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The significance of changes in the permeability of the plasma membrane of the living cell in the processes of stimulation and contraction.

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The general facts indicating that stimulation is dependent on a temporary increase in the permeability of the surface layer or plasma membrane of the irritable element are as follows :

A. The nature of the motile process in such plants as *Mimosa*, *Dionæa* and the *Cynareæ*, where the movement depends on a sudden loss of turgor. Such a change indicates either (1) a sudden decrease in the concentration of the osmotically active substances within the cell due to chemical action, or (2) a sudden loss of impermeability relatively to the osmotically active substances. The latter explanation is almost certainly the correct one.

B. The identity of the electrical change accompanying stimulation in motile plant cells with that observed in irritable animal tissues (Burdon-Sanderson), indicating a fundamental similarity in the conditions of stimulation in the two classes of organisms.

C. The fact that the post-mortem increase in permeability is accompanied by contraction in muscle cells; the same is, of course, true of motile plant organs where the movement depends on loss of turgor.

D. The nature of the electrical change accompanying stimulation. If the irritable element represents a concentration-cell in which a semi-permeable membrane (the plasma membrane) greatly diminishes the velocity of the anion, while leaving that of the cation practically unaltered (Ostwald-Bernstein membrane theory), any marked increase in permeability relatively to the anion must result in a fall of the potential difference between exterior and interior of the irritable element. Such an electrical change actually occurs on death or injury of the element; also momentarily during stimulation. A demonstrable increase in permeability occurs at death; inferentially, therefore, the same change occurs during stimulation.

E. The fact that an irritable tissue loses irritability for a variable (usually brief) period after stimulation (refractory period), — indicating that at that time the property of semi-permeability, on which electrical stimulation depends (Nernst), — is temporarily lost.

The special observations presented in this paper are as follows :

1. *Arenicola* larvæ are stimulated intensely by pure isotonic solutions of various salts (NaCl, KCl, NH_4Cl , LiCl, SrCl_2 , BaCl_2), contracting to half their length for several seconds when first introduced into the solution. At the same time a yellow pigment contained in the cells of the organism diffuses freely to the exterior and colors the solution.

2. Solutions which do not produce this strong initial contraction do not cause such loss of pigment. Isotonic CaCl_2 and MgCl_2 (especially the latter) are instances. In these solutions the muscles lose the power of contraction and the organism becomes stiff and motionless (though still propelled by the cilia which remain active). Addition of small quantities of CaCl_2 to a NaCl solution prevents the strong initial contraction and loss of pigment (antitoxic action).

3. MgCl_2 and similarly acting solutions appear to *decrease* the permeability of the tissues, and so prevent the ionic transfer on which stimulation depends. The general action of anæsthetics consists in *decreasing the normal permeability*; stimulating agencies, on the other hand, have the reverse effect.

4. Strong solutions of fat-solvents (chloroform, ether, benzol, (etc.) produce a contraction of the muscles accompanied by loss of pigment, even in $m/2$ MgCl_2 . This effect is to be referred to an alteration of the lipoid substances in the plasma membrane. Such alteration, if slight, *decreases* permeability (anæsthetic action in low concentrations); if extreme, it produces the reverse effect, with resulting stimulation.

5. The hypothesis is presented that the chemical effect of the above changes in permeability depends essentially on their influence in varying the rate at which carbon dioxid leaves the cell. The velocity of the oxidative energy-yielding processes whose end-product is CO_2 is thus varied with the rate of removal of this latter substance from the system; this velocity is accordingly increased during the increased permeability of stimulation, and is decreased

during anesthesia or inhibition. This view is supported by a consideration of the electrical changes accompanying inhibition and stimulation, respectively ("positive" and "negative variations").

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On the relative concentration of lysins, precipitins, agglutinins, opsonins and related substances in the different body fluids of normal and immune animals.

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The present work was suggested by some of our previous work with Prof. Carlson on the physiology of lymph. It was suggested that it would be of profit to establish the differences between serum and the other body fluids in their content of antibodies of various kinds in normal and immune animals, with the hope that it would have some bearing upon the problem of lymph formation, and also upon the origin of these antibodies. Thus far the hemolysins, hemagglutinins, bacterial agglutinins, bacterial opsonins, hemopsonins, and precipitins have been studied in the serum, neck lymph, thoracic lymph, pericardial fluid, cerebrospinal fluid, and aqueous humor. The bacterio-lysins are also under consideration.

The results with normal dogs have been the following: Hemolysins are found in the serum, thoracic lymph, and neck lymph in the normal animal. Serum and thoracic lymph contain them in almost equal quantities, with a slight balance in favor of the serum. The hemolytic power of the neck lymph is much lower than that of the serum, and is almost entirely wanting in the lymph which is secured without massage. In two of seven cases there was a small amount of hemolysis in the pericardial fluid, in the remaining cases there was no laking when the fluid was free from erythrocytes. There is no hemolysis in the cerebrospinal fluid, except in one case where there was a trace of free hemoglobin. There was no hemolysis in the aqueous humor. The hemagglutinins run parallel with the hemolysins except that they act in higher dilutions than the latter.