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The human body's response to glucose and three physical models

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Three physical models of the human body's response to a glucose challenge are presented from the medical literature. Glucose tolerance is evaluated using kinematical techniques, an exponential-decay analysis, and a damped harmonic-oscillator model. Each treatment contains material suitable as supplementary topics in physics courses, both introductory and intermediate.

I. INTRODUCTION

Medical topics can be very effective for stimulating the premedical student's interest in physics. This article illustrates how some medical research methods employed in the study of the human body's response to a glucose challenge use the same techniques learned in physics courses. Three treatments are given ranging from simple graphical analysis to more advanced discussions involving differential equations. The graphical approach is very suitable for a supplemental topic in a noncalculus-based physics course for life-science majors. The advanced treatment contains mathematical methods encountered in intermediate mechanics. Such can be presented briefly to physics majors, illustrating the power and scope of methods studied in physics.

In Sec. II a brief description of the oral glucose tolerance test (OGTT) is presented. Section III contains an analogy comparing glucose-tolerance response to a simple kinematical problem. Graphical techniques are employed to arrive at a proposed clinical index for the diagnosis of diabetes. In Sec. IV a model is discussed which approximates the body's response to an intravenous glucose challenge with an exponential-decay curve. Section V reviews a model comparing glucose-tolerance response to the oscillations of a damped harmonic oscillator. Concluding remarks are given in Sec. VI.

II. THE ORAL GLUCOSE TOLERANCE TEST (OGTT)

The OGTT measures the body's ability to respond to an oral load of glucose after a 12-h fast. A baseline blood sample is taken in order to determine the fasting glucose con-

centration. Then, the patient consumes a dose of glucose (e.g., 50 or 100 g) and blood samples are taken a few times during the next 2 or 3 h (e.g., at 30, 60, 90, and 120 min). Glucose concentrations are given in milligrams per deciliter (mg/dl); however, numerical values vary depending on whether venous or capillary blood is taken, and whether whole blood or plasma values are reported.

For normal glucose tolerance, glucose concentrations are virtually reduced to the fasting or baseline level by the end of 2 h after a glucose load. In cases of impaired glucose tolerance, the glucose concentrations remain high for extended periods of time. Patients with diabetes mellitus register high amounts of sugar in the blood due to insufficient amounts of insulin, a hormone secreted by the pancreas for the metabolism of carbohydrates.

There is no universal set of criteria for the diagnosis of diabetes; although, severe cases are readily recognized. According to one set of guidelines, the National Diabetes Data Group,² a fasting plasma glucose level reaching 140 mg/dl on more than one occasion is indicative of diabetes. For fasting levels not so high, diabetes is present if two blood samples, one taken at 2 h and one at a suitable point before 2 h, reach 200 mg/dl on more than one occasion (recommended oral dose is 75 g).

The difficulty with suggested guidelines is evident in a 1975 study which compared six published methods. Each set of criteria was employed to classify 340 subjects, representative of people likely to be examined in a clinic specialized in diabetic detection.³ The percentages of subjects diagnosed as diabetic ranged from as low as 18% using the criteria of the European Study Group for Diabetes to as high as 51% with the recommendations of the British Diabetic Association.

The difficulty in establishing a unique set of guidelines

has generated considerable medical research in modeling glucose-tolerance response. Three approaches discussed in the following sections employ standard material encountered in physics: (1) graphical kinematic techniques, (2) exponential decay, and (3) damped harmonic oscillations.

III. GRAPHICAL METHODS

The simple graphical approach to the study of glucose tolerance is analogous to the kinematical description of moving objects introduced early in a basic course in physics. Figure 1 provides a graph indicating the speed of an automobile as a function of time as it passes another car. The smooth curve in Fig. 1 indicates the actual speed of the car from moment to moment, while the dashed lines connecting the points at times 0, 30, 60, 90, and 120 s give an approximate description.

The distance traveled by the car during the 120 s is given by the area under the smooth curve (neglecting the effect of switching lanes). This area can be approximated by the area under the four dashed lines:

$$A = (1/2)(a + 2b + 2c + 2d + e)t, \tag{1}$$

where a = 80, b = 120, c = 100, d = 85, e = 80 (units in km/h), and t = 30 s, giving A = 3.21 km.

Figure 2, very similar to Fig. 1, is a plot of five values of plasma glucose concentration taken from the normal OGTT reported in Table I. The points are connected by straight lines. The blood sugar level rises initially after the glucose challenge at t = 0 min. A short delay in rising is due to gastrointestinal absorption time. The body responds by secreting insulin to metabolize the glucose and bring concentrations back down to the fasting level.

Billewicz et al., have proposed a single geometric measure of an OGTT for use in clinical settings. The total area is not suitable because the area under the fasting level is such a large percentage of the total area. Small changes in fasting levels have large effects on the total areas calculated. The incremental area, i.e., area above the fasting level,

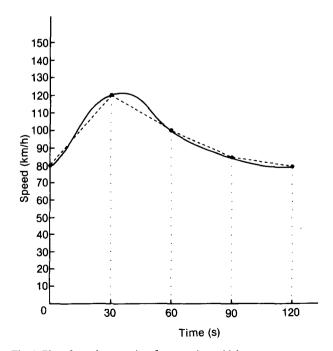


Fig. 1. Plot of speed versus time for a moving vehicle.

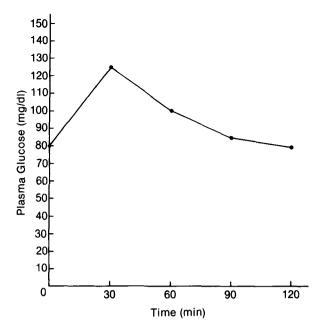


Fig. 2. Plot of plasma glucose versus time from an oral glucose tolerance test.

is a much better measure of the actual response to a glucose challenge.4

Their index is

$$H = nI_A (0-2 \text{ h})/I_A (0-1 \text{ h}),$$
 (2)

where n is the number of 15-min time intervals for the curve to peak, I_{A} (0-2 h) is the incremental area for the 2 h, and I_{A} (0-1 h) is the incremental area for the first hour.

Good responses peak early and readily return to the fasting level. In such cases, n is small and the bulk of the incremental area occurs during the first hour. Both of these characteristics produce low values of H for normal subjects. Suggested interpretation of the H index is as follows: H < 5 is normal, $5 \le H \le 9$ is suspect, and $H \ge 10$ is abnormal.4

For the OGTT values reported in Table I and Fig. 2, the time to peak is estimated to be 30 min; therefore, n is taken to be 2. The numerical value for the index defined in Eq. (2) is easily calculated: H = 2(65t)/(50t) = 2.6, well within the normal range. In Ref. 4, a nomogram is given for estimating n by fitting a parabola through the highest measured point and its neighbor on each side. However, physics students can be challenged to arrive at an improved estimate for n analytically.

For the OGTT values in Table I, the parabola must pass through the points (0.80), (30.120), and (60.100). Using a time coordinate where 1 unit is 15 min, these three points are $(x_1, y_1) = (0.80)$, $(x_2, y_2) = (2.120)$, and (x_3, y_3) = (4,100). One parabola, $y = Ax^2 + Bx + C$, passes through the three points. The maximum occurs at

Table I. Plasma glucose (PG) values from a normal oral glucose tolerance

Time (min)	0	30	60	90	120
PG (mg/dl)	80	120	100	85	80
_					

Table II. Plasma glucose values (mg/dl) from normal⁵ (N) and diabetic⁶ (D) OGTT results, compared with the H index.

		Index					
	0	30	60	90	120	Н	H_{P}
G.B. (N)	91	162	124	123	125	3.5	4.0
R.B. (N)	109	177	161	140	110	3.2	4.2
L.B. (N)	98	194	176	132	96	3.1	4.1
D.G. (N)	94	157	141	109	102	3.0	3.9
R.H. (N)	98	152	136	115	113	3.2	4.1
D.L. (N)	89	122	78	108	106	3.7	3.7
A.M. (D)	204	332	380	408	368	16.4	15.9
F.R. (D)	260	308	372	400	444	30.2	30.2
D.F. (D)	179	244	248	292	276	17.8	19.2
E.M. (D)	185	256	288	320	360	25.9	25.9
A.J. (D)	280	354	432	495	487	21.8	24.6
E.T. (D)	204	256	309	352	343	21.5	23.8

x = -B/2A = n, from setting dy/dx = 0. The algebra simplifies if coordinates are chosen with the vertical axis passing through the center point, shifting the time coordinate back afterwards. One readily finds $n = x_2 + \epsilon$, where $\epsilon = (y_3 - y_1)/(2y_2 - y_1 - y_3)$. For the case depicted in Fig. 2, n = 2.33, which is larger than the previous estimate of n = 2. The H index, using the estimate of n from the parabolic fit, is $H_P = 3.0$, somewhat higher than the value 2.6 found earlier.

Table II contains OGTT results for six normal⁵ and six diabetic⁶ subjects (glucose load of 100 g). The H index is listed for each case, along with the index value H_P using a parabolic fit through the highest point and its immediate neighbors. In calculating H, if glucose concentrations dip below the fasting level, values are replaced by the fasting value. When the last value is the maximum, n is taken to be 8

In some cases, considerable error is induced due to sampling blood at intervals of 30 min. For example, H_P for R.B. is lowered from 4.2 to 2.4 when 15-min blood samples are taken (see Ref. 5 for 15-min values for each of the normal subjects listed in Table II). However in practice, blood sampling every 15 min is uncomfortable and time consuming.

An advantage of the H index is its relative insensitivity to variations in laboratory testing. For example, the conversion from whole venous blood glucose to plasma glucose involves a linear transformation.³ It is a simple student exercise to show that the H index defined by Eq. (2) is invariant under a transformation of the form G' = mG + b, where G and G' are glucose concentrations (m and b are constants).

IV. EXPONENTIAL DECAY

The intravenous glucose tolerance test (IGTT) involves the direct injection of glucose into the blood stream. There is very little delay time in reaching the peak glucose concentration as the gastrointestinal track is avoided. When the initial time is defined at peak concentration, the plot of decreasing glucose excess⁷ (incremental values above the fasting level) as a function of time approximates a decaying exponential. Figure 3 is a plot of glucose excess as a function of time after a rapid intravenous glucose injection.⁸

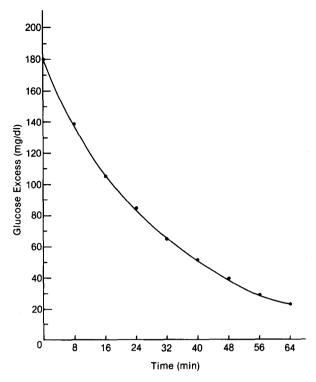


Fig. 3. Plot of glucose excess versus time from an intravenous glucose tolerance test. Reproduced from Ref. 8 by copyright permission of The American Society for Clinical Investigation, New York.

The simple model suggested empirically from the work of Amatuzio *et al.*⁸ indicates that the disappearance of glucose is approximately proportional to the glucose excess present, i.e.,

$$dg(t)/dt = -kg(t), (3)$$

where g(t) is the difference between the glucose concentration G(t) and the fasting value G_F , and k is a constant. The solution to Eq. (3) is the familiar decay law encountered in studies of radioactivity,

$$g(t) = g(0)e^{-kt}, \tag{4}$$

where g(0) is the initial peak excess due to the sudden glucose injection.

The decay constant k can be determined from the data by a least-squares fit for a plot of $-\ln[g(t)/g(0)]$ vs t. Table III lists some IGTT data for normal (N), mildly diabetic (MD), and severely diabetic (SD) subjects, all of which were diagnosed previous to the decay studies by other means. The intravenous load was 25 g and the time t = 0 was taken 4 min after injection. Blood samples were obtained from an ear lobe.

The decay constant k has been multiplied by 100 and reported as a removal rate R = 100k (%/min) in Table III. The percentage is relative to the amount of glucose present at any given instant, which decreases from moment to moment according to Eq. (4). The correlation coefficient r for the fits ranges from 0.94 to 1.00, with a typical value of 0.98.

In Table III, the normal subjects have an average removal rate of $R_{\rm N}=4$ %/min, the mild diabetics average $R_{\rm MD}=2$ %/min, and the severe diabetics have a mean $R_{\rm SD}=1$ %/min. However, difficulties arise when R is used as a clinical index due to the spread in values found in each group. For example, J.U. (SD), previously classified as

Table III. Excess glucose values (mg/dl) during an IGTT for subjects⁸ previously diagnosed as normal (N), mildly diabetic (MD), and severely diabetic (SD); and removal rates R(%/min).

	Time (min)							<i>R</i> (%/min)		
	0	8	16	24	32	40	48	56	64	
W.B. (N)	180	138	105	85	65	52	40	29	24	3.2
R.C. (N)	184	149	103	79	68	48	38	15	15	4.0
F.M. (N)	203	147	103	61	55	30	15	6	6	5.9
E.S. (N)	178	140	107	87	68	43	42	23	17	3.6
K.N. (N)	200	150	109	95	82	71	64	55	41	2.2
B.D. (N)	140	93	74	48	29	14	19	4	-4^a	5.7
O.D. (MD)	187	168	142	123	105	90	71	63	38	2.3
W. (MD)	149	134	109	100	88	81	66	48	42	1.9
E.J. (MD)	170	138	119	108	90	83	73	53	48	1.9
M. (MD)	153	138	105	98	85	79	79	46	28	2.3
M.B. (MD)	179	134	117	100	88	73	66	52	42	2.1
F.S. (MD)	125	109	99	83	78	73	67	61	55	1.2
J.U. (SD)	210	160	124	116	110	106	84	70	62	1.7
G.E. (SD)	152	116	114	102	104	78	76	74	66	1.2
M.C. (SD)	200	154	124	124	104	104	104	82	82	1.2
B.P. (SD)	161	152	146	132	122	108	109	102	102	0.8
A.N. (SD)	133	99	97	90	75	77	66	59	54	1.3
E.W. (SD)	65ª	73	70	67	64	62	65ª	65ª	62ª	0.5

^a Discarded in calculating R.

severely diabetic, has a value for R as high as 1.7 %/min (very close to the mildly diabetic average of 2 %/min). As another example, K.N. (N), a normal subject, has a value of R (2.2 %/min) in the mildly diabetic range.

The use of a decay or removal rate for evaluating response is not very different from using total incremental area. The total area under the glucose-excess curve is

$$A = \int_0^\infty g(t)dt = g(0) \int_0^\infty e^{-kt}dt = g(0)/k.$$
 (5)

The removal parameter, k = g(0)/A, is inversely proportional to the total incremental area.

V. DAMPED HARMONIC OSCILLATIONS

From Tables II and III it is evident that glucose levels can drop below the fasting level after a glucose challenge. Figure 4 illustrates oscillations in normal response that can

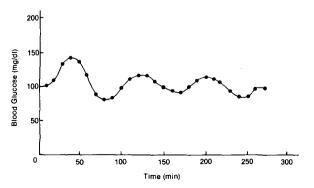


Fig. 4. A normal blood-glucose-response curve, illustrating damped harmonic oscillations. Reproduced from Ref. 9 by copyright permission of Georg Thieme Verlag, Stuttgart, West Germany.

be observed over time intervals of 3 h. 9 A simplified version of the harmonic-oscillator model for the OGTT proposed by Ackerman *et al.* 10 is presented below.

In Sec. IV it was assumed that the rate of change in glucose exess is proportional to the amount of excess glucose present in the blood. A more detailed model incorporates the excess amount of insulin hormone in the blood h(t) and an external source term S(t). Therefore, Eq. (3) is replaced by

$$dg(t)/dt = -k_1 g(t) - k_2 h(t) + S(t), \tag{6}$$

where k_1 and k_2 are constants.

Similarly, the rate of change in excess insulin hormone depends on the amount of insulin and glucose present.

$$dh(t)/dt = -k_3h(t) + k_4g(t),$$
 (7)

where k_3 and k_4 are constants. Note the plus sign in Eq. (7) for the glucose term since insulin production is positive when glucose excess is present. The insulin parameter h(t) can be eliminated from Eqs. (6) and (7), resulting in a differential equation for g(t),

$$d^{2}g(t)/dt^{2} + 2\beta dg(t)/dt + \omega_{0}^{2}g(t) = f(t), \tag{8}$$

where
$$\beta = (k_1 + k_3)/2$$
, $\omega_0^2 = k_1 k_3 + k_2 k_4$, and $f(t) = k_2 S(t) + dS(t)/dt$.

After a 12-h fast, the system is in equilibrium. The sudden administration of an oral load can be approximated by a rapidly rising source function S(t) at t=0, which then gradually drops off. The time derivative of the source function at t=0 can be taken to be a delta function, $dS(t)/dt=a\delta(t)$, where a is a constant with suitable units. Approximating f(t) by this dominant contribution, ¹⁰ the solution to (8) is of the form¹¹

$$g(t) = Ae^{-\beta t} \sin \omega_1 t, \tag{9}$$

where $\omega_1^2 = \omega_0^2 - \beta^2$. The glucose concentration $G(t) = G_F + g(t)$ is pictured in Fig. 4, a damped oscillatory function offset by the baseline fasting level G_F .

After detailed analysis, Ackerman et al. 10 suggest ω_0 as the best parameter in evaluating responses, and refer to ω_0^2 as the responsivity. For normal subjects investigated in Ref. 10 the characteristic time $T_0 = 2\pi/\omega_0$ was less than 4 h, while for diabetics T_0 extended beyond 4 h. Note that the observed period in Fig. 4 is $T_1 = 2\pi/\omega_1$, and not T_0 .

In order for a curve to be diagnosed as abnormal based on low values of $\omega_0^2 = \omega_1^2 + \beta^2$ (large T_0), both ω_1 and β must be low. ¹⁰ This means that abnormal responses will have both long observed periods T_1 and poor damping. Overdamped responses ($\omega_0 < \beta$, ω_1 imaginary) with β small can be found in extreme diabetic cases where the curve hangs high for hours. ¹²

Fitting the data of an OGTT with damped oscillatory functions is not easily accomplished. Therefore, it is difficult to extract the relevant parameters from the data. For this reason, the harmonic-oscillator model has not proved practical for clinical application.⁴

VI. CONCLUDING REMARKS

This article has discussed three physical analogies which have aided medical researchers in understanding the human body's response to a glucose challenge. While each model may appear different, they are all quite similar. The incremental area of the kinematical approach is closely related to the decay constant in the exponential-decay model

(see Sec. IV). The decay or removal constant, related to the half-life of the decay, represents an inverse characteristic time of the response. In the harmonic-oscillator model, a characteristic time is used to evaluate responses (see Sec. V).

These medical models include material that can be readily incorporated into physics courses, some of which is more suitable at the introductory level, other at more advanced levels. The author successfully introduced the kinematical treatment during the second week of an introductory one-semester physics course for nursing students. The premedical student is likely to acquire an early appreciation for physics when it becomes evident that techniques learned after only one or two weeks enable one to read a paper published in a medical journal. Similarly, intermediate mechanics students can realize the potential that theoretical methods encountered in physics have in their application across disciplines.

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Using videotapes to study underdamped motion of a pendulum: A laboratory project

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Using a video camera with a stopwatch feature and a VCR enabled my class to study the effects of air resistance acting on the following pendulum bobs: Ping-Pong ball, styrofoam spheres, and a brass sphere. We measured the maximum return angle on each swing for a pendulum $(L=1\,\mathrm{m})$ released from an angle of 70°. The students wrote a computer program to analyze the data, assuming that the force of air resistance equals cr^2v^2 , where $c=0.87\,\mathrm{kg/m^3}$. We found that c was larger than this and extracted the force of air resistance acting on the string. As part of the lab project, we also measured the period and position-versus-time when a pendulum with a brass bob was released at a large angle.

I. INTRODUCTION

My attention was drawn to this subject by an article by M. F. McInerney. ¹ He studied the underdamped motion of a pendulum by measuring the speed of a polystyrene pendulum bob as it passed through a photogate and observed the decrease in speed on each swing due to air resistance. Recently I reported on a laboratory project^{2,3} for my sophomore intermediate mechanics class in which we videotaped the overdamped motion of a mass at the end of a

spring immersed in glycerin. It seemed that videotaping could be used profitably to observe the motion of a pendulum and be the basis for another laboratory project. These experiments were sufficiently complex so that the students would have to write their own computer programs, one important goal for the project. This paper describes the following series of experiments that were performed by my class:

(1) Measuring the period of a pendulum released with a large amplitude.