As we have had inquiries concerning this subject, and particularly concerning the Birkeland-Eyde process, we add a few literature references. The description by S. Edström will be found in the Transactions of the American Electro-Chemical Society, vol. vi., page 17, 1904; the instructive lecture by Prof. Otto N. Witt on the process as now worked at Notodden, and on the whole problem, was published in the *Chemische Industrie*, Berlin, of December 1, 1905. The Birkeland-Eyde patents are: English patent, 1903, No. 20,079; French, No. 335,692; United States, Nos. 772,862 and 775,125; German (applied for), B 34,093; Norwegian patents, 13,240 and 13,280. The British patents of Lovejoy and Bradley are: 1901, No. 8230; 1902, No. 14,780. Most of the scientific researches to which we have referred have appeared in the *Berichte der Deutschen Chemischen Gesellschaft*, abbreviated "Ber.," these are: F. v. Lepel, Ber., 1903, page 1,251; 1904, page 712; 1905, page 2,524. Muthmann and Hofer, Ber., 1903, page 438; A. Stavenhagen, Ber., 1905, page 2,171. O. F. Tower, "Action of Nitrogen on Steam," Ber., 1905, page 2,945. We have further to mention: W. Nernst, *Nachrichten Ges. Wissensch.*, Göttingen, 1904, page 261; J. K. Clement, "Ozone Formation," *Annal. der Physik*, vol. xiv., page 334; E. Rasche, *Dingler's Journal*, vol. cclxii., page 318 (all three on the thermal equilibrium); O. Scheuer, *Zeitschrift für Elektrochemie*, September 1, 1905, page 565; and J. Brode, *ibid*, page 752, October 27, 1905.

THE CHANGES IN THE NERVE AND MUSCLE WHICH SEEM TO UNDERLIE THE ELECTROTIC EFFECTS OF THE GALVANIC CURRENT.*

By Prof. JACQUES LOEB.

WHEN we send a constant current through a nerve, the irritability of the latter is increased in the region near the cathode and decreased at the anode. While this so-called electrotonic effect lasts as long as the current goes through the nerve, there is another effect of the current, viz., a contraction which occurs only at the moment the current is made or broken (or its intensity suddenly changed). Since the impulse for the make contraction starts from the cathode and that for the break contraction from the anode it is generally assumed that the making of catelectrotonus and the disappearance of the anelectrotonic condition cause the contractions of the muscle at the making or breaking of the current.

Through the work of Faraday and Arrhenius the fact has been definitely established that in liquid conductors the current can only be carried by ions and that these ions exist already in the liquid conductor before the current goes through. Since tissues can only act as liquid conductors, a current cannot pass through a nerve or a muscle except through the motion of the ions.

Since the effect of a current only occurs at the electrodes (or wherever the free passage of ions is completely or partly blocked), an explanation for the effects of a galvanic current upon nerve or muscle must look for the possible phenomena at the electrodes (or where the progress of the motion of ions is blocked). In a liquid conductor two kinds of changes occur at the electrodes: first, changes in the concentration of ions, and second, a withdrawal of charges from the ions which come in contact with the electrode. It will be necessary to decide which of the two physical effects of the current is responsible for its physiological effects at the electrodes. Experiments which I published eight years ago[†] prove conclusively that the contraction caused by the making or breaking of a galvanic current cannot be caused by a withdrawal of charges from the ions. In these experiments I showed that a nerve which is entirely insulated and placed parallel to the spark discharge of a Toepler-Holtz machine or a Ruhmkorff will cause contractions, whenever a spark or a discharge is produced, while no or only minimal effects are noticeable when the nerve lies at right angles to the spark discharge. Since the same influence of the orientation of the nerve to the direction of a galvanic current has been known to exist when the current passes directly through it, it follows that the stimulating effects of a current are not due to a withdrawal of the electrical charges from the ions at the electrodes, but are due merely to a change in the concentration of the ions at the electrodes (or wherever the motion of ions is blocked inside a living organ). For in my experiments no electrical charges were withdrawn from the nerve, and the only effect the induction could have produced was a change in the concentration of the ions at the two sides of the nerve opposite the electrodes of the Ruhmkorff or Toepler-Holtz machine.

It is therefore obvious that no explanation of electrical stimulation can be correct unless it is based exclusively upon the effects which changes in the concentration of ions will produce. This eliminates such hypotheses as the one which assumed that protoplasm consisted of positively charged colloidal particles and that a loss of this charge at the cathode produced coagulation. It eliminates likewise all hypotheses which are based upon the assumption of secondary chemical effects due to the withdrawal of charges from the ions and subsequent chemical reactions caused by the transformation of ions into atoms.

It was clear to me that a solution of the riddle of the stimulating effects of the galvanic current could only come from a study of the effects of solutions of electrolytes upon nerve and muscle. When we put a

nerve or a muscle into a solution of an electrolyte, the ions of this electrolyte will migrate into the nerve or muscle, and an increase in the concentration of the ions of the electrolyte in question will be produced. I therefore endeavored to find out which solutions of electrolytes allowed us to imitate the various effects of the galvanic current upon nerve and muscle.

Since the stimulating effects of the current and the increase in irritability (catelectrotonus) occur at the cathode (when the current is made), and since the cations migrate to the cathode, I expected—as was perhaps natural—to find that certain of the cations present in the muscle and nerve were responsible for the catelectrotonic effect of the current and the production of twitchings by the same. The cations which were concerned were Na, K, Ca and Mg. I found that when the chlorides of these four metals are used NaCl and KCl cause rhythmical twitchings when a frog's muscle is put into a solution of one of these salts; in a m/8 solution of the former the twitchings may last for two days while in a pure KCl solution only a few, often only a single contraction of the muscle occurs at the moment it is put into the solution. But no condition resembling catelectrotonus is produced in the muscle. The chlorides of Mg and Ca, on the contrary, not only produce no contractions of the muscle but inhibit them when they are produced by NaCl. When I put the nerve into any of these four solutions (isotonic with the blood), no condition resembling catelectrotonus was produced and no twitchings occurred during the time of my observation.* The only application that could be made from these facts to the theory of electrical stimulation was this, that possibly the single contraction which starts from the cathode when the current is made might be due to the K ions. Since the migration velocity of the K ion is greater than that of the other three inorganic cations named, the making of the current must indeed increase the concentration of the K ions comparatively more at the cathode than that of any of the other three ions. I expressed this possibility in my lectures in Chicago, but never published it because the most essential feature of galvanic stimulation could not be explained in this way, namely, the increased irritability in the region at the cathode (catelectrotonus) and the decreased irritability at the anode. Moreover contractions could be produced by KCl in the muscle only but not from the nerve.

The fact that Ca and Mg inhibit the stimulating effect of NaCl suggested the idea of testing the effect of such sodium salts whose anion is liable to precipitate calcium (or Mg) or to form calcium salts with a comparatively low degree of dissociation. It was found that such salts not only produce rhythmical contractions but that they do so at a much lower concentration than NaCl. Moreover such salts, e.g., oxalates, fluorides, phosphates, citrates, etc., are liable to increase the irritability of the muscle in a striking way and produce in it a form of irritability which I called provisionally contact irritability. I found that these solutions acted in a still more striking way upon the nerve inasmuch as they produce here an increase in irritability, such as exists in the region around the cathode.† It is astonishing how rapidly such an increase is brought about in a nerve when put into the solution of a calcium precipitant, such as sodium fluoride, citrate, etc. I have described in the last mentioned paper several experiments which indicate how enormously sensitive the motor nerve becomes under this condition.

The further extension of experiments showed that the condition of increased irritability can be produced by the salts which precipitate calcium not only in the nerve and muscle of higher animals, but also in the lower forms, e.g., the isolated center of jelly fish.

It is an equally general fact that when this condition is produced in a nerve, muscle or any other organ tried thus far, the normal or diminished irritability can be established by adding a sufficient quantity of CaCl₂ or MgCl₂ to the solution, or better still by putting the nerve for a short time into a pure solution of one of these salts.

The result of these experiments has therefore been that an increase in free Ca or Mg ions in the nerve or muscle causes a condition of diminished irritability corresponding to the anelectrotonus caused by the galvanic current, while a decrease in the concentration of free Ca or Mg ions causes a condition of increased irritability corresponding to catelectrotonus caused by the galvanic current.

The question therefore presented itself: could it be possible that the effect of the current consists in increasing the relative concentration of the free Mg and Ca ions at the anode and decreasing it at the cathode? I think it can be shown that at the cathode similar effects may be produced by the galvanic current as when we put the nerve or muscle into a solution of a calcium precipitant (or a salt whose anion forms a Ca salt with a small degree of dissociation) while at the anode effects must be produced similar to those which we obtain when we put the nerve or muscle into a CaCl₂ or MgCl₂ solution.

The changes in the concentration of the various ions which will occur in a nerve at the electrode depend primarily upon the velocity of the migration of ions. This velocity varies considerably for the anions found in nerve and muscle. While the Cl ion has a very high velocity (65.4) the higher fatty acid anions, such

as oleate, have a very small velocity, probably below 30. The same must be true for palmitate and stearate. These anions of the higher fatty acids must be found in the nerve and muscle. It is known that these anions precipitate Ca and it has been shown directly by Friedenthal* that sodium oleate acts like sodium oxalate and sodium fluoride in the production of muscular twitchings and otherwise, when injected into an animal. On account of this enormous difference in the velocity of the Cl and oleate ions, the galvanic current must cause more Cl ions to leave the cathode in the unit of time than oleate, palmitate, etc., ions and consequently, in the region of the cathode, the current must bring about a relative increase in the concentration of the Ca precipitants such as oleates, etc., and a relative decrease in the concentration of CaCl₂, which is not only very soluble, but also highly dissociated. It is therefore obvious that the effect of the galvanic current at the cathode region must be the same as if we put the nerve into a solution of sodium oxalate, fluoride, citrate, etc. At the anode just the reverse must occur. In the unit of time comparatively more Cl than oleate ions must migrate and collect there and the result will be an increase in the concentration of free Ca and Mg ions.

We have only discussed thus far these few anions, inasmuch as we cannot speak with equal certainty about the velocity of migration of other anions in the nerve or muscle. It is known that CO₂ is formed constantly in the muscle. This formation of CO₂ must of course increase the amount of Ca held in solution and increase the concentration of the free Ca ions through the formation of the bicarbonate of Ca. It is therefore of interest to state that according to Kohlrausch the velocity of the CO₃ ion (and HCO₃?) seems to be comparatively great, even greater than that of the Cl ion, the former being 70, the latter 65.4.‡ The figure for CO₃ is however not considered as correct as that for Cl. It seems certain, however, that the CO₃ ions have a comparatively great velocity and their relative concentration will therefore be diminished at the cathode and increased at the anode. No reliable data seem to exist concerning the velocity of the PO₄ ions.

As far as the changes in the relative concentration of the cations at the two electrodes are concerned, they must be less than the changes in the relative concentration of the anions, inasmuch as the difference in the velocity of migration of the cations is considerably smaller than that in the migration of the anions. The velocity of Cl is more than twice, possibly three times as great as that of the oleate ion and is absolutely greater than that of any of the cations K, Na, Ca, and Mg. The relative velocities of these ions are for K = 64.7 for Ca 51.8, for Mg 46, and for Na 43.6. Since K is by far the fastest ion, the main effect will consist in a relative increase in the K ions at the cathode. The difference in the velocities of Ca, Na, and Mg is too slight to bring about marked and rapid changes of their relative concentration at the electrodes under the influence of a weak current such as is used to produce electrotonus. It thus seems as if the differences in the relative migration velocities of the four cations mentioned above could not contribute materially to the origin of the electrotonic conditions.

While the data in our possession at present seem to explain satisfactorily the origin of the anelectrotonus and catelectrotonus, they do not show why only at the making and breaking of a current a contraction occurs. It is possible that the two phenomena are only incidentally connected.

If we summarize the facts discussed in this paper we may say: that previous work has shown that the condition of catelectrotonus (increased irritability) can generally be produced by putting nerves or muscles into a solution of calcium precipitants such as sodium (oxalates, fluorides, citrates, oleates, etc.) and that a condition of decreased irritability can be produced by putting the nerves or muscles into solutions of CaCl₂ or MgCl₂.

This paper indicates that by considering the migration velocity of the various anions in nerve or muscle it can be shown that if we send a galvanic current through a nerve or muscle, at the cathode the concentration of those anions which are liable to precipitate Ca, e. g., oleate, is relatively increased, while that of the Ca solving ions, like Cl, is decreased; and that the reverse is true at the anode. It seems therefore as if the electrotonic effects of the galvanic current might be due to the comparative increase in the Ca precipitants at the cathode and the comparative increase of the Ca solvents at the anode.

A NEW STANDARD OF LIGHT.

PROF. J. VIOLLE, as is well known, suggested choosing as a standard of light the radiation given off by the surface unit of incandescent platinum at its point of solidification. This French scientist has recently been experimenting with a view of establishing a new secondary standard of light on a similar principle. Without altering the fundamental standard just referred to, he found it profitable to take advantage of the normal boiling of a metal to maintain the temperature of a vessel heated by vapors of this metal, at a constant figure. To this effect he arranged a kind of testing tube of carbon above the metal, which was brought to the boiling point in the electrical furnace. The vapor would surround the whole of the bottom and a considerable length of the test-tube, which was lengthened by a tube allowing the interior of the test-tube to be investigated at constant temperatures.

* Friedenthal, *Engelmann's Archiv*, p. 145, 1901.

† These figures are quoted from Landolt and Börnstein, *Tabellen*, p. 763.

* Reprinted from the University of California Publications.
† Loeb, *Pflüger's Archiv*, vol. lxxv., p. 483, and vol. lxxix., p. 99, 1897; and reprinted in *Studies in General Physiology*, vol. ii., p. 482, 1905.

* The results of these experiments were published in the *Festschrift für Prof. Fick, Würzburg, 1899*, where I mentioned also briefly the negative results I had obtained in regard to the nerve.

† Loeb, *American Journal of Physiology*, vol. v., p. 362, 1901. Also in *Studies in General Physiology*, vol. ii., p. 692.