

white eyes, to a male with the normal sex-linked allelomorphs, viz., gray body color and red eyes, but in addition the male carried a recessive non-sex-linked character, viz., ebony body color.

One gynandromorph appeared among many thousand offspring. It was male on one side (partially) and female on the other. Both sides had red eyes and gray (or dark gray) body color. An analysis of this case shows that the male side must have contained the sex chromosome of its father and a non-ebony autosome from the mother. In other words, the gynandromorph on the male side is like the father except that it carries in addition one of the autosomal characters of its mother. The result means that at some early division a sex chromosome failed to pass to one pole and became lost.

Since this explanation will cover also the first two types, and since neither the hypothesis for the first nor that for the second type will explain all three types the third hypothesis is to be preferred. It leads to the conclusion that *gynandromorphs and mosaics may arise through a mitotic dislocation of the sex chromosomes.*

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The applicability of Hermann's theory of alteration.

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1. Herrmann's theory of alteration, which is accepted to-day by many physiologists, assumes that the junction of dead and of living tissue is the seat of an electromotive force which acts in such a direction that the dead tissue is negative while the living tissue is positive. This theory was advanced by Herrmann against DuBois Reymond who tried to explain the currents produced by muscles and nerves by means of complicated structural assumptions. Herrmann's theory has the advantage of expressing in an extremely simple form a large number of physiological observations. It has met general recognition partly also because all the opposing theories were of a very unsatisfactory character. The arguments however which Herrmann advances to support his views are not so conclusive as to fully justify his views. Especially his observation that a

definite time elapses between the cutting of the muscle and the appearance of the current of injury must not necessarily be due to a chemical alteration resulting from the injury. This time is so exceedingly short ($5/1000$ of a second) that a mechanical explanation rather suggests itself than a biochemical.

2. The conception that a difference of chemical processes in the dead and in the living tissue produces currents is also contradictory to physical laws. This was already pointed out by DuBois Reymond and his arguments seem still valid to-day. According to well-established physical principles an E.M.F. may be produced as a result of a chemical alteration which is brought by a current passing through the system, not however through a local chemical reaction which liberates ions.

3. Moreover certain experimental facts are in direct contradiction to Herrmann's theory; if a muscle is brought in contact at one end with distilled water and at the other end with a physiological NaCl solution it is found that the part in contact with the water is positive. This means that the injured part of the tissue is positive in this case since the distilled water has a destructive influence in direct contradiction to the alteration theory. Biedermann¹ who first observed this phenomenon has tried to bring it in harmony with the alteration theory. He argues that the death of the tissue produced by means of distilled water is of a peculiar nature because the conduction of irritation still persists under certain circumstances. This argument however certainly also contains hypothetical factors.

4. Mac Donald² has described interesting experiments which show that the magnitude of the current of injury has no relation to the state of life or death of the tissue. The current of injury of a sciatic nerve of the cat is measured immediately after excision and some time later; it is then generally found that the magnitude of the current decreases, which might be explained as being due to the death of the nerve. If however the nerve is immersed for a short time in a dilute salt solution the magnitude of the current of injury increases up to or above the original value. It hardly need be said that this treatment does not restore to the nerve any

¹*Sitz. d. Wiener Akad.*, 81, Abt. 3, 74 (1880).

²*Proc. Roy. Soc.*, 67, 310 (1900).

of its vital properties. This shows that the alteration theory can by no means claim a general applicability.

5. The alteration theory certainly does not give any point of view concerning the physical nature of the currents produced by tissues. Among the more recent attempts to solve this problem the so-called membrane theory is especially prominent. This theory was put forward by Ostwald in 1895 on the assumption that a semipermeable membrane is more permeable for cations than for anions. It is however not thoroughly justified *from a physical standpoint* either and Tammann and Walden who tried to prove it by means of analytical methods in Ostwald's laboratory have got contradictory results. Apparently therefore an experimental study of the E.M.F.'s produced by tissues and their artificial imitation, is a more promising method for the solution of the problem in question.

6. One of the most characteristic properties of the E.M.F. produced by tissues is the positivizing effect of water and of dilute salt-solutions as shown by the experiments of Biedermann and of Mac Donald described above. Dr. Loeb and the author have studied this phenomenon in a more quantitative way, namely with uninjured plants.

An artificial imitation of this property has been possible. A systematic study of cell arrangements composed of aqueous and water immiscible electrolytes (undertaken by the author) has shown that all water immiscible acid substances—used as ventral conductor show the same phenomena as living tissue, especially solutions of fatty acids in substituted phenols (as found recently by Dr. Loeb and the author).

The presence of a water immiscible acid (most likely a fatty acid) in the skin or membrane surrounding the tissue is therefore essential for this positivizing effect, not a selective permeability to cations as one would expect from Ostwald's theory. (Also the negativizing effect of K salts which was observed by Biedermann on muscles could be imitated by means of pure water immiscible substances.)

7. These experiments make it possible to investigate the physical nature of the single potential differences which compose the E.M.F.'s produced by tissues. For the cell arrangements of aque-

ous and water immiscible substances which imitate the tissue so far as the production of currents is concerned can be analyzed in all details much more easily than the tissue itself. The work along this line is not yet entirely finished, the results obtained so far show that biological potential differences are located at the junction of water immiscible fatty membranes and aqueous solution and that their magnitude is determined by peculiar phenomena of distribution. These phenomena of distribution can be fully accounted for by well-established physiochemical laws, but they are of rather complicated nature.¹

The biological potential differences are not determined by ionic mobility as has been frequently assumed.

The methods used in this work are essentially physiochemical. The results obtained so far may appear insignificant to the physiologist as most of the more important electrophysiological observations especially those connected with irritation (action currents) remain unexplained. However the explanations for all these phenomena which the alteration theory can put forward are very hypothetical. It therefore seems justified at the present time to try a thorough explanation on the basis of well known physical laws of the very simplest electric phenomena observed in tissues.

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The synthesis and rate of elimination of hippuric acid after benzoate ingestion in man.

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Ten grams of sodium benzoate were administered to a healthy man on a diet of milk, butter, and cane sugar, *i. e.*, glycooll-free. The urine was collected at two hour intervals, and the relation between the elimination of hippuric acid and urea studied. As compared with the corresponding control periods on the same

¹ The details of this work are published in the *Journal of the American Chemical Society*, XXXV, 344 (1913), *Transactions of the American Electrochemical Society*, XXIII, 401 (1913), *Zeitschrift f. Electrochemie*, XIX, 319 (1913).