A Mathematical Model for the Determination of Total Area Under Glucose Tolerance and Other Metabolic Curves

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OBJECTIVE — To develop a mathematical model for the determination of total areas under curves from various metabolic studies.

RESEARCH DESIGN AND METHODS — In Tai's Model, the total area under a curve is computed by dividing the area under the curve between two designated values on the *X*-axis (abscissas) into small segments (rectangles and triangles) whose areas can be accurately calculated from their respective geometrical formulas. The total sum of these individual areas thus represents the total area under the curve. Validity of the model is established by comparing total areas obtained from this model to these same areas obtained from graphic method (less than ±0.4%). Other formulas widely applied by researchers under- or overestimated total area under a metabolic curve by a great margin.

RESULTS — Tai's model proves to be able to *1*) determine total area under a curve with precision; 2) calculate area with varied shapes that may or may not intercept on one or both *X/Y* axes; 3) estimate total area under a curve plotted against varied time intervals (abscissas), whereas other formulas only allow the same time interval; and 4) compare total areas of metabolic curves produced by different studies.

CONCLUSIONS — The Tai model allows flexibility in experimental conditions, which means, in the case of the glucose-response curve, samples can be taken with differing time intervals and total area under the curve can still be determined with precision.

Estimation of total areas under curves of metabolic studies has become an increasingly popular tool for evaluating results from clinical trials as well as research investigations, such as total area under a glucose-tolerance or an energy-expenditure curve (1,2). Three formulas have been developed by Alder (3), Vecchio et al. (4), and Wolever et al. (5) to calculate the total area under a curve. However, except for Wolever et al.'s formula, other formulas tend to under- or overestimate the total area under a metabolic curve by a large margin.

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RESEARCH DESIGN AND METHODS

Tai's mathematical model

Tai's model was developed to correct the deficiency of under- or overestimation of the total area under a metabolic curve. This formula also allows calculating the area under a curve with unequal units on the *X*-axis. The strategy of this mathematical model is to divide the total area under a curve into individual small segments such as squares, rectangles, and triangles, whose areas can be precisely determined according to existing geometric formulas. The area of the individual segments are then added to obtain the total area under the curve. As shown in Fig. 1, the total area can be expressed as:

Total area = triangle a + rectangle b + triangle c + rectangle d + triangle e + rectangle f + triangle g + rectangle h +...

If y = height, x = width

Area (square) = x^2 or y^2 $(x = y)$;

Area (rectangle) = xy;

Area (triangle) = $xy/2$

Let: $X_1 = x_2 - x_1; X_2 = x_3 - x_2$

$X_3 = x_4 - x_3; X_4 = x_5 - x_4;$

$X_{n-1} = x_n - x_{n-1}$

$$\text{Total Area} = \tfrac{1}{2}X_1 (y_2 - y_1) + X_1y_1 + \tfrac{1}{2}X_2 (y_3 - y_2) + X_2y_2 + \tfrac{1}{2}X_3 (y_4 - y_3) + X_3y_3 + \tfrac{1}{2}X_4 (y_5 - y_4) + X_4y_4 + \ldots + \tfrac{1}{2}X_{n-1} (y_n - y_{n-1}) + X_{n-1}y_{n-1}$$
$$= \tfrac{1}{2} (X_1y_1 + X_1y_2 + X_2y_2 + X_2y_3 + X_3y_3 + X_3y_4 + X_4y_4 + X_4y_5 + \ldots + X_{n-1}y_{n-1} + X_{n-1}y_n) = \tfrac{1}{2} [X_1(y_1 + y_2) + X_2 (y_2 + y_3) + X_3 (y_3 + y_4) + X_4 (y_4 + y_5) + \ldots X_{n-1} (Y_{n-1} + Y_n)]$$

If the curve passes the origin, $1/2[X_0y_1]$ should be added to above formula. If the curve intercepts at y_0 at the *Y*-axis, let $X_0 = x_1 - x_0$, $1/2[X_0(y_0 + y_1)]$ should be added to the above formula; Tai's formula applied to different conditions:

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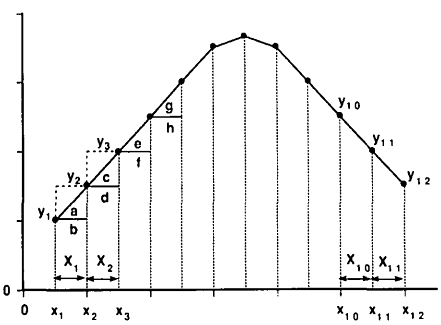

Figure 1—*Total area under the curve is the sum of individual areas of triangles a, c, e, and g and rectangles b, d, f, and h.*

$$\text{Area} = \frac{1}{2}\sum_{i=1}^{n} X_{i-1}(y_{i-1} + y_i)$$

(Tai's formula)

When the curve passes the origin: $x_0 = y_0 = 0$, $X_0 = x_1 - 0$;
When the curve intercepts Y-axis at y_0: $X_0 = x_1 - 0$
When the curve neither passes the origin nor intercepts at y-axis: $X_0 = y_0 = 0$

Example using Tai's model:
Blood glucose determined at six time periods: (6)

time (min)	0	30	60	90	120
Glucose (mg/dl)	95	147	124	111	101

$X_0 = x_1 - x_0 = 30 - 0 = 30$;
$X_1 = 60 - 30 = 30$; $X_2 = X_3 = 30$

$$Area = \frac{1}{2}[30(95 + 147) + (147 + 124) + (124 + 111) + (111 + 101)] = 14400 \text{ mg/dl/120 min}$$

RESULTS

Comparison of Tai's formula to other formulas

Five sets of laboratory data from the previous experiments of the author are used here for calculating the total area under a curve using the four different formulas as indicated above. The validity of each model was verified through comparison of the total area obtained from the above formulas to a standard (true value), which is obtained by plotting the curve on graph paper and counting the number of small units under the curve. The sum of these units represents the actual total area under the curve. Results are presented in Table 1. From Table 1, it is evident that total area I can not be obtained from Alder's formula. Total area II has underestimated the total area under a metabolic curve by a large margin. Total area III corresponds well (− 6.1%) with the actual area estimated from the plot (total area V). However, this formula only permits a single t value, which means the time interval has to be the same.

CONCLUSIONS

Verification of Tai's mathematical model

From Table 1, it is clear that Tai's formula (total area IV) has the most accurate estimation of the total area under a curve. Total area IV agrees extremely well with actual total area obtained from the graph (+ 0.1%). Because no statistically significant differences were found between areas from these two methods, the validity of Tai's model can thus be established.

This formula also permits accurate determination of total area under the curve when the curve intercepts with Y-axis, as well as when the curve passes the origin. Furthermore, in this formula, values on X-axis do not have to be the same as the t in Wolever et al.'s formula. It allows flexibility in experimental conditions, which means, in the case of glucose-response curve, samples can be taken with differing time intervals and the total area under the curve can still be determined with precision. Thus, if different authors estimate the total area under a curve from

Table 1—*Summary of results: (% area: % of total area V)*

Total area	I	II	III	IV	V
Test					
Glucose	N.A.*	480 (3.3%)	13517 (94.3%)	14400 (100.4%)	14337
TEF (SM)	N.A.*	336 (3.2%)	9588 (92.6%)	10326 (99.8%)	10349
TEF (LM)	N.A.*	452 (3.2%)	13367 (94.7%)	14163 (100.3)	14115
RMR (L)	N.A.*	1157 (3.9%)	N.A.†	30040 (100.0%)	30047
RMR (O)	N.A.*	1636 (4.6%)	N.A.†	35733 (100.0%)	35725
Ave		(3.6%)	(93.9%)	(100.1%)	

t tests: II:V $P < 0.005$; III:V NS; IV:V NS

Area I: Alder (3)*; Area II: Vecchio et al. (4);
Area III: Wolever et al. (5); Area IV: Tai's Model
Area: V: Graphic Method;

Metabolic studies:
Test I
Blood glucose at six time periods before and after a glucose load: (blood glucose: x, mg/dl; time interval between tests $t = 30$ min; obese women: $n = 6$) (6)
Test II and III
Thermic effect of food at ten time periods after one large meal (LM: 750 kcal) or six small meals (SM: 125 kcal)
(TEF: $\bar{x}$, 10^{-2} kcal · min^{-1} · kg^{-1} LBM; $t = 30$ min; lean women: $n = 7$) (2)
Test IV and V
Resting metabolic rate of lean (L) and obese (O) women.
(RMR: $\bar{x}$ 10^{-2} kg · min^{-1} · kg^{-1} LBM; L: $n = 7$, O: $n = 8$; $t_1 = t_2 = 20$ min; $t_3 = 25$ min; $t_4 = t_5 = t_6 = 30$ min) (6)

*Nonapplicable because of the irregular shape of the curve.
†Nonapplicable because of the uneven time intervals.

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Tai's formula, comparisons can be made between areas under curves produced under different experimental conditions.

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