TIME RELATIONS OF GROWTH.

I. GENETIC GROWTH CONSTANTS OF ANIMALS.*

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I.

The Viewpoint.

To guide us in our study of the time relations of growth, we have adopted the viewpoint that growth is a complex physicochemical process but that the velocity of growth during a given phase of growth is limited or governed by one chemical reaction—a master reaction as Robertson¹ terms the limiting reaction—and that the time relations of each phase of the growth process may therefore be represented by the expression representing the time relations of the single limiting reaction. The curve of growth indicates that there are several phases following each other consecutively, sometimes overlapping to a greater or less extent, and according to this viewpoint the course of growth as a whole is limited by several consecutive chemical reactions, and the specific velocity constants of each of the respective phases of growth.

The justification for the viewpoint that growth is a physicochemical

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¹Robertson, T. B., The chemical basis of growth and senescence, Monographs on experimental biology, Philadelphia and London, 1923.

process need not be gone into in this place. It is sufficient to recall that the life work of Jacques Loeb and of the school of physiologists associated with his name consisted in experimentally substantiating the hypothesis that life processes, including growth and senescence,² are physicochemical in nature and this viewpoint now rests on a fairly solid foundation of experimentally established facts. The more recent investigations of the biochemist and physiologist³ in the fields of nutrition and metabolism as related to growth and senescence, of secretion of certain ductless glands as related to growth and senescence, of products of bacterial growth and metabolism as related to the growth of a bacterial population, and finally of the tissue cultures *in vitro* (especially of Carrel, Ebeling, and associates⁴) all substantiate the early theories of Loeb and his associates that growth and senescence are physicochemical processes.

The viewpoint that a single and simple chemical reaction may and usually does limit or govern the time relations of complex chemical processes is one which has been accepted by the physical chemist at least since 1898,⁵ and represents one of the best experimentally established principles of chemical kinetics.

In harmony with the viewpoint that growth is a physicochemical process, we shall employ, whenever possible, the equations employed by the physical chemist in representing the time relations of chemical reactions to represent also the time relations of growth. Incidentally, but not primarily, the applicability of the equation of the chemist to the time relations of growth may be taken as further substantiating evidence that growth is limited by a chemical reaction.

² Cf. (inter alia) Loeb, J., Arch. ges. Physiol., 1908, cxxiv, 411. Loeb, J., and Northrop, J. H., Proc. Nat. Acad. Sc., 1917, iii, 382; J. Biol. Chem., 1917, xxxii, 103. Loeb, J., Scient. Month., 1919, ix, 578.

³ For a review of literature *cf.* Robertson, T. B., Principles of biochemistry, for students of medicine, agriculture, and related sciences, Philadelphia and New York, 2nd edition, 1924.

⁴ For an excellent description of the investigations of Carrel and associates, cf. Pearl, R., The biology of death, Monographs on experimental biology, Philadelphia and London, 1922.

⁵ Cf. Walker, J., Proc. Roy. Soc. Edinburgh, 1897-98, xxii, 22.

The Growth Curve and Its Constants.

The smoothed time curve of growth in weight is sigmoid, but the point of inflection, or rather region of inflection, is not in its center, but where slightly over one-third of the mature weight is reached. The growth curve of man is the only exception encountered (*cf.* Fig. 1). This exception raises a number of questions which will be mentioned in a later paper.

This communication is concerned only with the growth constants of equations which fit data following the point of inflection. We shall call these constants genetic growth constants because they are hereditary or genetic characteristics of the animals under consideration. The term genetic growth constant in equations of the growth process, is meant to correspond to the terms specific velocity constants and equilibrium constants in equations of chemical processes *in vitro*.

After the point of inflection, we have found the velocity of growth (i.e. gain in weight per unit time) to decline in a geometrical progression with age. The body weight thus increases, by successively decreasing gains in weight, approaching a certain value, A, as a limit. The limiting value A may, for practical purposes, be considered as representing the mature weight of the animal. The mature weight of the animal, A, is one genetic growth constant of the animal. The normal animal reaches, under a given set of favorable conditions, a mature weight which is characteristic of its own species just as the product of a chemical reaction *in vitro* reaches, under a given set of conditions, a definite equilibrium concentration characteristic of its kind. The mature weights, A, for several animal forms for which adequate data are available are presented in Table I. The method of obtaining A from a series of data will be presently explained.

We have said that after the point of inflection, the velocity of growth declines in a geometrical progression with age. It may be useful to make this statement clear by a concrete illustration. A population of male guinea pigs was found to add to its weight in successive months (after the point of inflection)

$$112, 90, 70, 56, 43, 35, 27, 21, \dots, gm.$$
(1)



FIG. 1. The relative course of growth in rat and man. The smoothed curve of growth of the rat, and other animals examined, is sigmoid, the point of inflection occurring when about one-third of the mature body weight is reached. The growth curve of man has quite a different form. It is noted that the point of inflection occurs before puberty. (Data on unmated female white rat by Donaldson, Dunn, and Watson and on man, female, by Roberts, all classes. Conception, and age and weight when 98 per cent of the mature weight is reached were made to coincide in the chart.)

If the gain in weight during any month be divided by the gain in weight in the immediately preceding month, the ratio will be found to be approximately the same for all pairs of monthly gains.

$$\frac{70}{90} = \frac{56}{70} = \frac{43}{56} = \frac{35}{43} = \frac{27}{35} = \frac{21}{27} = \dots = .78 \text{ or } 78 \text{ per cent}$$
(2)

The common ratio in series (1) is roughly .78. We shall designate the common ratio in a series of gains in weight by the letter P which is to represent the concept of fractional persistency of growth, or simple persistency of growth. Every animal has a characteristic numerical value of P under a given set of conditions. P, therefore, is a genetic growth constant. In Table I are presented the numerical values of P for several classes of animals.

The method of computing P as given in the preceding paragraph is simple enough but in the practical study of growth curves it is extremely helpful to employ equations, and for purposes of interpretating the growth processes from a physicochemical viewpoint, it is desirable to have equations of the form used by the chemist. Series (1) may be represented by an equation the form of which is familiar to the chemist,

$$V = V_0 e^{-kt} \tag{3}$$

in which V represents the velocity of growth or gain in weight per unit time at the age t (after the point of inflection), and V_0 is the *theoretical* velocity when t = 0, and e is the natural base of logarithms: k represents the fractional decline of growth, and is termed the specific velocity constant in the literature of chemical kinetics. From series (1)

$$k = \frac{112-90}{112} = \frac{90-70}{90} = \frac{70-56}{70} = \frac{56-43}{56} = \dots = .22 \text{ or } 22 \text{ per cent per month.}$$
 (4)

It is clear that k + P = 1, or 100 per cent.

The body weight increases by the successively decreasing gains illustrated in series (1), approaching the limiting, or practically mature, weight A. Now, if the decline in the velocity of growth may be represented by equation (3), then the course of increasing

| Rabbit. Males and females (Castle). | | | | | | | | |
|---|-------|------|------|------|------|------|------|------|
| Flemish | 3.2 | 7.1 | 8.0 | 43.4 | 2.1 | 3.7 | 5.3 | 11.1 |
| F_1 Himalayan X Flemish | 2.8 | 6.2 | 9.2 | 44.7 | 2.7 | 4.2 | 5.8 | 11.4 |
| F_1 Polish X Flemish. | 2.5 | 5.5 | 11.0 | 49.2 | 3.0 | 4.4 | 5.8 | 11.0 |
| F_{I} Himalayan X Polish | 2.0 | 4.4 | 7.0 | 47.4 | 2.6 | 4.1 | 5.6 | 10.9 |
| Polish. | 1.4 | 3.1 | 3.3 | 43.4 | 2.0 | 3.6 | 5.2 | 11.0 |
| Domestic fowl. | | | | | | | | |
| (Kempster <i>et al.</i>) | | | | | | | | |
| Females. | | | | | | | | |
| Rhode Island Red | 3.56 | 7.85 | 5.2 | 16.6 | 2.28 | 6.5 | 10.6 | 25.9 |
| Plymouth Rock | 3.40 | 7.50 | 5.43 | 19.5 | 2.40 | 6.0 | 9.5 | 22.5 |
| Rhode Island White | 3.00 | 6.61 | 4.65 | 20.6 | 2.10 | 5.5 | 8.9 | 21.1 |
| White Leghorn | 2.20 | 4.85 | 3.25 | 18.0 | 2.17 | 6.0 | 9.6 | 23.9 |
| Ancona | 1.65 | 3.64 | 4.0 | 34.4 | 2.57 | 4.6 | 6.6 | 15.0 |
| Guinea pig. | | | | | | _ | | |
| (Wright.) | | | | | 4 | | | |
| Males | .825 | 1.82 | 1.4 | 23.0 | 2.3 | 5.3 | 8.3 | 19.3 |
| Guinea pig. | | | | | ~ | | | |
| (Castle.) | | | - | | , | | | |
| F_1 , Arequipa X Race B, males | 1.30 | 2.87 | 1.95 | 19.8 | 2.05 | 5.6 | 9.1 | 21.8 |
| F_{a} , Arequipa X Race B, males | 1.04 | 2.29 | 1.46 | 20.9 | 1.63 | 4.9 | 8.3 | 20.5 |
| F ₁ , Cavia culleri \times Race B, males | .930 | 2.05 | 1.60 | 27.4 | 2.00 | 4.5 | 7.0 | 16.3 |
| Race B, males | .870 | 1.92 | 1.45 | 21.7 | 2.36 | 5.55 | 8.76 | 20.4 |
| Race B, females | .840 | 1.85 | 1.50 | 22.3 | 2.6 | 5.7 | 8.8 | 20.2 |
| F_1 , C. cutleri X Race B, females | . 785 | 1.73 | 1.26 | 26.1 | 1.8 | 4.5 | 7.1 | 17.0 |
| F_2 , C. cutleri X Race B, males | . 725 | 1.60 | 1.10 | 25.1 | 1.70 | 4.4 | 7.2 | 17.5 |
| F_2 , C. cutleri X Race B, females | . 590 | 1.30 | 1.45 | 40.5 | 2.22 | 3.9 | 5.6 | 11.9 |
| C., cutleri, males. | .400 | .882 | 1.7 | 52.9 | 2.74 | 4.0 | 5.4 | 10.1 |
| C. cutleri, females. | 333 | 124 | 780 | 12 1 | 1 06 | 20 2 | 20 2 | 11 0 |

| | | | | | 10021 | | Age² (fro | om concel | otion) at |
|-----|---|--------------|----------|------|--|-------|---|---------------------------------|-------------------------------|
| No. | Animal. | A (Mature | weight.) | εί | (Per- centage of monthly decline in growth.) | *. | One-balf mature weight. ⁸ | Three-fourths mature weight. | 98 per cent mature weight. |
| | | kg. | lbs. | | | mos.2 | mos. | mos. | mos. |
| | Norvay rat. (King.) | | <u> </u> | _ | | | | | |
| 33 | Females. | .370 | .816 | .415 | 12.9 | 68. | 6.3 | 11.7 | 31.2 |
| 34 | Males. | .385 | .849 | .43 | 12.2 | .906 | 6.6 | 12.2 | 32.4 |
| 35 | Albino rat. Specially well fed and cared for males (Greenman and | | | | | | | | |
| 2 | Duhring). | 350 | 222 | 59 | 35 0 | 1 77 | 2 75 | 5 72 | 17 0 |
| | Inbred, 7-15 generation series (King). | | | 8 | | | | 2 | |
| 36 | Males. | .335 | .738 | .57 | 38.3 | 1.4 | 3.21 | 5.00 | 11.5 |
| 37 | Females. | .215 | .474 | .42 | 49.0 | 1.4 | 2.6 | 4.2 | 9.3 |
| | On a whole milk and whole wheat diet (Sherman and | | | | | | | 1 | |
| | MacLeod). | | | | | | | | |
| 38 | Males | .330 | . 728 | .80 | 52.0 | 1.7 | 3.03 | 4.37 | 9.3 |
| 39 | Females. | . 223 | .492 | .88 | 70.7 | 1.94 | 2.92 | 3.90 | 7.5 |
| | Inbred, 16-25 generation series (King). | | | | | | | | |
| 40 | Males. | .320 | . 705 | .470 | 29.1 | 1.30 | 3.70 | 6.08 | 14.7 |
| 41 | Females. | .217 | .478 | .350 | 38.3 | 1.25 | 3.05 | 4.87 | 11.3 |
| | Stock rats (Donaldson <i>et al.</i>) | | | | | | | | |
| 42 | Males | .280 | .617 | .59 | 40.0 | 1.86 | 3.59 | 5.33 | 11.6 |
| 43 | Females. | .203 | .447 | .75 | 64.4 | 2.03 | 3.11 | 4.18 | 8.1 |
| | Stock rats (Ferry). | | | | | | | | |

TABLE I-Continued.

| : | | 010 | | 100. | | | | - c - c | |
|------------|--|-------|-------|--------|------|-------|-------|---------|------|
| 44 | Males | 0/7. | C6C. | UCT. | 04.I | P1 | cc.c | 000 | 2.01 |
| 45 | Females. | .172 | .379 | .280 | 41.8 | 1.17 | 2.8 | 4.5 | 10.5 |
| | Control rats for inbreeding experiments (King). | | | | | | | | |
| 46 | Males. | .255 | .562 | .400 | 33.0 | 1.38 | 3.46 | 5.57 | 13.1 |
| 47 | Females. | . 189 | .417 | .280 | 35.7 | 1.10 | 3.0 | 5.0 | 10.9 |
| | Stock rats (King). | | | | | | | | |
| 48 | Females | .210 | .463 | .39 | 48.5 | 1.27 | 2.7 | 4.1 | 9.3 |
| | Stock rats (Hoskins). | | | | | | | | |
| 4 9 | Males. | .230 | .507 | .86 | 81.0 | 1.62 | 2.5 | 3.3 | 6.5 |
| ß | Females. | .166 | .366 | 09. | 88.5 | 1.5 | 2.2 | 3.0 | 5.8 |
| - | "Runt" (Series 1, No. 1) (King). | | | | | | | | |
| 51 | Female. | . 147 | .324 | .33 | 62.1 | 1.3 | 2.4 | 3.5 | 7.5 |
| _ | Normal litter mate to runt (Series 1, No. 3). | | | | | | | | |
| 52 | Female | .170 | .375 | .460 | 70.7 | 1.4 | 2.4 | 3.4 | 6.9 |
| | White mouse. | | | | | | | | |
| | (Robertson.) | - | | | | | | | |
| 53 | Males. | .0275 | .061 | .044 | 62.0 | .76 | 1.88 | 3.01 | 7.10 |
| 54 | Females. | .0235 | .052 | .050 | 82.0 | .921 | 1.76 | 2,60 | 5.70 |
| | Pigeon. | | | | | | | | |
| | (Riddle and Frey.) | · | | | | | | | |
| 55 | Common pigeon, male and female | .340 | . 750 | .38 | 80 | .139 | 2.6 | 3.5 | 6.7 |
| 56 | Ring dove, male and female | .160 | .353 | .170 | 102° | .06 | .74 | 1.4 | 3.9 |
| | Man. | | | | | | | | |
| | Male | | | | | | yrs. | | |
| 57 | English non-laboring classes (Stephenson) | 69.2 | 152.6 | 183808 | 4.8 | 13.68 | 12.37 | 16.1 | 20.5 |
| 28 | English all classes (Roberts) | 68.0 | 149.9 | 5043 | 2.98 | 12.03 | 12.4 | 15.9 | 23.0 |
| 20 | Swedish (Kev). | 68.0 | 149.9 | 22851 | 3.62 | 13.4 | 12.4 | 16.6 | 22.4 |
| 8 | U. S. naval cadets (Beyer) | 65.8 | 145.1 | 2156 | 3.68 | 13.1 |] | 16.2 | 22.0 |
| 61 | U. S. Amherst College, and Nebraska students (Has- | | | | | | · | | |
| | tings) | 65.4 | 144.2 | 7113 | 3.14 | 12.44 | 12.7 | 16.1 | 22.8 |

| | TABLE IC | oncluded. | | | | | | | |
|------------|--|-----------|---------------|--------|--|-------|---|---------------------------------|-------------------------------|
| | | | | | 100&1 | | Age ² (fro | m concep | tion) at |
| No. | Animal. | (Mature | t weight.) | R | (Per- centage of monthly decline in growth.) | * | One-dalf mature weight. ⁸ | Three-fourths mature weight, | 98 per cent mature weight. |
| | | kg. | lbs. | | | mos.2 | mos. | mos. | mos. |
| | Man-Continued. | | | | | | | | |
| | Male. | | | | | | | | |
| 62 | English laboring classes (Stephenson) | 65.3 | 144.0 | 2037 | 2.38 | 12.1 | 12.3 | 17.0 | 25.8 |
| 63 | Polish Radom Gymnasium (Suligowski) | 62.0 | 136.7 | 15782 | 3.76 | 12.28 | 11.4 | 15.4 | 21.0 |
| 64 | English artisan classes (Roberts) | 61.6 | 135.8 | 13309 | 3.46 | 12.9 | 11.3 | 16.3 | 22.4 |
| 65 | Russian St. Petersburg School (Wiazemsky) | 61.5 | 135.6 | 79447 | 4.45 | 13.4 | 12.3 | 16.0 | 20.7 |
| 6 6 | Jews in South Russia (Weissenberg) | 58.0 | 127.9 | 171302 | 4.76 | 14.0 | 12.3 | 16.5 | 20.9 |
| 67 | Chinese students in Wuchang School (Merrins) | 55.0 | 121.3 | 6301 | 3.31 | 11.9 | 12.6 | 15.4 | 21.8 |
| 68 | Philippine (Babbitt) | 52.3 | 115.3 | 15326 | 3.83 | 12.4 | 12.0 | 15.4 | 20.9 |
| 69 | Japanese (Miwa) | 51.4 | 113.3 | 39694 | 4.46 | 12.4 | 11.7 | 15.0 | 19.7 |
| | Man. | | | | | | | | |
| | Female. | | | | | | | | |
| 20 | English all classes (Roberts) | 57.4 | 126.6 | 1331 | 2.6 | 10.1 | 11.1 | 14.5 | 22.6 |
| 71 | American well to do, New York (Baldwin) | 56.4 | 124.4 | 7944 | 3.97 | 10.4 | 10.1 | 13.3 | 18.6 |
| 72 | Russian Institutions (Diek) | 54.0 | 119.1 | 1398 | 2.66 | 10.2 | 1 | 14.5 | 22.5 |
| 73 | German (Camerer) | 51.6 | 113.8 | 12430 | 4.08 | 11.2 | 10.4 | 14.1 | 19.2 |
| 74 | Japanese (Miwa) | 46.0 | 101.4 | 2751 | 3.36 | 10.2 | 1 | 13.6 | 19.9 |

TABLE I-Concluded.

 1 The percentage of monthly persistency of growth, 100P, may be obtained by subtracting the percentage decline, $100k_{s}$ from 100; *i.e.*, 100P = 100 - 100k.

² By age is meant, in all cases, age as counted from conception. The following ages of the animals at birth are given should the reader desire to convert the conceptional ages to birth ages: Cattle 9.4 mos., swine 4.0 mos.; sheep 5.0 mos.; rabbit 1.0 mos.; fowl 0.7 mos. (21 days); guinea pig 2.2 mos. (67 days); rat 0.7 mos. (22 days); mouse 0.66 mos. (20 days); pigeon 0.6 mos. (18 days); man 0.79 yrs. (9.5 mos.).

(A-W) age charts as follows: When A - W = 1/2A, half of the mature weight is reached, and the age corresponding to this ³ Ages at one-half mature weight, three-fourths mature weight, 98 per cent mature weight, etc. are evaluated from equation These values may also be interpolated from the value is read on the age axis of the (A-W) age chart. Similarly, when (A-W) = 1/4A, three-fourths of the mature weight is reached, and when (A - W) = 2%A, 98 per cent of the mature weight is reached. (5) by solving for t after replacing W by 1/2A, 3/4A, 98%A, etc.

For this reason we are certain of the applicability of equation (5) based on the given constants only after the age of 2 years. It is certain that the numerical values of the mature weight A represent the facts, it is equally certain that B and t^* are too low to represent the facts. Such a low value of B and t^* implies that the point of inflection in the smoothed growth curve occurs before birth which we know ⁴ Data for Register of Merit Jersey Cattle are available only after the age of 2 years. from experience to be improbable.

⁵ The rabbit appears to differ from other domestic animals by the fact that the female tends to be larger than the male and apparently also tends to require a longer period to reach maturity than the male. Castle calls attention to the fact that such difference in mature weight is observed only in the larger breeds of rabbits.

ciation of growth velocity of 102 per cent for the dove when this bird required 3 months to reach only 98 per cent of its mature weight? This paradox is due to the fact that this is a rate of depreciation of a quantity (A - W) which declines from moment to moment in a geometric progression, and that the absolute "interest" on this quantity, that is the velocity of growth, also declines from moment to moment in a geometric progression. It follows from this fact that the time required to deplete (A - W) is longer than it would have been if the value of (A - W) continued constant over the entire month, and the percentage persistency, 100P, which is merely 100 per cent minus 100k, is negative. Hence, strictly speaking, when employing finite units of time, k and p are only relative indices of the decline in the velocity of growth with age that is relative ⁶ 100k is the monthly rate of depreciation of the growth velocity. But how is it possible to have a monthly rate of depreindices of the time required to reach maturity.

¹ The age at half mature weight for man was read from the smoothed growth curve, since equation (5) does not apply to the curve of man at half mature weight. body weight (including all the gains) with age may be represented by the equation

 $W = A - \frac{V_0}{k} e^{-kt}$

or

$$W = A - Be^{-kt}$$
(5)

In equation (5) W represents the body weight at the age t and B represents $\frac{V_0}{k}$. The significance of B and also of A may be most clearly visualized by inspecting Figs. 2 and 3.

Equation (5) may be written in the form

$$A - W = Be^{-kt}$$
(6)

Equation (6) indicates that (A - W), that is the weight remaining to be made to reach the limiting or mature weight, declines in a geometrical progression with age. Of course, this could be predicted from series (1) or equation (3). The ratios of the gains in weight per unit time to the values of (A - W) are constant, that is

$$V = k \left(A - W \right) \tag{7}$$

Thus, the gains in weight in successive months for the previously mentioned guinea pigs were found to be (series (1))

and the values of (A - W) were found to be

therefore, the ratios of $\frac{V}{(A-W)}$ are

$$\frac{90}{420} = \frac{70}{330} = \frac{56}{260} = k = .23$$
 (approximately).

Thus, the numerical value of k as found with the help of equation (7) is the same as the value found in series (4).

All the above exponential equations of geometrical progression represent different forms of the same idea, an idea which when ap-

plied to the time relations of a chemical reaction *in vitro* is known as the law of mass action as applied to monomolecular change.

From the physicochemical viewpoint, one may interpret the applicability of the monomolecular equations to growth data as indicating that the velocity of growth, V, is proportional to a limiting "growth substance" which is used up in the course of growth according to the monomolecular law. Equation (7) is an especially helpful form in visualizing such a situation. The constant A may be considered as representing the amount of "growth substance" at the beginning of growth. W may be considered as representing the amount of limiting "growth substance" converted into body weight (A - W), the concentration of the growth substance at the given moment, and the velocity of growth at any moment is directly proportional to the amount (A - W), of growth substance at the given moment.

One may, of course, with equally good logic, interpret equation (7) as indicating the production during the course of growth of a growthretarding substance according to the monomolecular law, and (A -W) representing the degree of freedom from the retarding substance which limits growth. This interpretation is more in harmony with our present state of knowledge about growth. The discoveries of Carrel⁴ that certain tissues-probably all tissues-can grow indefinitely under appropriate conditions and that some product of growth has a retarding influence on growth of tissues in vitro, and the common observations that bacterial cells can grow indefinitely providing the products of growth are removed and food is supplied, favor the view that it is some product of growth which exerts the retarding effect on the inherent tendency of cells to multiply indefinitely, and that A merely represents the concentration of the limiting product of growth which just balances the inherent growth tendency. The inhibition of growth of lactic acid-producing bacteria by the lactic acid produced by the bacteria is a well known example in which growth is retarded by a chemical product of growth. After the point of inflection in the curve of growth of lactic acid-producing bacteria, the velocity of growth of the bacteria may be represented by equation (7).

Before leaving this subject, it is perhaps necessary to point out

that A and B in equation (5) usually have the same numerical values when representing monomolecular change *in vitro*. However, there may be a delay or lag in the beginning of the process in which case the numerical value of B is greater than of A. The greater the delay,



FIG. 2. The significance of A and B in equation (5) illustrated graphically, also of the constant t^* which will be utilized in the second paper of this series.

the greater the numerical value of B as may be seen in Fig. 2. B is a parameter the value of which increases with the increase in length of the process which precedes the point of inflection for the phase under consideration.

An interesting illustration of a delay in the growth process is

furnished by the rat that Osborne and Mendel⁶ kept (by limiting the food supply) from the age of about 40 days to the age of 510 days at the constant weight of 60 gm. (normal weight at maturity is about 220 gm.). In such a case, the numerical value of the constant B is merely increased to account for the longer period of delay preceding the point of inflection. The fundamental idea which must be remembered in connection with equations (5) and (7) is that after the point of inflection the velocity of growth under optimum conditions is a function not of chronological age, but of (A - W).

We have developed the following simple graphic method for evaluating the constants A, B, and k in equation (5). Since, as pointed out, the numerical values of (A - W) normally decline in a geometrical progression with age, it therefore follows that if the numerical values of (A - W) are plotted against age on paper in which the scale of ordinates is divided in a geometric progression and scale of abscissæ in the usual arithmetic progression, there should result a straight line provided the correct value of A (mature weight) were chosen. A few reasonable values of A are chosen by inspection from the growth curve, and the corresponding values of (A - W) are plotted as shown in Fig. 3. The value of A giving the straightest line is the best estimated value of A. The constant k is determined by measuring the slope that the (A - W) line makes with the age axis. B is found by substitution, or by inspection from the figure.

The agreements between the observed values, and the values computed from equation (5) are indicated to some extent in Fig. 4. In Fig. 4, the value of A of each animal is represented by 100 per cent and the weights at other ages are expressed as percentages of the respective values of A. The numerical values of k are not changed by replacing the absolute values of the mature weight, A, to 100 since k is only an index to the velocity with which the limiting value (100 or the absolute numerical value of A) is approached. Such a plot has the advantage of showing in a striking manner the relation between the numerical values of k, the more rapidly the mature weight is approached.

⁶ Osborne, T. B., and Mendel, L. B., J. Biol. Chem., 1915, xxiii, 439; Am. J. Physiol., 1916, xl, 16.



FIG. 3. A graphic method of determining the numerical value of the mature weight, A, of an animal. The correct mature weight of a given animal (male albino rat of Greenman and Duhring) is 350 gm. If (350 - W) is plotted against age, a straight line results. If a larger or smaller value for A is assumed, the curves deviate from a straight line as illustrated by the curves when A is assumed to be 300 to 400 gm. The numerical values of B and t^* may also be read from this graph, B is the value of (A - W) when t = 0; t^* is the age when (A - W) = A.

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Percentage of mature weight

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Age(from birth) man

සි ۶ 2 68 64 8 ß Age (from conception) of animals 52 ٠ -48 • 4 -6 CON. 1 36 32 • -23

illustrated graphically. The mature weights of the animals are represented by 100 per cent, and the weights at other ages by the percentages of the mature weight. This chart also shows the satisfactory agreement between observed values FIG. 4. The relation between the numerical values of the velocity constant k and the steepness of the growth curves represented by circles and the smooth curves computed from equation (5); also the striking difference between the curve of man and of other forms.



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SUMMARY.

This paper is the first in a series proposing to evaluate growth constants from the viewpoint of and by the methods of the physical chemist. After discussing the physicochemical conception of growth, tentative numerical values of two growth constants are given for several species of animals including man, and the methods of computation are discussed in detail.

SOURCES OF DATA.

Animals.—

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- Supplementary data on swine were kindly furnished for this analysis by Director F. B. Mumford of this station from his unpublished records.
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