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The dynamics of cell-division.

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[*From the Eugenics Record Office.*]

From the structural point of view mitosis is a process by which a living cell, through continuous and orderly transformations, divides so that (*a*) in equational division each daughter cell duplicates the mother cell exactly at the latter's comparable stage of existence; or (*b*) in ontogenetic division each daughter cell duplicates the mother cell at the latter's comparable stage of existence, exactly in chromatin content, but not necessarily exactly in any other detail.

From the dynamical point of view mitosis is a process related and characterized as follows: Beginning in a single living cell at a stage of high metabolic activity but of divisional stability thence continuing by means of metabolism to a condition of low metabolic activity and divisional instability the mitotic potential is established. Thence reactions still proceed by virtue of the cell's self-contained structural and chemical organization, and its environmental complex. These successive reactions are so timed, localized, and successively interdependent upon their preceding and adjacent activities, that in equational division mitotic stability and metabolic activity are again achieved only when this self-contained process-chain of reactions reaches a stage wherein are found, in place of one cell, two cells, which if the division be equational are exact duplicates of the one parent cell at the same stage. If, however, the mitosis be ontogenetic the daughter cells will exactly resemble the parent cell at the latter's comparable stage in chromatin content only; their cytoplasmic form and functions may vary greatly.

The structural stages and ends of the mitotic process have been analyzed much more thoroughly than have the dynamical. The analysis of the latter seeks not to find form but to explain what is happening in terms of interplay of forces. It should yield even greater returns in understanding vital and evolutionary phenomena. In attempting such an analysis it is necessary first to learn how to measure[1] a characteristic of mitotic activity, such as its velocity in passing through successive stages. The actively dividing cell must then be subjected to definite measures and quality of light, heat, gravity, pressure, electricity, or chemical influence, and next the behavior of the dividing cell as modified by the definite quantitative and qualitative influences must be measured. We may then examine the behavior of such elementary processes as have been measured while reacting to these definite influences. It is finally in order to seek for similarity of behavior which, when found, suggests very strongly similarity of organization and forces. The completeness and accuracy of such an analysis depends, of course, upon the degree of refinement in the isolation and measurement of factors and the exactness of the parallel to known processes.

This takes us immediately into the realm of physical chemistry. The present paper will discuss a definite problem in this study, namely, the influence of temperature upon the dividing root-tip cells of the onion, and will then seek a preliminary or working analysis by comparing the reaction thus found with similar reactions which physical chemists have found in other and simpler complexes. The following table shows the effect of temperature upon the velocity of the several mitotic stages calculated in the usual Q_{10} form of the chemist.

[1] Laughlin, H. H., "The Duration of Mitotic Stages in the Root-tip Cells of the onion," Carnegie Inst. of Wash. Pub., No. 267.

Mitotic Stage.	Q_{10} Velocity at 20° C. Compared with Velocity at 10° C.	Q_{10} Velocity at 30° C. Compared with Velocity at 20° C.
1. Early prophase	−1.1340 (.8818)	+1.1525
2. Early prophase	+2.6832	+4.9406
3. Mid-prophase or spireme	+2.9599	+2.6404
4. Late prophase	+1.3859	+2.7593
5. Metaphase	+1.4071	+3.0663
6. Early prophase	−1.1701 (.8546)	+2.3440
7. Mid-anaphase	+1.1523	+2.7571
8. Late anaphase	+1.6334	+2.6038
9. Early telophase or di-spireme	+1.3329	+2.1694
10. Late telophase	+1.1240	+3.0931
Resting or metabolic	+1.2215	+4.9463
Stages 2 to 10 inc.	+2.0476	+3.2311
Stages 1 to 10 inc.	+1.1990	+1.3962
Entire cycle, *i. e.*, the 1 resting and the 10 active stages	+1.2139	+2.6218

Next we shall list and classify according to the sign of their temperature coefficients such other elementary and complex physical, chemical and physiological processes as have been described in the literature of the subject, and which may throw light upon the nature of the temperature-reactions shown in the above table.

A. The following forces and processes within medium ranges of temperature (5° C. to 35° C.) react in the positive direction to temperature-increments, that is, they have the Q_{10} value with the + sign:

1. Velocity of chemical reaction.
   In homogeneous reactions $Q_{10} = +2.0$ to $+3.0$.
2. Osmotic pressure. (Always low in colloids.)
3. Plasmolysis. (Protoplasmic permeability.)
4. Diffusion of fluids. (Always low in colloids.)
5. Electric conductivity of solutions.
6. Migration rate of ions.
7. Ionization.
8. Rate of conduction of nerve impulse.
9. Rapidity or rhythm of electric phenomenon.
10. Velocity of protoplasmic streaming.
11. Coagulation.

[1] Loc. cit.

12. Speed of destruction of spores of anthrax by carbolic acid.
13. Velocity of ontogeny in the frog.
14. Velocity of bulk increase in maize seedlings.
15. Rate of digestion in cold blooded vertebrates.
16. Rate of respiration in *Pisum sativa*.
17. Activation of star-fish eggs by chemical agents.
18. Velocity of CO_2 assimilation by the leaves of the cherry-laurel.
19. Expansion of liquids.
20. Vapor pressure.

B. The following forces and processes show the negative coefficient to temperature-increments. Q_{10} values with the $-$ sign.

1. Surface tension.
2. Polarization capacity.
3. Electromotive force of electro-chemical cell.
4. Electromotive force of nerve.
5. Duration of latent period of smooth muscle.
6. Solubility of gases in water.
7. Duration of life in *Drosophila*.
8. Elasticity.
9. Viscosity (absolute internal friction) of dog serum.
10. Cohesive properties generally.

C. Besides these two classes there is another group of activities which shows a positive or a negative coefficient, depending upon conditions, $Q_{10} = \pm$, as follows:

1. Osmosis.
2. Dialysis.
3. Cataphoresis.
4. Tendency toward precipitation.
5. Solubility of salts:

Most salts $+$
$Na SO_4$ $-$
Many organic salts $-$

6. Strength of linkage in the second chromosome of *Drosophila*, $-$ at low temperatures, $+$ at high temperatures.

Of the processes here listed[1] 8 were secured from Kanitz's compilation,[2] 8 from Snyder's,[3] one—that of Q_{10} values of the several mitotic stages—was supplied by the experiments of the writer,[4] and the remainder were found either in isolated cases in the literature of related subjects, or one current in text-books.

These are the materials at present available for beginning the analysis of the dynamics of mitosis by means of differential temperature-reactions. The question is, which, if any, of the more elementary of these forces, and what other forces, in what combination and to what degree, are active in each stage of mitosis? Certainly for the most part the several mitotic stages are manifestations of chemical and physico-chemical forces showing a positive index.

Stages Nos. 1 and 6 deserve special attention. Stage No. 1 is the earliest prophase; Stage No. 6 is that in which the chromosomes have left the equator but have not yet reached the poles. Both of these stages manifest a negative coefficient from 10° C. to 20° C. The activities of these stages within such temperatures must, therefore, as shown by the behavior of their resultants of forces, be composed of those processes most of which, or at least the most effective of which, react negatively to temperature increments. This fact alone halves the complexity of the puzzle for these particular mitotic stages, and sets them apart as being characterized by distinctive sets of forces.

Another general observation is worthy of note, physiologists,[5] point out that in simple chemical processes Q_{10} values are greater in the upper ranges of temperature than in the lower, while in vital processes generally the reverse is true. In mitosis the complex of forces is such that in most stages a given increment of temperature will cause a greater velocity-response in the particular

[1] The references to each of the experiments providing the listed data on Q_{10} values will be given in the completer paper now being prepared by the writer.

[2] Kanitz, A., "Temperatur und Lebensvorgange." Berlin, 1915.

[3] Snyder, Charles D., "A Comparative Study of Temperature coefficients of the Velocities of Various Physiological Actions," *Am. Jr. Physiol.*, Vol. XXII, Aug., 1908.

[4] Loc. cit.

[5] Harvey, E. Newton, "Effect of Different Temperatures on the *Medusa cassiopea*, With Special Reference to the Rate of Conduction of the Nerve Impulse." Carnegie Inst. of Wash. Pub. 132. 1910.

ranges of vital temperatures than in the lower. This indicates by the method of the chemist that which the cytologist has long held, namely, that the mitotic complex is something more than a sum total of continuous and independent physiological actions; it is an interrelated system of forces, vastly complex and which system varies in its complex at each stage of mitotic progress.

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Diet and roughage in relation to the experimental scurvy of guinea pigs.

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It has been repeatedly demonstrated that exclusive diets of cereals produce scurvy in the guinea pig. We have fed filter paper, sawdust and hay respectively, as supplements to an oat diet without averting the appearance of scurvy. Duration of the disease and decline were not appreciably different when these supplements were fed. The addition of 7, 10, or 18 per cent. of paper pulp to a special soy bean diet[1] failed to supply an antiscorbutic property.

Feeding raw milk in addition to oats induces marked constipation with impaction of feces in the cecum. Animals fed 40 c.c. milk daily showed definite symptoms of scurvy in about a month. As the daily allowance of milk was increased, the symptoms seemed to recede in severity. Yet even when 80 c.c. milk were consumed daily, the animals became very constipated and died; but there were scarcely any signs of scurvy. Autopsy of such a case revealed absence of the typical macroscopic hemorrhages or of fragility of the bones. These observations appear to confirm the findings of Chick, Hume and Skelton,[2] which indicate that a sufficient *amount* of milk fed to guinea pigs will prevent scurvy. Such observations render debatable the hypothesis that

[1] Barnett Cohen, PROC. SOC. EXP. BIOL. AND MED., April 17, 1918, p. 102.

[2] Chick, Hume, and Skelton, *The Lancet*, Jan. 5, 1918.