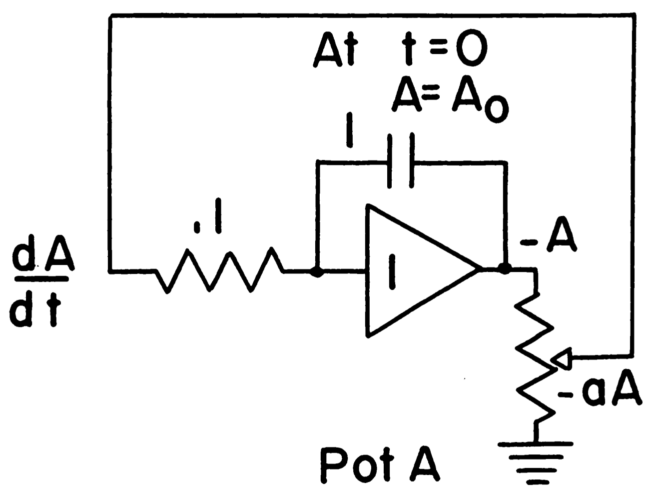

Fig. 2: Schematic showing the computer setup for simple radioactive decay. The half-life is determined by the setting of Pot A. The capacitance is in microfarads, and the resistance is in megohms.

TYPICAL PROBLEMS AND THEIR ANALOGUE SOLUTIONS

The first problem is concerned with a hypothetical isotope, *A*, having a decay constant, *a*. It is desired to describe the decay of the isotope with respect to time.

The differential equation describing the decay is:

$$\frac{dA}{dt} = -a.A ,$$

and the algebraic solution, obtained by separating the variables and integrating is:

$$A = A_0 e^{-at} .$$

The analogue solution is simply obtained by setting a portion of the output of an integrating amplifier equal to the input (Fig. 2). The constant of integration is obtained by inserting the voltage representing the initial quantity of isotope into the integrating capacitor at the start of the solution. The "machine time" solution is then obtained. Four different solutions, obtained from four different settings of pot A, and recorded on a direct writing oscillograph, are shown in Fig. 2a.

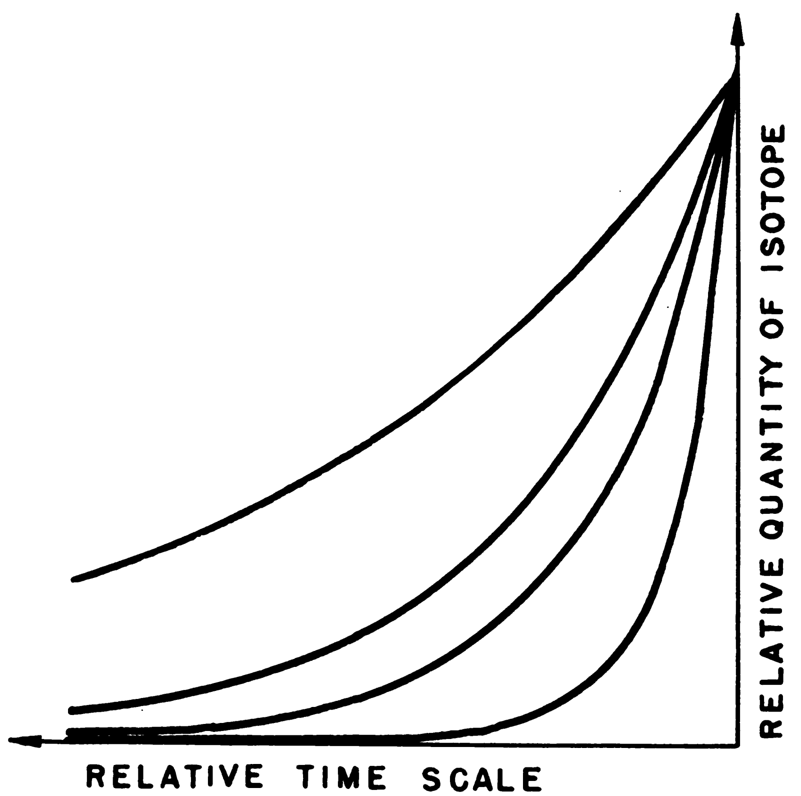

Fig. 2a: Representation of the decay of different isotopes with different half lives, produced by varying the setting of Pot A in Fig. 2.

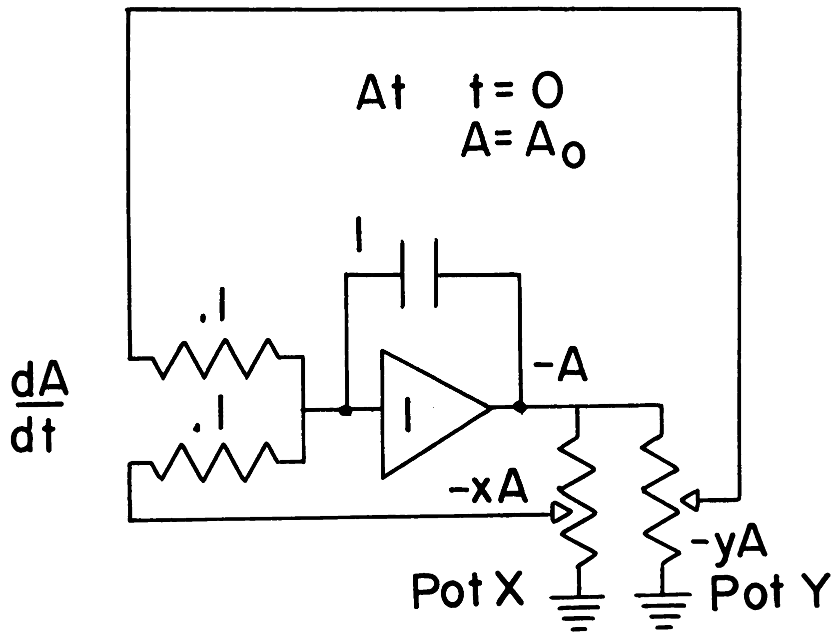

Fig. 3: Schematic of the analogue solution to the second problem. The capacitance is in microfarads and the resistance is in megohms. Refer to the text for details.

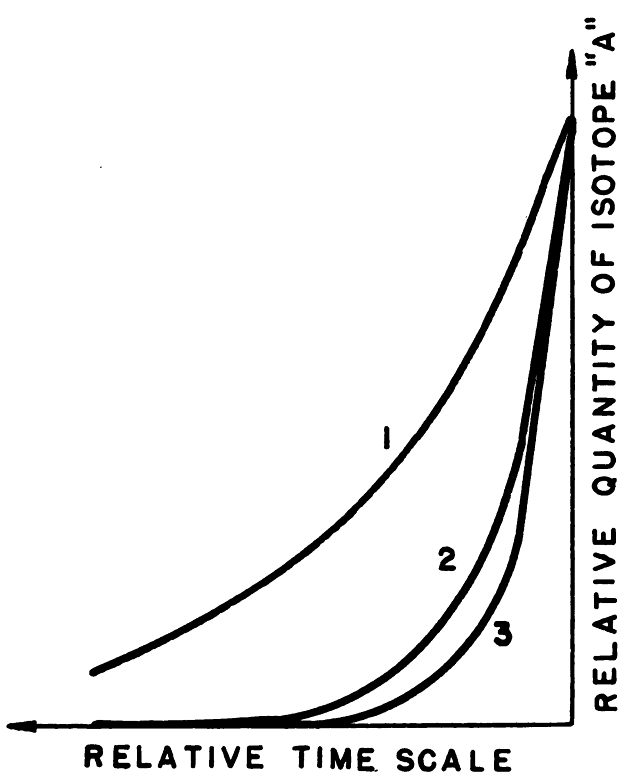

Fig. 3a: Output of integrating amplifier 1 in figure 3 at different settings of pots X and Y.

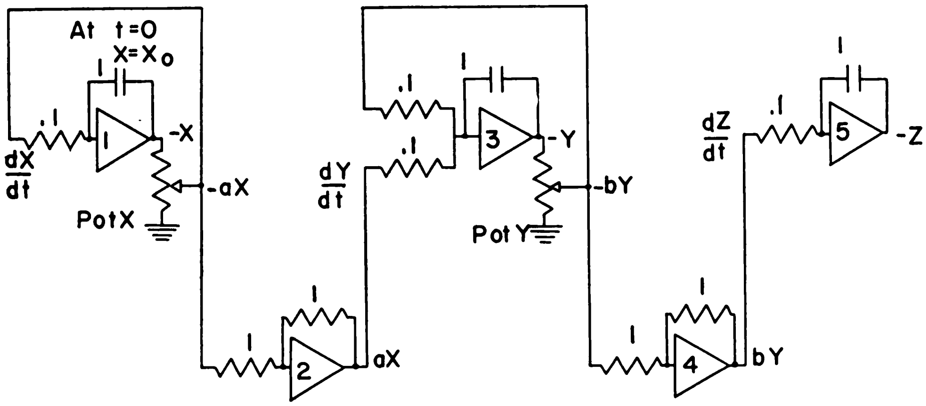

Fig. 4: Schematic of the analogue solution to the third problem discussed in the text. Capacitance is in microfarads and resistance in megohms.

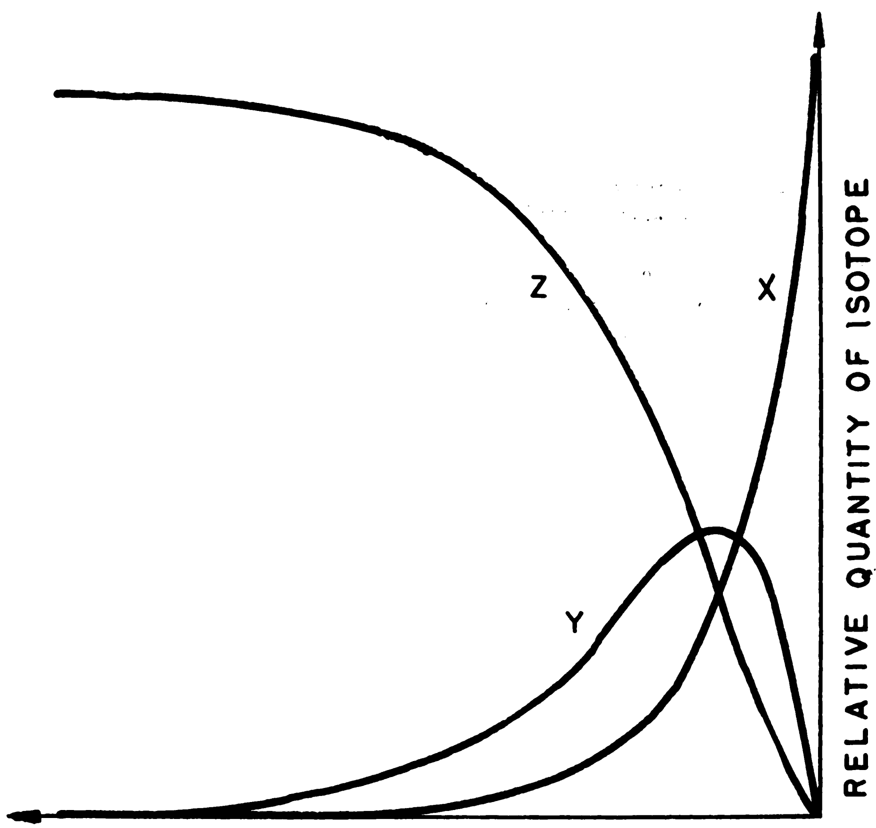

Fig. 4a: Simultaneous representation of X, Y, and Z, from the differential equations of the third problem.

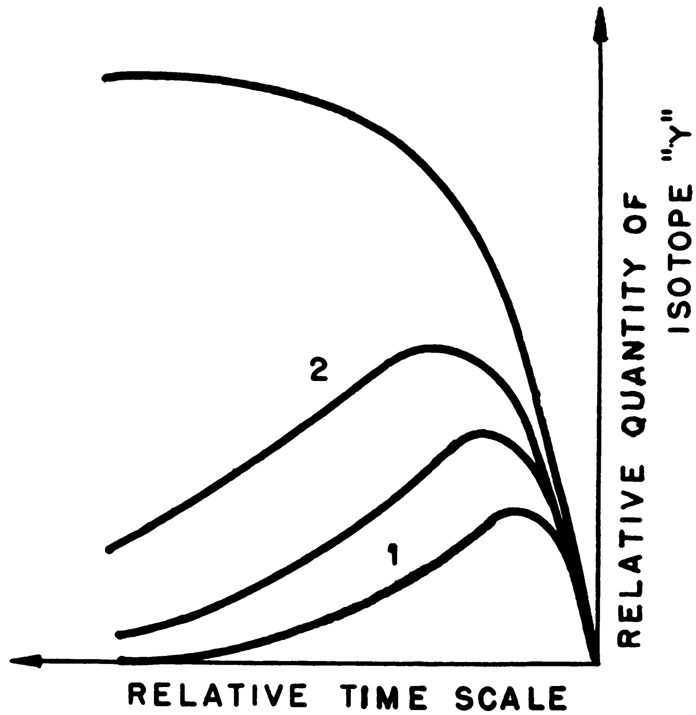

Fig. 4b: Effect on Y when *a* is varied and *b* remains constant. Curve 1 is produced by a large value of *a*, and curve 2 by a small one.

The second problem involves an isotope *A*, which has both a physical and biological half life. The physical decay constant is *x*, and the biological decay constant is *y*. It is desired to depict the total decay of the isotope within a bio-

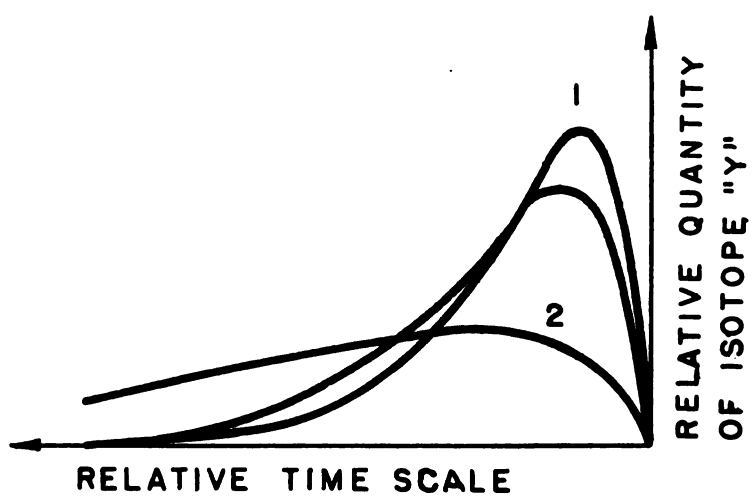

Fig. 4c: Effect on Y when *a* is varied and *b* remains constant. Curve 1 is produced by a large value of *a*, curve 2 by a smaller one.

logical organism, as well as the decay of the isotope outside the organism, and the disappearance of the isotope from the organism.

The differential equation representing the solution to the problem is:

$$\frac{dA}{dt} = -xA - yA \ ,$$

and the algebraic solution is:

$$A = A_0 e^{-(x+y)t} \ .$$

Physical decay alone is obtained by setting $y = O$, and independent biological decay is obtained by setting $x = O$.

The analogue solution is shown in Figure 3. Curve 1 in Figure 3a represents physical decay alone and is obtained by setting pot Y to zero (ground potential), curve 2, representing biological decay alone, is obtained by setting pot X to zero, and curve 3, representing the observed decay of the isotope within the organism, is obtained with x and y set to the proper decay constants.

The third problem is of greater complexity. Assume that isotope X having decay constant a decays into isotope Y with decay constant b, which in turn decays into stable isotope Z. (An example of such a situation is the preparation of I^{132} from Te^{132} according to the following reaction):

$${}_{52}Te^{132} \longrightarrow {}_{53}I^{132} \longrightarrow {}_{54}Xe^{132} \ .$$

It is desired to plot the decay curves of X and Y, and the curve representing the appearance of F.

The differential equations representing the above system are:

$$\frac{dX}{dt} = -aX \ ,$$

$$\frac{dY}{dt} = aX - bY \ ,$$

$$\frac{dZ}{dt} = bY \ .$$

The algebraic solutions are:

$$X = X_0 e^{-at} \ ,$$

$$Y = \frac{aX_0}{b-a}\left(e^{-at} - e^{-bt}\right) \ ,$$

$$Z = X_0\left(1 - \frac{b}{b-a}e^{-at} + \frac{a}{b-a}e^{-bt}\right) \ .$$

The plot of the solutions to the above equations is a very time consuming process without the analogue computer.

The analogue solution is shown in Figure 4. The input to amplifier 1 is the expression of the decay of isotope X, $\frac{dX}{dt} = -aX$, the input to amplifier 3 is the decay of Y, $\frac{dY}{dt} = aX - bY$, and the input to amplifier 5 is the production of Z, $\frac{dZ}{dt} = bY$. Amplifiers 2 and 4 are sign inverters. A typical solution, as recorded on the direct writing oscillograph, is shown in Figure 4a.

One of the advantages of analogue simulation is the rapidity with which a complex solution may be examined under the influence of varied parameters. This provides a feel for a system which is almost impossible to obtain using the analytical approach. Figure 4b shows the effect of varying the decay constant of the second isotope, Y, on the amount of Y present at a given time, the decay constant of X remaining constant. (Physically, this would represent a different system.) This is effected by a change in the setting of pot B. Readily apparent by increasing the decay constant is the earlier time at which isotope Y reaches its maximum, as well as the smaller total amount present at this time.

In a similar fashion, a, the decay constant of X, is varied by changing the setting of pot A, and the effect on Y is noted (Fig. 4c). In this case, increasing the value of *a* causes the maximum of B to be reached more rapidly, but, unlike the previous example, increasing a produces *a* larger amount of *B* at its maximum.

SUMMARY

Applications of a simple, relatively inexpensixe analogue computer to a few hypothetical problems in nuclear medicine involving radioactive decay are discussed. The only prerequisite for using this device is a basic understanding of differential equations. Besides the solutions to specific problems, the student of nuclear medicine obtains a better, more sophisticated understanding of the dynamic, time dependent nature of radioactive material and its interaction with the biological organism.

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