investments must be safe and the net income large. It is believed that no guardian would more surely fulfill these conditions than the corporation of Harvard College.

EDWARD C. PICKERING.

CAMBRIDGE, MASS.,
April, 1903.

THE NATURE OF NERVE IRRITABILITY, AND OF CHEMICAL AND ELECTRICAL STIMULATION. PART II.

THE present paper contains results confirming and extending those given in my paper in SCIENCE, Vol. XV., pp. 492–498, 1902. The results previously reported were interpreted to mean that chemical stimulation by salts, apart from the osmotic stimulation of strong solutions, was really an electrical stimulation due to the electric charges of the dissociated ions. Of these ions the negative or anion always tended to stimulate the nerve, while the positive or cathion always tended to reduce nerve irritability and prevent stimulation. Whether any salt stimulated or annihilated nerve irritability without stimulation depended upon the predominance of the anion or the cathion. Chemical stimulation was shown to be in reality electrical, instead of electrical stimulation being chemical as had hitherto been supposed. These results made it possible to understand electrotonus and electrical stimulation. The cathode increases nerve irritability and stimulates, because in this region anions are predominant during the passage of the current; while the anode depresses because here the cathions preponderate. Stimulation on the break of the current was due to the reverse of these processes, the accumulated anions diffusing toward the cathions, and a fall in the positivity of the nerve in the anode region resulting. Furthermore, the specific action of the ions upon the nerve was supposed to be due to a production of a change in state in the colloids in the nerve, extending Loeb's hypothesis in this particular and making it specific that stimulation meant a precipitation of the colloids, inhibition the reverse; the colloids of the motor nerve reacting as if they were electro-positive.

Since the publication of this paper, illness and the pressure of other work have prevented my bringing the matter to a conclusion as soon as I had hoped, and meantime Loeb has published an attack on my hypothesis so far as it applies to muscle.*

Loeb has been led to abandon this hypothesis because of certain exceptions, among them being the action of barium chloride. Further work, of which the following is a preliminary statement, establishes, I believe, the truth of the main conclusions in my former paper, so far at least as motor nerves are concerned. In the case of the muscle I can not but think, from Loeb's results, that a careful study of apparent exceptions might show the same facts there, and explain these exceptions, as has been the case with the nerve. As regards the possibility of sensory nerves showing a different reaction to motor, Grützner long ago pointed out the fact that they were readily stimulated by potassium chloride and acids, while motor nerves were not. Every one knows that acids will stimulate some sensory end organs, presumably by means of the positive ions the acids contain. Knowing these facts, it was easy to infer that sensory nerves were electro-negative and were stimulated by salts having a predominant positive ion, while motor nerves were electropositive and were stimulated by the anion. Were this true, we should have a positive variation in sensory nerves and a reverse electrotonic effect from that in motor.

* Loeb, *Pflügers Archiv f. die ges. Physiologie*, Bd. 95, 1902, p. 255.

I accordingly tried experiments on the sensory nerve trunks of frogs more than a year ago, but I found the response to sensory stimuli so uncertain as to make the results valueless. Further experiments are necessary before speaking definitely, but thus far I have been unable to obtain any conclusively different results in sensory from motor nerves. I mention this fact to show that the argument that positive ions stimulate sensory end organs is not incompatible with my own conclusions and the facts were well known to me.

1. *The anion stimulates motor nerves; the cathion reduces irritability.* Loeb contradicts this statement for muscle because barium chloride stimulates muscle. The stimulating action he refers to the cathion. Barium chloride of an M/10 or weaker solution will also stimulate motor nerves, and is in these strengths a better stimulus than an equivalent sodium chloride solution. My former statement including barium chloride among the nón-stimulants was wrong, the mistake arising from a series of negative observations. Mr. O. H. Brown called my attention to this error. The stimulating action of barium chloride is, however, due to the anion and not to the barium, although barium nitrate and acetate will also stimulate. That it is the chlorine and not the barium which stimulates may be shown by stimulating the nerve or the muscle with non-polarizable mercury, calomel, barium chloride electrodes. If barium stimulates the contraction should begin at the positive electrode on the make of the current, as well as at the negative, for at the anode barium ions are passing into the nerve. It was found that the contraction always began at the cathode on the make as with sodium chloride. The experiment was also tried of soaking the nerve or muscle in barium chloride for many minutes previous to stimulation, so that barium chloride might be present in the muscle and nerve in large amounts. No change in the nature of the response could be observed. Similar experiments with electrodes of aluminum chloride, manganese chloride, magnesium chloride, zinc chloride and other metals gave the same results as sodium chloride, except that a greater depression may occur at the anode. These facts show that the stimulation is due to the anion and not to the cathion.* Further evidence will be given to support this conclusion. Barium chloride resembles sodium chloride in many of its reactions, so that there is little doubt that if the sodium salts stimulate by their anions the barium salts do also. I think it probable that barium chloride stimulates because the two charges on the chlorine overbalance the two charges on the barium. This physiological difference between barium and calcium and sodium and potassium is in line with their chemical behavior. Barium chloride solutions contain no hydrogen ions produced by electrolytic dissociation, while calcium and magnesium do; and potassium chloride, while not containing hydrogen ions itself, facilitates catalyses produced by such ions, while sodium has not this property. Why the two calcium charges are more efficient than the two barium charges is still obscure, but may be due to the charge being more firmly attached to the barium than to the calcium, or that the charge has a different motion in the two cases.

2. *The relative stimulating efficiency of the anions* is primarily, as already stated, proportional to the number of charges on the anions. Further observations on more nerves and other salts show that the monovalent anions are to the divalent and the

* I owe the suggestion of using electrodes in this way to Dr. Lingle, who has already employed it on heart muscle.

trivalent in their stimulating capacity approximately as $1:2+:3.5$, and not as Hardy found in colloidal solutions proportional to a power of the valence. There are variations from this rule, some monovalent anions, *i. e.*, hydroxyl, being nearly as powerful as divalent. The formate, however, is not an exception to the rule in the nerve, whatever it may be in muscle. It is, however, somewhat stronger than the chloride. Such variations are in no way antagonistic to the general conclusion that it is the charge which stimulates, and attention was called to them in my original paper. They probably mean that the number of charges is not the sole factor, but possibly, as already suggested, it is rather the motion of the charge around or with the atom or the affinity of the charge for the atom.

3. The general rule that the inhibiting action of the cathion is proportional to its valence or its electrical charges holds true, but here even more than in the anions there are exceptions, monovalent ions sometimes being stronger than one half of a bivalent ion. These exceptions need further study and do not invalidate the general conclusions, for, so far as I have examined, the only bivalent cathion which is weaker than two monovalent anions is barium.

4. That barium chloride stimulates by means of the anion is shown also by the fact that its stimulating action may be neutralized by any of the agents used to neutralize the stimulating action of sodium chloride, *i. e.*, by the addition of small amounts of $CaCl_2$, KCl, LiCl, NH_4Cl and probably other salts having predominant positive ions. More of these salts are required than are required to neutralize NaCl, which agrees exactly with the theory. These facts were predicted, and experiments confirmed the prediction even to the amounts of salts necessary to add. Furthermore, barium chloride, like sodium chloride or other sodium salts, places the end of the nerve in a condition of catelectrotonus, so that if the end of the nerve is cut off after immersion in any of these salts, the muscle goes into a tetanus and may remain in a tetanic contraction for many minutes, in some cases even half an hour. This tetanus corresponds closely to the tetanus observed on cutting the nerve between the electrodes with the anode near the muscle during the passage of the current, and is, I believe, due to the same cause. This similarity of action between sodium and barium salts shows them to act in the same way in the nerve, but the barium salts somewhat more strongly. The fact that barium chloride may be neutralized in its poisonous and stimulating action by calcium chloride is difficult to reconcile with the hypothesis that antitoxic action occurs between monovalent and polyvalent positive ions.

5. If sodium chloride stimulates by the anion, as electrical stimulation clearly indicates, it should be possible to neutralize its stimulating action by adding small amounts of any salt of which the positive ion preponderates, but not by any salt of which the negative ion preponderates. This is the case: The stimulating action of sodium chloride may be neutralized by small amounts of the chlorides of lithium, potassium, hydrogen, ammonium, aluminum, calcium, strontium, zinc, cobalt, manganese or magnesium. The amount of salt necessary to neutralize varied in different cases, more lithium being necessary than potassium. The salts were found to range themselves in this action in the same order of efficiency as previous experiment had shown them to act as depressors of irritability. The order was predicted from the theory and confirmed by experiment. The exact figures will be given in the full

paper. By this method we can arrive at the exact relative physiological efficiency of the different positive ions, and, so far as I have gone, it corresponds closely with the chemical or catalytic action of these ions.

The addition to sodium chloride of any salt of which the anion overbalances more than chlorine does over sodium should not neutralize the poisonous or stimulating action of sodium chloride, but should increase the latter. This is the case: The addition of barium salts, or of sodium sulphate, phosphate, citrate or ammonium citrate increases the stimulating action of sodium chloride.

6. If sodium chloride is poisonous because the chlorine predominates, we should be able to neutralize its poisonous action by predominant positive ion salts, but not by predominant negative ion salts. This is the case so far as observations go: The addition to sodium chloride of small amounts of calcium chloride, as found by Howell, or potassium or lithium, will greatly prolong the life of the nerve immersed in the solution. The toxic and antitoxic action, so far as the nerve is concerned, and I believe in other cases also, is thus shown to be due to a neutralization of a predominant ion by an ion of an opposite charge, and is not due to any antitoxic action between monovalent and divalent positive ions. The stimulating action of the sulphate or citrates can not be referred primarily in my opinion to their precipitation of calcium or rendering it inert. The stimulating action of these salts may be neutralized, for example, by potassium where there is no question of precipitation. The antagonistic action is thus shown to be due probably not to a combination between the toxin and antitoxin, but to the fact that each of these acts on the protoplasm, but in an opposite manner.

7. The theory that positive ions act like the anæsthetics and depress protoplasmic activity or inhibit has been confirmed by observations on the eggs of echinoderms. The anæsthetics liquefy these eggs; liquefaction is also caused by the electric current on the anode side. These results were obtained by Mr. O. H. Brown. Further analogies of action were observed by Dr. Spaulding and will be published shortly. Preliminary experiments on the nerve indicates that this resemblance extends possibly to protoplasmic respiration, salts of a predominant positive ion checking respiration while those of predominant negative ion increase respiration, at least temporarily. My experiments are, however, still too few to enable positive statements to be made.

8. The current of rest of motor nerves shows marked fluctuations if the tip of the nerve is dipped into acids, alkalies or salt solutions. The acids quickly depress the current, alkaline salts increase it. The current may thus be many times abolished by acids and reappear on dipping in sodium hydrate. These results are being carried further. They indicate the general truth of the conclusions of the opposite physiological action of anions and cathions.

9. The results recorded of the antagonistic physiological action of the anions and cathions hold also for the central nervous system and for the kidneys. This work has been done by Dr. S. A. Matthews and Mr. O. H. Brown and others in this laboratory and will be shortly published. They show that the motor nerve is not unique, but that its reaction corresponds to those of many other tissues.

I believe that the exceptions observed by Loeb in muscle may be explained in part by the fact that when a muscle is put into a salt solution it is impossible to state whether the contractions arise from the nerves, nerve ends, the muscle substance or a disturbance of the electrical equilibrium within the muscle mass. It must not be forgotten also that the relaxation of the muscle is possibly an active process, and, as experiments indicate on cilia, the relaxation may be stimulated by the positive ions, the contraction by the negative, somewhat as Howell suggested for potassium and calcium in the case of muscle. Lingle has already worked in this direction and will no doubt be able to clear up some of the discrepancies.

10. I believe the results so far obtained support strongly the truth of the hypothesis of the antagonistic action of the anions and cathions on protoplasm. They support Loeb's original suggestion of the importance of valence and of my conclusion that in motor nerves and some other tissues the anion stimulates, while the cathion inhibits. They also support the explanation of chemical and electrical stimulation and electrotonus given in my former paper.

11. The results obtained indicate also the truth of the general law, *i. e., the physiological action of any salt is equal to the algebraic sum of the actions of its ions.*

A. P. MATHEWS.

CHICAGO,
March 3, 1903.

STREMMATOGRAPH TESTS. PRINCIPLES AND FACTS RELATING TO THE DISTRIBUTION OF THE STRAINS IN THE BASE OF RAILS UNDER MOVING TRAINS.

BEFORE it was possible to make any tests of precision showing the distribution of the stresses in rails under moving locomotives, it was necessary to improve the tracks, and introduce stiffer rails than were in use prior to 1884. The $4\frac{1}{2}$-inch 65-pound rails, with their splice bars, were too weak to distribute the loads of the locomotives and cars in an efficient manner. While the distribution theoretically follows the same general law in the lighter rails, yet the efficiency is so much less that it is impossible to obtain comparative tests in practice to confirm the theory of the distribution of stresses under locomotives.

On the $4\frac{1}{2}$-inch rails, the heaviest axle loads on passenger locomotives prior to 1889 were about 27,500 pounds. When many miles of the stiffer 5-inch 80-pound rails were in the track, the axle loads were increased to 40,000 pounds per pair of driving wheels.

The stiffer rails permitted better joints, capable of holding up the ends of the rails, which continued the functional action of a rail as a continuous girder to adjacent rails.

After the stiffer rails have been well surfaced in the track, the portion under the driving wheels becomes practically a restrained beam with numerous supports, the front end being held down by the forward truck wheels, and the other portion of the rail by the tender wheels.

The stiffer rails have been laid upon the same road-beds, without increase of width, to distribute laterally the heavier wheel loads to more breadth of road-bed.

The track for steam railroads is by construction flexible, but notwithstanding the high standards of smoothness which have been secured by reducing the looseness of the superstructure and its flexibility to small limits by stiffer rails, it is not a limited flexible structure like a bridge, in which the strains in the members may be analyzed and calculated.

The problem—or series of problems—in reference to the strains in rails and their distribution under moving locomotives and cars, is so complicated by the looseness of the superstructure and the imperfect elasticity of the road-bed, that it has not yielded to mathematical analysis, as for