

## ON THE NATURE OF THE EQUATION FOR GROWTH PROCESSES.

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### I.

It was found by Bliss (1925-26) that there are certain deviations in the temperature characteristic when part of a given developmental period of *Drosophila* (prepupa) is passed at a lower temperature. If the equation used by Robertson (1923) to express the course of growth were correct, then an animal should pass corresponding portions of its development, as expressed in per cent of total developmental time, at any temperature that was favorable for development at all (Crozier, 1926-27). Just why this relation between temperature and partial times for development should be true in the case of Robertson's equation may be seen by an examination of the implications of the equation. Its differential form is

$$\frac{dx}{dt} = Kx(a - x),$$

where  $a$  is the initial endowment of a growth-promoting substance and  $x$  the amount formed after time  $t$ . A sigmoid curve results from the well known integrated form of this equation

$$\log \frac{x}{a - x} = k(t - t_1),$$

where  $k = Ka$ , and  $t_1$  is the time at which the reaction is half completed; *i.e.*, when

$$x = \frac{a}{2}.$$

Since there is but one velocity constant ( $k$ ), the growth curve for an animal raised at 25° should be made to coincide with the growth

curve of the same kind of an animal at 15° by bringing the two curves together at the end-point of development when  $x = 100$  per cent, or some lesser value (*cf.* Crozier, 1926-27). But if the equation describing growth has more than one velocity constant and these constants are unequally modified by temperature changes, then the two curves for growth, when brought together at the end-point for development, will not coincide at all points along the time course of development. In other words, if an animal is allowed to develop for 50 per cent of the total normal time at 15°, and then is transferred to a temperature of 25°, it may take less time or more time to finish development than would be predicted on the basis of the fact that it has still to go 50 per cent of its total normal time at 25°. The differences between two such curves may be expressed in per cent gain or loss in time when a transfer is made from one temperature to another.

## II.

A series of experiments of this type was made with *Pseudosida bidentata*. This species yields a constant value of the temperature characteristic ( $\mu = 19,800$ ) between 14° and 28° (Brown 1926-27). The animals used were adult parthenogenetic females. These mothers, when about to release a brood of young, were isolated in test-tubes containing 25 cc. of culture water and the tubes were placed in a water bath. The bath set to operate at 25° was heated by an immersion heater, while the bath set to 15° was cooled below room temperature by means of the low temperature thermostat described by Crozier and Stier (1926-27). The control was in each case very good, as the temperature varied less than 0.01°C. The length of time required for the completion of an adult instar during these experiments was within the limits of the times determined for this species a year earlier (Brown, 1926-27) with somewhat less precise temperature control.

The average time for the completion of an adult instar (Table I) was obtained at 15° and at 25°. Then animals were allowed to develop at 15° for approximately  $\frac{1}{4}$ ,  $\frac{1}{2}$ , and  $\frac{3}{4}$  of the full time for completion of the instar at this temperature and then transferred to 25° and allowed to finish development (*i.e.*, until the release of the next brood). The reverse experiments were also made, by allowing the

animals to begin development at 25° and then making transfers to the lower temperature. The time gained or lost as the result of a transfer was computed as a percentage of the total time. The two theoretical curves (Fig. 1, C) which are drawn are separated from each other by an amount represented by this gain or loss. Of course it is not known that the curves are really sigmoid, but they probably are since most

TABLE I.

Apparent gain or loss in time when developing *Pseudosida bidentata* are transferred from 25° to 15° and from 15° to 25°. The "calculated total time" for development is the time passed at Temperature 1, plus the computed time for the remaining proportionate fractional time at Temperature 2. The gains and losses in time are given in the last vertical column as percentages of the total time, with their probable errors.

Condition of experiment	At 25°	At 15°	Actual total time	Calculated total time	Gain or loss in time
	<i>hrs.</i>	<i>hrs.</i>	<i>hrs.</i>	<i>hrs.</i>	<i>per cent</i>
Full time at 25°.....	46.0±.5				
33.1 hrs. at 25°, then transferred to 15°.....		35.4±.9	68.5	72.2	+5.0±.7
22.1 hrs. at 25°, then transferred to 15°.....		69.1±.8	91.2	94.6	+3.6±.5
11 hrs. at 25°, then transferred to 15°.....		108.0±1.7	119.0	117.1	-1.6±.4
34.3 hrs. at 15°, then transferred to 25°.....	35.7±.4		70.0	69.0	-1.3±.7
70.2 hrs. at 15°, then transferred to 25°.....	24.5±.8		94.7	93.0	-1.8±.5
105 hrs. at 15°, then transferred to 25°.....	13.2±.6		118.2	116.4	-1.5±.4
Full time at 15°.....		139.6±.4			

growth curves are of this shape, and at least the experimental points cannot be represented as falling on straight lines.

Two cases already published by others give data which may be compared with the foregoing. The curves shown in *A* of this figure are from data by Titschak (1925) for the pupal development of the clothes moth *Tineola biselliella* at 20° and 30°. Data are not given which would enable one to determine the presence or absence of a break in the graph for *log rate* against *reciprocal absolute temperature*

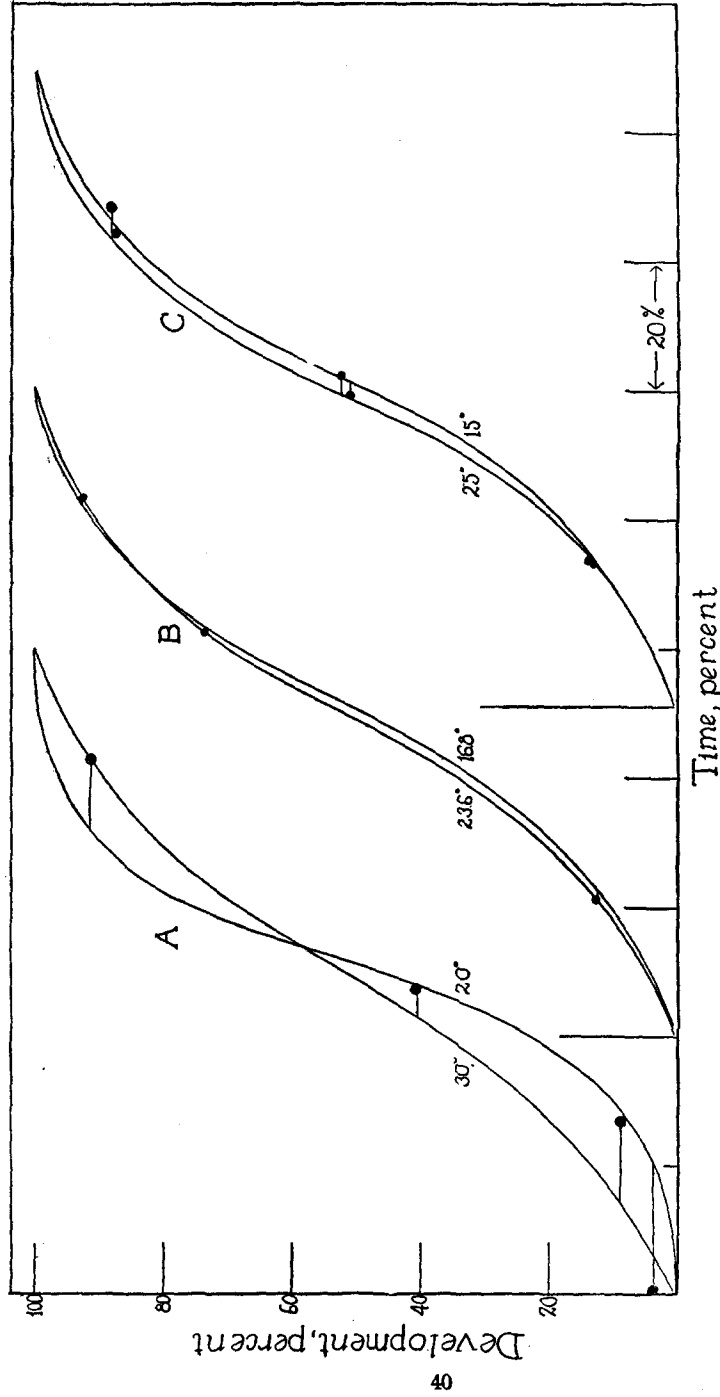


FIG. 1. A. *Tineola biselliella* (Titschak, 1925). B. *Drosophila melanogaster* (Bliss, 1925-26). C. *Pseudosida bidentata*. Graphs showing the general character of theoretical growth curves at two temperatures, as determined by the apparent gain or loss in time resulting from a transfer of developing animals from one temperature to the other. The curves are brought together at 100 per cent development by expressing the time in per cent. The horizontal lines and the symbols represent experimental transfers; those drawn to the left are losses in time and those to the right gains in time. The diameters of the symbols approximate the probable errors of the observations.

between these temperatures. The middle pair of curves (*B*) in this figure are from the data of Bliss (1925-26) for the prepupal development of *Drosophila*. These data were very carefully collected and the differences while small are statistically significant. In the graph for *P. bidentata* (*C*), as is also approximated in the two other cases, the diameter of the symbols represents the probable error of the observations. Of especial significance is the fact that the two transfers near 50 per cent on the time axis give approximately the same difference, but one (15-25°) represents a loss of time while the other represents a gain.

### III.

The fact that it is impossible to make such pairs of curves coincide throughout, means that the growth equation of Robertson (1923) cannot hold; but that an equation with at least two velocity constants, which are unequally affected by temperature, must apply. Crozier (1926-27), in the paper referred to, has used such an equation, which is also apparently the correct one for a first order process with positive autocatalysis. The differential form of this equation is

$$\frac{dx}{dt} = (K_1 + K_2x)(A - x),$$

where  $K_1$  is the velocity constant proper to the reaction  $A \rightarrow x$ , but in the absence of the catalytic effect of  $x$ , while  $K_2$  is the velocity constant associated with  $x$  as a catalyst. The velocity of the formation of  $x$  will pass through a maximum (inflection point of the growth curve) when

$$x = \frac{K_2A - K_1}{2K_2}.$$

This equation was found to apply to the complete growth cycle of another species of cladoceran (Brown and Crozier, 1927-28), and presumably applies to the course of development within a single adult instar.

The integral form of the differential equation is

$$t = \frac{1}{K_1 + K_2A} \ln \frac{A(K_2x + K_1)}{K_1(A - x)}.$$

The curve of this equation is sigmoid, but the inflection point depends on the ratio between the two velocity constants, and the resulting curves may be decidedly asymmetrical.

Results of the type indicated in Fig. 1 may be taken to prove that the curve describing the course of a developmental epoch must contain at least two velocity constants, and the equation proposed (Crozier, 1926-27) has made it possible to predict that the effects of changing temperature during development should be of the sort actually found. It was implied in the original account of this equation that such effects might be employed for the mapping out of the curves for processes otherwise "unseen." It is also obvious that these effects are of major significance for the understanding of the influence of fluctuating environmental temperatures.

#### SUMMARY.

An analysis of the growth curves of a cladoceran for one adult instar at each of two temperatures is made by comparing the apparent gains or losses in time when the animals are transferred from one of these temperatures to the other during the course of the developmental period. Since the curves for the two temperatures when brought together at their end-point do not coincide, the equation used to describe growth must have at least two velocity constants unequally affected by changes in temperature.

#### CITATIONS.

- Bliss, C. I., 1925-26, *J. Gen. Physiol.*, ix, 467.  
Brown, L. A., 1926-27, *J. Gen. Physiol.*, x, 111.  
Brown, L. A., and Crozier, W. J., 1927-28, *J. Gen. Physiol.*, xi, to appear.  
Crozier, W. J., 1926-27, *J. Gen. Physiol.*, x, 53.  
Crozier, W. J., and Stier, T. J. B., 1926-27, *J. Gen. Physiol.*, x, 501.  
Robertson, T. B., 1923, *The chemical basis of growth and senescence*, Philadelphia.  
Titschak, E., 1925, *Z. wissenschaft. Zool.*, cxxiv, 123.