THE NATURE OF GROWTH

DR. H. S. REED
UNIVERSITY OF CALIFORNIA

I

One of the most conspicuous characters of organic beings is their power to grow—to become what, at a previous stage of their existence, they were not. The acorn becomes an oak tree, the helpless babe becomes an Aristotle. What is the cause of the transformation? What forces are involved in these non-reversible processes which we term development, or growth? The oak tree can not be put back into the acorn, neither can the man be put back into the baby. It is needless to say that much of our philosophy of the universe has arisen from the attempt to answer questions which man has asked concerning these phenomena. In biology there have been two distinct schools—the vitalists, who held that the processes in organic beings are qualitatively different from those occurring in other forms of matter, and the mechanists, who hold that the differences, if any, are merely quantitative. The vitalistic naturalists have attempted to explain the organism in terms of a soul either connected with or separate from some superior soul. The mechanistic naturalists have attempted to explain the organism in terms of mass, time and space. It is not necessary to judge the successes or failures of the two schools in the present discussion. I do feel constrained, however, to remark that the students of the growth process (especially the growth of plants) have busied themselves with the irrelevant and unimportant aspects of the subject and have neglected most of the problems which might explain

1 Read at a symposium on "Growth and permeability," held by the Pacific Division of the Plant Physiological Section of the Botanical Society of America, Los Angeles, September 19, 1923.
growth. In the words of a recent article by Kidd and West: 2

A few fundamental principles are necessary for the study of growth and development. These are conspicuous by their absence in existing text-books of plant physiology, which excel in the assemblage of interesting curiosities and of uncorrelated details. The phenomena of normal growth seem to call for further study and analysis and for the application of mathematical treatment.

In view of the great diversity of organic life and of its complex manifestations, it is not surprising that biology should be one of the last of the sciences to abandon the grab-sample methods of study with which man originally tackled the problems of the universe.

It is my purpose to show how the problem of growth may be quantitatively studied by the application of methods already in use in other departments of science and how their use simplifies the problem. I think it fair to assume that most of us have come to the realization that it is necessary to extend the application of quantitative methods in the study of physiology. In addition to measuring the factors of the environment, we must measure the response of the organism. Of the many responses of organisms, the two of paramount biological importance are growth and reproduction, yet their study has been long neglected.

II

One of the first results of the application of quantitative methods to biological processes is the discovery of their continuity. The organism of to-day is the organism of yesterday plus or minus a certain number of molecules of water, carbohydrate, et cetera. The processes of hydration and dehydration which play such an important part in the changes of carbohydrates, proteins and fats are mainly brought about by oxidases, reductases and other enzymes. These processes go slowly in comparison with many chemical reactions and are often reversed, but they are the principal centers of metabolic activity in the organism.

Studies of growth phenomena should eventually lead to a consideration of the energy relationships involved. We can not but believe, in the absence of contrary evidence, that the growth processes of living organisms are manifestations of the energy relationships prevailing in other parts of the universe. The study of these energy relationships ought not, therefore, to be disregarded. Our aspirations for such knowledge, which have received so much encouragement from the discovery of the principle of the conservation of energy, can never be entirely suppressed.

For purposes of this discussion the major phases of growth will be considered to be enlargement, differentiation and senescence. The organism which begins as a single cell becomes larger. As it becomes larger, its parts become differentiated. The little seedling is originally little more than a slender rod. But the rod grows and becomes differentiated into shoot and root, and the former undergoes further differentiation into vegetative and reproductive organs, each of which may become highly complex in structure and function. These processes constitute development or growth. Following them come changes which betoken the end of the growth process, leading to senility and eventually to death.

III

If we concur in the view that growth is an increase in size accompanied by a differentiation in members, we may inquire concerning the factors which are related thereto.

The organism acquires materials from its environment and by means of them becomes larger or different. Water is one of the substances which is acquired in large quantities and is of general importance for vital processes. A plant’s ability to grow is, therefore, highly dependent on its ability to absorb water. The structure of most organisms is such that considerable water must pass through them every day. The lack of no other sub-
stance (oxygen excepted) is more quickly or keenly felt than the lack of water. These statements are so evident and so trite that you are perhaps impatient with me for taking the time to make them. My purpose in introducing them is to call attention to the dependence of growth upon imbibition. MacDougal\(^3\) has unquestionably shown that imbibition is dependent upon the colloidal state of the cell and that the amount of water imbibed depends as much upon colloidal state as on access to an adequate supply. From MacDougal’s experiments it is evident that proteins have the greatest water capacity in acid solutions and that pentosans show the greatest degree of hydration in neutral or slightly alkaline solutions. Miss Carey\(^4\) has shown that gelatin absorbs more CO\(_2\) after soaking in water and still more after soaking in HCl solution than the fresh gel absorbs. This may be due to the fact that gelatin absorbs more water from acid solutions than from pure water. Slight changes in the conditions cause conspicuous changes in the rate of imbibition. The ions of the common constituents of soil solutions have varying effects upon the imbibition and swelling of protoplasm and other colloidal substances. The studies on this question are legion, but they too often concentrate their attention on the water and ions which go through the cell colloids, whereas the importance belongs to what stays in them. In the case of root cells of a terrestrial plant the transmitted substances are obviously important because from them the rest of the plant acquires many of the necessary materials.

IV

The growth of an organism usually begins at a slow rate, gradually increases for a time, then becomes slower until it stops. The same is true of an autocatalytic reaction. It begins slowly, but as more of the catalyzing substance is produced, the reaction proceeds at an in-


creasingly rapid rate. As the supply of reacting substances is used up, and as the products of the reaction increase in amount, the reaction slows down and comes eventually to a stop.

Robertson\(^5\) has shown that the rate of a reaction like this may be expressed by the differential equation

\[
\frac{dx}{dt} = kx(A - x)
\]

When integrated this becomes

\[
\log \frac{x}{A-x} = K(t - t_1)
\]

In these equations \(x\) = size of the plant at time \(t\); \(A\) = final size of the plant; \(t_1\) = time at which half the final size is reached; \(k\) = a constant; and \(K = Ak\).

This equation has been used to express the growth of sunflowers,\(^6\) of pear shoots,\(^7\) of cucumber leaves,\(^8\) of lemon shoots,\(^9\) and of white rats.\(^10\) The production of flowers on the cotton plant,\(^11\) of ammonia by ammonifying bacteria,\(^12\) and of carbon dioxide by yeast\(^13\) follow the same equation. The results of these and of other investigations have shown the general applicability of this equation to the study of the growth of organisms. Considering the nature of the materials studied, it must be said that the equations give results of satisfactory accuracy.

V

Our next question may well be: "What do these equations teach us concerning growth?" "Are we to regard

\(^12\) Miyabe, K., Soil Science, 2: 481–497, 1916.
them as evidence of physiological principles, or merely as evidence of successful jugglery?" Some physiologists maintain that the resemblance between observed and calculated values is entirely superficial and without significance.

This is an important question, and no effort should be spared in attempting to answer it. It seems to me that we are at the beginning of a new epoch in plant physiology and that we have a responsibility in orienting our ideas to the wider view we are gaining.

![Graph](image)

**Fig. 1.** The growth of pear shoots calculated from the equation

\[
\log \frac{x}{114 - x} = 0.0242 (t - 47.4)
\]

The S-shaped curves (Fig. 1) representing the growth of an organism may be divided into three parts. The lower part \((a)\) represents the initial period in which the size increases rather slowly; the middle portion \((b)\) represents the period of most rapid growth; and the third portion \((c)\) represents the period commonly known as the period of senescence.\(^\text{14}\)

Since the curve plotted from the equation represents the growth of a wide range of organisms, we must guard against giving it too narrow an interpretation.

The growth represented by \(a\) undoubtedly is the result of an increase in the number of cells when they increase.

at a geometrical rate (the growth is an exponential function of time), while the supply of raw material in the environment is greatly in excess of the absorbing capacity of the organism. In the case of yeast and bacteria the number of cells is small in proportion to the volume of the nutrient medium. In the case of the higher plants, the young seedling or young shoot first draws on accumulated products of metabolism of the parent plant, gradually supplementing them with products synthesized in its own tissues. In the case of mammals, the young are utilizing during this period the nutrient fluids of the mother, which are especially rich in growth-promoting materials, and are gradually supplementing them with food from other sources.

The portion of the curve represented by $b$ covers the period of most rapid growth and is the most conspicuous to the observer. Many physiologists who have studied growth have confined themselves to this part of the growth process. During this time the increase in size is almost (but not exactly) proportional to the time, i.e., the cells increase (in size or number) at an arithmetical rate. We may assume that during this period the catalyst of growth is abundant, but that the growth is conditioned upon the rate at which the organism can obtain from the environment the materials upon which the catalyst can work. During this period growth is more apt to be influenced by fluctuations in the external medium than in the other two periods. In many cases growth during this period must depend upon the rate of oxygen absorption, and in the case of green plants, upon the rate of carbon-dioxide absorption. In all cases it is closely conditioned upon the rate of water absorption, and may therefore depend upon the rate at which acids are produced.

The last portion of the curve covers the period of senescence. The growth during this period comes to a point where no further increase in size takes place; as a matter of fact, some organisms may shrink because of the loss of water. The portion of the curve represented
by $c$ is symmetrical with $a$ in the case of most organisms whose growth curves have been studied. Both portions are obtained when the values of $\pm K(t - t_i)$ approach a maximum. During the period represented by $c$ the cells increase in size or number at a rate only slightly greater than that at which cells die. Since the means for obtaining material are well developed, and the supplies of external material are not commonly depleted, we must assume that something has happened to retard the growth of the organism. In our present state of knowledge it seems most logical to assume that the catalyst which directs growth has become inactivated to such a degree that it no longer functions as formerly. Leaving aside the combined effects of limiting factors, there is still an inner factor which puts an end to further growth. We may plant a rose bush and an apple tree in the same garden and give each the best of conditions, yet the rose bush will never attain the size of the apple tree. Something in the internal organization of the rose bush terminates its growth at a certain point within a few years, whereas the apple tree will grow many years before its growth is terminated.

The study of growth of living organisms reveals an almost universal action of some sort of inhibiting substance which sooner or later brings growth to a stop. It has long been known that many micro-organisms produce substances which are inimical to prolonged growth. In many cases the stale culture medium may be reconditioned by boiling or by treatment with solid absorbing agents.

The condition known as dormancy in seeds, buds, bulbs and tubers must be also referred to the action of some substance (in some cases volatile esters$^{15}$) which prevent growth until they have been eliminated or destroyed.

Certain internal secretions of the animal body are known to inhibit growth and to perform very definite form-regulating functions. The term chalone, proposed

some years ago by Henry Fairfield Osborn,\textsuperscript{16} is an appropriate and convenient designation for this class of substances.

The evidence for the existence of growth-inhibiting substances or chalones in the higher plants is accumulating. Loeb,\textsuperscript{17} Appleman,\textsuperscript{18} Halma\textsuperscript{19} and the writer\textsuperscript{20} have obtained evidence that the growth of plants in different families is regulated by chalones of some sort.

It is no part of my present purpose to discuss the nature of the evidence, neither will time permit a consideration of the criticisms advanced by those who find it difficult to abandon the timeworn, traditional viewpoint that growth regulation depends upon the presence of nutritive materials. My intention is to discuss the rôle of this class of inhibiting substances in the growth process. Since the old ideas upon this subject have never given an adequate explanation of the nature of growth, it may be well to indicate the bearing of these recent investigations upon the problem. The whole question is greatly simplified if we assume that the chalone is some sort of a substance which inactivates the growth-catalyst. Substances of this nature are well known in zymology and in physical chemistry. Iredale\textsuperscript{21} has shown that the catalysis of hydrogen peroxide by colloidal platinum may be inhibited by gelatin, as well as by several other colloids. It is entirely unnecessary to assume that the chalone of every organism belongs to the same class of chemical substances. Colloids, acids, esters or even carbohydrates may act in different cases to retard the growth process of different organisms.

It is highly important to understand that the growth-retarding agencies are present from the beginning of the

\textsuperscript{17} Loeb, J., \textit{Science}, 46: 547, 1917.
\textsuperscript{19} Halma, F. F., unpublished results.
process. The amounts may be for some time so small that they have no material effect upon the catalyst, but, as time goes on, they accumulate and gradually inactivate the catalyst. Their retarding action may be increased or decreased by changes in the external medium whereby the absorption of oxygen or of other substances is altered, but the effect of external conditions on the form of the growth curve is not as great as generally assumed.

VI

The concept of growth-inhibiting substances throws much-needed light on the problem of cyclic or periodic growth. Many, if not most, organisms have more than one growth cycle. The intra-seasonal cycles in the growth of shoots of certain fruit trees are well marked. Studies on the fluctuating growth of apricot shoots produced evidence that their growth rate was alternately increased and diminished by some factor which varied harmonically during the growing season. So far as the evidence now in hand permits, it seems logical to assume that cyclic growth is related to the accumulation of some growth-inhibitor of a colloidal nature which inactivates the catalyst. After a time the physical or chemical state of the growth-inhibitor is altered, or the amount of catalyst present is in excess of the inhibiting power of the materials, and a new cycle of growth is begun.

VII

This discussion has dealt primarily with the equation for autocatalysis

$$\log \frac{X}{A-x} = K(t - t_i)$$

without any intent to ignore the other equations which have been used to express the growth of organisms. For some purposes Wilhelmy’s equation,

$$x = A(1 - e^{-kt})$$


is well suited to express the growth curve. Blackman\textsuperscript{24} has shown that for short intervals the growth of a plant may be expressed by the compound interest formula

\[ W = W_o e^{rt} \]

where \( W \) = dry weight of the plant at time \( t \), \( W_o \) = initial dry weight of the plant, \( r \) = the rate of interest, or "efficiency index" of dry-weight production, and \( e \) = the base of the natural logarithms. It is evident that \( r = \log_e W - \log_e W_o \).

Mitscherlich\textsuperscript{25} proposed the formula

\[ \log^n (\sqrt[n]{A} - \sqrt[n]{y}) = \log^n \sqrt[n]{A} - e \cdot x \]

where \( n \) = a variable indicating the probable number of environmental factors, \( A \) = maximum possible dry weight, \( y \) = dry weight at time \( x \), the time \( x \) being expressed in vegetative periods of arbitrary length.

It is not my present intention to discuss the relative merits of one or another of these equations but to stress the importance of expressing growth as an orderly dynamic change in which increase in size is equal to an exponential function of time. He who wishes may discard any or all of the equations mentioned, but there is no escape from the conclusion that the growth of plants should be studied as a problem in chemical mechanics.\textsuperscript{26}

\textbf{VIII}

Without attempting to discuss additional data we may stop now to inquire what we may conclude from the facts already presented.

Primarily, it seems that growth is a dynamic process which causes enlargement and differentiation in organisms. It seems to me that these facts show a continuity in the growth process which has hitherto been unappreciated by physiologists. If we will replace our former ideas of the haphazard character of growth by the idea

that it is a slow chemical reaction of the first order, our ideas will more nearly accord with the observed facts. This may be nothing more than exchanging the idea that organic beings are the sport of the gods, for the idea that they are the result of a divine harmony achieved through the operation of natural laws.

The question which is often raised by those who have been accustomed to think of the organism in terms of its environment is, "How does the organism manage to maintain such an even growth rate in spite of the myriad fluctuations in its surroundings?" This applies especially to plants. Animals having the power of movement can, to some extent, get out of unfavorable surroundings, but the higher plant is fixed, and must take the environment as it finds it. We must admit that raising or lowering some essential factor, such as heat, to the death point or near the death point, will so alter the growth rate as to invalidate the foregoing assumptions. But, unless the conditions become too nearly lethal, organisms show a constancy in their development which merits our attention and study.

Our understanding of the behavior of the organism will be clarified if we apply the theorem of Le Chatelier, a theorem which has been derived from physico-chemical conceptions. It may be stated as follows: If a system in equilibrium is subjected to a constraint by which the equilibrium is shifted, a reaction takes place which opposes the constraint, i.e., one by which its effect is partially annulled. In all cases, whenever changes in the external condition of a system in equilibrium are produced, processes also occur within the system which tend to counteract the effect of the external changes.

Let us see if we can apply this theorem. A plant growing in the field is in dynamic equilibrium with its surroundings, otherwise it is dead. If cloudy days or drought or other changes ensue, the activities of the plant take such a course that the effect of the changed conditions is minimized, and the growth rate generally suffers
little change. This appears to be an integration of the activities of the plant which results in its specific response—a response which is far more dependent upon the inherent nature of the plant than upon the surroundings.

I am aware that many, if not all, of the views here expressed will be criticized, and often adversely, in the next few years. If there be anything of truth in them, it will be sifted out. Undoubtedly I have erred in the direction of over-simplification, but this is due to an attempt to lay aside, so far as possible, all irrelevant matters and to discuss growth simply as a problem involving slow transformations of material at a rate proportional to time.