

ON CURVES OF GROWTH, ESPECIALLY IN RELATION TO TEMPERATURE.

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I.

Growth generally manifests an accelerated velocity during the mid-portion of a developmental cycle, so that the curve of bulk with time is sigmoid. This fact gave rise (Ostwald, 1902; Errera, 1899-1900; Robertson, 1907-08) to the view that the accumulation of material during growth may be described by the equation for a first-order process in which one of the products of the transformation acts as catalyst. This conception has had a vigorous enlargement (Robertson, 1923), looking toward the description of the velocity of development as governed by a succession of first-order chemical processes, "master reactions," which are self-accelerated.

Several difficulties are connected with the application of this idea. One of these is that in fitting simple logistic (autocatalytic) curves to actual data, it has usually been assumed (*cf.* Robertson, 1923; 1925-26) that the curve of growth in any cycle is symmetrical about a mid-point of inflection. This follows from the nature of the equation commonly taken to give the course of such an autocatalyzed process:

$$\frac{dx}{dt} = K x (A - x), \quad (1)$$

where A signifies the initial endowment of the growth-promoting precursor, x the amount formed after time t . The point of inflection in the integral curve of this equation is located at

$$x = A/2.$$

A method of testing the sufficiency of this form of the autocatalysis equation is afforded by the study of rates of development as controlled

by temperature. The autocatakinetic relationship (Lotka, 1925) is of so very general a character, arising in any kind of a situation where a limited progress is facilitated by the conditions created through its initiation¹ but progressively inhibited by proportionately enforced exhaustion, that some test of this sort is necessary if the form of growth curves is to be satisfactorily understood. Thus if the simple logistic were an adequate description of growth velocity, temporary alteration of the temperature of the development would not be expected to modify the temperature characteristic (Crozier, 1924-25, *a*) for the remainder of the development. Since the temperature characteristic for the velocity constant K must be constant, changing the temperature therefore merely multiplies the time coordinates of the growth curve by a constant. The temperature characteristics obtained from what may be termed "partial developmental periods" should be the same as for the total developmental interval (within one cycle). There is adequate indication (Bliss, 1925-26) that this may not be the case. Consideration of this fact results in a modification of the formulation of the "autocatalytic" curve of growth. The modification has the merit of greater consonance with chemical theory, and of indicating a direct interpretation of the sort of results to be expected when the temperature is changed during the course of a developmental cycle. It may also give some light upon the nature of temperature characteristics for development at constant temperatures.

Let it be supposed that at the beginning of a developmental cycle there is available an unrenovable quantity, A , of a substance giving rise to another, x , which determines the velocity of growth. We are especially interested in "velocities of growth" as measured by the reciprocals of the times required to attain a given stage of development. We will suppose that the material A gives rise to x by a first order reaction, and that x serves as catalyst for this change. The reaction $A \rightarrow x$ will therefore be governed by a velocity constant (K_1) proper

¹ An interesting instance is given by the growth of knowledge of the variety of the amino acids, as plotted by Cohn (1925). A still different type of S-shaped curve may result from estimations of growth in which the numbers of cells of colonial protozoans are counted (Fauré-Fremiet, 1922); in certain species the mode of dichotomy results in the curve for number of individuals against time appearing "autocatalytic."

to it in the absence of the influence of x , and also by the velocity constant due to catalysis by x . The decomposition of A must therefore be conceived as made up of two parallel reactions, and its differential equation is then

$$\frac{dx}{dt} = (K_1 + K_2 x) (A - x), \quad (2)$$

where K_2 is the velocity constant associated with x as catalyst.

The velocity of formation of x will pass through a maximum when

$$x = \frac{K_2 A - K_1}{2 K_2}. \quad (3)$$

Therefore, if any change of condition, such as temperature, influences K_2 and K_1 unequally, the form of the curve connecting x with time will be changed and the point of inflection will move to a new relative position. Thus when K_2 is made relatively smaller, the inflection point occurs earlier (assuming A the same), and the shape of the curve is significantly altered.²

It is to be noticed that in such a system the point of inflection is found at $x = A/2$ when K_1 is of inappreciable magnitude; whereas, in case K_2 is very small the equation approaches that of the usual monomolecular curve without detectable autocatalysis.

II.

Integration of (2) yields

$$t = \frac{1}{K_1 + K_2 A} \ln \frac{A (K_2 x + K_1)}{K_1 (A - x)} \quad (3)$$

The curve of this equation may be applied to various series of observa-

² This formulation seems simpler, and leads to more suggestive consequences so far as concerns the planning of experiments, than does Robertson's (1923) suggestion of the pseudo-reversible character of the "master process" in growth; moreover, it would appear to be the obviously correct equation for an autocatalytic system. Robertson pointed out that if a reverse process in the growth equation is of higher order than the direct, the curve of increasing bulk with time becomes asymmetric about the inflection point; many if not most growth-cycles are in fact asymmetric (*cf.* Brody, 1925-26). A different mode of dealing with the asymmetry has more recently been employed by Robertson (1925-26), which amounts to assuming that x has a positive value at the beginning of a cycle.

tions; for example, to the growth in height of sunflower plants (data of Reed and Holland, 1919). The fit (Fig. 1) may be made distinctly better than when the "simple" curve of autocatalysis is employed. An adequate test of the descriptive validity of this equation for growth might be sought in the curve of increasing weight for a mammal, where temperature variation may be neglected. Donaldson's data on

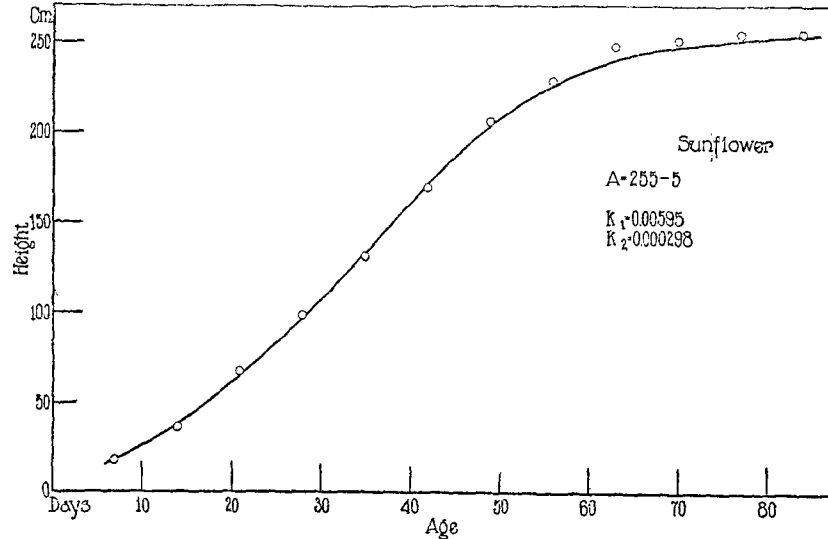


FIG. 1. Growth in height of the sunflower; data of Reed and Holland (1919); the curve is that of the equation

$$t = \frac{1}{k_1 + k_2 A} \ln \frac{A (k_2 x + k_1)}{k_1 (A - x)},$$

the cycle starting at $x = 5$ cm., with $k_1 = 0.00595$, $k_2 = 0.000298$; A , the mature height, is taken = 250.

the growth of the rat (Donaldson, 1915) are suitable for such a test, though undoubtedly complicated by the cyclic character of growth in mammals (Donaldson, 1906; Robertson, 1907-08; Brody and Ragsdale, 1922-23). Robertson (1923) has fitted to this data two "fused" logistic cycles, but the agreement is not especially good. In Fig. 2 it is shown that these data are fitted sufficiently well by the autocatalytic equation in the form $dx/dt = (K_1 + K_2 x)(A - x)$, except that for a

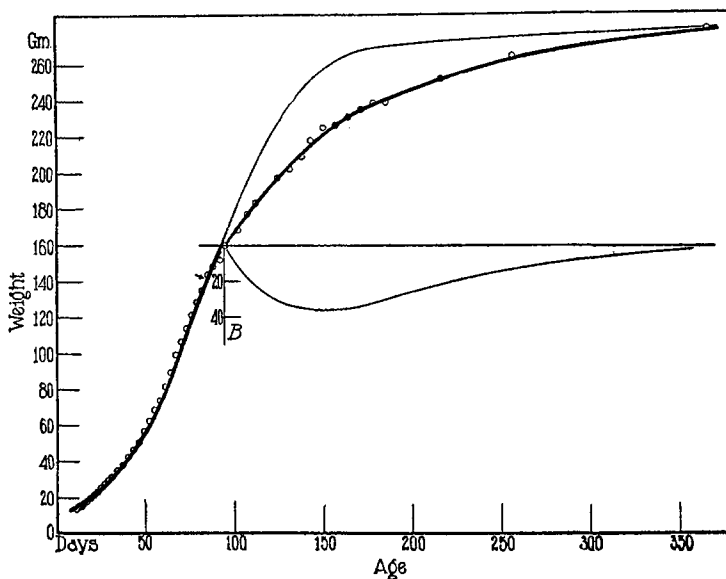


FIG. 2. Data on the growth of un-mated male white rats (Donaldson, 1915) adhere fairly well to the equation

$$t = \frac{1}{k_1 + k_2 A} \ln \frac{A(k_2 x + k_1)}{k_1(A - x)}$$

for the first 100 days. It is assumed that the weight reflects the amount of a growth-determining material x , produced in a reaction $A \rightarrow x$, which is catalyzed by x ; that the value of A is given by the maximum weight (for convenience, 280 gm.); and that the cycle starts at $x = 10$ gm. The constants for the curve as drawn are $k_1 = 0.00135$, $k_2 = 0.000135$; $x = \text{weight} - 10$.

Beyond 95 days age, it may be supposed that the material x is inhibited by another, B , produced in a system of the type $M \xrightarrow{K_3} B \xrightarrow{K_4} N$, where M is unrenewable. The thin inverted curve is the curve of this process with $M_0 = 121$, $k_3 = 0.01663$, $k_4 = 0.02375$; the equation is

$$B = M_0 \frac{k_3}{k_4 - k_3} (e^{-k_3 t'} - e^{-k_4 t'}),$$

t' being counted from $t = 95$.

The curve drawn through the observed weights (circles) is obtained by subtracting B from x .

period after 100 days age the deviation is great. It is an interesting fact, which may perhaps be used to obtain another view of the mechanism of growth "cycles," that the deviation after 100 days from the formula fitting the earlier course of the data and also its terminal range, may be accounted for quantitatively and exactly by assuming that beyond age 95 days the growth-controlling substance, x , is inhibited (but not destroyed) in proportion to the amount of a substance B produced in a system of the type $A \xrightarrow{K_3} B \xrightarrow{K_4} C$. Assuming suitable values of A , K_3 , and K_4 as found from the deviations of the data from the calculated autocatalytic curve, the accessory curve in Fig. 2 gives the values of B to which the deficiency of x is assumed to correspond. The curve drawn through the plotted points is obtained by taking the difference between B and the calculated x . From this standpoint it may be legitimate to regard the decrease in growth velocity between two cyclic accelerations as due to the presence of an inhibitor, which disappears with time and does not destroy x . It should be possible to relate an inhibition of bulk-increase to known physiological events in the organism dealt with. For the rat it can be pointed out that the maximum in the "correction curve" (B) occurs at an age of 150 days, at which time (Donaldson, 1924) the activity of the thyroid seems to attain a definite maximum and then to decline. This implies that thyroid activity is to be taken as hindering growth in bulk (at this age). Miss King's measurements of growth of rats (Donaldson, 1924) may be fitted in a similar way, with the maximum of the "correcting curve" at very nearly the same age. There is indication that the peculiar growth curve of man (summary of data in Davenport, 1926) may be accounted for in a similar way, with the maximum growth inhibition (male) at about 14 years; but the deviation from calculated autocatalytic curves is so extensive as to make difficult the adjustment of a "correction curve."

III.

The way in which the curve of equation (3) may be modified by changing the temperature is illustrated in Figs. 3 and 4. We may assume that for the completion of a developmental stage, say an instar or other definite interval in the differentiation of an insect, there must occur the production of a definite amount of a substance,

x , arising in a first order reaction $A \rightarrow x$, and that x is a catalyst for the reaction. We must suppose that in general the temperature characteristic for the catalytic effect of x will not be the same as that for the catalytic influence promoting the reaction apart from the action of x . As already pointed out, this will so affect the shape of the curve that the graphs at two temperatures are not superimposable. If one-half of the developmental period under consideration were to be passed at $t^\circ\text{C}$., this would not mean that one-half of the development would be completed, since the curve is not symmetrical. Then on passing to

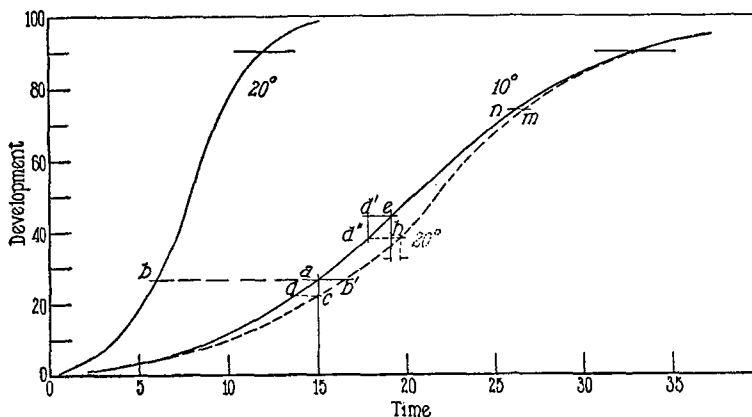


FIG. 3. Curves of the equation

$$t = \frac{1}{k_1 + k_2 A} \ln \frac{A(k_2 x + k_1)}{k_1(A - x)},$$

with $A = 100$ in each case. (Time is in arbitrary units.)

At 20° , k_1 is assumed = 0.010

k_2 " " = 0.005

At 10° , k_1 " " = 0.005 (i.e., $Q_{10} = 2$)

k_2 " " = 0.0017 (i.e., $Q_{10} = 2.94$)

These curves are not superimposable; the dashed curve is that for the 20° conditions, expanded by multiplication of the abscissæ by a factor which makes the curves coincident at $x = 0.90A$.

If such curves are assumed to underlie development, and if we assume that at completion of a given stage $x =$ a definite fraction of A , say = 90 per cent, then Q_{10} for velocity of development is (from the curves) $32.92 \div 12.02 = 2.74$. As A is assumed larger and larger, the Q_{10} ratio for velocity of development approaches nearer and nearer to the Q_{10} for k_2 . (If the assignment of Q_{10} 's is reversed, Q_{10} for $x = 0.90A$ is 2.13.) Additional details are discussed in the text.

another temperature, the development still to be completed would be (depending on the alteration in the ratio K_1/K_2) either more or less than the fraction uncompleted before the transfer; and the time required to produce the necessary fixed amount of x would be correspondingly greater or smaller than what would be calculated; hence the apparent temperature coefficient for the velocity of the partial de-

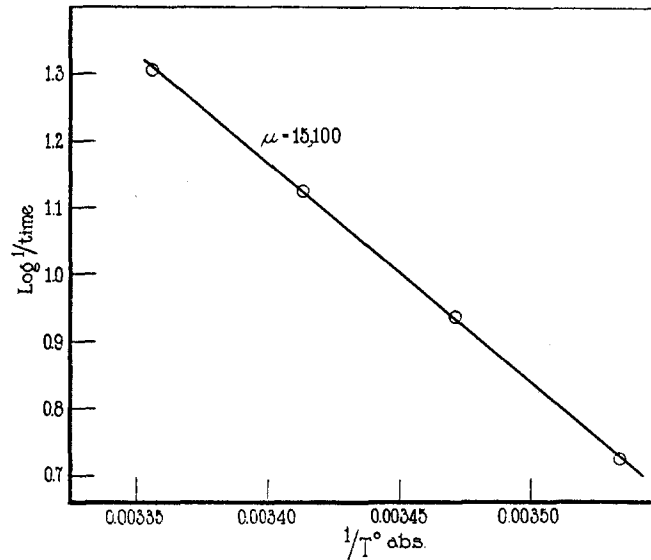


FIG. 4. From the autocatalytic curve, with assumed values $A = 500$, $k_1 = 0.08$, $k_2 = 0.0015$, and with μ for $k_1 = 11,000$, for $k_2 = 16,000$, values of the time are calculated to give $x = 490$. The reciprocals of these times are plotted logarithmically against $1/T^{\circ} \text{ abs.}$, at 10° , 15° , 20° , 25°C . The relationship is almost exactly rectilinear, and the temperature characteristic obtained from the graph (fitted line) is $\mu = 15,100$. This shows that in a system of the sort discussed in the text it is possible to estimate an apparent critical increment which agrees fairly closely with that for one of two catalytic velocity constants concerned in an autocatalytic activity.

velopment would not be the same as for the total development when passed at constant temperatures. (No account is here taken of differences produced by "breaks" in the curve of developmental rate with temperature.)

The assumption of a definite amount of x as marking the termina-

tion of a developmental interval is required because the end-product of growth is the same at each temperature. It is convenient to regard this amount as a fraction of A , the original endowment. With arthropods in particular, the succession of developmental intervals is so definite that one is forced to think of their termination as controlled by "trigger effects," such as might be provided through the accumulation of a governing substance to a critical concentration rather than by the asymptotic approach to completion which would correspond to the extinction of A in our model.

It is desirable to show that deviations in apparent temperature coefficient when part of a developmental period is passed at another temperature, such as those recorded by Bliss (1925-26), may be systematically accounted for. (1) If, in Fig. 3, the organism is maintained at 10° for a calculated fraction of the developmental time interval (*i.e.* to a) it is then ahead of schedule by comparison with the curve of development at 20° (b'); hence the supposed portion of the development still to be completed (from b') is actually less, on transfer to 20° , and the apparent temperature coefficient in consequence is larger than if rates of complete development at 10° and at 20° are compared.

(2) On the other hand, if exposure to low temperature occurs during an intermediate fraction (from c to e), the development is "behind schedule" at c (by the amount $c a$ corresponding to the time $c d$), and on arrival at time e , calculated to give a certain fraction of the total developmental time, this will actually be fallen short of so far as concerns differentiation by the amount h , so that the degree of development is then in fact that represented at point d' . If now the organism be brought back to 20° , the developmental level is indicated at point h , which is ahead of that assumed at time e ; during subsequent development at 20° the developmental course still to be completed is thus less than that calculated and hence appears faster; but with the conditions shown the apparent acceleration is less than in the first case, where transfer from the 10° to the 20° curve results in a considerable time-saving and therefore in a marked increase of calculated temperature coefficient.

(3) Again, if transfer from the 20° curve to the 10° be made late in development, as at point m , time is lost, because the relative develop-

ment is greater at the same time along the 10° curve; therefore the calculated temperature coefficient is actually less than that obtained from uninterrupted developments at 10° and at 20°.

For the prepupal period of *Drosophila*, with a normal temperature characteristic 16,850, Bliss (1925-26) found that in experiments of type (1) the apparent μ was 20,220; of type (2), 18,770; of type (3), 16,570. There is additional indication of just this sort of relationship in data given by Titschak (1926) for the rate of development in the clothes moth *Tineola*. The particular curves drawn in Fig. 3 are of course intended merely to show that it is possible to explain such results. It is significant that this explanation turns upon properties of an equation which describes with some precision the time course of growth and differentiation such as can be visibly evidenced by increasing weight, and which it is therefore legitimate to suppose may describe even more accurately the progress of developmental changes measurable only by the incidence of their end-results.

IV.

Although few investigations of growth permit very precise estimations of critical thermal increments, it is nevertheless important that there is indication of diverse magnitudes of μ , the temperature characteristic, for different cases; and that these values are suggestively close to those known to be associated with various other vital processes (Crozier, 1925-26). A careful investigation of a particular developmental stage in *Drosophila* has been made by Bliss (1925-26); Brown (1926-27) has determined the temperature characteristics for a developmental interval in cladocerans; the values of μ derived for these phenomena correspond to values repeatedly found in processes of quite different sorts (Crozier, 1925-26; Crozier and Stier, 1925-26). This is a striking fact, because one would be inclined to believe that chemical mechanisms controlling growth might be very different from those having to do, for example, with the regulation of the heart-beat or of breathing movements. This suspected difficulty might be overcome if it could be shown that the velocity of development, or the duration of life in particular stages, is determined, not by the magnitude of some simple underlying chemical change, but by the velocity with which this change is taking place. Northrop (1925-26) has indeed

shown that the duration of life in *Drosophila* does not depend upon the transformation of a definite amount of energy (Rubner), since the amount of CO_2 produced during life is not a measure of the life duration.

Aside from this possibility, however, the curve of equation (3) has some interesting properties which indicate another mode of interpretation. The reciprocal of the time for production of, say, $x = 0.90 A$, will have a temperature coefficient which depends on the magnitudes of K_1 , K_2 , and A , and of the temperature coefficients of K_1 and K_2 . If A be put = 100, and $K_1 = 0.010$, $K_2 = 0.005$, at 20° , with the respective temperature coefficients Q (10° - 20°) = 2.0 and 2.94, then Q (10° - 20°) for $1/t$ will be 2.74. Thus the temperature coefficient for $1/t$ may agree very closely with that for one of the two velocity constants.

This kind of relationship may be illustrated by one particular set of assumptions as to the values of A , K_1 , and K_2 , when it is supposed that $\mu = 11,300$ for K_1 and $\mu = 16,500$ for K_2 . We desire to see whether the values of $\log 1/t$ will in such a case give a rectilinear relationship to the reciprocal of the absolute temperature, as seems to be the case in growth. It is seen that with very small deviation, such as would probably be overlooked in practical cases, they, indeed, do give this relationship (Fig. 4).³ This is sufficient to demonstrate that an autocatalytic system in which two velocity constants are implicated may permit the approximate evaluation of temperature characteristics, and that these may even be quite close to those corresponding to the

³ It is easily seen that with other values of K_1 , K_2 , the agreement could be very much closer. The values used in this illustration are chosen merely to show the slightly curvilinear character of the plot (Fig. 4), which would otherwise be detected with difficulty.

It may be pointed out that calculations of $1/\text{time for completion}$ of a stage of development based upon the integral form of $dx/dt = (K_1 + K_2 x)(A - x)$ do not yield "breaks" in the curve of $\log(1/\text{time})$ vs. $1/T^\circ \text{ abs.}$, even when such temperature characteristics are assumed as reverse the sign of the difference between K_1 and K_2 at the extremes of temperature. In such a case the μ calculated from the times required to produce $x = 0.90 A$ agrees rather closely with that μ , whether of K_1 or K_2 , which happens to be smaller. It is of interest that in a system of this kind it is the magnitude of the *temperature characteristic*, rather than of the velocity constant, which chiefly determines the apparent μ of the resultant.

action of specific catalysts. The calculated curve is not exactly rectilinear, but in practice it may be very difficult to decide the origin of deviations at the extremes of the temperature range. It may be pointed out, however, that one may, from this standpoint, expect to find evidence of: (1) slight differences in critical increments when contrasting growth phenomena with other common activities, (2) relationships between $\log 1/time$ and $1/T^\circ$ abs. which are not exactly rectilinear, but concave toward the $1/T^\circ$ axis, and (3) deviations of critical increment when development is passed in part at one temperature, in part at another. The testing of these, especially (1) and (2), is at present handicapped by absence of precise data.

v.

In discussing growth rates as controlled by temperature it must be kept in mind that the momentary growth rate may vary with time. This may result not merely from the form of the growth-curve, but also because the growth-curve may smooth out recurrent cyclic variations in rate. An instance has already been given (Crozier, 1924-25, *b*), derived from Leitch's measurements of root elongation in the sweet pea. The temperature characteristics in this case differ markedly, depending upon the time period (0.5 hour or 24 hours) involved in the measurement. This is probably related to the fact that cell division occurs at a fairly definite point in a diurnal growth-rhythm (Stålfelt, 1921). Other kinds of complexity are not unexpected, for no one in his senses regards growth as an uncomplicated process. Lehenbauer's (1914) data show that the mean hourly elongation of maize seedlings increases abruptly at 20° , and with time. The average μ above 20° is about 15,500. Where such "breaks" occur in the temperature graph the effects to be expected when time is a significant variable are difficult to predict.

It is, nevertheless, of interest to examine the available measurements of growth to see if they yield anything in the nature of consistent temperature characteristics. A number of observers have studied the growth of fungal colonies as related to temperature. The data are not always presented in the most directly usable form, nor can the probable retarding effects of changes in the medium be discounted with any sureness. In the growth of such colonies on agar plates it is to be

supposed that in the absence of retarding or accelerating effects the rate of enlargement should be constant. A correct measure of growth, assuming only extension in area to occur, would be given by the increase in area per unit of circumference per unit time. When growth of such a colony gives a sigmoid curve with time it is certainly inap-

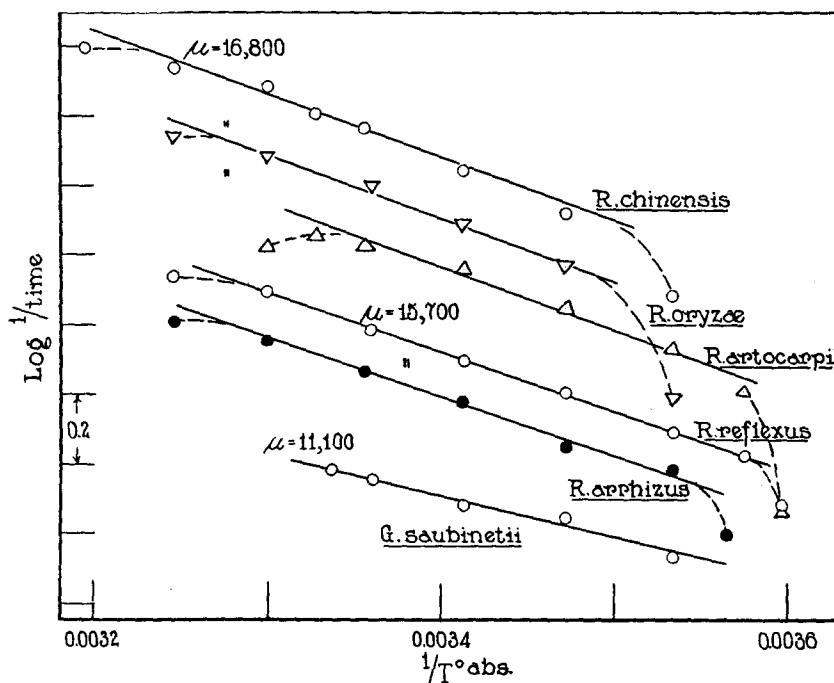


FIG. 5. The velocity of early growth in 5 species of *Rhizopus*, measured by the time required for the germinating hypha to become as long as the diameter of the spore (data from Weimer and Harter, 1923); and the growth of *Gibberella saubinetii*, taken as $1 \div$ time for colony to attain a diameter of 2.5 cm. (by interpolation from data of MacInnes and Fogelman, 1923). It is apparent that aside from terminal deviations such as are usually encountered the temperature characteristics closely resemble those calculated from data on respiration (Crozier, 1924-25, b).

appropriate to regard the curve as describing an inner autocatalyzed growth-controlling process, and hence probably useless to attempt analysis of its precise relations to temperature. Fawcett (1921) records the growth in diameter of colonies of several fungi. These figures have been used to calculate the areal increase per unit time

(24 hours) per unit of growing edge at successive intervals. The rate of enlargement so computed changes with time, in such a way as to suggest that more extensive measurements would, at each temperature, pass through a maximum. The initial growth of the colony so affects the medium that growth is accelerated. Estimations of the temperature characteristic of the inner growth-promoting process would, therefore, require the separation of the effects of temperature upon growth from those involving changes induced in the medium.

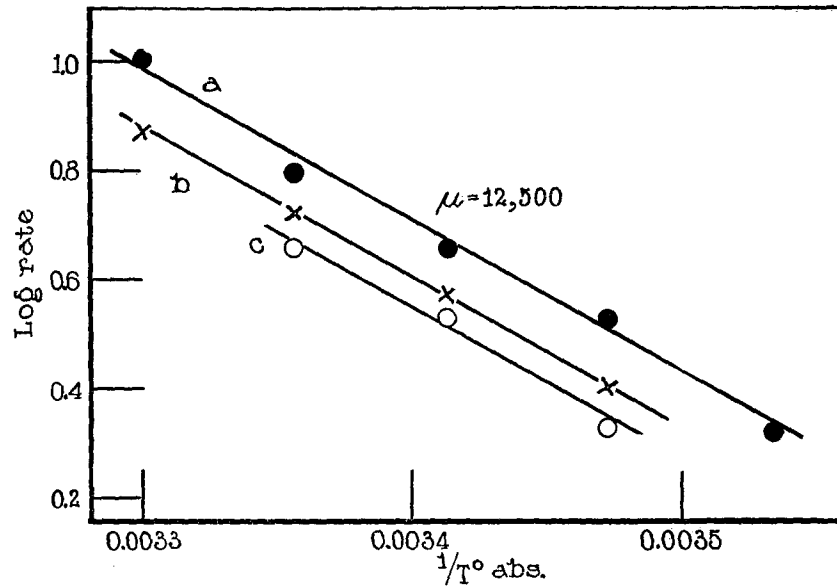


FIG. 6. The rate of decay of sweet potatoes inoculated with *Rhizopus*. The temperature characteristic is sensibly independent of the end-point chosen (*i.e.*, the amount of destruction, presumably determined in greater part by the activity of the fungus). Data from Lauritzen and Harter (1925).

Weimer and Harter (1923) studied the germination and growth of a number of species of *Rhizopus*. From their curves it is possible to plot the reciprocals of the times required for the germ tubes to grow until the length equals the diameter of the spores; these figures provide mean velocities of growth for the attainment of a constant amount of growth (Fig. 5). The agreement with the Arrhenius formula is usually excellent, since the deviations at high and at low temperatures

are no different from those generally encountered in other vital systems. The values of μ accord sufficiently well with those known in other growth phenomena.

In such a case it is to be presumed that the temperature characteristic obtained is not a property of the constants in an autocatalytic system, but pertains merely to a metabolic mechanism immediately responsible for increase in bulk.

MacInnes and Fogelman (1923) measured the growth of colonies of *Gibberella saubinetii*, and from their figures it is possible to obtain by interpolation the time required at several temperatures to form a colony of given size (diameter). Data from Lauritzen and Harter (1925) may be used in a similar way, giving the time required for *Rhizopus* to produce a given amount of decay in sweet potato. These measurements are plotted in Figs. 5 and 6, where the corresponding temperature characteristics are indicated.

These instances illustrate the applicability of the Arrhenius equation but they do not permit critical examination of the meaning of the corresponding temperature characteristics. It can be said merely, that in general the critical increments resemble in their magnitudes those already encountered in various other vital activities. A similar vagueness of interpretation is necessary in connection with studies of growth and regeneration in animals. Moreover, and aside from experimental difficulties in temperature control, many cases are disturbed by the fact that the developmental process under examination was not exactly begun at the temperature indicated, but the lot of organisms was distributed to thermostats some little time *after* development had begun. Bearing this difficulty in mind, we may, however, examine the velocity of development in several instances. It should be noted that there is direct justification for regarding a morphological end-point as a legitimate end-point for our purpose, provided it be timed with precision; Terroine and his associates (Terroine, Bonnet, and Joessel, 1924; Barthélemy and Bonnet, 1924) have indicated that thermal acceleration of development to a constant stage (*e.g.* to absorption of external gills, in the tadpole; germination of seeds) does not modify the utilization of energy during the growth process,—in other words, the chemical “balance” is the same at the same stage of development. But in many instances it may be impracticable to obtain a significant morphological end-point.

The speed of early cleavage of the fertilized ovum has been measured by Loeb and Wasteneys (1911) and by Loeb and Chamberlain (1915), for the egg of *Arbacia*. These two series of measurements are concordant, and exhibit critical increments 12,400; 21,000; 41,000,

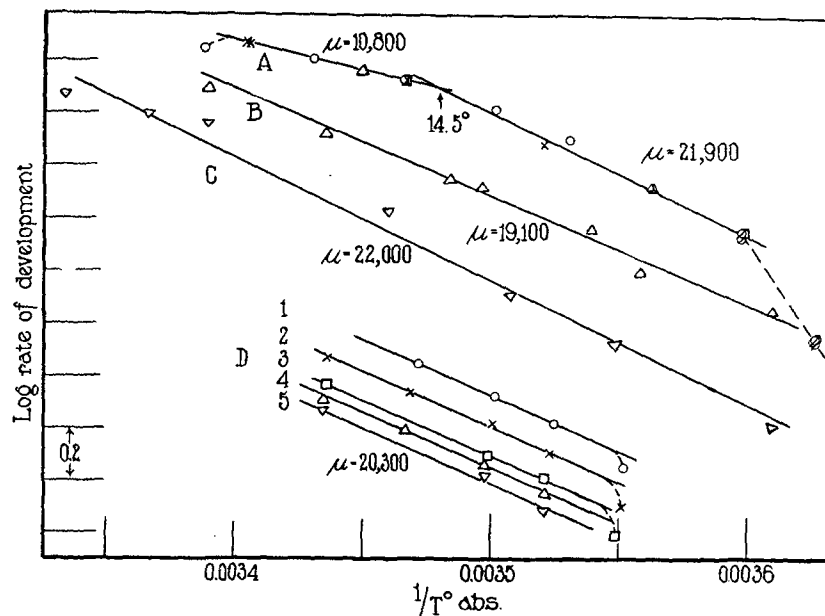


FIG. 7. Data upon the rate of cleavage and upon early stages of development in anurans.

A. Processes involved in the first cleavage, *Rana* (from Krogh, 1914).

B. From first cleavage to disappearance of yolk-plug (from Lillie and Knowlton, 1897).

C. From first, second, or third cleavage to disappearance of yolk-plug (Lillie and Knowlton, 1897).

D. From fertilization to: (1) medullary groove, (2) external gills, (3) 3 gill plumes, (4) a length of 7.0 mm., (5) a length of 7.8 mm.; *Rana* (Data from Krogh, 1914).

It is clear that there is a measure of consistency in the occurrence of $\mu = 20,000 \pm$. This is indicated also in some fragmentary data from Barthélemy and Bonnet (1924). Hertwig's data (cf. Cohen, 1901) also show parallelism in the effect of temperature at different stages of development, but indicate for the intermediate range of temperatures a distinctly lower μ , $17,000 \pm$. Estimations of the rate of growth of the body, and of the tail, in *Rana* and *Bufo*, agree in indicating $\mu = 24,000 \pm$ (data from Lillie and Knowlton, 1897).

with "breaks" at 11° and at 20° (Crozier, 1924-25, b). The velocity of segmentation in eggs of the frog (first cleavage) is plotted in Fig. 7, from data by Krogh (1914). The velocity of subsequent early

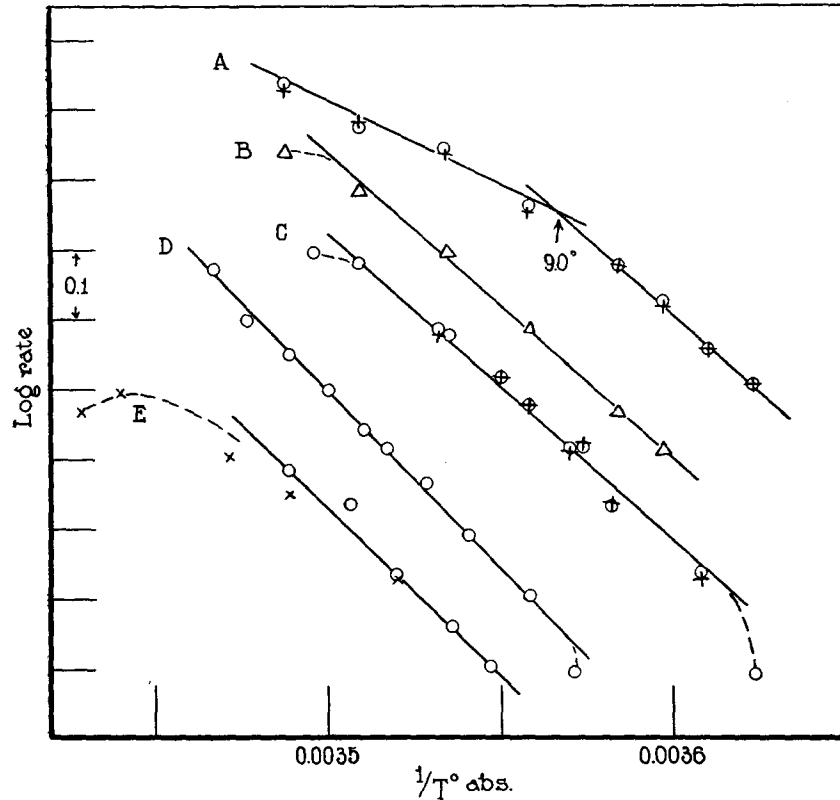


FIG. 8. Data upon the development of teleosts:

A, *Gadus morrhua* and *G. æglefinus*; B, *G. merlangus*; average velocities of development up to hatching; observations by Dannevig (in Johansen and Krogh, 1914); for A, $\mu = 11,800$ and $\mu = 20,200$, with break at 9.0°C; for B, $\mu = 20,000$.

C, Plaice; to length 4.6 mm., circles; to length 4.9 mm., crosses; the two series brought together by multiplying the members of the second by a factor; $\mu = 20,000$. (Johansen and Krogh, 1914).

D, *Hypomesus olidus* (Higurashi and Tauti, 1925); $\mu = 23,700$.

E, *Plecoglossus altivelis*; two series, one from Higurashi and Tauti (1925), the second from Higurashi and Nakai (1926); $\mu = 23,000$.

It should be noted that in the cases of deviation at extreme temperatures there is independent evidence of abnormal differentiation.

development of the frog, in Krogh's experiments, exhibits a constant increment not significantly different from that for the mid-range of temperatures (15° to 4.7°) in the case of the first cleavage, but the critical temperatures are different.

It is noteworthy that in the case of amphibian development the temperature characteristics calculated from the data of Lillie and Knowlton (1897) upon the early development of *Rana* and of *Amblystoma* (Fig. 7) may be said to agree quantitatively with the magnitude obtained over the lower temperature range (4° to 15°) in Krogh's (1914) experiments.

The rate of development of teleost embryos has been studied by Krogh and others. The more extensive series of observations are collected in Fig. 8. More recent experiments on the rate of insect development provide data showing for *Dytiscus marginalis* $\mu = 19,300$, for *D. semisulcatus* $\mu = 20,000$ (to 15°) and $\mu = 10,400$ (data from Blunk, 1923). Some figures from Ziegelmayr (1926) for rate of development of *Cyclops* give $\mu = 15,700$. Such data have been treated in a different way by Krogh (Johansen and Krogh, 1914), but the most direct utilization of the measurements shows that there is a striking constancy in the occurrence of $\mu = 20,000$, with one series showing $\mu = 24,000$; thus there is evidenced a suggestive parallelism with the values obtained for amphibian development.

For the full interpretation of such graphs it is necessary to know the effect of the preliminary period during which the objects (*e.g.*, fertilized eggs) have been maintained at some constant or nearly constant temperature before distribution to thermostats at different temperatures. In the light of the view previously set forth in this paper it would be expected that if at all prolonged this preliminary interval might well have a definite and detectable effect. It would be expected to accentuate any innate departure from the rectilinear character of the plots, or might seriously affect the apparent magnitude of the temperature characteristic. This especially makes it impossible to use critically much of the early material on insect development (*cf.* Sanderson, 1910; Sanderson and Peairs, 1913), although it supplies interesting suggestions. In the most carefully conducted experiments the

adherence to rectilinearity is certainly satisfactory (*cf.* Crozier, 1924-25, *b*; Bliss, 1925-26; Brown, 1926-27).

The fact that the same temperature characteristic holds for mean growth velocities at different points on a curve of development (Fig. 7) must be taken to signify that within the range considered the shape of the underlying curve very nearly is the same at different temperatures; hence, that only one "velocity constant" is materially effective, or else that if more than one be involved, their temperature characteristics are the same.⁴

The net result may be stated by saying that while the control of growth velocities by chemical reaction velocities seems adequately shown, it is yet highly desirable that further data be secured by improved methods; there is some indication that the controlling reactions may belong in categories with those found by their temperature characteristics to be implicated in other and quite diverse vital processes. There is as yet scarcely sufficient evidence to verify the prediction that the curve relating log velocity of growth to $1/T^\circ$, when "velocity" = reciprocal of time required to reach a defined stage, should be slightly curvilinear. But there is indication that growth velocities, where evidenced as constant rates of increase, adhere satisfactorily to the Arrhenius formula; and even when we may quite reasonably expect that an "autocatalytic" system is involved, the agreement is often as good as might be desired. The values of the temperature characteristics secured for growth phenomena are quite varied, yet they cluster rather definitely about the following magnitudes; 7-8,000; 11-12,000; 16-17,000; 20,000; 24,000; 27,000 (this summary is based upon studies of a number of cases additional to those specifically mentioned in this article). Consideration of the properties of the equation which describes the velocity of an autocatalytic process (Section IV) shows how this sort of result may be obtainable.

⁴ With regard to velocities of regenerative growth, which in certain cases at least appear to adhere to typical growth curves, there does not exist any considerable body of data. We may cite the following instances. The regeneration of hydranth in *Tubularia* (Moore, 1910) has been cited in an earlier paper (Crozier, 1924-25, *b*). Measurements of the rate of regeneration (morphyllaxis) in planarians indicate a high temperature coefficient (Lillie and Knowlton, 1897; Vandel, 1921-22), but are insufficient for analysis.

VI.

SUMMARY.

The velocity of growth, taken as the reciprocal of the time required to attain a given size or stage of development, obeys with some exactness the Arrhenius equation for relation to temperature. The values of μ , and the type of "breaks" found in the curves connecting velocity and temperature, are similar to those found in the case of various other vital activities. More precise data, particularly from experiments in which parts of the given developmental stadium are passed at different temperatures, may strengthen present indications that this relationship is not absolute. It is pointed out that the equation for an autocatalytic process, taken as descriptive for growth, predicts particular sorts of deviation under these conditions, which have in one instance been obtained experimentally; and may at the same time nevertheless permit the apparent temperature characteristic for (average) growth velocity to agree rather closely with that for one of the two velocity constants present in the correct autocatalytic equation.

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