**The injury current of nerve, the key to its physical structure / by J.S. MacDonald.**

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## THE KEY TO ITS PHYSICAL STRUCTURE

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# ERRATA

P. 264, line 34. For 'conductor' read 'conduction.'
P. 309, line 10. For 'simply' read 'simple.'
P. 346, line 14. For 'organic' read 'inorganic.'

# THE INJURY CURRENT OF NERVE

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## PREFACE

IN justification of this attempt to secure a hearing for an already elaborately-handled theme, it may be pardonable to emphasize the importance of a very obvious fact, that the joint work of chemists and physicists has made the present time extremely opportune for the conduction and consideration of such research.

It may be said that this phenomenon of the injury current was most exhaustively examined at a time when physical science was not ripe to deal with such possibilities, and that the physiologist was obliged at great inconvenience to grope for correlated physical data; whereas, at the present time, such a mass of the required information has been collected, codified, and arranged according to simple and sufficing explanatory hypotheses by the physicist, that physiological research of this kind can with great advantage be carried out upon easily anticipated lines.

It may, on the other hand, be said that at the present date it is much more necessary to apologize for the carrying out of any study of electrical phenomena occurring in animal tissues, and especially such as are consequent upon injury, than to be imbued with a sense of their importance; for it is now realized that every process of diffusion occurring between solutions of electrolytes, such as solutions of inorganic salts, is a probable source of electrical phenomena, and also that every injury is necessarily succeeded by processes of diffusion following the destruction of pre-existing barriers. It is, for example, an absolutely certain prediction that differences of potential must be found between electrodes placed upon the external and internal surfaces of glandular organs, upon which it is an otherwise amply determined fact that solutions of inorganic salts are present differing in concentration or in nature in these two positions. And again, when it is otherwise known that stimulation of nerves leading to these structures causes a further difference to arise between the two solutions, it is certain that new differences of potential will arise as the result of such stimulation. In such cases it may seem doubtful whether the information gained from an examination of differences of potential can be of interest in comparison with the more direct information attainable by other means.

In the case of nerve no such apology is needed, for no other means have yet been found for detecting and measuring its intrinsic changes, even if these can finally be shewn to be of chemical rank ; nor can the study of the injury current be exempted from this claim.

There still remains the great probability that a nervous impulse may be a change propagated by electrical agency, and even in its essential nature an electrical phenomenon ; a travelling and temporary dislocation of pre-existing discrete particles, and not a travelling process producing new and differently gifted particles from the old.

If so, it is as solutions of electrolytes confined to minute cylinders that nerve fibres have a most important interest ; and yet the characteristics of these solutions are beyond the reach of methods of ordinary chemical investigation.

Therefore, any method which promises to reveal, even in an indirect way, the nature and concentration of these solutions, should be considered deserving of immediate and zealous application.

The investigation of the injury current stands alone in offering such possibilities ; and its diligent prosecution is not a matter for apology, nor even of secondary though legitimate importance, but is the only means by which a knowledge of the fundamental structure of the nerve can be obtained.

# HISTORICAL SECTION

The occurrence and distribution of differences of potential between points upon the surface of excised nerve, was discovered in 1842 by Du Bois Reymond, published in 1843,[1] and described in an exhaustive manner in his first collection of researches[2] in 1849. The general account given by him of this phenomenon provides one with an example of the possible truth and completeness of experimental observation. Rapidly as the research must have been carried through, for it forms only an incident in a larger theme, the statement is a perfect one, and an intimate acquaintance with the phenomenon reveals the amount of observation concealed behind each one of its carefully considered sentences. The salient points were gathered into three generalizations, the well-known *laws of the nerve current*. They define the spatial distribution of points upon the surface of the nerve, between which the differences of potential were (1) large, (2) small, (3) non-existent.

These laws describe the ideal case, which it is carefully noted was rarely, if ever, obtained, and in their application to the facts of any single experiment are stated generally to require modification. The most important modifications being due to the occurrence of a potential difference between the two cross sections and to the dislocation of the equatorial point from the mid point of the nerve.

Morgan, in 1863,[3] pursued the investigation one step further, and demonstrated the existence of a nerve current in minutely thin longitudinal fragments of nerve trunk, obtained for the experiment in a manner described by Harless[4]. He also noted the presence of 'weak longitudinal currents' in these fragments, and ascertained the symmetrical arrangement of potential distribution round an equatorial point.

The remaining work which has been undertaken in this subject has, to a large extent, only been concerned with the comparison of results obtained from various nervous tissues, and with modifications devised to test theories of its mode of origin, or with results obtained in abnormal or pathological conditions of the nerve.

The relation between the conditions thus found upon the surface of the nerve trunk, and its microscopical fragments, and the conditions of greater interest and importance legitimately inferred from a consideration of these to exist in the more

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[1] Du Bois Reymond, *Poggendorf Annal.* Bd. LXVIII. January, 1843.

[2] *Untersuchungen.* II (1), p. 262.

[3] Charles E. Morgan, *Reicherts Archiv.*, 1863, p. 340; also *Electrophysiology and Therapeutics.* New York, 1868, p. 465.

[4] E. Harless, *Abhandl Konigl Bayerisch Akad. d. Wiss.* 2nd Class, Bd. VIII. Abth. II, p. 539.

deeply-situated nerve fibres, was elaborately investigated by Du Bois Reymond.[1] His inferences strengthened by the mathematical work and physical experiments of Helmholtz[2] explained the complex distribution of potential differences upon the nerve trunk surface, as due to a simple distribution of oppositely electrically charged surfaces upon the individual nerve fibres. The zinc-copper model exemplifies these inferences, and its composition is a standing witness to the fact that the complex superficial conditions are, to a great extent, the outcome of an examination of the nerve trunk when longitudinally isolated from the surrounding structures, and examined in air. The complex condition then found upon the surface of the nerve trunk is new, is not the same as the conditions existent upon its surface when clothed in the neighbouring tissues, nor is it the same as the conditions existent upon the important elements of its structure.

In concentrating attention upon the individual nerve fibre and its physical structure, and after a laborious investigation of surface distribution, legitimately delving from this the essential nature of the problem as it affected the individual nerve fibre, Du Bois Reymond may be said to have not only discovered the 'apparent' but also the 'real' phenomenon. The whole longitudinal surface of the individual nerve fibre is probably equally positive, the whole transverse surface uniformly negative. The gradual transition, which apparently takes place in the surface conditions as we pass from the cross section in towards the unbroken nerve fibre, has probably no parallel in a varying state of the nerve fibre. The nerve fibre at its cut end is negative. The longitudinal surface in the neighbourhood of this cut end appears less positive than the remainder of the longitudinal surface, simply because of its physical juxtaposition to this negative surface.

## Section I

### Explanatory Theories. Du Bois Reymond

Of these facts and legitimate inferences, various explanations have been offered. Du Bois Reymond based his explanation entirely upon the constitution of one primarily important structural element of the nerve fibre. He used, in fact, the data obtained from observations upon the manner of origination and conduction of electrical currents by the nerve as a base from which to obtain knowledge of the main physical characteristics of the structure of the nerve fibre. It is a matter for regret that he did not sufficiently recognize in the nerve fibre the existence of not one but several structures of possible importance. It is true that before committing himself finally to such a position he was careful to examine the other two lines upon

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[1] Du Bois Reymond, *Untersuchungen.* Bd. I, p. 672. 1849. The original work was done upon muscle but confirmed for nerve.

[2] Helmholtz, *Pogg. Ann*, Bd. LXXXIX, p. 212. 1853. For a full account see also A. Fick, *Die Medizinische Physik*, Braunschweig, 1858 ; or C. Morgan, *Electro-physiology*, New York, 1867.

which an explanation might be sought, namely (1) a difference between the chemical constitution and physical characteristics of the molecules forming the longitudinal surface and transverse section respectively, due to secondary changes (acidity, etc.) at the transverse section ;[1] and (2) a pre-existing difference beween the nerve substance proper and its sheath.[2]

The first of these two rejected alternatives is closely akin to Hermann's 'alteration' theory, and was dismissed because of the apparent disproportion in extent between the phenomenon to be explained and the chemical change which could otherwise be demonstrated. The second alternative is as closely akin to Grünhagen's theory, and was dismissed because of an apparently decisive contradictory experiment (see later).

Having once selected a line of explanation, his further developments of it were foreordained by the scientific attitude of the time, which translated wholesale the attributes discoverable within and at the surface of a mass of homogeneous material to each of the individual molecules of which it was formed. The peripolar[3] molecule was a minute zinc-copper model unit, and its conception was then the necessary outcome of the legitimately formed belief that the nerve or muscle fibre was alone the physical structure upon which the phenomenon depended, and that this could practically be treated as a homogeneous structure.

Similarly when Du Bois Reymond discovered that under certain circumstances the muscle fibre could not be treated as homogeneous, and that the condition then present in localized portions of the fibre prevented the demonstration of the phenomenon, it was only possible to consider that such localized portions (parelectronomic layer)[4] offered an opposing electromotive force: it not being known that neutral 'membranes' might eliminate the display of electrical differences by offering an impermeable obstacle to the movement of diffusing particles, and that there was, therefore, no necessity to credit such obstacles as were discovered with what one might call 'electromotive functions.'

### Note on the Parelectronomic Layer

Du Bois Reymond's conception of the parelectronomic layer has been misunderstood, and even ridiculed, as if invented when the trend of a controversy compelled him to meet new evidence and satisfy impossible claims upon his original 'peripolar molecule' conception. It may therefore be of some advantage to consider the following quotation taken from a book published in 1852, and, therefore, fifteen years before the appearance of the 'alteration theory':—

H. Bence Jones, *Animal Electricity* (being an abstract of the discoveries of Emil Du Bois Reymond), page 116; published by Churchill, London, 1852—'The current obtained from the longitudinal section and the natural transverse section is seldom, if ever, so strong as the current obtained from the longitudinal

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[1] *Monatsberichte d. Konigl. Akad.*, 2 Berlin, 1859, p. 288. Republished in Du Bois Reymond's *Gesammt Abhandl*, II, I, 5. 'After my discovery in 1842 of the muscle current, naturally one of my first experiments was undertaken to discover whether the longitudinal surface and the artificial cross section of muscle possessed different reactions.'

[2] *Untersuchungen*, I, 558. 1848.

[3] Du Bois Reymond, *Untersuchungen*, I, p. 561, 1848 ; see also C. Morgan, *Electrophysiology, etc.*, p. 279, 1867.

[4] Du Bois Reymond, *Untersuchungen*, II, p. 39 ; or C. Morgan, *loc. cit.*, pp. 294-309.

section and the artificial transverse section. Very often, indeed, the former appears incomparably weaker; and by keeping the frogs for twenty-four hours at least at a temperature of 32° F. (0° C.) it is possible wholly to deprive the natural transverse section of its negative power when it is included in a circuit with the longitudinal section. But even the direction of the current can be reversed by means of cold. . . . . Whichever of these various modifications of the electric power of the natural transverse section may prevail, the usual current immediately appears when this section is injured in any way, so as to deprive an extremely thin layer of its vital properties, and thereby of its electromotive action. . . . Since the layer of muscular substance on the natural transverse section tends to reverse the laws of the muscular current, Du Bois Reymond proposes to call it the parelectronomic layer (from παράνομος contrary to the law), and he likewise calls that the parelectronomic state of the muscle, in which the muscle, in consequence of the parelectronomic layer having the intensity of its action increased, either appears inactive, or even becomes inactive in the negative direction,' etc.

## Section II. Hermann

Beginning in 1867, Hermann[1] produced a series of papers which proved that the phenomenon of the current of rest could not be demonstrated in uninjured tissue, and that injury, sometimes of an unsuspected kind, was an essential factor in its production. This proof he accompanied by an emphatic and controversial insistence upon the importance of the secondary results of injury, and in deference to his views the phenomenon has changed name, becoming the current of injury and subsequently the demarcation current. The extreme emphasis laid by him upon the secondary results of injury has since been abandoned,[*] and in 1898 he is found deliberating between his own 'alteration theory,' which embodies these views, and a 'pre-existence' theory belonging to that general class of theories against which he so strenuously contended.

It has been said that Du Bois Reymond's 'peripolar molecule' was formulated upon a basis of assumption, that the matter giving rise to the phenomenon was preexistent and homogeneous. It must also be said that Hermann's 'alteration theory' is confessedly based upon an assumption,[2] which must be considered, too, as possibly obnoxious; for it is an assumption of knowledge which is, in this case, unfortunately not otherwise attainable.

'Let us suppose that the dying substance is negative to the living, then all these phenomena are explained.'[3]

The acceptance, even temporarily, of such a postulate as this is equivalent to the surrender of a legitimate spirit of enquiry, and is impossible to a mind seeking to unravel the intricacies of 'vital' phenomena by gratefully received details of chemical

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[1] Hermann, *Untersuchungen zur Physiologie der Muskeln und Nerven.* Berlin, 1867-1868.

[*] See later, p. 223.

[2] Hermann, *Pflügers Archiv.*, 1898. LXXI, p. 299.

[3] Hermann, *Handbuch.* Th. I, p. 235.

Note.—Hermann's alteration theory is expressed in terms of vital states. For a reduction of these to the terms of chemical and electrochemical nomenclature—see (1) Bernstein, *Pflugers Archiv.*, 1897, who evolves a theory which, superficially similar to Du Bois Reymond's in that it is a molecular one, nevertheless involves a chemical difference at the seat of injury and is therefore similar to Hermann's; (2) Tschagowetz, 1897, *Ztscht d. russ Gesellsch f. phys. Chem.*, XXVII, 5, p. 430; (3) Max Oker Blom, 1901, *Pflügers Archiv.*, LXXXIV, p. 191.

composition and physical conditions. 'Vital' phenomena, not otherwise known to exist, are practically created to explain an interesting physical phenomenon; and are suitably arranged in the course of the nerve fibre in a manner which is not open to corroboration.

To Du Bois Reymond such an acceptance would have involved not only the abandonment of a particular theory, but also the relegation of his whole subject to the regions of empirical symbolism. It is not surprising, therefore, that immediately the theory was promulgated he entered the field against it.[1]

The extent of the controversy is well known. The experimental data collected during its prosecution will, doubtless, be remembered, when the words which hurled them into the possession of contemporary science have long been forgotten; but Du Bois Reymond will then have been reinstated as the founder of a scientific method of physiological research, and will thus have a more honoured remembrance than as the discoverer of a fact or a series of facts, or as the defender of a perhaps too confidently-held position. In the meantime the indirect outcome of the controversy and of its lessons has been a philosophy, which sees in comparative 'negativity' a long sought-for rule, by which to measure accurately the relative intensity of life in two contrasted situations.[2] In repose positive, in activity negative, only given a standard of candle power the value of any vital spark could immediately be assessed by the galvanometer.

In 1877, Hermann[3] published experimental data, which very largely moulded the general opinion as expressed in contemporary and in subsequent text-books. These data, obtained by the use of his 'fall rheotome,' proved that the current of injury did not traverse the galvanometer circuit in fully developed strength for a short interval (·0025″) after the occurrence of the injury.

The fact was advanced as conclusive evidence against all 'pre-existence' theories; so that Du Bois Reymond's and Grünhagen's and every similar point of view must be abandoned. The conclusion was practically accepted, and has been followed by consequences of importance.

To regard the injury current as possibly the outcome of pre-existing conditions is to regard it as a phenomenon of primary interest, as, in fact, a possible key to the desired knowledge of the physical structure of the nerve, and, therefore, to the knowledge of the possibilities of the meaning of its physical change during function.

The fall rheotome experiments temporarily removed any general confidence which had been maintained in such a possibility, and, as a consequence, deposed the phenomenon to a rank of secondary importance.

The delay measured by means of the fall rheotome is, however, by no means conclusive evidence of a time spent in the initiation of chemical or of vital change.

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[1] Du Bois Reymond, *Monatsberichte d. Konigl. Akad. d. Wiss.*, Berlin, 1867, p. 597; reprinted in Du Bois Reymond's *Gesammt Abhandl.*, II, p. 319.

[2] E. Hering, *Lotos*, Prague, 1888; translated 'Brain, 1897, p. 232.'

[3] Hermann. *Pflüger's Archiv.*, XV., p. 191. 1877. Experiments upon muscle.

There have first to be considered such factors as polarization, self-induction, and, not least, the fact that chemical substances in solution only give rise secondarily, by processes of diffusion, to electrical phenomena. It is not, therefore, surprising that Hermann, in 1898, is somewhat less confident of the truth of the alteration theory than in 1867. Its establishment as the prevalent hypothesis has rested not so much upon evidence adduced directly to support it as upon evidence which temporarily cut the ground from beneath the feet of its opponents.

It is necessary to realize this fact, and to remember the powers of adverse criticism which indefatigable research and a skilful handling of physical and mathematical detail, and the position of authority which the victory in this controversy and the esteem in which his other contributions to physiological literature are held, have conferred upon Hermann.

## Section III. Grünhagen

Grünhagen[1] in 1866, a year before Hermann's promulgation of the alteration theory, advanced a theory, like Du Bois Reymond's in so far that the conditions of importance were assumed to be 'pre-existent' in the nerve before the injury, but unlike it in that it involved, as prime factors, conditions existent in the ensheathing tissues of the nerve trunk, as well as in the physiologically important elements of structure. Grünhagen's advance to this position was due to a consideration of the histological structure of the nerve, and to experiments undertaken by him in which he brought to notice circumstances of importance hitherto unconsidered in this problem: for he discovered in combinations of various solutions and 'membranes' a possible source of definitely-directed electrical currents.

The first 'membranes' used by him were porous clay pots, and his explanation of the value of the whole combination was given in terms of the capillary pores of these structures, and of the Quincke[2] 'diaphragm currents' arising from the passage of water through them. Further examination revealed other possible explanations, and in 1874[3] one finds him as the discoverer of a 'new kind of electrical current' as distinguished from currents thus originated by the passage of water. This new source of electromotive force was, undoubtedly, what would now be described as a partially permeable 'membrane' separating solutions of electrolytes. Of the efficacy of such combinations there now seems little room for doubt, as also of the similar ones examined previously by Buff in 1854, and ridiculed by Hermann in 1871 (see later). There can also be little doubt but that Grünhagen insisted upon the importance of the membrane in the combinations described by him, and this point must be remembered in considering Hermann's criticism. Hermann, one must

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[1] Grünhagen, *Konigsberger Med. Jahrb.* IV, p. 199. 1886.

[2] Quincke, *Pogg. Ann.* CVII, p. 37, CX, p. 56; also paper by Kunkel, *Pflüger's Archiv.*, XXV, p. 342. 1883.

[3] Grünhagen, *Pflüger's Archiv.*, VIII, p. 573. 1874.

also remember, at first regarded the axis cylinder as an artefact,[1] and has, until quite recently, stoutly resisted the attempt to consider the axis cylinder and myelin sheath as necessarily the possessors of different physical characteristics. Hermann has wrongly[2] depreciated[3] the importance of a dividing membrane in deciding the occurence of polarization phenomena, and in his polarization experiments the presence of such membranes was rigidly excluded.[4]

There are many grounds, therefore, to justify one in considering that Hermann did not appreciate the important part played in Grünhagen's models by the dividing membrane, nor the extreme probability that analogous parts were really to be found in the nerve.

In Hermann's Handbook, 1879 (Bd. I, p. 234), we find the arguments which the propounder of the 'alteration theory' uses to dismiss Grünhagen's theory based upon the assumption of pre-existing heterogeneous structures in the nerve. It is taken that its most decisive refutation is to be found in the manner in which it leaves unexplained, or badly explained, the correlated phenomenon of the action current. It may, indeed, be true that the particular explanation of the action current which Grünhagen advocated may be insufficient or even of little interest. It may be true that the alterations of resistance which he invoked may not occur, nor even if occurring may fail to provide a direct explanation of this other phenomenon. But it is equally true that Hermann's own explanation of the action current almost necessarily entails the occurrence of alterations of resistance, and that the failure to discover such alterations would also greatly militate against this.[5]

But, disregarding the particular explanation of the action current offered by Grünhagen, and also the possible non-coincidence of the two phenomena of action and injury current, it can hardly be said that the physical structures invoked by Grünhagen are such as would by their arrangement prevent the development of the current of action; for these are just the structures upon which now, and with a great shew of reason, the attempt is being made to explain this phenomenon (Boruttau, Strong, etc.).[6]

In the second place, Hermann uses Du Bois Reymond's[7] contra indicating experiment, which was undertaken by Du Bois Reymond as a crucial test of a tentative hypothesis he temporarily advanced, and has been accorded a 'classical position' by Hermann until recently. It is apparent upon consideration that this test, whereas

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[1] Hermann, *Pflügers Archiv.*, LXXI, p. 283. 1898.

[2] Nernst quoted by Boruttau, *Pflüger's Archiv.*, LXXVI, p. 626.

[3] Hermann, *Pflüger's Archiv.*, VI. p. 342.

[4] Hermann, *Nachrichten v. d. Gottinger Gesell z d. Wiss*, pp. 326-347. 1887.

[5] The alteration theory sees in both dying and active tissue the presence of a similar state of activity accompanied by a similar chemical change. If, as is most usually supposed, this chemical change involves the breaking down of complex organic compounds, and the separation from them of simple dissociation products, it almost certainly follows that non-electrolytes are broken down into electrolytes, and so cause alteration in resistance. In fact, upon this assumption a simple explanation of both action current and injury current might readily be produced, the membrane by its selective influence upon the velocity of positive and negative ions might lead in the resulting diffusion processes to electrical phenomena.

[6] Boruttau, Strong, *loc. cit.* Cremer, *Ztschrft fur Biologie*, pp. 37, 550.

[7] Du Bois Reymond, 1848, *Untersuchungen*, I, p. 558; also a repetition of the same experiment for nerve, C. Morgan, *Electrophysiology*, p. 465.

valid and sound as applied to Du Bois Reymond's idea, loses all interest when applied to Grünhagen's.

Du Bois Reymond's experiment was as follows :—The muscle was torn into minute strips so as to obtain longitudinal fragments containing only a few muscle fibres. One of these longitudinal strips was laid upon one electrode; another was placed so as with its transverse section to touch the longitudinal surface of the first, and with its own longitudinal surface upon another electrode. *The normal 'current of rest' of the second strip was observed to be present.*

The idea which Du Bois Reymond tested by this experiment was the possible presence of two heterogeneous structures in the muscle fibre, two physical structures capable of causing an electrical current, when in contact, as, for instance, do copper and zinc. Such a probability was forced upon him by the histological distinction between the sarcolemma and the contents of the muscle fibre. The results of the experiment given above were taken, and, it is obvious, legitimately so, as conclusive evidence against the possibility; for, as Du Bois Reymond said then, the structures were arranged as follows :—

$$\overbrace{\text{Sarcolemma. Contents. Sarcolemma.}}^{\text{First Fibre}}$$

$$\overbrace{\text{Contents. Sarcolemma.}}^{\text{Second Fibre}}$$

The arrangement is thus symmetrical, and is incapable of giving rise to an electrical current if the assumption tested were true, as, for instance, would also be the case with the similar arrangement—

Copper. Zinc. Copper. Zinc. Copper.

Since the experiment did, however, result in the exhibition of the usual current, the assumption and this method of regarding the arrangement of structures in the experiment were necessarily excluded.

But this test is meaningless when applied to Grünhagen's theory, as was done by Hermann, for the structures as seen in its light are as follows :—

$$\overbrace{\text{Nutritive fluid. Membrane. Contents.}}^{\text{First Fibre}}$$

$$\overbrace{\text{Nutritive fluid. Membrane. Contents. Membrane. Nutritive fluid.}}^{\text{Second Fibre}}$$

The arrangement is here seen in its true light as an asymmetrical one, *and as necessarily productive of an electrical current*, and the discovery of such a current in the experiment is, therefore, a circumstance capable of anticipation. The application of such a test to this idea is, therefore, without point, and in its result a confirmation and not a contradiction of the hypothesis.

After reviewing the evidence which influenced Hermann in rejecting Grünhagen's theory, including the two points just dealt with, and also the results of the fall rheotome experiments previously considered, we may pass to consider Hermann's position in 1898.[1]

We find the sufficiency of the 'alteration' theory unabandoned.[2] This is but natural. But we find Hermann very seriously considering the claims of a pre-existence theory based upon the assumption of two heterogeneous physical structures in the nerve fibre.

We find, in fact, Hermann coming forward with proof of the existence of such a difference between the sheath and contents of the nerve fibre, as would, if conclusive, fully justify an *à priori* plea for the formation of such a theory. And the theory which Hermann thus revives is not Grünhagen's, but is Du Bois Reymond's tentative hypothesis.

It is necessary, therefore, to turn again to Du Bois Reymond's crucial test as criticized both in 1879 and in 1898 by Hermann; in fact, as necessarily unfavourably criticized by him 1867, for the complete refutation of this supposition could alone have prepared the way for the promulgation of the alteration theory.

Du Bois Reymond thought that he was arranging symmetrically the muscle fibre contents and sheath, and paid no attention to the 'nutritive solution' bathing these structures, for he regarded it merely as a neutral conducting medium, and did not know that it might play an active part in the production of the phenomenon.

Hermann saw[3] and sees[4] that the arrangement is asymmetrical, and that Du Bois Reymond's test is unconvincing, but he does not see the asymmetry as given above, but in the light of the vital states postulated by the 'alteration theory'—

First Fibre

Sarcolemma. Normal contents. Sarcolemma.

Second Fibre

Dying contents. Normal contents. Sarcolemma.

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[1] Hermann, *Pflüger's Archiv.*, LXX, p. 523. 1898. The experiments related by Hermann in this paper and in another (*Pflüger*, LXVII, p. 240) are of a somewhat remarkable kind. The passage of the strong currents through microscopical fragments of nerve are observed to produce protrusions of the myelin from the nerve fibre. Upon this bodily movement of tube contents upon the tube, arguments are based which lead Hermann to consider the essential physical difference between these structures.

[2] Hermann, *loc. cit.*; also *Pflüger's Archiv.*, LXXI, p. 296 *et seq.*, 1898.

[3] Hermann, *Handbuch*, *loc. cit.*

[4] Hermann, *Pflüger's Archiv.*, LXX, *loc. cit.*

That is to say, that in attempting to decide between the two theories, the alteration theory and this pre-existence theory, he does not place them in clearly alternative positions, but considers the second as a corollary to the first. No proofs have ever been produced of the existence of a dying condition at the cut end of a nerve or even of a localised chemical change. Both may, indeed, exist, but the primary reason for considering the possibility of such a state is that HERMANN propounded the alteration theory. *Hermann is, therefore, considering the pre-existence theory from the point of view of the teachings of the alteration theory, and not as a quite separate and distinct possibility, and must have done so from the first.*

The general impression left upon one's mind is that GRÜNHAGEN's theory has never met with the consideration nor with the acute criticism which it deserved as a logical deduction from a valuable appreciation of the relative values of the structures of the nerves.

### NOTE

GRÜNHAGEN's theory in its most acceptable form was completely anticipated by BUFF in 1854, although applied to electrical currents obtainable from plant tissues, and not from muscle or nerve. (*Ann. d. Chemi. u. Pharm.*, Bd. 89, 76. 1854.) The currents obtained were explained as the result of—

(1) A negativity of the sap ;
(2) A positivity of the surface water ;
(3) A sharp delimitation of the two solutions by the epidermis.

BUFF also supported his conclusions by physical experiments of interest.

JURGENSEN, in 1861, also working with plants, came to very similar conclusions supported by similar experiments. (*Studien. d. Physiol. Institut. zu Breslau*, I, 87-109. Leipzig, 1861.

J. REINKE, in 1882, also discussing plant currents, refused to admit an explanation couched in terms of vital states, and anticipates a possible explanation in the complex arrangement of moist conductors contained in plants. (*Pflüger's Archiv.*, XXVIII, 143, 1882.)

J. S. MACDONALD, in 1900, produced certain evidence obtained from mammalian nerve, and considered this to be in support of a similar theory.

BUFF's and JURGENSEN's conclusions were adversely criticized by HERMANN in 1871. He also criticized the value of their physical experiments, performing similar experiments with uncertain results. The value of BUFF's, JURGENSEN's, and GRÜNHAGEN's physical experiments are, however, now easily assessed by an appeal to the new subject of electrochemistry. (HERMANN, *Pflüger's Archiv.*, IV, p. 148, 1871.

## SECTION IV. BORUTTAU

DU BOIS REYMOND used the current of rest as a phenomenon from which to extract a practical conception of the physical structures of the nerve, and proceeded with this structure in his mind to explain the other electrical phenomena which could be demonstrated in it. BORUTTAU has used the polarization phenomena in a similar manner. The polarization phenomena entail a 'core model' structure for the nerve, and have been held to do so by several investigators. Granted the 'core model' structure of nerve, all the other electrical phenomena of nerve are stated as explained by it.

It has been stated previously (see note, p. 221) that a 'core model' structure (such as was assumed by Grünhagen) might be used to explain the electrical phenomena of the 'action current,' even if they were the secondary consequences of chemical change taking place in the axis cylinder. This possibility has been considered by Boruttau, forming, as it does, one of the two only probable lines upon which this phenomenon can be investigated and perhaps explained. But he has taken a greater interest in the other possible explanation, and has sought confirmative suggestions from experiments upon 'core models,' and has also sought confirmatory facts from experiments upon nerve.

According to this second explanation, the nerve has not only a core model structure, but also that structure is just of the kind required to act as the purely physical conductor of electrical change, and to conveniently transmit energy from point to point without involving the development of new sources of energy (chemical changes) in its line of progress. Such a conception of the arrangement of structures in the nerve has also been frequently debated since the date of Galvani's discovery. The possibilities of the insulating or semi-insulating sheath of the nerve, that is to say of the core model structure of the nerve, have been discovered from every point of view, but without any very direct attempt having been made to obtain experimental data which might place definite limits to these possibilities.

Boruttau and Strong,[1] and perhaps Hoorweg (although his methods of illustrating his conception are open to objection), have realised the necessity entailed by the core model structure, namely, that its fracture must provide one with a current of injury. Strong has presented a detailed description of his hypothesis, and Boruttau has illustrated a similar one by a working model,[2] but neither seem to have grasped the important corollary which their statements, if true, must entail, namely, that the injury current and its modification, under known conditions, may, or rather must, give valuable information as to the details of the core model structure.

The appreciation of this position necessitates a return to Du Bois Reymond's point of view and the establishment of the injury current as a phenomenon of primary importance.

### Note on the Purely Physical Theory of Nerve Function

The greatest objection to a physical theory of nerve function is the existence of recorded instances in which the transmission of the nervous impulse is proved to have taken place unaccompanied by a demonstrable physical phenomenon. Many of these instances are open to considerable suspicion, as are all physical experiments made by investigators satisfied with approximate and inexact methods and apparatus. Criticism of such recorded instances has already been undertaken by Boruttau, but there are certain broad principles affecting experiments of this kind which have not been as much insisted upon as is necessary.

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[1] Strong, *Journal of Physiology*, XXV, p. 427.

[2] Boruttau, *Pflüger's Archiv*. LXIII, p. 154. 1896. Gelatine cylinders of K.Cl. solution surrounded by a mantle of ·6 per cent. NaCl. solution. The model so formed shews a negativity of cross section to longitudinal surface.

In the first place, experimental modifications designed only to affect the physiologically interesting units of structure of the nerve (the axis cylinders) are also capable of producing great modifications in recorded electrical changes by altering the conditions of the complex wrappings which surround the axis cylinders. There is often reason to suppose that modifications in recorded electrical changes obtained after immersion of nerves in solutions of electrolytes, and even of non-electrolytes, are merely variations in the relative value of the outwardly demonstrable change. The real phenomenon being, perhaps, unaltered in value or else altered in a manner quite different from that in which its 'externally visible' moiety is affected.

The need of such cricticism is obvious when variations are produced by such extreme means as the immersion of nerves in saturated salt solutions, but it is also applicable and almost invariably neglected in other less striking instances.

The relative value of the outwardly demonstrable change to the real phenomenon in the axis cylinder depends upon at least three factors—the physical characters (electrical conductivity, etc.) of the lymph, the nerve fibre sheath, and the axis cyclinder. It is more than conceivable that a reagent which affects only the nerve sheath should, even if not in any way modifying the condition of the axis cyclinder, produce an important variation in the outwardly accessible phenomenon ; and there is no difficulty in extending such a proposition to include also the effect of reagents which alter the surrounding 'lymph' without affecting any part of the nerve fibre itself.

This proposition also holds good for experiments in which modifications are produced in the so-called 'excitability' by immersion of the nerve in solutions, etc., which may produce their apparent effects by altering the conditions under which the stimulating current arrives in or leaves the axis cylinder without affecting the axis cylinder itself in any manner.

Immersions in solutions, exposure to gases, variations of temperature, all alike may produce the major effect observed by altering the quantity of change which can make its way to the surface, or in the case of stimulation, by varying the amount of stimulation which reaches the axis cylinder from the surface of the nerve.

Nor is this the only consideration which places negative results under suspicions unless stringently examined, for some of the experiments which are presumed to present results of value in this connexion have involved other complications still more undesirable.

The ordinary diphasic record obtained by the usual means does not, it is acknowledged, present in either of its phases a correct, or even approximately correct, idea of the magnitude and duration of the electrical change traversing successive sections of the nerve. The record is the algebraical sum of two such real phases. In the generally chosen conditions of experiment, when the interval of nerve between the electrodes is a short one, and traversed by the nervous impulse in a time which is a fraction of the whole time occupied by the complete passage of the changes accompanying it past either point ; under these circumstances large portions of the two opposite phases occur at the same time, and to a great extent are, therefore, eliminated from the record.

When statements are made as to the non-occurrence of portions of the anticipated electrical change, it is as well to immediately consider the possibilities of such elimination. Important as this is when only a single nervous impulse is presumed to have passed the two electrode points, it becomes of vital interest when a second has been despatched in rapid succession to the first, for then the record becomes the algebraical sum of four phases, and is unrecognizable for any useful purpose. It is an easy matter to demonstrate that such an algebraical sum may apparently present four phases, or three, or even two ; and in fact may so closely imitate a diphasic record, the record resulting from the passage of a single nervous impulse, as to be mistaken for this. Such a record may then be, and probably has actually been, held out as a proof that the second nervous impulse did not in its passage give rise to a second travelling electrical change.

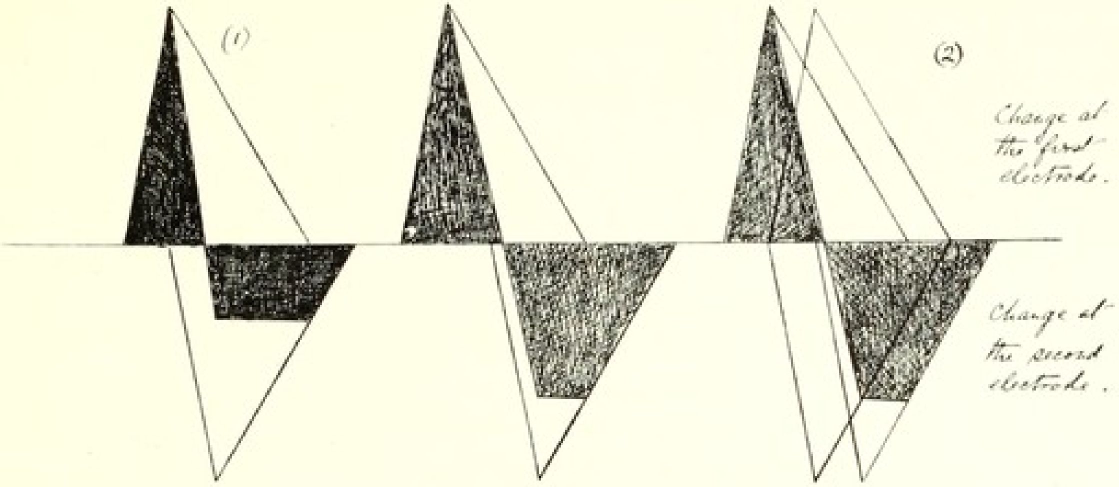


FIG. 1

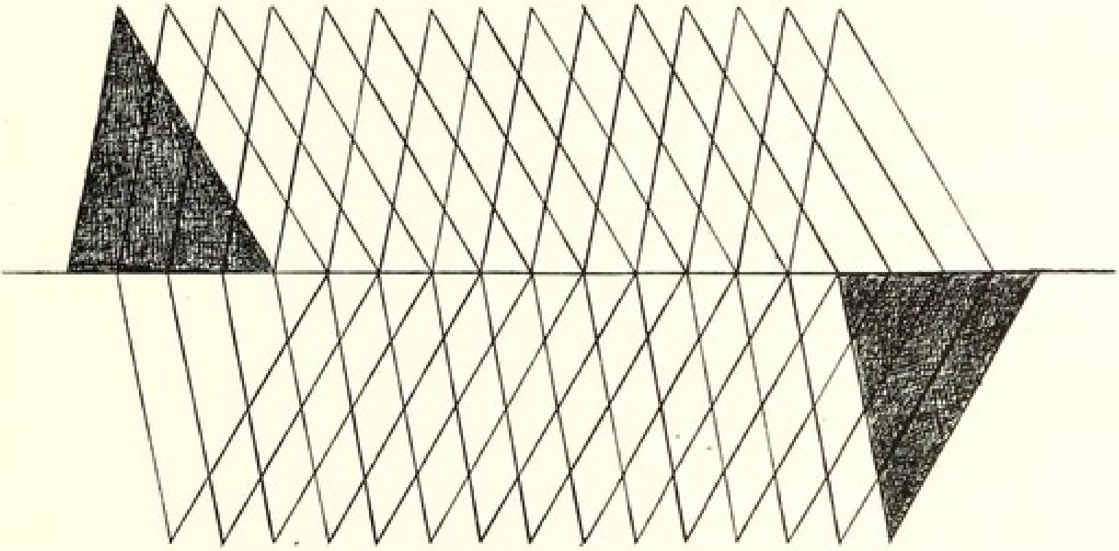


FIG. 2

Fig. 1. The three drawings represent—

(1) A diphasic record, the result of one nervous impulse passing two points separated by a time interval of ·001″.

A diphasic record. One nervous impulse. Two points ·002″ apart.

(2) A diphasic record. *Two nervous impulses.* Two points ·001″ apart.

Fig. 2. A diphasic record. *Fifteen nervous impulses.* Two points ·001″ apart.

In the accompanying figure the two darkly-shaded records (1 and 2) are two diphasic records of not very different character. The first is the outcome of *one change*, affecting two points in succession, at an interval of onset of ·001 second, and lasting at each point for ·004."

The second is the result of *two such changes* passing the same two points with an interval between them of ·001."

It is obvious that in the second two out of the four phases actually occurring are entirely unrepresented in the record, since occurring at the same time and being equal and of opposite sign they are completely eliminated from it. *The actual record, although the result of two nervous impulses, let us say, passing at an interval of* ·001, *is exactly the same as the record would be of one nervous impulse passing along the nerve if its passage was observed by placing electrodes upon two points separated by double the distance which divides the two points arbitrarily chosen.*

To emphasize the statement, it is interesting by an examination of fig. 2 to convince oneself that the passage of ten nervous impulses at the rate of one thousand per second, or of one thousand nervous impulses at the same rate, and even if each in succession produced at every point its appropriate electrical change might in a record give rise to a *diphasic* variation. In this extreme case the diphasic record could hardly be interpreted as due to the occurrence of only one electrical change at each point.

Such considerations hold good for every experimental record taken as the observed effect of two or more successive stimuli, and vitiate, in a very great number of cases, conclusions drawn in their neglect. When many successive stimuli are used, as in faradisation, and when imperfect recording instruments add further fallacies to the record, as in galvanometric observations, it is impossible to base any conclusion of even suggestive interest upon such records. It may even be reasonably said that such criticism applied to diphasic and multiplied diphasic records obtained by the observation of two points in the continuity of the nerve, may be transferred to records of 'negative variations,' taken from the longitudinal surface and cross section. Confidence is only implicitly placed in such records when it is imagined that electrical change only occurs at the point on the longitudinal surface, and that the real change is, therefore, monophasic. This is, however, far from being the truth, for even exactly-taken records of such single negative variations are triphasic: and no one can satisfactorily declare what the nature of the real phases occurring at either point was, which has resulted in this triphasic record.

# THE CURRENT OF INJURY

The statements subsequently made are all based upon observations taken from experiments upon mammalian nerve, which offers several advantages for the purposes of this enquiry.

In the first place, mammalian nerve can be obtained in comparatively long stretches, and in the case of the phrenic or the vagus nerves in long stretches free from branches and, therefore, from undesirable accessory cross sections. The phrenic nerve, in addition, offers the advantage of containing only medullated fibres of uniform size and relative value of axis cylinder and myelin ; it is, however, not easy to remove as neatly from its pleural covering as are nerves placed in a bed of loose areolar tissue, and on this account, although at first made use of, it has been for the present abandoned.

Certain mammalian nerves, such as the vagus of the dog, although for many reasons preferable, suffer from the disadvantage of exhibiting a relatively small difference of potential between the longitudinal surface and the cross section. It is in such cases naturally more difficult to form a correct opinion of the real distribution of potential upon the surface of the nerve.

This apparent disadvantage is, however, discounted by the comparatively small resistance of mammalian nerve in general, as contrasted with the relatively minute sciatic nerve of the frog. The resistance in the nerve being small, a slight potential difference gives rise to an appreciable current through the galvanometer, and compensation and determination of potential difference is in this manner rendered far more exact. The disadvantage has also in the present case been of no interest since an extremely sensitive galvanometer (Thompson pattern, Muirhead and Company) of 50,000 ohms. resistance has been used throughout the whole series of experiments.

The differences of potential measured in the case of the vagus nerve recently removed from the dog were rarely as great as ·010 volt, averaging about ·007 volt. In the case of the sciatic nerve of the dog and cat the potential differences obtained are much greater, and are greater than the potential difference ordinarily obtained from the sciatic nerve of the frog. The frequent examples given subsequently in this paper will be found fully to bear out this statement. Consequently, it is easy in the case of the mammalian sciatic nerve, dealing with a low resistance and a large difference of potential, to measure accurately the comparatively large currents which are found and to compensate the potential differences with ease. The results of a typical examination of a sciatic nerve are given in Experiment I.

In this case, as in all cases examined, certain irregularities will be noticed, showing a departure from the ideal case depicted by Du Bois Reymond's laws. It is convenient to assume that such irregularities are produced by accessory cross sections; it is is not however believed that all, nor even the most important, irregularities are the outcome of such an accidental cause. It will be seen that experiments made upon carefully prepared and treated vagus nerves are not free from irregularities of an exactly similar kind, and in this connexion attention is drawn to the facts of Experiment (Tap Water, fig. W, see p. 279), in which the irregularities are demonstrated in a very striking manner by the use of a special expedient.

In this section the important details of experiments are given which may serve to demonstrate the conditions actually to be met with. No attempt is made to arrange them with reference to any hypothetical simplicity, it being considered that the examination of actual curves, experimentally obtained, is of greater value. It is necessary to exhibit the phenomenon in some detail, because such a demonstration of actual measurements has never been previously undertaken, and because great pains have been taken to correct the observations made from the consequences of an unavoidable source of error most frequently neglected.

This source of error is due to the alteration in the phenomenon taking place with lapse of time, but fortunately taking place, as will subsequently be seen, in a regular and definite manner. The change with lapse of time is not greater in mammalian nerve than in frogs; it is, however, in either case considerable, and as the data of the experiment given below show, the error, unless corrected, is always vitiating the conclusions drawn from observations. Comparisons between differences of potentials found between sets of points, such as are made when an attempt is made to study the distribution of potential, are valueless, unless the routine method of conduction of the experiment permits the comparison to be made between corrected values *inferred to exist at the same moment of time.*

## EXPERIMENT A

### Vagus Nerve of Cat

Piece of Nerve 6 centimetres long

The nerve was laid upon a dry ebonite scale forming a platform in the moist chamber. One non-polarizable electrode was placed in contact with a cross section and retained there throughout the experiment; the other non-polarizable electrode was first placed in contact with a point distant 1 centimetre from this, then upon a second point distant 2 centimetres, a third at 4 centimetres, a fourth at 5 centimetres distance, an observation being taken in each case of the potential difference between each point and the cross section. The experiment was continued by a return of the second electrode to point (4), then to point (3), then to point (2), then to point (1). Thus two observations were taken at each point, once going up and once going down the nerve, *and a definite interval of time was allowed for each observation.*

In the figures given below, and in the case of all other experiments recorded in this section, the arrows indicate the order in which the observations were taken :—

| Distance of point from the cross section | Potential Difference between this point and the cross section | | | |
|---|---|---|---|---|
| | (*a*) | | (*b*) | |
| (1) 1 centimetre ... | ·01904 | | ·01416 | Daniell |
| (2) 2 „ ... | ·01696 | ↓ ↑ | ·01624 | „ |
| (3) 3 „ ... | ·01696 | | ·01688 | „ |
| (4) 4 „ ... | ·01672 | | ·01688 | „ |
| (5) 5 „ ... | ·01520 | | ·01520 | „ |

If the two sets of observations (*a*) and (*b*) of this experiment are taken singly, it is obvious that a different idea is capable of being formed from each of them of the distribution of potential upon the longitudinal surface. The maximum of the curve representing this distribution is in case (*a*) obviously to be placed between points (2) and (3), point (3) being the mid-point of the piece of nerve examined. The maximum in case (*b*) is to be placed between points (3) and (4) and, therefore, on the other side of the mid-point. The reason for this difference between the two sets of observations is readily seen from the fall in the potential difference which has taken place at point (1) in the time necessary to take the whole set of observations, a fall of ·005 volt, that is of almost 25 per cent. of the initial value. The effect of this fall is not noticeable in the two observations at point (4) which rapidly followed upon one another ; in fact, there is apparently a slight increase, due probably to the selection of a slightly different point upon the return visit. The fall has nevertheless been taking place all the time, and, provided that it is regular and that the observations have been taken at regular intervals, its effects can be eliminated by taking the average of such a set of observations ; for corrected values are then obtained, which are almost accurately those actually existent at the moment of 'mean time' of the whole set of observations.

Taking this set of average values from this experiment, we have :—

| | | |
|---|---|---|
| Point (1) | ·01665 | Daniell |
| „ (2) | ·01660 | „ |
| „ (3) | ·01697 | „ |
| „ (4) | ·01680 | „ |
| „ (5) | ·01520 | „ |

This set of figures provides a totally different idea of the distribution of potential. There is not a great difference between the whole set of values, the curve of distribution is, therefore, a comparatively flat-topped one ; and its small maximum is at the mid-point of the nerve.

Necessary as is such a precaution when only five points are examined, it becomes doubly necessary when, for the sake of accuracy, more points are dealt with, and when a longer piece of nerve is taken. It has been found, with practice, possible to take twenty observations, two at each of ten points (travelling up and down in this way) in ten minutes. The success of the method and the value of the precaution are, in my opinion, both shown in the details of the following experiment :—

## EXPERIMENT I

### Sciatic Nerve of Dog

Piece of Nerve 8 centimetres long, clean cut at both ends

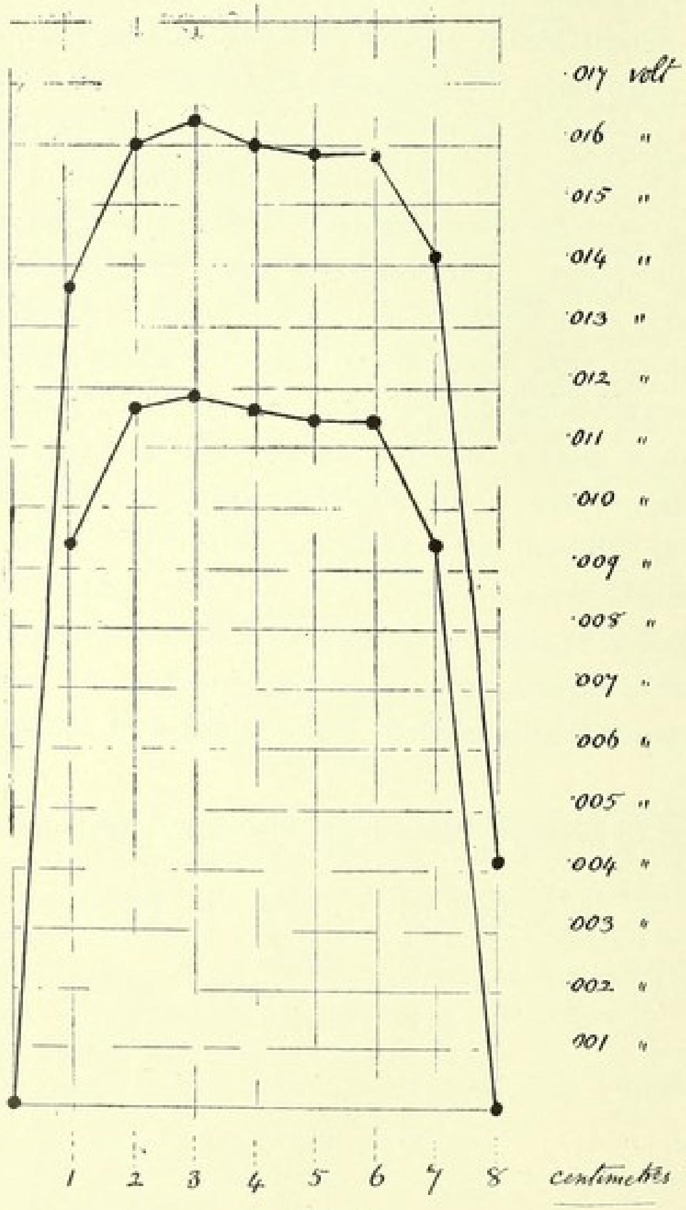


Fig. 3

*Three double sets of observations were taken :—*

(1) The potential differences between points upon the longitudinal surface and the upper cross section.

(2) The potential differences between the same points and the lower cross section.

(3) A repetition of (1).

Each double set of observations occupied ten minutes. The total time spent over the three sets was thirty minutes ; no interval was allowed between one set and another, and the taking of every observation was accurately timed.

For the sake of simplicity, the description of the geometrical position of each point is always the same throughout the whole set of observations. Whether the potential difference is being taken between a point and the upper or the lower cross section, the distance of the point from the upper cross section provides it with its name. Thus point (1) is always a point distant 1 centimetre from the upper cross section, etc.

*The order in which the figures are given and the arrows drawn alongside of them fully indicate the order in which the observations were made.*

*The difference between the two cross sections was only once measured*, and the upper cross section was found to be negative to the lower by ·00422 volt, the relative time at which this measurement was taken will be seen from the list of observations in which it is recorded. *It was measured at the mean time* of the whole set of observations. Point (8) is marked with an asterisk to emphasize the measurement taken between the two cross sections, and the same plan has been followed in all the other experiments of this section.

*There was no potential difference between the electrodes*, and there never is in the experiments given any reason to apply a correction for such a difference. Differences between electrodes are usually the result of a slight difference in the concentration of the zinc sulphate solution in the two tubes, the result of pouring zinc sulphate solution into imperfectly dried tubes. This error has been completely avoided by the use of very wide **U** tubes, having a bore of 1·5 centimetres, so that they contain a large volume of the solution, and by cleaning them always the night previous to the experiment, and using them dry in the morning without resorting to any further cleaning process.

The nerve was, as in the last experiment and all succeeding ones, laid on an ebonite scale in a large moist chamber (25 centimetres long and 25 centimetres broad by 10 centimetres deep), the electrodes were freely moveable upon ebonite runners placed in this moist chamber, parallel to and one on either side of the scale on which the nerve was placed. The greatest care was taken to secure perfect insulation of every piece of apparatus made use of.

| | A | | | B | | | C | | |
|---|---|---|---|---|---|---|---|---|---|
| | Potential Differences taken from the Upper Cross Section | | | Potential Differences taken from the Lower Cross Section | | | Potential Differences taken from the Upper Cross Section | | |
| (1) | ·01491 | | ·01439 | ·00950 | | ·00898 | ·01307 | | ·01214 |
| (2) | ·01755 | | ·01737 | ·01209 | | ·01130 | ·01492 | | ·01426 |
| (3) | ·01795 | ↑ | ·01803 | ·01228 | ↑ | ·01156 | ·01555 | ↑ | ·01452 |
| (4) | ·01795 | | ·01756 | ·01188 | | ·01135 | ·01465 | | ·01412 |
| (5) | ·01769 | ↓ | ·01742 | ·01162 | ↓ | ·01120 | ·01412 | ↓ | ·01399 |
| (6) | ·01769 | | ·01756 | ·01148 | | ·01135 | ·01399 | | ·01399 |
| (7) | ·01565 | | ·01531 | ·00924 | | ·00924 | ·01294 | | ·01294 |
| (8)* | ·00422 | | ·00422 | | | | | | |

### Below are given the Average Values taken from A, B, and C respectively

| | A<br>Potential Differences to upper | B<br>Potential Differences to lower | C<br>Potential Differences to upper |
|---|---|---|---|
| (1) | ·01465 | ·00924 | ·01260 |
| (2) | ·01746 | ·01169 | ·01459 |
| (3) | ·01799 | ·01192 | ·01503 |
| (4) | ·01775 | ·01161 | ·01438 |
| (5) | ·01755 | ·01141 | ·01405 |
| (6) | ·01762 | ·01141 | ·01399 |
| (7) | ·01548 | ·00924 | ·01294 |
| (8)* | ·00422 | | |

* Point (8) represents the second lower cross section.

### Below is given an Average of A and C for comparison with B

| A and C<br>Potential Differences to upper | | | |
|---|---|---|---|
| (1) | ·01362 | (5) | ·01580 |
| (2) | ·01602 | (6) | ·01580 |
| (3) | ·01651 | (7) | ·01420 |
| (4) | ·01606 | (8) | — |

We have in the figures of this experiment the means of contrasting the distribution of potential on the nerve at the same moment of time as found by comparison with the upper and the lower cross section, and that also at a moment of time when the potential difference between these two cross sections was observed (·0042 volt).

| | Potential Differences to upper | Potential Differences to lower | Arithmetical Differences |
|---|---|---|---|
| (1) | ·01362 | ·00924 | ·00438 |
| (2) | ·01602 | ·01169 | ·00433 |
| (3) | ·01651 | ·01192 | ·00459 |
| (4) | ·01606 | ·01161 | ·00445 |
| (5) | ·01580 | ·01141 | ·00449 |
| (6) | ·01580 | ·01141 | ·00449 |
| (7) | ·11420 | ·00924 | ·00496 |

The two curves drawn from these numbers are given in fig. 3, and it is obvious, both in the figure and in the numbers given above, that the curves are parallel and reproduce at a different level every minute phase. Further, the difference of level between the two curves ·004 volt (approx.) is almost exactly the difference found at that moment of time between the two cross sections. If the mill of observations out of which this similarity has been evolved is considered, it will serve to establish confidence in the meaning of every curve taken in this routine fashion. The difficulties to contend with are found not only in the fall of level with lapse of time, but also, as more curves drawn from the numbers given above would show, an alteration in the form of the top of the curve. The alteration in form is, however, as regular as the fall of level, and, like it, may have a meaning which will repay investigation ; it is most clearly appreciable in the cases of nerves removed from animals dead some hours (when the surface of the nerve is in a peculiar condition, which is subsequently discussed) ; in the case of freshly removed nerves from recently killed animals it is, as in this case, only slight.

## Summary

In general the points which one would like to emphasize in the data of this experiment are :—

(*a*) That, as Du Bois Reymond noted, the 'equatorial' point, or highest point of the curve, does not correspond with the geometrical centre of the nerve.

(*b*) That there is a difference between the two cross sections ; but that in this case, although by no means in all cases, the highest maximum of the curve is nearer to the more negative cross section.

(*c*) That the fact of changing the point of reference from one cross section to another does not, in the slightest degree, alter the relative value of points upon the longitudinal surface to one another.

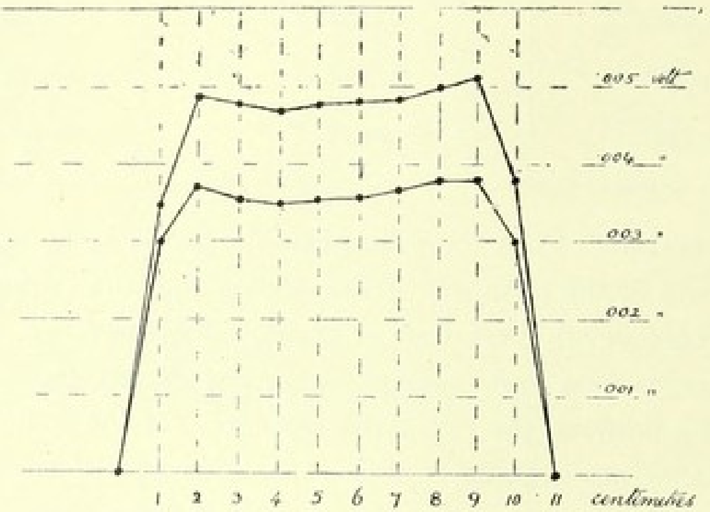
(*d*) That the lapse of time does reveal a definite but small alteration in the relative value of points upon the longitudinal surface. In this case the alteration is such as to make the potential curve a more obviously asymmetrical one.

The experiments upon vagus nerves which follow are given for the present without comment as examples, carefully worked out, of the distribution of potential upon excised nerve.

## EXPERIMENT II

### Vagus Nerve of Dog

Piece of Nerve 11 centimetres long. Ligatured and cut at both ends



II

| Points upon the longitudinal surface distant from the other end | Potential Differences measured from the upper injury | | Average Value (correction for alteration with time) |
|---|---|---|---|
| 1 centimetre ... | ·00352 D. | ·00328 D. | 34·0 × $10^{-4}$ D. |
| 2 ,, ... | ·00508 | ·00446 | 47·7 |
| 3 ,, ... | ·00500 | ·00432 | 46·6 |
| 4 ,, ... | ·00492 | ·00432 | 46·2 |
| 5 ,, ... | ·00508 | ·00444 | 47·6 |
| 6 ,, ... | ·00500 | ·00452 | 47·6 |
| 7 ,, ... | ·00508 | ·00452 | 48·0 |
| 8 ,, ... | ·00508 | ·00480 | 49·4 |
| 9 ,, ... | ·00520 | ·00504 | 51·2 |
| 10 ,, ... | ·00372 | ·00372 | 37·2 |

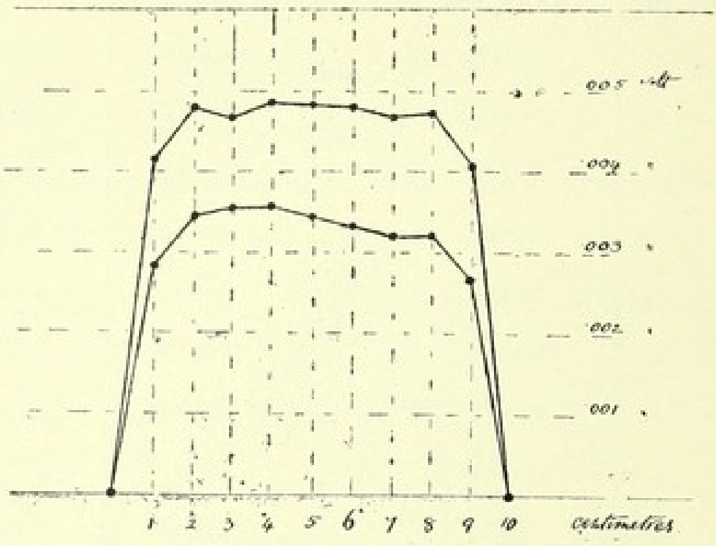
After an interval of thirty-five minutes, a second double set of observations was taken. The interval between the mean times was forty-five minutes.

| Points upon the longitudinal surface distant from the other end | Potential Differences measured from the upper injury | | Average Value (correction for alteration with time) |
|---|---|---|---|
| 1 centimetre ... | ·00272 D. | ·00296 D. | $28{\cdot}4 \times 10^{-4}$ D. |
| 2 " ... | ·00348 | ·00360 | 35·2 |
| 3 " ... | ·00348 | ·00340 | 34·4 |
| 4 " ... | ·00340 | ·00340 | 34·0 |
| 5 " ... | ·00348 | ·00344 | 34·6 |
| 6 " ... | ·00348 | ·00352 | 35·0 |
| 7 " ... | ·00348 | ·00368 | 35·8 |
| 8 " ... | ·00372 | ·00376 | 37·4 |
| 9 " ... | ·00372 | ·00372 | 37·2 |
| 10 " ... | ·00280 | ·00286 | 28·3 |

## EXPERIMENT III

### VAGUS NERVE OF DOG

Piece of Nerve, 10 centimetres long, both ends cut



III

| Point on the longitudinal surface distant from the upper end of the nerve | Potential Differences measured from the Upper Cross Section | | Average Value (Correction for alteration with lapse of time) |
|---|---|---|---|
| 1 centimetre ... | ·00448 D. | ·00400 D. | $42{\cdot}4 \times 10^{-4}$ D. |
| 2 " ... | ·00520 | ·00472 | 49·6 |
| 3 " ... | ·00500 | ·00472 | 48·6 |
| 4 " ... | ·00544 | ↑ ·00472 | 50·8 |
| 5 " ... | ·00544 | ·00456 | 50·0 |
| 6 " ... | ·00544 ↓ | ·00451 | 49·7 |
| 7 " ... | ·00520 | ·00440 | 48·0 |
| 8 " ... | ·00520 | ·00464 | 49·2 |
| 9 " ... | ·00416 | ·00424 | 42·0 |

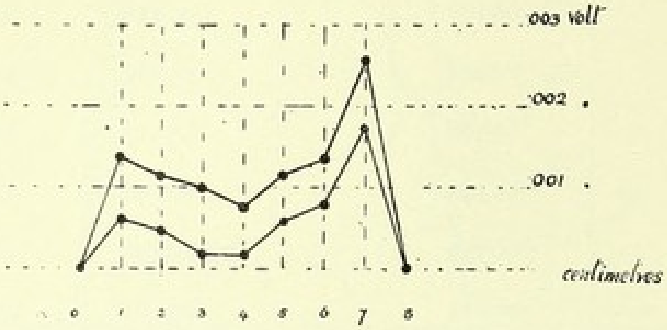
A second set of observations, taken after an interval of thirty-five minutes, *i.e.*, with an interval between the mean times of the two sets of forty-five minutes.

| Point on the longitudinal surface distant from the upper end of the nerve | Potential Differences measured from the Upper Cross Section | | Average Value (Correction for alteration with lapse of time) |
|---|---|---|---|
| 1 centimetre ... | ·00328 D. | ·00248 | $28{\cdot}8 \times 10^{-4}$ D. |
| 2 " ... | ·00392 | ·00320 | 35·6 |
| 3 " ... | ·00406 | ·00320 | 36·3 |
| 4 " ... | ·00408 | ·00320 | 36·4 |
| 5 " ... | ·00392 | ·00317 | 35·4 |
| 6 " ... | ·00368 | .00317 | 34·2 |
| 7 " ... | ·00349 | ·00296 | 32·2 |
| 8 " ... | ·00349 | ·00296 | 32·2 |
| 9 " ... | ·00272 | ·00272 | 27·2 |

## EXPERIMENT IV

### Vagus Nerve of Dog

Piece of Nerve, 8 centimetres long, removed seven-and-a-half hours after death. Distance measured from upper end. Point (1) = 1 centimetre from upper end. Point (2) = etc.



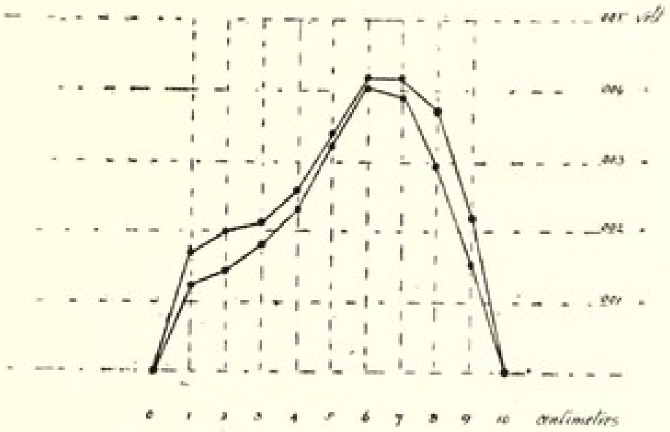
### Differences of Potential

| | To Upper Cross Section | | Average | To Lower Cross Section | | Average |
|---|---|---|---|---|---|---|
| (1) | ·00128 | ·00140 | ·00134 | ·00056 | ·00064 | ·00060 |
| (2) | ·00104 | ·00128 | ·00116 | ·00024 | ·00064 | ·00044 |
| (3) | ·00096 | ·00104 | ·00100 | ·00008 | ·00024 | ·00016 |
| (4) | ·00072 | ·00080 | ·00076 | ·00008 | ·00024 | ·00016 |
| (5) | ·00112 | ·00120 | .00116 | ·00056 | ·00064 | ·00058 |
| (6) | ·00128 | ·00144 | ·00136 | ·00064 | ·00104 | ·00082 |
| (7) | ·00264 | ·00264 | ·00264 | ·00224 | ·00224 | ·00224 |

## EXPERIMENT V

### Vagus Nerve of Dog

Piece of Nerve, 11 centimetres long. Cross section, upper end. Ligature below. Distances all measured from the upper cross section. Nerve removed two-and-a-half hours after the death of the animal.



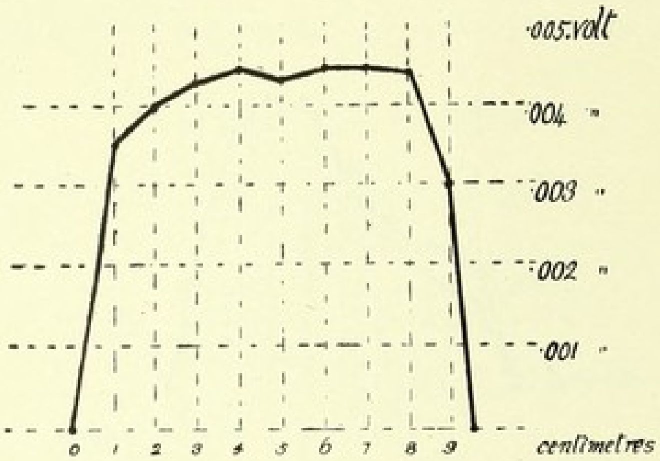
Differences of Potential

| | To Upper Cross Section | | Average | To Lower Cross Section | | Average |
|---|---|---|---|---|---|---|
| (1.5) | ·00140 | ·00216 | ·00178 | ·00124 | ·00124 | ·00124 |
| (2.5) | ·00136 | ·00260 | ·00198 | ·00140 | ·00156 | ·00148 |
| (3.5) | ·00160 | ·00260 | ·00210 | ·00164 | ·00220 | ·00192 |
| (4.5) | ·00216 | ·00312 | ·00264 | ·00180 | ·00300 | ·00240 |
| (5.5) | ·00292 | ·00404 | ·00348 | ·00308 | ·00352 | ·00330 |
| (6.5) | ·00380 | ·00464 | ·00422 | ·00424 | ·00400 | ·00412 |
| (7.5) | ·00380 | .00464 | ·00422 | ·00412 | ·00372 | ·00392 |
| (8.5) | ·00312 | ·00360 | ·00386 | ·00288 | ·00308 | ·00298 |
| (9.5) | ·00224 | ·00224 | ·00224 | ·00152 | ·00164 | ·00158 |

# EXPERIMENT VI

## Vagus Nerve of Dog

Piece of right vagus, 9·5 centimetres long, removed immediately after death. Clean cut cross section at either end. No ligatures. Distances measured from the upper cross section.



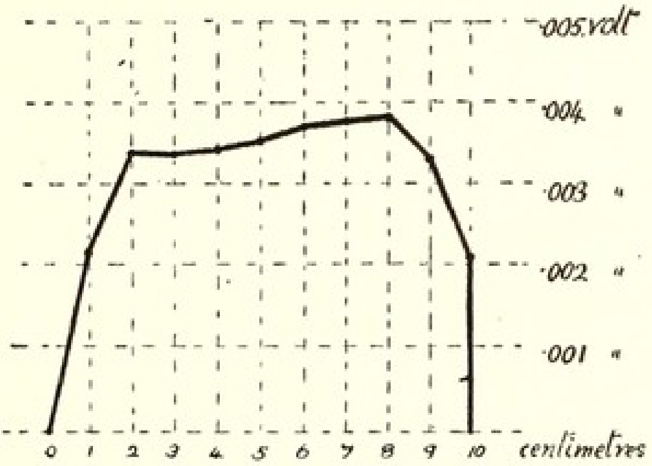
| Potential Differences from the Upper Cross Section | | | Average |
|---|---|---|---|
| Point (1) | .00360 | ·00312 | ·00336 |
| " (2) | ·00432 | ·00372 | ·00402 |
| " (3) | ·00452 | ·00400 | ·00426 |
| " (4) | ·00460 | ·00428 | ·00444 |
| " (5) | ·00460 | ·00400 | ·00430 |
| " (6) | ·00460 | ·00432 | ·00446 |
| " (7) | ·00460 | ·00432 | ·00446 |
| " (8) | ·00460 | ·00424 | ·00442 |
| " (9) | ·00288 | ·00307 | ·00297 |
| " (9·5)* | 0 | 0 | 0 |

Points marked thus * are in each case the second cross section.

## EXPERIMENT VII

### Vagus Nerve of Dog

Piece of Nerve, 10 centimetres long, removed immediately after death. Both ends ligatured and cut close to the ligature. Distances measured from the upper cross section.



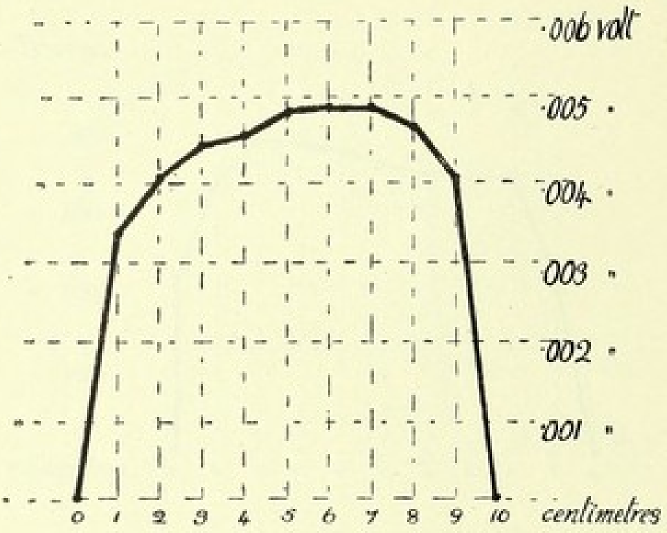
| | Potential Differences from the Upper Cross Section | | Average |
|---|---|---|---|
| Point (1) | ·00224 | ·00216 | ·00220 |
| „ (2) | ·00344 | ·00344 | ·00344 |
| „ (3) | ·00344 | ·00340 | ·00342 |
| „ (4) | ·00360 | ·00340 | ·00350 |
| „ (5) | ·00360 | ·00344 | ·00352 |
| „ (6) | ·00364 | ·00368 | ·00366 |
| „ (7) | ·00372 | ·00368 | ·00370 |
| „ (8) | ·00384 | ·00368 | ·00376 |
| „ (9) | ·00328 | ·00328 | ·00328 |
| „ (10)* | ·00212 | ·00212 | ·00212 |

Points marked thus * are in each case the second cross section.

## EXPERIMENT VIII

### VAGUS NERVE OF DOG

Piece of Nerve, 10 centimetres long, removed immediately after death. Both ends cut. No ligatures. Distances measured from the upper cross section.



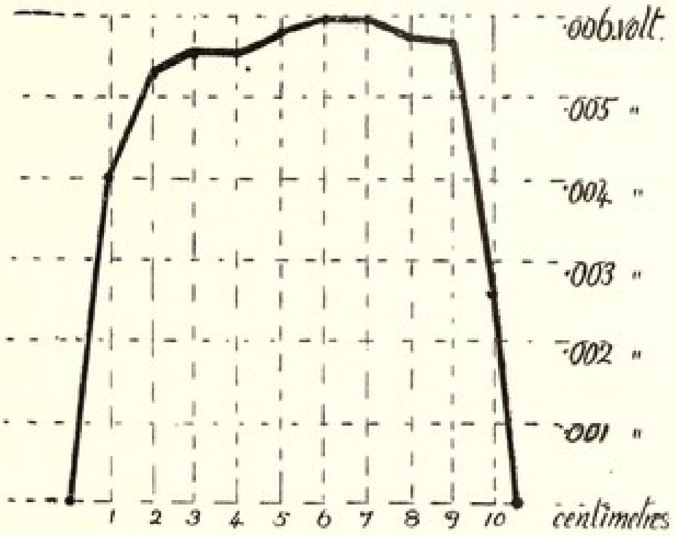
| | Potential Differences from Upper Cross Section | | Average |
|---|---|---|---|
| Point (1) | ·00360 | ·00296 | ·00328 |
| „ (2) | ·00424 | ·00368 | ·00396 |
| „ (3) | ·00456 | ·00424 | ·00440 |
| „ (4) | ·00488 | ·00412 | ·00449 |
| „ (5) | ·00520 | ·00432 | ·00476 |
| „ (6) | ·00504 | ·00456 | ·00480 |
| „ (7) | ·00496 | ·00472 | ·00484 |
| „ (8) | ·00496 | ·00424 | ·00460 |
| „ (9) | ·00412 | ·00384 | ·00397 |
| „ (10)* | ·00016* | ·00016 | ·00016 |

Points marked thus * are in each case the second cross section.

## EXPERIMENT IX

### Vague Nerve of Dog

Piece of Nerve, 10·5 centimetres long, removed one hour after death. Nerve ligatured and cut at both ends. Distances measured from the lower injury.



| Potential Differences Measured from the Lower Cross Section | | | Average |
|---|---|---|---|
| Point (1) | ·00320 | ·00468 | ·00394 |
| ,, (2) | ·00468 | ·00584 | ·00526 |
| ,, (3) | ·00520 | ·00584 | ·00552 |
| ,, (4) | ·00520 | ·00584 | ·00552 |
| ,, (5) | ·00552 ↑ | ·00604 | ·00578 |
| ,, (6) | ·00572 | ·00600 | ·00586 |
| ,, (7) | ·00572 | ↓ ·00600 | ·00586 |
| ,, (8) | ·00556 | ·00584 | ·00570 |
| ,, (9) | ·00552 | ·00576 | ·00564 |
| ,, (10) | ·00256 | ·00256 | ·00256 |
| ,, (10.5)* not observed | | | |

Points marked thus * are in each case the second cross section.

# MODIFICATION OF THE DISTRIBUTION OF POTENTIAL BY THE 'EXTERNAL ARC'

## Changes in the Distribution of Potential Produced by the Conditions of an Experiment

A necessary step in the process of examination of the nerve is the application to it of two electrodes and a connecting wire path. The whole arrangement with the included galvanometer may conveniently be termed an observation circuit, or, simpler still, an 'external arc.' It is a well-known fact that the distribution of potential on the surface of the nerve, as on any other conductor, is unaffected by the presence of such an external arc when the current found traversing it has been accurately compensated. It is also a well-established, but by no means so generally known, fact that the presence of such an external arc profoundly modifies the distribution of potential upon the surface and in the interior of the intervening piece of nerve, when the current traversing the arc is left uncompensated.

The first part of this statement, namely that the external arc with compensated currrent is not a disturbing factor, is of obvious importance to the actuality of the results obtained by this method of examination, and it was shown by Helmholtz[1] to be mathematically true. The value of the error due to an absence of compensation was also calculated by him, and that, too, with a special reference to the case of animal tissues and the centres of electromotive activity, assumed by Du Bois Reymond to be imbedded in them ; the calculation showed that the distribution of potential was modified in a very precise manner. The effect of placing an external arc upon such a conductor, and the consequent derivation of a current through the arc, was shown so to alter the distribution of potential in the conductor as if the conductor formed a portion of the circuit through which the current through the arc was flowing. Thus in the case of a nerve, the current flowing in the galvanometer circuit from longitudinal surface to cross section exactly modifies the pre-existing distribution of potential in the nerve, as if it also flowed in the nerve from cross section to longitudinal surface.

The truth of the calculations was also demonstrated in experiments performed upon conductors in which sources of EMF were placed ; but the actual demonstration of the quantitative influence of this condition in experiments upon nerve has never been undertaken. The presence of the condition has, indeed, been noticed in physiological experiments, as, for example by Von Fleischl,[2] in observations

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[1] For a detailed account of Helmholtz's postulates see Adolf Fick, *Die Medizinische Physik*, 1858, p. 354 ; Morgan, *Electrophysiology, etc.*, p. 265. New York, 1868.

[2] E. v. Fleischl, *Electrotonus, etc.*, *Sitzungber d. Wien, Acad.*, LXXVIII, Abth. 3.

upon electrotonic currents (when HERMANN[1] identified it as being due to this cause, confirming his statements by experiments upon the core-model), nevertheless, it has not been directly examined.

The experiments given below may serve to supply such a deficiency, although not made with this intention, since they were undertaken in ignorance of the general principle enunciated by HELMHOLTZ, and with a view to experimentally investigate the disturbance produced by the placing of an 'external arc.' The examples, which are quoted, all exhibit special instances of the manner in which the pre-existing difference of potential is affected, *e.g.* :—

(*a*) The creation of differences of potential where none existed previously.

(*b*) The diminution, elimination, or reversal of pre-existing differences of potential.

The agreement of the results actually found with those anticipated by a law unknown to the investigator is evidence of the general exactness of the measurements taken in this research, and also, and this is of importance, to the correctness of certain assumptions made in dealing with the measurements of resistance.

## EXPERIMENTS

In each experiment the nerve, having been removed from the animal, was placed upon four nonpolarizable electrodes—A, B, C, D; the cross section being always placed upon electrode A, and the other end of the nerve, extending beyond electrode D, was suspended from the wall of the moist chamber by a silk thread.

The wires connected to the four electrodes—A, B, C, D—were fitted into brass plugs, which could readily be inserted and removed from positions in circuits arranged for the measurement of potential differences or resistances, or could be placed into adjoining holes in an insulated piece of brass. In this way it was possible to measure the resistance, take the potential difference, or complete the 'arc' joining the electrodes simply, or through an inserted resistance.

The length of the nerve and of its various sections, as divided by the position of the electrodes, was carefully measured.

The resistances of the nerve and of its various sections were also measured. Each value given for a resistance being the mean of two measurements taken with the nerve placed in the two positions possible in the limb of the Wheatstone bridge. This precaution was taken to avoid the error due to the presence of differences of potential.

The resistances between the electrodes themselves were measured, for each pair, before and after the experiments. The values obtained for these have in each case been subtracted from the values obtained of the resistances of pieces of nerve inclusive of electrodes.

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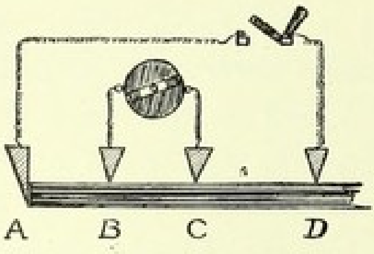
[1] Hermann, *Pflüger's Archiv.*, XX, 1879; also H. Weber, *Borchardts Journ. of Math.*, LXXVI, p. 13.

The potential differences between the electrodes were measured before and after the experiments; no experiments are recorded in which any such were found, and, as has been previously stated, this latterly has never been the case.

A complete set of such measurements having been taken, the experiment was performed. Electrodes A and D were connected together through the plug key, so as to allow the injury current to traverse the arc AD. When this was done it was always found that the potential difference between the intermediate points, B and C, was greatly altered. The alteration remaining constant as long as AD was closed, and disappearing immediately when this arc was broken.

The performance of the experiment was followed by the making of a simple calculation from the data then obtained, by which it was sought to reveal the relation which might exist between the alteration in the potential difference between points B and C and the resistance between these points in the path of a current traversing the arc DA and the nerve AD as a complete circuit.

The basis of this calculation was the value of the resistance between points B and C, and also the resistance in the whole circuit inclusive of the nerve AD.



It is necessary, before proceeding to the details of the actual experiments, to consider the comparative value and meaning of the measured resistances of the pieces of nerve—AD and BC.

There is no difficulty in determining the required resistance of the whole circuit, and thus of the piece of nerve AD to the terminal points of which the observation arc is applied. For the resistance in this case is necessarily measured by the resistance to a current entering and leaving the nerve at the points A and D, that is at the points and traversing the same path as the current determined by the position of the arc.

The measurement of resistance of the short piece of nerve BC is different, since the current used to measure this resistance must enter and leave the nerve at points B and C, and encounter a 'transverse' resistance in so doing which is not encountered by a current passing, as in the assumed conditions of the experiment, from A to D and through points B and C, situated within the longitudinal resistance.

This objection invalidates all conclusions made as to the resistance of nerve measured between two points upon its longitudinal surface, just as the measurement of the resistance between two points upon the surface of an insulated, or rather badly insulated cable, is of no value, when one is seeking information as to the conductivity which the cable offers to currents traversing the same section of cable but passing in the interior of the cable from and to points beyond the terminals of the small stretch considered.

There can be no question but that the direct measurement of the resistance of short pieces of nerve is rendered in this way fallacious, it seems possible, however, that a study of the extent of the fallacy may be of interest. Direct experimental evidence justifying the rejection of such measurements may be taken from the observation of differences in the resistance per centimetre of long and short stretches of nerve. For if a piece of nerve is laid upon several electrodes, and the resistance of the whole piece of nerve and of its parts separately measured, it is always the case that the directly measured total resistance is less than the same resistance computed by the addition of the resistances of the several parts ; a fact undoubtedly due to the repeated inclusion of the transverse resistance in the measurements of the shorter stretches. The finer the calibre of the nerve and the longer the distance between each pair of electrodes the less true this statement becomes, obviously because there is then a closer approach to 'infinity' of resistance of each small piece of nerve. The fact is, however, readily demonstrated upon the sciatic nerve of the frog, and disappears in such a nerve upon 'cooking,' in company with the excess transverse resistance. The fact is very apparent in large calibred mammalian nerve.

### Preliminary Experiment. Sciatic Nerve of Dog

The nerve was laid upon five electrodes—A, B, C, D, E

| | | | |
|---|---|---|---|
| The resistances by sections ... | AB | 6,150 | ohms. |
| | BC | 7,890 | ,, |
| | CD | 10,450 | ,, |
| | DE | 11,450 | ,, |
| Addition ... | | 35,940 | ohms. |
| Resistance of AE, directly measured ... | | 24,000 | ,, |
| Difference ... | | 11,940 | ohms. |

*i.e.*, an excess of 48 per cent. above the direct estimation.

The facts from similar experiments upon vagus nerves (dogs) are tabulated below to show in the briefest possible manner the magnitude of the error introduced into the examination of the resistance of short stretches of nerve.

## TABLE OF PRELIMINARY EXPERIMENTS

### Resistance of the Vagus Nerve of the Dog from Seven Separate Experiments

| Number of Experiment | Length of Nerve in Centimetres | Number of Sections | Resistance in Ohms | | Excess | |
|---|---|---|---|---|---|---|
| | | | Direct Measurement | Summation of Resistance of Parts | In Ohms | Per Cent. |
| I | 8 | 5 | 100,952 | 128,720 | 27,768 | 27·5 |
| II | 8·3 | 5 | 121,500 | 149,500 | 28,000 | 29·1 |
| III | 7·8 | 4 | 88,500 | 105,950 | 17,450 | 19·7 |
| IV | 7·3 | 4 | 91,000 | 111,000 | 20,000 | 22·0 |
| V | 6·2 | 4 | 70,900 | 94,780 | 23,880 | 33·6 |
| VI | 5·3 | 3 | 65,200 | 82,400 | 17,200 | 26·3 |
| VII | 3·8 | 3 | 50,200 | 79,200 | 29,200 | 36.6 |

A consideration of such evidence and of the probabilities of the case examined by themselves make the avoidance of values obtained by direct measurement for the resistance of short stretches of nerve a matter of necessity. It seems clear that the resistance per centimetre obtained from the measurement of the longest stretch of nerve available, provided, if possible, with two cross sections, is a measurement as free as possible from errors due to transverse resistance and polarization phenomena, and gives the best determination of the gross longitudinal resistance of the nerve.

In the following experiments, therefore, all resistances have been directly determined, but the directly determined resistances of the shorter stretches of nerve are not used for purposes of calculation. The nerves were laid upon an ebonite ruled scale during the measurement of resistances and the distances of the electrodes from one another were read upon the scale and noted, from these lengths the resistances of the shorter stretches of nerve have been calculated by use of the standard resistance per centimetre obtained from the whole length of nerve. Both values are, however, given to show the magnitude of the error thus avoided, and also to serve as material for the purposes of any criticism directed against this method of procedure.

## EXPERIMENT A

### Vagus Nerve of Cat

Nerve laid upon four electrodes—A, B, C, D

| | | |
|---|---|---|
| Length of AD (piece of nerve between electrodes A and D) | 4·3 cms. | |
| ,, BC | 1·8 ,, | |
| ,, AB (distance of B from the cross section) | 1·3 ,, | |
| Resistance of AD directly determined | 128,000 ohms | (1) |
| ,, BC | 63,000 ,, | (2) |
| ,, a pair of electrodes | 7,000 ,, | (3) |
| ,, circuit AD, including electrodes | 135,000 ,, | |
| Calculated resistance of BC from the resistance per cm. obtained from (1) and from the length BC | 54,000 ,, | |
| Potential difference between A and D | ·00712 Daniell | |
| ,, ,, ,, B and C | 0 ,, | |

These data having been collected, the experiment was performed :—

(1) Electrode A was permanently connected to electrode D.

The potential difference between points B and C was re-examined—B, the point nearer to the cross section, was found positive to C, the more distant point, by ·0028 Daniell.

The experiment was repeated rapidly several times, in each case B and C were equipotential when A was not connected to D, when this connection was made, B was positive to C, as given.

(2) Electrode A was connected to D through 100,000 ohms. resistance—B positive to C again, but by ·00168 Daniell.

(3) Electrode A was connected to D by 150,000 ohms resistance—B positive to C, ·00128 Daniell.

(4) Electrode A connected to D through 200,000 ohms—B positive to C, ·00108 Daniell.

Finally, the connexion between A and D being broken, B was found as formerly equipotential to C.

The potential difference between A and D, examined at the end of this experiment—A was negative to D, ·00648 volt.

## EXPERIMENT B

### Vagus Nerve of Cat

Nerve laid upon four electrodes—A, B, C, D. Cross section at A.

| | | |
|---|---|---|
| Length of AD | 6·2 cms. | |
| ,, BC | 2·6 ,, | |
| ,, AB | 0·8 ,, | |
| Resistance of AD | 204,400 ohms | (1) |
| ,, BC | 104,200 ,, | |
| ,, Pair of electrodes | 6,000 ,, | |
| Total resistance in circuit AD (nerve and electrodes) | 210,400 ohms. | |
| Calculated resistance of BC obtained from its length and the resistance per cm. from (1) | 85,800 ,, | |

## EXPERIMENT B—*continued*

| | |
|---|---|
| Potential difference between AD (A −) ... ... ... | ·00840 Daniell. |
| ,, ,, ,, BC (B −) ... ... ... | ·00068 ,, |
| (*a*) Electrode A connected up to electrode D, then it was found that B was positive to C ... ... ... ... | ·00252 ,, |
| (*b*) Electrode A connected to D through a resistance of 100,000 ohms, then B was positive to C ... ... ... | ·00144 ,, |
| (*c*) Connexion between A and D broken, then B was negative to C | ·00068 ,, |

## EXPERIMENT C

### Vagus Nerve of Cat

Nerve laid upon four electrodes—A, B, C, D. Cross section at A.

| | | |
|---|---|---|
| Length of Nerve AD ... | 3.9 centimetres ... ... ... | (1) |
| ,, BC ... | 0.7 ,, ... ... ... | (2) |
| ,, AB ... | 0·7 ,, | |
| Resistance of AD ... | 102,200 ohms. ... ... ... | (3) |
| ,, Electrodes... | 6,000 ,, | |
| ∴ of AD + electrodes ... | 108,200 ,, | |
| Resistance of BC ... | 28,460 ,, | |

| | |
|---|---|
| Calculated resistance of BC (from 3, 2, 1) ... ... | 18,300 ohms. |
| Potential difference between AD (A −) ... ... ... | ·00752 Daniell. |
| ,, ,, BC (B −) ... ... ... | ·00144 ,, |
| A connected to D. B remained negative to C ... ... | ·00012 ,, |

## EXPERIMENT D

### Sciatic Nerve of Cat

Nerve was laid upon four electrodes—A, B, C, D. Cross section at A.

| | | |
|---|---|---|
| Length of nerve | AD ... ... ... | 3·4 cms. |
| ,, | BC ... ... ... | 0·7 ,, |
| ,, | AB ... ... ... | 0·7 ,, |
| Resistance of | AD ... ... ... | 18,500 ohms. |
| ,, | Electrodes ... ... ... | 6,000 ,, |
| ,, | AD and electrodes ... ... | 24,500 ,, |
| ,, | BC ... ... ... | 10,870 ,, |
| Calculated resistance of BC ... ... ... | | $\frac{18{,}500}{3{\cdot}4} \times {\cdot}7. = 3{,}800$ ohms. |

| | |
|---|---|
| Potential Difference between AD (A −) ... ... ... | ·00960 Daniell. |
| ,, ,, BC (B −) ... ... ... | ·00224 ,, |
| (*a*) Electrode A having then been jointed to electrode D, the potential difference between BC (B −) ... ... ... | ·00076 ,, |

If, in these experiments Helmholtz's general principle is applied and examined by means of the data given, it will be seen that it explains all the results obtained.

If it is true that the moment a current is derived through the arc DA that then the distribution of potential in the nerve is precisely altered as if the same current passed from A to D along the nerve, it must follow that the difference of potential between any two points, whether upon the wire path or the nerve, are affected in a manner which can readily be calculated.

The newly created difference of potential between points B and C upon the nerve should be equal to

$$\frac{\text{Resistance between B and C}}{\text{Total resistance in circuit}} \times \text{Potential difference between AD}$$

Where a pre-existing difference of potential is found between B and C, the old and the new should algebraically sum. These simple calculations, made for the four experiments given, are embodied in the following table :—

DATA

| | Resistance of BC | Total Resistance | Potential Differences between Points AD | Potential Differences pre-existing between Points BC |
|---|---|---|---|---|
| Experiment A. (*a*) | 54,000 | 135,000 | ·00712 Daniell. | 0 |
| (*b*) | 54,000 | 235,000 | ,, | 0 |
| (*c*) | ,, | 285,000 | ,, | 0 |
| (*d*) | ,, | 335,000 | ,, | 0 |
| Experiment B. (*a*) | 85,800 | 210,400 | ·00840 Daniell. | ·00068 Daniell. |
| (*b*) | ,, | 310,400 | ,, | ,, |
| Experiment C. (*a*) | 18,300 | 108,200 | ·00752 | ·00144 ,, |
| Experiment D. (*a*) | 3,800 | 24,500 | ·00960 | ·00224 ,, |

VALUE FOR SUBSEQUENT POTENTIAL DIFFERENCES BETWEEN POINTS B AND C.

| | Calculated | Found |
|---|---|---|
| A. (*a*) | ·00284 | ·00280 |
| (*b*) | ·00163 | ·00168 |
| (*c*) | ·00133 | ·00128 |
| (*d*) | ·00114 | ·00108 |
| B. (*a*) | ·00274 | ·00252 |
| (*b*) | ·00164 | ·00144 |
| C. (*a*) | — ·00017 | — ·00012 |
| D. (*a*) | — ·00076 | — ·00076 |

Adding together the figures from the four experiments obtained by the application of the general principle to the data collected.

Calculated 1225 × $10^{-5}$ Daniell.
Found 1168 × $10^{-5}$ ,,

Total Difference 57 × $10^{-5}$ Daniell.

or a difference of 4·6 per cent.

The experiments have naturally been selected from others providing similar evidence, and have been chosen on account of the exactness of the agreement between value calculated and found.

Nor is this unfair as practice was obtained in performing the series of measurements required: for each experiment increased the rapidity with which they were taken, and led to important modification in the convenient arrangement of the necessary apparatus. The experiments were also made unsupported by the knowledge that their results must, if correct, be of the nature given.

The next and last experiment recorded in this section affords not only a confirmation of the results previously given, but also illustrates a new point. From its data it may be seen that Helmholtz's general principle is not only true of the injury current but also of 'longitudinal currents.' In either case the institution of the outer observation circuit modifies the distribution of potential upon the surface and in the interior of the nerve and in the same way. The current which passes from point (1) to point (2) in the outer wire path also traverses as a new phenomenon the nerve from point (2) to point (1).

## EXPERIMENT E

### Sciatic Nerve of Cat

Nerve on electrodes A, B, C, D. Cross section at A.

Length of AD ... ... 4 centimetres.
,, BC ... ... 1·6 ,,
,, AB ... ... 0·7 ,,

Directly measured resistance of AD ... ... 13,000 ohms.
,, ,, BC ... ... 10,700 ,,
,, ,, Electrodes ... 6,000 ,,

Resistance of BC calculated $= 13{,}000 \times \frac{1·6}{4} = 5{,}200$ ohms.

Potential difference between AD (A—) ·01450 Daniell.
,, ,, BC (B—) ·00448 Daniell.

## EXPERIMENT PERFORMED

(*a*) Electrode A connected to D through a closed key.

Potential difference between BC now (B –) ·00064 Daniell.

Key connecting A to D opened.

Potential difference between BC now (B –) ·00448 ,,

(*b*) Electrode A connected to D through a resistance of 100,000 ohms.

Potential difference between BC now (B -) ·00390 Daniell.

Connexion between A and D removed.

Potential difference between BC now (B ) ·00448 ,,

(*c*) *Experiment of new type.*

Electrodes B and C were connected through a key.

When this key was closed, the potential difference between points A and D was measured and found (A –) ... ·01305 Daniell.

When this key was opened, the potential difference between points A and D was measured and found (A –) ... ·01450 Daniell.

Treating as before the data from this experiment.

In case (*a*).—The potential difference between B and C due to the closure of the circuit forming AD,

$$= \cdot 0145 \times \frac{5{,}200}{19{,}000} = \cdot 00397\ (\mathrm{B}+)\ \text{Daniell.}$$

The pre-existing potential difference between these points ... ·00448 (B –) Daniell.
The algebraical sum of these values ... ... ... ·00051 (B –) ,,
and this is the calculated value.
The value actually found ... ... ... ... ·00064 (B –) ,,

In case (*b*)

The potential difference between BC due to closure of the circuit AD.

$$= \cdot 0145 \times \frac{5{,}200}{119{,}000}\ \text{Daniell}\ (\mathrm{B}+)$$

$$= \cdot 00062\ \text{Daniell}\ (\mathrm{B}+) \quad \ldots \quad (1)$$

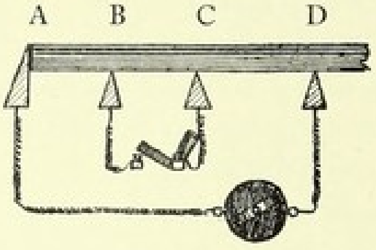
But B was originally ·00448 (B –) ... ... ... ... ... (2)

The algebraical sum of these values = ·00386 Daniell (B –), and this calculated value closely agrees with the value found which was ·00390 Daniell (B –)

| | Value calculated | Value found |
|---|---|---|
| In case (*a*) | ·00051 (B –) | ·00064 (B –) |
| (*b*) | ·00386 (B –) | ·00390 (B –) |

Case (*c*) requires to be considered by itself.

In considering the data from case *c* (Experiment E), the circuit formed by the closure of electrodes B and C, and by the intervening stretch of nerve BC is alone considered. The remaining pieces of nerve AB and CD are treated, for the purposes of calculation, as if they were a continuation of the terminal conductors of the galvanometer and compensator circuit up to the points B and C.



According to Helmholtz's principle the closure of the key K gives rise to a current in the complete circuit KBC, the magnitude of which is determined by the source of **EMF**, which is of the value of the pre-existing difference of potential between points BC, and by the total resistance in this circuit BCK.

It should be possible to determine the resistance of any portion of this circuit when the current is traversing it from a discovery of the difference of potential existing then between the terminal points of the resistance.

In this way it is possible to determine the longitudinal resistance between B and C, using as 'leads' to the terminals of this resistance the pieces of nerve AB, CD.

$$r = \frac{e}{E} R.$$

Where E = ·00448, the pre-existing potential differences between points BC.
R = 10,700 + 6,000 = 16,700 ohms.
e = the newly-found potential difference between B and C.
= pre-existing potential difference between points AD—new potential difference between AD.
= ·01450— ·01305 = ·00145 Daniell.

$$r = \frac{e}{E} R.$$

$$= \frac{\cdot 00145}{\cdot 00448} \times 16{,}700 \text{ ohms.}$$

$$= 5{,}405 \text{ ohms.}$$

This value, obtained from this experiment, for the 'longitudinal resistance' between points B and C closely agrees, as a reference to the data of case (*c*) shows, with the value as otherwise calculated and used as the basis of the calculations made in case (*a*) and case (*b*), namely,

5,200 ohms.

The agreement of experimental results and prediction are so close in these experiments that one is inclined to place confidence in the measurements upon which the simple calculations depend, and one is, therefore, inclined to draw further conclusions from them.

In the first place, it is apparently obvious that the resistance of the longer stretches of nerve examined, as obtained from the WHEATSTONE bridge method, was also the actual resistance encountered by the nerve's own current when led through the outer path to the cross section, and so back through the nerve. Also, that a variation in the nerve's own current produced by the insertion of resistance in the outer path did not produce any effect upon this resistance. A reference to experiment A will show that the value for this resistance used in the calculations was the same, and led to the same satisfactory result, when the resistance in the whole circuit was varied from 135,000 ohms to 335,000 ohms; and when, therefore, the new current was in one case three times as great almost as in the other.

This longitudinal resistance apparently remains constant when the current traversing it is greatly varied, which would not be the case if any very large fraction of the resistance was due to polarization, and if, as is supposed, the polarization increased largely with the current.

This is a fact of considerable interest since, in dealing with the general problem of the electromotive phenomena of the nerve, it is necessary to know the nature and quantity of the electrolytes present in the nerve. The first guide to such knowledge is provided by measurements of electrical conductivity, and if these measurements are once acknowledged to be misleading by reason of special conditions present, then the main source of information is rendered valueless.

Measurements of electrical conductivity of nerve can be undertaken, by determining the resistance of a cut piece of nerve from cross section to cross section, in which it would seem that the error introduced by polarization would be absent, if it be assumed that all the polarization phenomena are due to the fact that stream lines pass from one constituent structure of the nerve fibre to another. For in this method of examination, when all the parallel constituent structures are traversed by stream lines parallel to them, this cannot occur, except as a negligible error due to artificially produced bends in the course of nerve fibres.

It is possible that even to such measurements exceptions may be taken, since there is some reason to fear the presence of a true 'longitudinal polarization,' the outcome of circumstances of physical structure not understood.

It is noteworthy, therefore, that in the measurements given above there is no reason to consider such a complication: so that the errors due to polarization are so small as to be negligible, and do not interfere with a practical use of these measurements as the basis of calculation.

The confidence obtained from such results has led to the institution of the measurements of conductivity in the next section, and their use as guides to the quantity of electrolytes contained in solution in the nerve, and, therefore, as assisting to form an opinion of the quantity of matter upon which all the electromotive phenomena of nerve depend.

## MEASUREMENTS OF ELECTRICAL CONDUCTIVITY

The average resistance of the sciatic nerve of the cat is four thousand ohms per centimetre when given as based upon measurements of long stretches of nerve (five centimetres). The value of this statement (and it is of the orthodox character) is limited, in so far as it offers no basis for a real comparison of the resistance of the sciatic nerve with that of any other nerve of different average calibre, and also since it gives no information as to the varying nature of the resistances of the differing elements of structure entering into the composition of the nerve.

The first limit is only to be surmounted by a determination of the calibre, and this is a matter of some difficulty when use is made of nerves from which subsequently data of a different kind are to be sought, and which must not, therefore, be damaged in the process.

In the present series of measurements, this difficulty has been avoided by the use of an indirect method, which does not injure the nerve, and which affords results that are certainly not more than 5 per cent. in error.

The second limit it is not possible, for the present, to surmount, and the value of the information attainable is thereby greatly reduced. The reduction in value is not, however, so great as to leave the taking of these measurements merely an 'academic' interest ; since the information obtained, scanty though it be, is from one point of view of extreme value. The nerve, being a 'moist conductor,' owes its conductivity to the solutions of electrolytes which it contains, and measurements of conductivity, therefore, can be used as guides to a knowledge of the quantity of electrolytes present in solution in the nerve, although giving no guide as to their relative distribution in its component parts. The information so obtained is by no means perfect, but is of value, since the limits to its accuracy are not such as to render the errors introduced more than a fractional part, even if a large fraction, of the true value which they tend to conceal.

The measurements, indeed, form the only means by which any approximate notion can be acquired of the total amount of electrolytes in solution, that is of the amount of matter which can partake in the production of the electromotive phenomena of the nerve ; and it is obvious that in a study of these electromotive phenomena it is desirable to decide, even if roughly, the proportion which this amount bears to that of the total matter in the nerve.

### MEASUREMENTS

The following data are taken from eleven separate experiments upon sciatic nerves obtained from eleven cats, from the bodies of which they were removed immediately after death. The measurements of resistance were made by an ordinary 'bridge' method, the circuit being so arranged that a current of less than ·01 milliampère traversed the nerve at the time of measurement. The sensitive galvanometer used in the previous sections was also used in these measurements, and the determination was always finally made with this, and without a 'shunt.'

To avoid any error due to the presence of an injury current, the measurement was always repeated with the nerve arranged in a reverse direction, so as to cause this current to add to and to subtract from the measuring current; the values given are always the mean of two such measurements.

In each case given the piece of nerve, cut so as to be as near as possible five centimetres in length, was provided with a clean cross section at each end. It was arranged rectilinearly between two electrodes and upon a dry ebonite scale, and its length was accurately measured when thus in position. Immediately after the measurement of resistance the weight was accurately ascertained.

DATA FROM ELEVEN EXPERIMENTS

| Experiments | Resistance in ohms | Length in centimetres | Weight in grammes |
|---|---|---|---|
| Experiment I ... ... | 17,000 | 5·0 | ·287 |
| " II ... ... | 14,200 | 4·8 | ·237 |
| " III ... ... | 17,300 | 5·0 | ·239 |
| " IV ... ... | 23,800 | 4·9 | ·201 |
| " V ... ... | 15,900 | 4.8 | ·255 |
| " VI ... ... | 17,800 | 4·8 | ·216 |
| " VII ... ... | 23,500 | 5·0 | ·195 |
| " VIII ... ... | 18,000 | 4·0 | ·145 |
| " IX ... ... | 20,300 | 5·0 | ·236 |
| " X ... ... | 20,700 | 4·5 | ·210 |
| " XI ... ... | 26,000 | 4·9 | ·207 |
| Average of 11 Experiments | 19,500 | 4·8 | ·221 |

If, in these experiments, the determination of weight is treated as if it were a determination of volume, and the error so introduced is certainly less than five per cent., we have all the data necessary to determine the 'specific' conductivity of the nerve. The error would of course be eliminated by a correction for the specific gravity of the nerve, but this is difficult to obtain, owing to the peculiar behaviour of the nerve when immersed in solutions. Failing this determination of the specific gravity the error is left uncorrected; since it appears only once in the value of the specific conductivity, and is, therefore, not increased by multiplication to a higher power.

The 'specific' resistance of the nerve is taken as that of a closely packed pile of similar nerves, one centimetre in length, and offering a united cross section of one square centimetre.

In any single case such a 'specific' value may be found by dividing the value of the resistance by the length and multiplying by the ascertained value of the cross section.

$$\text{Specific resistance} \quad \ldots \quad \ldots \quad = r \times \frac{1}{\text{length}} \times \frac{\text{volume}}{\text{length}}$$

$$\text{or approximately} \quad \ldots \quad = r \times \frac{1}{\text{length}} \times \frac{\text{weight}}{\text{length}}$$

Thus taking the figures obtained as the average of the data of the eleven experiments—

$$\text{The specific resistance of the sciatic nerve of the cat} = 19{,}500 \times \frac{{\cdot}221}{4{\cdot}8 \times 4{\cdot}8} \text{ ohms.}$$

$$= 180 \text{ ohms (approx).}$$

Similar values given from the eleven separate experiments are—

| | | | |
|---|---|---|---|
| I ... ... | 195 ohms | VII ... ... | 183 ohms |
| II ... ... | 146 „ | VIII ... ... | 163 „ |
| III ... ... | 165 „ | IX ... ... | 191 „ |
| IV ... ... | 195 „ | X ... ... | 205 „ |
| V ... ... | 176 „ | XI ... ... | 165 „ |
| VI ... ... | 160 „ | | |

Taking the average value of 180 ohms, it is of interest for purposes of comparison to compare it with the specific resistance of mercury at 18° C, with which value the resistance of solutions of electrolytes is commonly compared.

| | |
|---|---|
| The specific resistance of mercury at 0° C. ... ... | $94{\cdot}07 \times 10^{-6}$ ohms |
| The temperature co-efficient ... ... ... | ·00077 |
| ∴ The specific resistance of mercury at 18° C. ... | $95{\cdot}4 \times 10^{-6}$ „ |

$$\frac{\text{The specific resistance of nerve} \;\ldots\;\ldots\;\ldots}{\text{The specific resistance of mercury} \;\ldots\;\ldots\;\ldots} = \frac{180}{95{\cdot}4 \times 10^{-6}} \text{ „}$$

$$= 1{\cdot}885 \times 10^{6} \text{ „}$$

Taking the 'specific conductivity' of nerve to be the reciprocal of its 'specific resistance,' as defined above, it is equal to—

$$\frac{1}{1{\cdot}885} \times 10^{-6}$$

$$= 53 \times 10^{-8} \text{ in terms of mercury at } 18^{\circ}\text{ C.}$$

The conductivity of nerve is now expressed in a form in which it can conveniently be compared to that of solutions of electrolytes. Thus, taking solutions of NaCl as our standards of comparison, we have the following determined specific conductivity of such solutions.[1]

SPECIFIC CONDUCTIVITY OF SOLUTIONS OF NACL

| Concentration of Solution | | Specific Conductivity in terms of Mercury |
|---|---|---|
| Gram molecules per litre | Grammes per cent. | |
| 1·00 | 5·620 | 695·0 × $10^{-8}$ |
| 0·50 | 2·865 | 378·5 × $10^{-8}$ |
| 0·10 | 0·583 | 86·5 × $10^{-8}$ |
| 0·05 | 0·292 | 44·8 × $10^{-8}$ |

The specific conductivity of nerve is, therefore, approximately the same as that of a solution of sodium chloride of ·35 grammes per cent. concentration. *In other words, the conductivity of the nerve would, so far as we are at present considering it, be adequately imitated by that of a saline solution occupying the same space, which was only half the strength of the ordinary 'normal saline' solution.*

It is of interest to compare the value so obtained with that of previous investigators. The data given by I. TEREG[1] are presented in a form most suitable for comparison. This author, in a general examination of the conductivity of the tissues and the modifications produced by changes of temperature, obtained a value for the resistance of nerves as follows :—The nerves were laid side by side in an accurately calibred hard glass tube (diameter 12 mm.) The length of the tube used was 34·5 mm. The nerves were presumably packed closely in this tube and accurately cut to the required length. Amalgamated zinc electrodes were brought to each end of the tube and the resistance of the enclosed nerves determined.

The following values are given for this resistance :—

| | |
|---|---|
| At 21° C. ... ... ... | 700 ohms. |
| 25° C. ... ... ... | 670 ,, |
| 32° C. ... ... ... | 600 ,, |
| 35° C. ... ... ... | 570 ,, |
| 39° C. ... ... ... | 530 ,, |
| 45° C. ... ... ... | 460 ,, |

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[1] Kohlrausch, *Wiedeman's Annal*, XXVI., p. 195.

[1] *Archiv. fur Anat. : und Physiologie*, 1899, p. 318.

From these figures of Tereg's, and preferably from the value obtained of the resistance at 21° C, a value can be calculated for the so-called 'specific resistance.'

$$\begin{aligned} \text{Specific resistance} \quad \ldots \quad \ldots \quad &= \text{R} \times \text{cross section} \times \frac{1}{\text{length}} \\ &= 700 \times \frac{\pi r^2}{l} \\ &= 700 \times \frac{({\cdot}6)^2 \times 3{\cdot}14}{3{\cdot}45} \\ &= 700 \times \frac{1{\cdot}13}{3{\cdot}45} \\ &= 230 \text{ ohms approx.} \end{aligned}$$

The specific conductivity in terms of mercury therefore is (for data see previous example)—

$$\begin{aligned} &= \frac{95{\cdot}4 \times 10^{-6}}{230} \\ &= 41 \times 10^{-8} \end{aligned}$$

A value which an examination of the table of specific conductivities of solutions of sodium chloride will shew is approximately the same as such a solution of the strength of ·3 grammes per cent. The figures given by Tereg, therefore, closely agree with those found from the previous experiments, and like them set the electrical conductivity down at a very low value.

The modifications with temperature, as observed by him, are also of considerable interest, since they show this agency affecting the values in a quantitative manner, exactly agreeing with that known to occur with change of temperature in solutions of electrolytes.

Thus the conductivity at 21° C. is $\frac{1}{700}$, at 45° C. it is $\frac{1}{460}$. The alteration thus consequent upon a rise of temperature through twenty-four degrees is $\frac{1}{460} - \frac{1}{700}$ or $\frac{6}{8050}$. Treating this latter figure as a fraction of the original conductivity of $\frac{1}{700}$ it is seen to represent a rise in the original value of almost exactly fifty per cent., *or two per cent. per degree of temperature.*

The value of such a result is considerable, as is seen from a reference to the following quotation : 'The molecular conductivity of a given electrolyte depends in the first instance on the temperature, increasing almost without exception with rise of temperature, and mostly by about 2 per cent. per degree.'[1]

The nerve, owing, as has been previously stated, all its electromotive phenomena, inclusive of electrical conductivity, to the solutions of electrolytes contained in it, is seen from the point of view of this modification with temperature to behave like any solution of electrolytes. This is a fact worthy of consideration when, as has sometimes been attempted, assumptions are made as to the mobility of the particles contained in it with the conduction of an electrical current other than that of the motion of ions in solution.

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[1] *Outlines of General Chemistry*, Ostwald, translated by J. Walker, London, 1895, p. 276.

If the electrical conductivity of nerve seems disappointingly small when it is sought to discover as its main function that of an electrical conductor, and when the prominence of the electrical phenomena discovered in it is considered, it is no longer so when a glance is taken at the known chemical constitution of the nerve. Thus, taking the figures collected in HALLIBURTON's[1] article on the chemical constitution of nerve, sciatic nerves contain 61·3 per cent. of water and 38·7 per cent. of solids.

The solids are given in the following estimation made from human sciatic nerve :—[2]

SOLIDS OF HUMAN SCIATIC NERVE

| | | |
|---|---|---|
| Proteids ... ... | 36·80 | per cent of the total solids. |
| Lecithin ... ... | 32·57 | |
| Cholesterin and fat ... | 12·22 | |
| Cerebrins ... ... | 11·30 | |
| Neurokeratin ... ... | 3·07 | |
| Other organic matters ... | 4·00 | |
| | 99·96 | |

None of these bodies, which are arranged here, contributing to the solids of the nerve offer much prospect of a capability of acting as electrolytes : the only substances which would seem in this company to be characterized as such, the inorganic salts, are omitted from the table presumably from a failure to estimate the unimportant constituents. To form an estimate of the amount of inorganic salts present, we are compelled to use the quantity estimated as present in the white matter of the brain, namely, ·57 per cent. of the total solids, or in the spinal cord forming 1·1 per cent. of the total solids.

These figures, while providing no exact guide, might lead us to infer that the inorganic salts of nerve formed ·3 or ·4 per cent. of its mass, a value which is suggestively similar to that of the total electrolytes as roughly estimated by the conductivity method.

More point is given to these figures by the fact that the inorganic salts of nerve are not expressible as so much sodium chloride, a large quantity of potassium salt being also present, the electrical conductivity of which is greater. To explain the conductivity of nerve in terms of its inorganic salts, it is, therefore, necessary only to find present a quantity of these less than ·3 per cent., and there seems every possibility of doing so.

The small value of the electrical conductivity of nerve has long been appreciated, although few attempts have been made to exactly determine it. The fact in its gross form was, subsequently to the discovery of the electrical current by GALVANI, made of

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[1] Schafer, *Textbook* I, p. 116.

[2] Moleschott, *Physiol. Chem.*, p. 335.

great polemical use as a conclusive argument against the advisability of seeking a purely electrical function for nerves in the body. It has, however, also been repeatedly pointed out that the nerve is not a homogeneous conductor, and that measurements of gross conductivity give no information as to the conductivity of the very different longitudinal elements of structure which compose it. From such a point of view it is seen, especially if one of these structural elements is assumed to have a semi-insulating character (very low conductivity), that such gross measurements may be most misleading if used in any way to limit the possibilities of conductivity of any individual element of structure.

Given a tissue of extremely high electrical conductivity, arranged in exceedingly fine threads within the general mass of poor conductors, its presence might be totally unsuspected, and might even be said to be concealed by the general low conductivity found.

It is of interest, therefore, to consider the only case in which careful investigation has led its authors to the conclusion that nerves are after all characterized by a high electrical conductivity much greater than that of any other of the tissues.[1]

These authors, Alt and Schmidt, have, by use of a new and peculiar method, compared the resistance of different animal tissues, and find them arranged in the following order ; in which, it will be seen, the standard of comparison is an arbitrary one, the resistance of muscle—

| | |
|---|---|
| Nerve | 0·17 |
| Heart muscle | 0·86 |
| Muscle | 1·00 |
| Blood | 1·00 |
| Aponeuroses | 4·41 |

etc., etc.

Such a statement places nerve in the position of being as an electrical conductor six times superior to muscle in opposition to the common view, that it is, on the contrary, inferior to it.

The experiments bear every mark of careful and repeated work, and the conclusion to which the authors have come seems, therefore, to be fully justified by them. The method is, on the other hand, quite new, and can only be adequately criticized by a physicist. In this method the tissues placed within and filling a glass tube of standard size were placed in line with other conductors to form an alternative path for the conductor of 'Franklin currents from a Holtz influence machine.' The other path was a spark gap.

The method would seem to depend upon a comparison of the resistance of the tissue and the resistance of a column of air, which would seem to be an absurdity. As a matter of fact, probably this is far from being the case, the spark conducted

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[1] Alt & Schmidt, *Halle Pflügers Archiv.* LIII, p. 575, etc.

through the air being conveyed not by particles of the air but by charged particles discharged from the conductor, and the real resistance of the air gap is not, therefore, open to calculation.

The authors believe that a high general conductivity is revealed in the nerve by this method, since, in their opinion, the method eliminates all error due to polarization. It must be admitted that such a revelation would place the longitudinal polarization of nerve in a position of extreme importance as an agent capable, under ordinary circumstances, of masking 90 per cent. of the electrical conductivity of the nerve. This extreme value of the longitudinal polarization has no direct evidence in support of it, and all the available evidence (as that obtained in the last section) points to the opposite conclusion, that polarization, though characteristically present and of importance, is not able to mask more than a fraction (less, say, than one-fifth) of the gross conductivity, and adds but a small fractional addition to the measurable resistance.

The difference found between nerve and the other tissues must have some reason, even if this is not expressible in the terms chosen by the authors, and there seems the remote possibility that the method has revealed the possession by the nerve of extremely fine paths of high specific conductivity.

# THE PHYSICAL STRUCTURE OF THE NERVE

*The pre-existing structures of the nerve are such as to primarily determine the fact that local injury is productive of an injury current: and this is true whether the differential distribution of electrolytes giving rise to it is* (1) *also pre-existent*, *or* (2) *the result of chemical change*, *a secondary consequence of injury.*

To explain fully the intended meaning of this statement it is necessary to briefly consider the nature and arrangement of materials in the nerve from a purely physical point of view. It is not, and never has been considered, sufficient to dwell solely upon details of histological structure, and to read into them an appropriate physical meaning, and it is at the present date more obvious than ever that this is not the primary method of examination. The data of primary importance are provided by a knowledge of the manner in which the structures of the nerve behave, when the electrolytes contained in solution in them are set in movement by a source of electromotive force; or it might also be said by the manner in which the electrolytes, when diffusing, give rise to a source of electromotive force.

From such a point of view an intimate acquaintance is necessary with :—

(*a*) The conductivity of the nerve.

(*b*) Secondary features of its conductivity, such as the polarization phenomena.

(*c*) The injury current.

The consideration of the last aid to knowledge, the injury current, is, although held to be the most important, abandoned in this section as begging the question set in the research.

The facts which have been determined by purely physical methods of examination are contained in the statement that the nerve behaves as a core model, and that a core model is always a complex conductor composed of materials of at least two different specific conductivities, arranged cylindrically, the one surrounding the other.

Practically it has always been found necessary to place in the core of the core model a material of higher specific conductivity than that of which the mantle is composed, and this fact may be used as an argument that the core of the nerve fibre is of higher specific conductivity than its sheath (it being universally acknowledged that the comparison between core model and nerve trunk can, without fallacy, be used as if in reality a comparison between the core model and nerve fibre).

The argument is not as good a one as might at first sight appear, since this property of the core model structure is necessitated by a characteristic which may be peculiar to it, and may not adequately represent a condition present in the nerve. For the successful imitation of the physical characteristics of the nerve by the core model is due to the acknowledged fact that, although commonly only composed of two materials, it opposes resistances of three kinds to the passage of an electrical current through it:

(1) the surface resistance of the mantle ;
(2) a high resistance at the surface of separation of core from mantle, due to internal polarization, and therefore only existing during the passage of the current ;
(3) the internal resistance of the core.

Three conditions are, therefore, obtained in the core model by the presence of two materials: but in order to obtain these three conditions from two materials, it is necessary that an extraordinary difference should be found between them. The conditions are only adequately so obtained by using a metallic conductor as the core, a dilute moist conductor as the mantle. The high specific conductivity of the core substance of the model is therefore possibly only an accidental attribute, due to the fact that a metallic conductor is necessarily chosen to obtain the polarization resistance.

The nerve fibre is, however, throughout a moist conductor. It seems an absurd, but is a necessary, statement that no metallic conductor exists within its core. The nerve, therefore, may indeed imitate the three conditions present within the core model carrying a current, it cannot, however, imitate them so successfully as to be composed of two analogous sets of materials. It is necessary to consider how the three conditions can be obtained by the use of moist conducting material alone without the assistance of the metallic core. The result of such a consideration is of extreme importance, for it has been found impossible to represent the three conditions by the use of moist conducting material without making use of three materials of different specific conductivity,

| | |
|---|---|
| (1) of fair conductivity . . . | mantle. |
| (2) of bad conductivity . . . | intervening structure. |
| (3) of conductivity better than (1) . | core. |

To carry the lesson learned from the core model to the structure of the nerve fibre we must, therefore, seek in the nerve fibre and the solution covering its surface for the analogues of these three different materials of different specific conductivity.

It is to be noted that in such a core model polarization resistance developed during the presence of the current (and only present then as in the case of the two material core model) is now of secondary importance. A pre-existing resistance now partially at least occupies its place, and the polarization which occurs is only a secondary addition to this pre-existing resistance.

The statement made above, though so briefly given, has involved years of controversy and experiment upon the part of several investigators, notably HERMANN and GRÜNHAGEN. This controversy has been now brought to a clear termination by the introduction into the subject of knowledge of the possibilities, within which the conduction of electrical currents by moist conductors is limited, by the 'electro-chemist' NERNST.

The statement of electro-chemistry is definite. Polarization cannot occur between two moist conductors (solutions of electrolytes) unless they are separated by a physical membrane (pre-existing high resistance). The introduction of the third material is, therefore, a necessity, and its nature is even to a certain extent defined, for the term 'physical membrane' implies a material which habitually acts as a barrier, limiting material particles moving in diffusion processes, and also, as in this case, the particular particles 'Ions' which are set in motion during the passage of an electrical current.

Practical experience is, therefore, amply confirmed by theoretical consideration.

Definite as is the statement of 'electro-chemistry' as well represented by NERNST, it is of interest that a similar statement was also simultaneously made by a physiologist making use in other fields of electro-chemical data and methods. This statement is, unfortunately, hidden away from the special literature of 'muscle and nerve,' inasmuch as it appears in an article on blood and blood corpuscles. It seems therefore pardonable to quote it in some detail. G. N. STEWART discovered the important fact (amply confirmed by its simultaneous discovery by ROTH, BUGARSKY, and TANGL, etc.) that the limiting surface of the red corpuscle offers an extremely high electrical resistance, when immersed in its natural surrounding fluid, the blood plasma.

The ions contained within the blood corpuscles in solution are capable of free movement within the confines of their walls, as is shewn by the osmotic pressure which they are known to be capable of exerting upon them. Conduction of an electrical current would therefore also freely take place within the corpuscular walls. Observations therefore which place the corpuscles in the position of poor or non-conductors can be used in evidence against the conductivity of the walls themselves, since they cannot be directed against the contained solutions.

Ions moving through the blood plasma in the orderly conduction of an electric current are stopped by the surfaces, and do not penetrate the mass of the red corpuscles. In other words, the limiting surfaces are only partially permeable membranes, even if not strictly semi-permeable membranes; and this statement so made is amply confirmed by evidence of a different kind. For such experimental evidence is only an additional confirmation of a long well-known fact, that the inorganic salts of the plasma and of the blood corpuscles are not the same, and of the corollary which this fact implies, namely, that the walls of the blood corpuscles form barriers to diffusion processes between the solutions within and without them.

The fact is, however, capable of extension to other tissue elements such as nerve fibres, which are only finely-drawn processes of cells also containing inorganic salts within them differing, in proportional amount at least, from those contained in the solutions without. The extension of the fact enables the enunciation of an apparently unobjectionable general statement, that all cell walls (walls of nerve fibres included) are possessed of this property of limited permeability to the particles in motion in the solutions surrounding them, and this no matter what be the force under the action of which these particles are moving. The general statement therefore includes the movement of ions carrying an electrical current.

From such or similar consideration G. N. STEWART[1] comes to the following conclusion as to the value of the polarization resistance stated by HERMANN to be found on the surface of nerve fibres during the passage of an electrical current:—

> 'But if nerve fibres are surrounded by an envelope whose specific resistance is much greater than that of the contents of the fibre, there must be a very abrupt change of potential as we pass along current lines that cut the envelope, and the surface of the envelope may therefore become strongly polarized. The fact discovered long ago by HERMANN, that the apparent conductivity of nerve across the fibres is many times less than its conductivity in the longitudinal direction, although explained by him as due to the relatively great capacity for polarization of the nerve when the polarizing current passes transversely across it, receives a more natural explanation if we suppose that the nerve fibres are surrounded by badly-conducting envelopes. Of course if this is the case, a part of the apparent excess of transverse resistance may still be due to polarization, but not the whole of it, nor probably any large proportion of it.'

Such a view is a repetition of GRÜNHAGEN's original position, that the major portion of the transverse resistance was due to a pre-existing high resistance envelope, separating the core of the nerve fibre from the outer 'nutritive fluid.' It is based like it upon a knowledge of the histological structure of the nerve, but whereas GRÜNHAGEN's envelope was peculiar to the nerve as its fatty sheath, and was, therefore, rejected on appeal to the similar existence of a property by muscle where such a sheath is non-existent; STEWART's envelope is the common property of the nerve fibre and of all cells. The envelope may include the neurilemma and the myelin sheath or both. Its thickness is not of such importance as its quality, and its quality is the common property of all limits to cellular structures no matter how microscopically minute they may be.

Such opinions based upon the one hand upon an intimate acquaintance with the properties, and the limits to the properties, of moist conductors (NERNST), and on the other hand, upon an intimate acquaintance with the physical value of histological structures, come to the same conclusion. The nerve fibre, covered with its surrounding solution, can only be successfully imitated by a concentric arrangement of three materials of different specific conductivity, and the theoretical considerations indicate amply that no simpler arrangement is possible.

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[1] G. N. Stewart, *Journal of Physiology*. XXIV, p. 212-3

The physical structure of the nerve fibre is therefore a 'core model' structure, and necessarily comprises—

(1) an outer solution of electrolytes.
(2) a partially permeable membrane.
(3) an inner solution of electrolytes.

Having come to a definite conclusion, that the three conditions of conductivity inferred as existing concentrically in the nerve fibre must be the outcome of a concentric arrangement of at least three different structures, we are in a position to ask whether the statement is still justified that the most internal structure has a specific conductivity of great comparative importance.

Is conduction of an electric current by a nerve trunk a phenomenon mainly occurring in the axis cylinders of the nerve fibres? If so, is this to be explained by the presence of a relatively greater volume of an uninterrupted (by membranes, etc.) solution of electrolytes here than elsewhere in the nerve, or is it to be explained by the presence of a solution of small volume but great concentration and conductivity?

The question seemed answered in the affirmative by a reference to the metallic core of the metallic core model. Such a core model does not, as has been stated, however, adequately represent the distribution of structures in the nerve fibres. Core models, however, such as GRÜNHAGEN's, have been frequently used, which attempted more completely to imitate the distribution of structures in the nerve, being entirely composed of moist conductors. It is of great practical interest, that in such models it has always been found necessary to make the internal solution of relatively great specific conductivity before a resemblance was experimentally found between the nature of the electrical conductivity of the model and the known nature of the conductivity of the nerve, which it was designed to imitate.

The characteristic feature of electrical conductivity in nerve is provided by the electrotonic currents *and by their distribution.* The electrotonic currents can be imitated by the core model, the distribution of such currents in the nerve can only be imitated by a core model in which the internal solution is of high specific conductivity.

This experimental fact is at least an indication which cannot be neglected, and is universally recognized as such. It is taken to mean that the axis cylinder of the nerve fibre is a better conductor than the tissues which ensheath the fibre, and, therefore, that more electricity is conveyed along the axis cylinders than is simultaneously carried by the other tissues of the nerve, when both are carrying an electrical current.

It has been taken, however, by HERMANN to mean that more conducting material is present in the axis cylinder and not that the conducting material present is of a better kind.

Such a conclusion is, however, difficult to follow ; since in the first place there is small ground for entertaining a belief in a relatively greater volume of the solutions of electrolytes placed there, and in the second place such a conclusion is in contradiction to the fact that in the model the conditions were obtained otherwise, namely, by the use of an internal solution of greater specific conductivity and not of greater volume.

One is, therefore, justified in stating, that the only obtainable evidence is in favour of the view that the solutions of electrolytes present within the axis cylinder are of greater specific conductivity than the solutions present elsewhere in the nerve trunk.

Since such a greater conductivity can only be explained in one of two ways, namely, that the electrolytes in the internal solution are different in nature or greater in concentration than those found in the external solution ; such an inference may be used to point to one of these two conditions as of probable occurrence. and this is of great importance from the point of view of the 'injury current.' Immediately it is granted that the internal and external solutions are not the same, it becomes almost necessary to assume that the rupture of such a compound conductor would give rise to new processes of diffusion, and so to an 'injury current.'

Even if we abandon this most probable view, that there is a pre-existing difference between the solutions, and for the time being suppose that the internal and the external solution are one and the same in nature and in concentration ; still we cannot afford to neglect the importance of this tubular membrane, capable of maintaining a difference between the solutions, should any new cause for such a difference arise.

Let any chemical change occur in the matter within the tubular diffusion obstacle, and lead to the formation of new electrolytes and to their appearance in the solutions therein contained ; at once is seen the possibility that they may be confined to this situation by the enclosing membrane.

Let, for example, carbonic acid be produced from the destruction of some complex organic body in the axis cylinder, then it is conceivable that this substance might diffuse with greater ease along the track of the internal solution than through the membrane into the external solution. At once a difference is created between the two solutions, and, were the nerve ruptured, then at the injury the carbonic acid would have its first chance of freely escaping from the internal into the external solution.

Granted the core model structure of the nerve fibre and the existence of this tubular surface of separation of the solutions contained in the nerve, we are at once presented with an important factor determining the origination of an 'injury current.'

The first effect of injury is to disturb this barrier between the internal and external solutions, and whenever differences already exist between them, to give rise *ipso facto* to a 'current of injury.'

A second effect of injury may be to lead to new chemical change, and to new differences between the two solutions. Even if so, it is extremely probable that the localization of the resulting electrical phenomena to the region of the injury may be a consequence, not of the localization of the chemical change, but of the injury to the tubular membrane.

In considering the physical structures of the nerve, therefore, the greatest stress is laid upon this separation of structures into 'internal' and 'external,' and upon the presence of the limiting surface which determines this separation.

The experiments recorded in the subsequent sections of this paper have been devised to test the opinion that this is a matter of primary importance.

# REPLACEMENT OF THE EXTERNAL SOLUTION OF THE NERVE BY WATER

## EXPERIMENTS ON NORMAL, ABNORMAL, AND DEGENERATED NERVE

In the last section it was stated that the main characteristic of nerve of interest from the point of view of the injury current was the presence of 'membranes,' which confine the important structures of the nerve cell processes from too familiar contact with the surrounding lymph. Such an arrangement is by no means peculiar to nerve, but seems to be the common property, in varying degree, of every cellular structure. The peculiar characteristic of nerve is the longitudinally unbroken continuity of its constituent parts, and their arrangement side by side in the nerve trunk in parallel tubular compartments. In a sense this peculiarity is shared with muscle; but in that case there is a secondary transverse segmentation which is not obvious in nerve, and also the limits of the peculiarity are there narrowed by the incomparably shorter length of the muscle fibres.

If it is believed that the internal solution of electrolytes found within cells in general is not the same as that which is found bathing their external surface, then the case of the nerve cell process of the nerve trunk offers itself as the most suitable for the testing of this opinion. For such a difference must give rise upon rupture of the membranes to diffusion processes, and consequently to differences of potential; and the prolonged surface of the nerve cell process obviously offers the best case for the examination of these electrical differences.

If such electrical differences as are found in the phenomenon of the injury current are to be totally explained in this way, they should be capable of modification in a manner entirely the same as that which would be expected from a process of diffusion. The value of a diffusion process depends upon the ratio between the concentration of the two solutions in contact, between which diffusion is taking place, and it can be greatly increased by diminishing the concentration of the weaker solution. Let us, therefore, reduce the concentration of the external solution of the nerve trunk to a minimum, the value of the diffusion process consequent upon rupture of the 'membranes' (which confine the internal solution) should be greatly enhanced, and with this there should also occur a great increase in the injury current.

Such a modification of the conditions of the nerve trunk is easily obtained by immersing it in water. For there is no reason to doubt that the primary effect of such an immersion is the extreme dilution of the external solution; although, as a later consequence, a dilution of the internal solution must also inevitably occur. This differential modification of external and internal solution is the usual result of immersion in solutions, and is a fact continually taken advantage of in the impregnation of tissue with dyes for purposes of histological research. In such researches the artifice of immersion is freely used to remove some impregnating solution from the external surface, and to leave it within the internal solutions of the cellular elements of the tissue. It is an occurrence, however, which does not require for its confirmation such evidence as this, if it be granted* that the limiting surfaces of cell, as shewn by the osmotic pressure exerted by the solutions in them during immersion in water, are barriers which limit the extent to which diffusion can take place through them. For it at once follows that it is easier to remove particles in solution outside the barrier, than those which are protected by such obstacles to their removal. Moreover, this differential modification by immersion in water is seen to be the converse of a modification of which no one will deny the actuality, namely, the easier access of an impregnating solution to the external solutions of the nerve than to the axis cylinders of its nerve fibres.

Granted that an immersion in water affects first the external solution, the modification in the injury current produced by such an artifice is of great interest. *Immersion in water always very sensibly increases the injury current of nerve.* The result of the experiment is entirely in agreement with the anticipation, which foresaw such a result following upon the dilution of the external solution ; and in so far as it is a confirmation of this, it may itself be used to strengthen the evidence in favour of the great importance of the core model structure of the nerve.

Nor is this the limit to the interest of the information which can be obtained from such experiments. There is no circumstance under which nerve shews an injury current, that the current is not increased by an immersion in water. But further, whereas nerve can be placed in, what is ordinarily considered, such a debilitated condition that it shews no injury current, it sometimes happens that even then an immersion in water will evoke from it an injury current as great as that which can be obtained by the same artifice from the most ' vigorous ' nerve. These latter conditions are, in fact, such as to justifiably provoke the following statement :—*Even when all the solutions in the nerve*, *external and internal*, *have been brought by processes of diffusion to a common level*, *then an immersion in water is of itself productive of such a new difference in concentration of the external and internal solution as to reproduce*, *and to reproduce to its full extent*, *the phenomenon of the injury current.* This statement is based, as will be seen, upon the examination of the injury current of degenerated nerve. Such a nerve removed from the body and provided with a new cross section may shew no injury current, and yet an immersion in water may reveal a current as great as that obtainable from a healthy nerve taken from the same animal and subjected to the same artifice.

In such a nerve there is reason to believe that the tubular limiting ' membranes ' are yet intact, their contents, on the other hand, are gravely altered. There is still, in such a nerve cell, substance limited by the neurilemma : although the cell substance

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* See Preliminary communication, *Proceedings Royal Society*. J. S. Macdonald, vol. lxvii, 315-320.

is not that of the nerve cell process, the myelin and the axis cyclinder being broken up and discontinuous. The usual explanation of the presence of a small injury current in such nerves is a 'vital' one, and in terms of the discontinuous fragments of the axis cylinder. On such lines, if it is possible to explain a small current, it is quite impossible to explain a phenomenon as great as that obtainable from the intact nerve.

The explanation which is offered now in the terms of the statement given above, is based upon the fact that the value of a diffusion process (or of a potential difference caused by one) is dependent upon the ratio between the two solutions, the same value being obtainable by the contact of several sets of solutions occupying different places in the range of possible concentrations.

If it were possible to obtain pure water free from disolved matter, the greatest possible difference between two solutions of approximately similar concentration would be between such pure water and a water in which there was only a slight trace of added electrolyte. The difference given by such a combination would be greater than that obtained by 'contrasting' impure water with any obtainable solution, for in the first case the ratio is infinitely great, its denominator being zero. Such a combination could, however, only exist for an infinitely short space of time, since contact with the impure water would rapidly soil its theoretically pure neighbour. Similarly, when there is any great difference such as this between the two solutions in contact, the difference is rapidly diminished by what we may term the soiling of the standard of comparison—the more dilute solution. Considerations such as this render a satisfactory explanation feasible for the practical impossibility of obtaining infinitely great differences of potential between solutions in contact.

In the extreme case when water is offered as the standard of comparison to any solution, the actual result obtained is always smaller by reason of this error, and the greater the concentration of the contrasted solution the greater the diminution due to the error.

Granted in the experiments quoted that the tubular membranes are intact or still serviceable. Granted, also, the small current found is to be explained as due to the existence of only a small difference between the internal and external solution. There is, then, every reason to conclude that it might be possible to obtain as great a current from such a nerve after an immersion in water as from a normal nerve. For in neither case, when the observation is taken, is the outer solution actually replaced and maintained as replaced by water; and the depreciation in the value of this standard of comparison (water) is likely to be greater when the internal solution is of considerable concentration.

It is worthy of note that, once granted the schematic structure which is claimed for the nerve, every difference between its internal and external solutions is liable to lead to an injury current, the direction and amount of which is determined by the difference. The only circumstance which can lead to the absence of an injury current is the temporary equality (in essential particulars) of the two solutions. The circumstances which determine a final disappearance of the phenomenon are:—

1. The destruction of the physical characteristics of the tubular membranes.
2. And the total removal of all electrolytes from both solutions by a prolonged washing of the nerve in water.

One other point is also worth attention. Some reason has been given for concluding that the internal solution of electrolytes is the more concentrated of the two. Granted the correctness of the view which is here taken as to the causation of the injury current, then these experiments with water are in confirmation of such an opinion. *The fact that an increased dilution of the external solution leads to an increase of the phenomenon may be taken as confirmative of the opinion that the phenomenon is due to the comparative dilution of the external solution.*

The measurements of resistance given in the following experiments were undertaken as indices of the extent to which the immersion in water succeeded in washing electrolytes from the nerve.

## EXPERIMENT (TAP WATER)

### Vagus Nerve of Dog

Piece of right vagus ten centimetres long. Removed immediately after death. The potential differences given were measured between the upper cross section and points upon the longitudinal surface.

Points (1) (2) (3), etc., refer in each case to a point on the longitudinal surface distant 1, 2, 3, etc., centimetres from the upper end of the nerve. Point (10), therefore, is the second cross section, and the difference between the two cross sections recorded under this heading is here as in the other experiments marked by an asterisk.

| | Potential Differences | | Average Values |
|---|---|---|---|
| Point (1) | ·00248 | ·00296 | 27·2 × $10^{-4}$ D. |
| ,, (2) | ·00300 | ·00328 | 31·4 |
| ,, (3) | ·00324 | ·00328 | 32·6 |
| ,, (4) | ·00348 | ·00328 | 33·8 |
| ,, (5) | ·00364 | ·00328 | 34·6 |
| ,, (6) | ·00364 | ·00328 | 34·6 |
| ,, (7) | ·00364 | ·00348 | 35·6 |
| ,, (8) | ·00360 | ·00336 | 34·8 |
| ,, (9) | ·00312 | ·00304 | 30·8 |
| ,, (10)* | ·00008 | ·00008 | *00·8 |

Points marked thus * are in each case the second cross section.

Below are given the resistances measured from the upper of the nerve to each point observed.

| | | | | |
|---|---|---|---|---|
| Point (1) | ... | 10,600 ohms | or | 10,600 ohms per centimetre |
| „ (2) | ... | 17,900 „ | | 8,950 „ „ |
| „ (3) | ... | 26,000 „ | | 8,660 „ „ |
| „ (4) | ... | 33,100 „ | | 8,520 „ „ |
| „ (5) | ... | 41,500 „ | | 8,300 „ „ |
| „ (6) | ... | 50,700 „ | | 8,450 „ „ |
| „ (7) | ... | 59,600 „ | | 8,510 „ „ |
| „ (8) | ... | 69,100 „ | | 8,640 „ „ |
| „ (9) | ... | 78,700 „ | | 8,700 „ „ |
| „ (10)* | ... | 82,200 „ | | 8,200 „ „ |

The nerve was now removed from the moist chamber and placed in a large quantity (2 litres) of *tap water, in which it was immersed for ten minutes.* At the end of this time the nerve was removed, dried in filter paper and replaced in position in the moist chamber. A re-examination was then made of the potential differences between the upper cross section and points upon the longitudinal surface.

| Potential Differences | | | Average Values |
|---|---|---|---|
| Point (1) | ·00673 | ·00568 | $62{\cdot}0 \times 10^{-4}$ D. |
| „ (2) | ·00766 | ·00673 | 71·9 |
| „ (3) | ·00935 | ·00800 | 86·7 |
| „ (4) | ·01030 | ·00937 | 98·3 |
| „ (5) | ·01214 | ·01096 | 115·5 |
| „ (6) | ·01307 | ·01214 | 126·0 |
| „ (7) | ·01650 | ·01500 | 157·5 |
| „ (8) | ·01404 | ·01325 | 136·4 |
| „ (9) | ·00713 | ·00739 | 72·6 |
| „ (10)* | 0 | 0 | 0 |

Points marked thus * are in each case the second cross section.

The potential differences between the same points and the other cross section were next determined.

| Potential Differences | | | | | Average Values |
|---|---|---|---|---|---|
| Point (1) | ·00568 | | | ·00436 | $50{\cdot}2 \times 10^{-4}$ D. |
| „ (2) | ·00634 | | | ·00528 | 58·1 |
| „ (3) | ·00726 | | | ·00634 | 68·0 |
| „ (4) | ·00837 | | ↑ | ·00726 | 78·1 |
| „ (5) | ·00924 | | | ·00800 | 86·2 |
| „ (6) | ·00977 | ↓ | | ·00919 | 94·8 |
| „ (7) | ·01135 | | | ·01096 | 111·5 |
| „ (8) | ·01016 | | | ·00977 | 99·6 |
| „ (9) | ·00488 | | | ·00488 | 48·8 |

Finally, the resistances between each point and the upper cross section were again taken to determine the alteration produced in them by immersion in water.

| From Upper Cross Section to | Resistance | |
|---|---|---|
| | In ohms | In ohms per centimetre |
| Point (1) | 13,500 | 13,500 |
| „ (2) | 30,000 | 15,000 |
| „ (3) | 39,300 | 13,100 |
| „ (4) | 51,700 | 12,950 |
| „ (5) | 61,700 | 12,340 |
| „ (6) | 92,400 | 15,400 |
| „ (7) | 99,700 | 14,240 |
| „ (8) | 109,000 | 13,620 |
| „ (9) | 120,000 | 13,300 |
| „ (10)* | 110,300 | 11,600 |

Points marked thus * are in each case the second cross section.

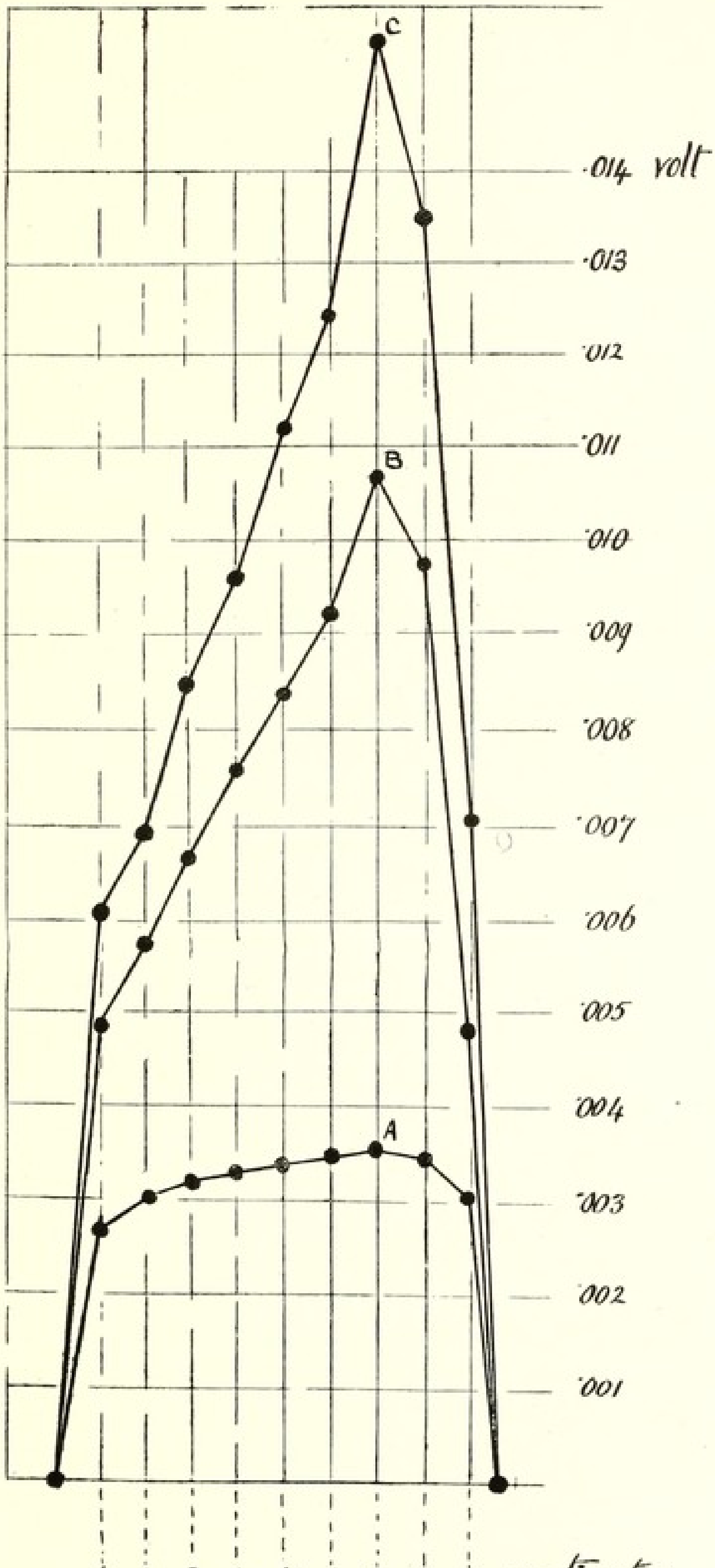

Fig. W

### Experiment (Tap Water)

(Fig. W)

A is the curve of distribution of potential upon the nerve when removed from the body. It will be seen that, in all essential details, it is similar to the curves given in the preceding section upon the 'current of injury.'

C is the curve of distribution of potential after the immersion of the nerve in tap water (p. 277). The point of reference was in this case, the upper cross section.

B is the similar curve obtained later (it is, therefore, lower). The point of reference in this case was the lower cross section (p. 278).

Attention is drawn to the position of the maximum point in each of the three curves A, B, C.

In this experiment the resistance of the nerves is increased from 82,200 ohms to 110,300 ohms by the immersion in water, an increase which can immediately be assigned to the removal of electrolytes from the nerve. There is also an indication in the data that the superficial resistance is more affected than the 'longitudinal resistance,' and, therefore, some confirmation of the otherwise amply justified belief that the electrolytes removed from the nerve come largely from the surface solutions.

Support for this last statement is found in the measured resistance of points (9) and (10). In the measurements of the resistance after immersion the paradoxical result is obtained that the resistance of 10 centimetres of nerve is 110,300 ohms, whereas the resistance of 9 centimetres of nerve is 120,000 ohms.

The resistance of the 10 centimetres is, on consideration, obviously less, because taken from cross section to cross section and not through the transverse resistance, whereas the 9 centimetre resistance includes some of this transverse resistance. In this case, also, the transverse resistance must be relatively much greater than before; since in the resistance measurement taken before immersion the influence of the same factor can be detected, but not present in sufficient force to produce the same paradoxical result.

Attending this loss of electrolytes, inferred to be mainly from the 'outer solution,' there is a great increase in the potential difference between longitudinal surface and cross section.

**(Before, 35·6. After, 160·0)**

**an increase of more than four times the original value.**

The curves of distribution of potential taken are of interest, in so far as they are typically asymmetrical. The curve taken after immersion in water is very obviously so, and the repetition of the curve taken from the second cross section, which was undertaken to prove that the asymmetry was not the artificial product of the order in which the observations were taken, is an ample confirmation of this.

If the curve taken before immersion is examined it will be seen that the asymmetry was already present before the immersion in tap water, that the maximum of the curve in fact remains in a position unaltered by the modification.

It is worthy also of incidental notice that at the time when the asymmetry was most marked, after the immersion, there was no potential difference between the two cross sections to account for it; that also the repetition of the same curve by a subsequent examination taken from the second cross section as reference point leaves no possibility of considering the asymmetrical form of the curve as the outcome of the mode of observation; that the measurements of resistance do not reveal any variation in the calibre or in the specific resistance of the nerve in different portions of its length which could make 3 centimetres of the nerve on one side of the maximum point equivalent to 7 centimetres upon the other; and finally that a consideration of the form of the curve leaves little room for the suggestion that its irregular form is due to the presence of accessory local injuries.

It may, from the experience of many similar experiments, be definitely said that the results of this experiment, whatever be the assumption to test which it was made, or whatever the explanation offered, conclusively demonstrates an experimental fact capable of constant repetition, namely, that a short immersion in water leads to a great increase in the value of the potential difference between longitudinal surface and cross section of the nerve, and even, since the resistance is not proportionately increased, to a great increase in the injury current.

Nor is this effect of an immersion in water confined to an effect upon nerve in any particular condition, for it is capable of being repeated upon nerves with very different previous histories. One condition, however, in which it is unattainable is worthy of especial attention, a long continued previous immersion in water, for in this case there can be no question of the meaning of the exception. *When the electrolytes in solution are all removed by processes of diffusion there can occur no further electrical phenomena.*

The following are briefly recorded further examples of this effect of an immersion in water :—

### (1) A Nerve Freshly Removed

| | | |
|---|---|---|
| Sciatic nerve of cat on removal ... ... ... | ·024 | Daniell. |
| After 10 minutes in tap water ... ... ... | ·053 | „ |

### (2) A Stale Nerve with Diminished Current

| | | |
|---|---|---|
| Phrenic nerve of dog on removal ... ... | ·0060 | Daniell. |
| After 3 hours in the moist chamber ... ... | ·0008 | „ |
| After 10 minutes in tap water ... ... ... | ·0101 | „ |

### (3) A Nerve which has been placed in Strong Salt Solutions

| | | |
|---|---|---|
| Sciatic nerve of cat on removal ... ... ... | ·0152 | Daniell. |
| After 1 hour 40 minutes in 9% NaCl ... ... | ·0010 | „ |
| After 45 minutes in tap water ... ... ... | ·0224 | „ |

### (4) Nerves which have Remained Long in the Body of a Dead Animal

| | | |
|---|---|---|
| (*a*) Sciatic nerve of dog removed 24 hours after death ... | ·0001 | Daniell. |
| After 10 minutes in tap water ... ... ... | ·0040 | „ |

(*b*) Dog dead 3 days and 2 hours, during two days of which the body was placed in a refrigerator, and then for 24 hours was allowed to lie in a warm room (August).

| | | |
|---|---|---|
| Sciatic nerve on removal ... ... ... | ·001 | Daniell. |
| After 5 minutes in tap water ... ... ... | ·003 | „ |

A short immersion was chosen under these circumstances, for it has been found that a long immersion in such a case results in a reversal of the injury current, a matter which will be further treated later.

## (4) NERVES WHICH HAVE REMAINED LONG IN THE BODY OF A DEAD ANIMAL—*continued*

(*c*) Cat dead 7 days. Placed in the refrigerator during the whole of this period, except the first 4 hours.

Sciatic nerve on removal ... ... ... ·003 Daniell.
After 10 minutes in tap water ... ... ... ·008 „

## (5) DEGENERATED NERVE

The two following experiments are recorded in some detail, since the results obtained in them are of an obvious interest. The main facts have been previously recorded* and are here quoted, the details being given in an appendix.

### (*a*) VAGUS NERVE OF DOG

*Preliminary operation.* 1 centimetre of nerve excised at upper, and 1 centimetre at lower limit of nerve in the neck.

*Examination nine days afterwards.* The animal was killed and the degenerated nerve immediately removed ... ... ... ·000 Daniell
After 25 minutes in tap water ... ... ·020 „

### (*b*) SCIATIC NERVE OF DOG

*Preliminary operation.* 1 centimetre of nerve excised.

*Examination twelve days afterwards.* The animal was killed and the degenerated nerve immediately removed ... ... ... ·003 Daniell
After 40 minutes in tap water ... ... ·023 „

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[*] See Preliminary communication, *Proceedings Royal Society, loc. cit.*

# APPENDIX

## EXPERIMENTS UPON DEGENERATED NERVE

### Experiment I

### Vagus Nerve of Dog

Professor Sherrington most kindly performed the preliminary section of the nerve, thereby placing the completeness and reality of the operation beyond dispute.

Two pieces, each about 1 centimetre in length, were removed from the left vagus nerve of this animal. One at the extreme upper limit of the nerve in the neck, and one at the extreme lower limit.

On the ninth day (ten inclusive of the day of operation) the piece of nerve which extended between the sites of the operation was removed.

From this piece the upper centimetre was excised, so as to present a new cross section distant 1 centimetre from the site of operation.

### Degenerated Vagus Nerve

Potential difference between points on the longitudinal surface (normally +) and the cross section

Point (1)* o
,, (2) positive. A deflection observed current too small to compensate, and, therefore, less than the unit of compensation (·00008 Daniell).
,, (3) ,, ,, ,, ,,
,, (4) ,, ,, ,, ,,
,, (5) ,, ,, ,, ,,
,, (6) ,, ,, ,, ,,
,, (7) ,, ,, ,, ,,
,, (8) The second cross section was negative. The deflection observed, but current again too small to compensate.

A fresh section was now made at point (6), the subsequent examination revealed the same small difference between this point and the longitudinal surface as for the original cross section.

*Resistance* of piece 6 centimetres long measured = 30,100 ohms or 5,000 per centimetre. A fresh section was now made at point (5), subsequent examination revealed a similar state of things as before.

**The nerve, 5 centimetres long, was now placed in tap water and left in this for 25 minutes,** at the end of which time it was removed and dried in filter paper. Upon removal its altered appearance was noted. It was swollen and shorter, length 4·7 centimetres. It was rigid but pulpy in appearance, unlike the clean rigidity of a normal nerve after immersion in water.

*Resistance* measured was 51,400 ohms or 10,280 ohms per centimetre. *Potential differences* between longitudinal surface and upper cross section, and subsequently to lower cross section.

| | | Daniell | | Daniell |
|---|---|---|---|---|
| Point (1) | positive to upper section ... | ·017424 | to lower section ... | ·012936 |
| ,, (2) | ,, ,, ... | ·020064 | ,, ... | ·012936 |
| ,, (3) | ,, ,, ... | ·015312 | ,, ... | ·012012 |
| ,, (4) | ,, ,, ... | ·010296 | ,, ... | ·007920 |
| The lower cross section (5) | o | | | |

---

* Point (1) as usual means point distant one centimetre.

### A Piece of the Right, intact, Vagus was now Removed, in length 8 centimetres

The potential differences between points upon the longitudinal surface and the two cross sections were measured.

| | | | Daniell | | | Daniell |
|---|---|---|---|---|---|---|
| Point (1) | positive to upper section | ... | ·000264 | to lower section | ... | ·002376 |
| „ (2) | „ „ | ... | ·001320 | „ | ... | ·004092 |
| „ (3) | „ „ | ... | ·001320 | „ | ... | ·004092 |
| „ (4) | „ „ | ... | ·002376 | „ | ... | ·005016 |
| „ (5) | „ „ | ... | **·003036** | „ | ... | **·005808** |
| „ (6) | „ „ | ... | ·002640 | „ | ... | ·005280 |
| „ (7) | „ „ | ... | ·002376 | „ | ... | ·004356 |

„ (8) the lower cross section negative to upper ·000792 Daniell.

A new cross section was now made at point (6). The potential difference between longitudinal surface and this (maximum) was ·007392 Daniell.

The resistance of nerve 6 centimetres long 69,300 ohms, or **11,550** per centimetre.

The lower centimetre was now excised, leaving the nerve 5 centimetres long.

*This piece of nerve was then immersed in tap water* and left in this for twenty-five minutes. Upon removal the nerve was slightly rigid, shortened to 4·7 centimetres, but did not appear swollen or pulpy.

The resistance was 96,300 ohms or **19,260** per centimetre.

The potential differences measured—

| | | | Daniell | | | Daniell |
|---|---|---|---|---|---|---|
| Point (1) | positive to upper section | ... | ·013068 | to lower section | ... | ·014114 |
| „ (2) | „ „ | ... | ·014520 | „ | ... | ·015182 |
| „ (3) | „ „ | ... | ·015048 | „ | ... | **·015182** |
| „ (4) | „ „ | ... | **·016632** | „ | ... | ·014256 |

„ (5) the lower cross section negative to the upper ·002904 Daniell.

The examination of the second nerve was as the observations recorded shew, a repetition of the procedure of the examination of the first.

## Experiment B

### Sciatic Nerve of Dog. Bk. II, 102

On Thursday, July 26, 1900, Professor Sherrington performed the preliminary operation upon this dog.

A piece 1 centimetre long (about) was removed from the extreme upper end of the right sciatic nerve trunk. The wound healed subsequently in the usual manner with no accident. On Tuesday, August 7, 1900, the dog was killed, that is on the twelfth of the days succeeding the day of the operation. The right sciatic nerve was removed, 4 centimetres being cut off below the operation section and thrown away, and a piece 5 centimetres being taken from below this for the purposes of the experiment.

(In all the succeeding statements of the potential differences, point (1), point (2), etc., means a point on the longitudinal surface distant 1 centimetre, 2 centimetres, etc., from the upper cross section).

(*a*) The resistance of piece of 5 centimetres was 14,800 ohms, or **2,960** per centimetre. The potential differences between points on the longitudinal surface and the upper cross section were—

| | | | |
|---|---|---|---|
| | Point (1) | + **·000264** | Daniell |
| | ,, (2) | + ·000264 | |
| | ,, (3) | + ·000132 | |
| | ,, (4) | + ·000132 | |
| Other cross section | ,, (5)* | + 0 | |

The differences were therefore normal in direction, but small.

(*b*) **The nerve now (ten minutes after its removal) was placed in tap water, and left in this for twenty minutes.** Upon removal it was dried in filter paper. It was now slightly rigid, and measured 5 centimetres. Its resistance was 20,200 ohms, or **4,040** ohms per centimetre.

| | | | | | |
|---|---|---|---|---|---|
| | Point (1) | + ·002772 | volt | potential differences | to upper cross section. |
| | ,, (2) | + ·003960 | ,, | ,, | ,, |
| | ,, (3) | + ·007128 | ,, | ,, | ,, |
| | ,, (4) | + **·008712** | ,, | ,, | ,, |
| Other cross section | ,, (5)* | + ·000132 | ,, | ,, | ,, |

(*c*) *The nerve was now replaced in tap water, and left for a further twenty minutes in this.* The results of this, as of similar successive repetitions of the same manoeuvre, are given in the following table :—

(*d*), (*e*), (*f*), (*g*), (*h*), (*i*) in the table, represent repetitions of the same manoeuvre, and the subsequent observations made.

After this, that is to say, four hours after the death of the dog, the nerve was placed in tap water, and examined after being in it twenty-four hours ; the nerve was still tense, rigid, and swollen, and provided a demarcation current in the normal direction, as in the table line (*j*).

A similar observation was made the next day (*k*), the nerve having been now forty-eight hours in tap water—it was still rigid.

## THE INTACT NERVE OF THE OTHER SIDE OF THE SAME ANIMAL

The left sciatic nerve was excised immediately after the first examination of the degenerated nerve was completed, and whilst the degenerated nerve lay in its first bath of tap water. This nerve was examined and then treated exactly in the same manner as the degenerated nerve was treated, the observations upon this nerve alternating with those upon the other, and so also the immersions in tap water. The main facts of this examination are given on following page.

---

Points marked thus * are in each case the second cross section

| Immersion of Nerve in tap water | Length | Resistance | | Maximum Potential Difference found |
|---|---|---|---|---|
| | | In ohms | In ohms per centimetre | |
| (*a*) Nerve at once ... ... | 5 | 15,900 | 3,180 | ·0182 |
| (*b*) After 20 min. in tap water ... | 5 | 20,400 | 4,080 | ·0267 |
| (*c*) Another 20 min. in tap water | 5·2 | 23,100 | 4,440 | ·0269 |
| (*d*) „ „ „ ... | 5·2 | 28,800 | 5,540 | ·0175 |
| (*e*) „ „ „ ... | 5·2 | 39,800 | 7,650 | ·0151 |
| (*f*) „ „ „ ... | 5·2 | 51,100 | 9,830 | ·0129 |
| (*g*) „ „ „ ... | 5·2 | 54,900 | 10,540 | ·0166 |
| (*h*) „ „ „ ... | 5·2 | 61,000 | 11,730 | ·0130 |
| (*i*) „ „ „ ... | 5·2 | 88,700 | 17,060 | ·0174 |
| The nerve was now placed in tap water for 24 hours, at the end of which time it was removed rigid, but not swollen, like the nerve of other side. | | | | |
| (*j*) After 24 min. in tap water | — | 307,500 | 60,000 | ·0045 |

Contrast these observations with the similar observations made upon the first nerve, the degenerated nerve. These are found in full detail in the table upon the next page.

## EXPERIMENT B

### DEGENERATED NERVE (SCIATIC OF DOG)

| Examination of nerve upon removal and after immersion in tap water | Length in centimetres | RESISTANCE | | POTENTIAL DIFFERENCES OF POINTS | | | | |
|---|---|---|---|---|---|---|---|---|
| | | In ohms | In ohms per centimetre | On longitudinal surface to the upper cross section (all points positive as in normal nerve) | | | | Lower cross section to upper cross section |
| | | | | Point (1) | Point (2) | Point (3) | Point (4) | Point (5) |
| (*a*) Nerve examined at once upon removal ... ... ... | 5 | 14,800 | 2,960 | ·0003 | ·0003 | ·0001 | ·0001 | 0 |
| (*b*) After having been placed for 20 min. in tap water ... ... | 5 | 20,200 | 4,040 | ·0028 | ·0040 | ·0071 | ·0087 | —·0001 |
| (*c*) Another 20 min. in tap water ... | 5·2 | 23,600 | 4,540 | ·0166 | ·0231 | ·0174 | ·0230 | —·0031 |
| (*d*) After another 20 min. in tap water | 5·2 | 30,500 | 5,860 | ·0220 | ·0256 | ·0195 | ·0238 | —·0001 |
| (*e*) " " " ... | 5·2 | 35,300 | 6,790 | ·0209 | ·0256 | ·0209 | ·0227 | —·0001 |
| (*f*) " " " ... | 5·2 | 34,700 | 6,670 | ·0211 | ·0259 | ·0177 | ·0186 | —·0001 |
| (*g*) " " " ... | 5·2 | 45,800 | 8,800 | ·0132 | ·0221 | ·0127 | ·0157 | —·0026 |
| (*h*) " " " ... | 5·2 | 54,100 | 10,400 | ·0100 | ·0207 | ·0124 | ·0153 | —·0037 |
| (*i*) " " " ... | 5·2 | 59,600 | 11,460 | ·0091 | ·0178 | ·0107 | ·0116 | —·0018 |
| The nerve was now placed in tap water, left in this all night, and | | | | | | | | |
| (*j*) Examined after 24 hours in tap water ... ... ... | 5·1 | 192,500 | 37,740 | ·0001 | ·0046 | ·0055 | ·0055 | +·0039 |
| Again left all night in tap water, and | | | | | | | | |
| (*k*) Examined after 48 hours in tap water ... ... ... | 5·1 | 442,500 | 86,760 | 0 | ·0005 | ·0003 | ·0003 | ·+0002 |

## THE ACTION OF SOLUTIONS OF ELECTROLYTES

### Preliminary Experiments Deciding the Choice of a Convenient Duration and Temperature for Immersion of the Nerve

Three statements previously made are here repeated :—

(1) That the 'core model' structure of nerve is a fact and demands at least the presence of—

(*a*) An external solution,
(*b*) A diffusion obstacle,
(*c*) An internal solution.

(2) That probably the internal solution is the more concentrated of the two, that at least the two are certainly different.

(3) That the injury current is the inevitable outcome of such a set of conditions.

These three statements are repeated because, with them in view, it is possible to intelligently follow all the modifications produced in the value of the injury current of nerve by the action of solutions of electrolytes. Thus granted that the value of this current (more strictly of the P.D.) depends upon the ratio existing between the concentrations of the two solutions, it at once follows that a replacement of the outer solution by a still more dilute solution should increase this value, and that replacement by a more concentrated solution should diminish it. It will be seen that this apparently antagonistic action between more dilute and more concentrated solutions has been found in the case of solutions of several electrolytes, it may be said in every such case in which it has been sought.

There is, in fact, however, no real antagonism between the action of dilute and concentrated solutions of electrolytes. There is an apparent antagonism, because an arbitrary standard is chosen for comparison, namely, the concentration of the external solution already present upon the nerve when removed from the body. All appearance of paradoxical action is at once removed by the acceptance of water as a zero of concentration.

The action of water was studied in the last section ; it is now our intention to study this action diminished by the addition of electrolytes to the water used, and it will be seen that the diminution increases with the quantity of electrolytes which is added.

Before doing so, however, it is necessary to examine the limits within which such a study can be pursued, limits which have already made their appearance as modifying the action of water. The first and most important of which is that set by the nature of the diffusion obstacle separating the external and internal solution.

It is not claimed for this 'membrane' that it is an absolute barrier to processes of diffusion between the two solutions. Such a claim would place it in a unique position amongst all the other limiting cell surfaces of the body as a strictly defined 'semi-permeable membrane;' would place it in fact, if logically maintained, in a unique position amongst the membranes studied by the physicists and called by them 'semi-permeable.' This membrane was called into theoretical being by necessities which arose in explanation of the polarization phenomena, and, once postulated, its existence was found, from general analogy and from other circumstances, to be not only not contra-indicated but even to be confirmed. Even if it be admitted, and it is not, that the necessities of the polarization phenomena form, after this subsequent examination, its only claim for existence ; still, it must be granted that these necessities are far from demanding a strictly semi-permeable membrane. All that is required by them is that the membrane shall be a 'partial' barrier to the movement of dissolved electrolytes, and shall so give rise to the accumulation of charged particles on its surfaces, particles left behind by their fellows which have successfully traversed it, and so conducted the electrical current. In short, neither theoretical necessity nor the teachings of physiological analogy point to the presence of anything but an imperfect obstacle to processes of diffusion between the solutions of the nerve.

Granted that this is so, and that as observed in the action of water (see page 275) the effect of immersing a nerve in a given solution is not merely to replace with this the external solution of the nerve, but also by penetration of the diffusion obstacle to modify the internal solution ; then here certainly we have a reason for accepting the formerly rejected standard of concentration, namely, that of the 'isotonic solution,' which is removed with the nerve from the body.

Granted that an immersion affects both the solutions of the nerve, then immersion in a dilute solution

(1) dilutes the external solution and so increases the injury current,

(2) dilutes the internal solution and so diminishes the injury current ;

whereas immersion in a concentrated solution

(1) concentrates the external solution and so diminishes the injury current,

(2) concentrates the internal solution and so increases the injury current.

It is fortunate that the second effect must in both cases be completed later than the first, and that so an opportunity is left for the study of the first : even if it is not as perfect as a physicist, with the advantages of determining his own conditions, would choose for the examination of the differences of potential caused by diffusion into contrasted solutions. To make the most of the opportunity it is necessary to accept the indication of preliminary experiments in choosing the duration of time most suitable for the immersion of the nerve in the solutions used. The shorter the time the less will be the undesired modification of the internal solution of the nerve. It is thus necessary to fix a time not too short for the best replacement attainable of the outer solution, and yet as short as possible so as to ward off this antagonistic modification.

## EXPERIMENT I

### Sciatic Nerve of Cat

A piece of Nerve 5 centimetres long

| | |
|---|---|
| Value of injury 'current' upon removal ... | $15 \times 10^{-3}$ Daniell |
| After an immersion of 1 hour and 40 minutes in 9 per cent. NaCl solution ... ... | 1 ,, ,, |
| After a subsequent immersion of 15 minutes in tap water ... ... ... | 11 ,, ,, |
| *After a further immersion of* 30 *minutes in tap water* (45 *minutes in all*) ... ... ... | 22 ,, ,, |

The solution of NaCl used was maintained at 17° C. After each immersion the nerve was dried in filter paper. The nerve was examined several times during its prolonged immersion in the concentrated NaCl solution, after the first twenty-five minutes, a second twenty-five minutes, a third twenty-five minutes, and then ten minutes; on each occasion the value of the injury potential difference (longitudinal surface to upper cross section) was found equal to ·001 Daniell.

## EXPERIMENT II

### Sciatic Nerve of Cat

A piece of Nerve 5 centimetres long

| | |
|---|---|
| Value of injury 'current' upon removal ... | $17 \times 10^{-3}$ Daniell |
| After 5 minutes in ·45 per cent. NaCl solution | 24 ,, ,, |
| After 45 minutes (in all) in ·45 ,, ,, | 3 ,, ,, |
| *After a subsequent immersion of* 20 *minutes in tap water* ... ... ... ... | 0 ,, ,, |

The data from these experiments give point to the remarks just made. One of these experiments shews the effect of immersion in a concentrated solution ten times the strength of the isotonic solution; the other the effect of immersion in a dilute solution one-half the strength of the isotonic solution.

In both cases, prolonged immersion in the solution has reduced the original value of the potential difference down to a small fraction. The reduction in the case of the nerve immersed in the dilute solution is irreparable by the subsequent immersion of the nerve in water. On the other hand, an immersion in water succeeds in bringing back to and beyond its original value the potential difference from the nerve which has been lying in the highly-concentrated solution.

The inference to be drawn from such facts seems an obvious one. The 'internal solution' of the nerve which had been immersed in the concentrated solution had become more concentrated, that of the nerve which had been immersed in the dilute solution had become more dilute; the distinction between their final states is revealed by a subsequent extreme dilution of their 'external solutions' (action of tap water) and subsequent testing.

## EXPERIMENT III

### Sciatic Nerve of Cat

A piece of Nerve 5 centimetres long

| | | | |
|---|---|---|---|
| Nerve immediately after removal ... ... | 17·0 | × $10^{-3}$ | Daniell |
| After 25 minutes in 1·8 per cent. NaCl solution ... | 6·6 | „ | „ |
| After a further 30 minutes in 1·8 per cent. NaCl solution | 3·6 | „ | „ |
| After a further 15 minutes „ „ „ | 2·9 | „ | „ |
| After a further 15 minutes „ „ „ | 2·6 | „ | „ |
| After a further 15 minutes „ „ „ | 2·6 | „ | „ |

## EXPERIMENT IV

### Sciatic Nerve of Cat

A piece of Nerve 5 centimetres long

| | | | |
|---|---|---|---|
| Nerve immediately after removal ... ... | 14·8 | × $10^{-3}$ | Daniell |
| After 25 minutes in ·9 per cent. NaCl solution ... | 11·6 | „ | „ |
| After a further 25 minutes in ·9 per cent. NaCl solution | 9·6 | „ | „ |
| After a further 25 minutes „ „ „ | 6·9 | „ | „ |
| After a further 25 minutes „ „ „ | 6·5 | „ | „ |

## EXPERIMENT V

### Sciatic Nerve of Cat

A piece of Nerve 5 centimetres long

| | | | |
|---|---|---|---|
| Nerve immediately after removal ... ... | 13·5 | × $10^{-3}$ | Daniell |
| After 25 minutes in ·6 per cent. NaCl solution ... | 14·8 | „ | „ |
| After a further 25 minutes in ·6 per cent. NaCl solution | 14·5 | „ | „ |
| After a further 25 minutes „ „ „ | 8·6 | „ | „ |
| After a further 25 minutes „ „ „ | 5·0 | „ | „ |
| After a further 25 minutes „ „ „ | 1·6 | „ | „ |

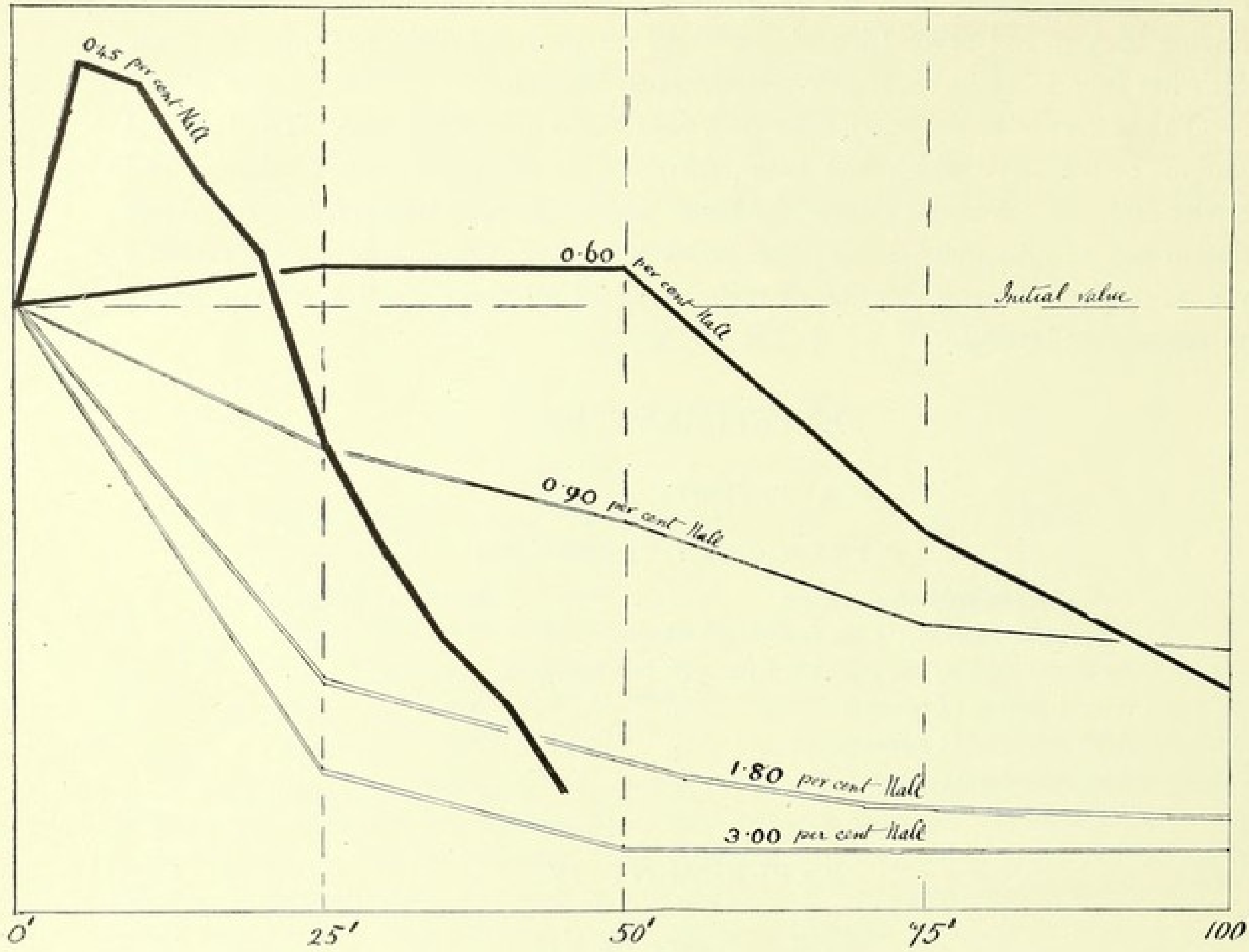

Fig. A

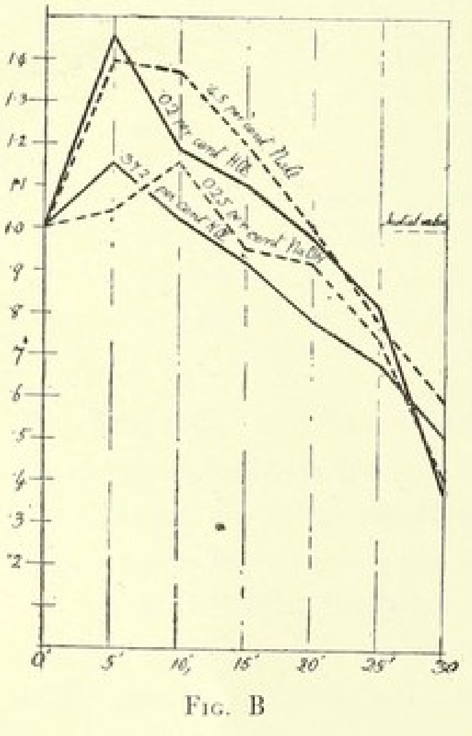

Fig. B

Fig. A includes curves drawn from Experiments IIa, III, IV, and V.

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Fig. B includes curves drawn from Experiments IIa, VI, VII, and VIII.

In these experiments all the solutions used were dilute. The curves represent the action of dilute solutions of different electrolytes. In the previous figure, A, the curves represent the action of the same electrolyte at different concentrations.

The curves in figure A have been obtained in the following manner. In each experiment the original potential difference determined immediately after removal of the nerve from the body is treated as unity, and all the modifications obtained by the effect of immersion in the solution are expressed in terms of this.

Thus taking the data from the three experiments—

| Experiment III | | Experiment IV | | Experiment V | |
|---|---|---|---|---|---|
| 1·8 % NaCl | | ·9 % NaCl | | ·6 % NaCl | |
| Original | 1·000 | Original | 1·000 | Original | 1·000 |
| In 25 min. | 0.388 | In 25 min. | 0·786 | In 25 min. | 1·060 |
| In 55 ,, | 0·211 | In 50 ,, | 0·643 | In 50 ,, | 1·059 |
| In 70 ,, | 0·170 | In 75 ,, | 0·482 | In 75 ,, | 0·635 |
| In 85 ,, | 0·153 | In 100 ,, | 0·429 | In 100 ,, | 0·365 |
| In 100 ,, | 0·153 | | | In 125 ,, | 0·115 |

The curves serve to shew the orderly fashion in which solutions of different concentration modify the injury current, or a better form of statement, perhaps, modify the decline of the injury current. The more concentrated the solution, the more rapid and complete the apparent decline ; the more dilute the less rapid, so that the most dilute solutions temporarily enhance the value of the injury current.

As will be seen from the curves, this statement is unexceptionable when the early portion of the curves is considered. In this portion it is realized that the concentration limits—of pure water on one side and saturated solution on the other—are associated with the extremes of effect produced, increase of the injury currrent on one side and elimination on the other. Between the limits of concentration the effect is dependent upon the concentration, the graduated effect being only adequately described by taking the effect of one of these limits of concentration—pure water—as the maximum, and describing the remainder as the effects of solutions more concentrated than this.

It is only when the later portions of the curves is considered that the isotonic solution demands attention as the solution in which the injury current normally declines ; separating more concentrated solutions which continue to follow the course described throughout the whole time of the experiment from less concentrated solutions, which adopt a new and paradoxical course.

The later action of these less concentrated solutions is quite characteristic, and in direct opposition to their earlier effects. For they are seen secondarily to cause a more rapid and more complete decline of the injury current the less their concentration. This later decline is advisedly called 'more complete' since the previous experiments have shewn it to be irreparable, and quite unlike the decline observed after immersion in more concentrated solutions, which can be recovered from by a subsequent immersion in water.

Such a comparison of the effects of solutions of different concentrations is also fully justified by an examination of the numerical values.

Let us, as a test of this statement, assume that during the first twenty-five minutes of immersion the 'internal solution' of the nerve is not greatly modified, then the modifications in the value of the potential difference should be comparatively simple, and should, crudely, vary inversely with the concentration of the solution used to replace the external solution.

$$\text{Experiment III— } \cdot 388 = \frac{x}{1 \cdot 8} \qquad \therefore x = \cdot 6984$$

$$\text{Experiment IV— } \cdot 786 = \frac{x}{\cdot 9} \qquad \therefore x = \cdot 7074$$

$$\text{Experiment V—} 1 \cdot 060 = \frac{x}{\cdot 6} \qquad \therefore x = \cdot 6360$$

The value x obtained upon the assumption that the values vary inversely with the concentration of the experimental solution made use of, are seen to be approximately similar enough to justify the assumption within these limits of concentration. It is even possible to extend these limits widely, and still the facts remain fairly closely within the limits of this relation.

Thus, from experiments performed, including those given above, the following table was constructed and published in a preliminary communication* :—

| Strength of Experimental Solution of NaCl | Value of x as calculated above |
|---|---|
| 0·6 grammes per cent. ... ... | ·6360 |
| 0·75 ,, ,, ... ... | ·6908 |
| 0·9 ,, ,, ... ... | ·7074 |
| 1·8 ,, ,, ... ... | ·6984 |
| 3·0 ,, ,, ... ... | ·7110 |
| 6·0 ,, ,, ... ... | ·6420 |
| 9·0 ,, ,, ... ... | ·5580 |

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* *Proceedings Royal Society*, 67, 321

The limits within which the relation is most true is seen to be from ·75 per cent. to 3·0 per cent., within which it may be said that the relation is actually that here stated. But when solutions are used much below the strength of the isotonic solution, the limit of even approximate truth is rapidly reached and passed. The reason, or certainly one of the reasons, of this fact is not far to seek, and is clearly brought out by the details of the following experiment, and by the curve drawn from them and placed in the diagram given (·45 per cent. curve) :—

## EXPERIMENT IIA

### (AN EXPANSION OF THE DETAILS OF EXPERIMENT II)

| | POTENTIAL DIFFERENCES | |
|---|---|---|
| | $\times 10^{-3}$ Daniell | In terms of the original as unity |
| Upon removal ... ... ... ... | 17·1 | 1·00 |
| (5) After 5 min. in ·45 NaCl ... ... | 24·0 | 1·40 |
| (10) Another 5 min. in ·45 NaCl ... ... | 23·9 | 1·37 |
| (15) ,, ,, ,, ... ... | 20·6 | 1·20 |
| (20) ,, ,, ,, ... ... | 18·7 | 1·09 |
| (25) ,, ,, ,, ... ... | 13·6 | 0·79 |
| (30) ,, ,, ,, ... ... | 10·3 | 0·60 |
| (35) ,, ,, ,, ... ... | 7·9 | 0·46 |
| (40) ,, ,, ,, ... ... | 6·1 | 0·35 |
| (45) ,, ,, ,, ... ... | 3·4 | 0·20 |

In this case the value of the potential difference after 25 minutes in the solution is 0·79.

$$\cdot 79 = \frac{x}{\cdot 45} \quad \dots \quad x = \cdot 35$$

The value of x is just half of that which would be found if the value of the potential difference varied inversely with the concentration of the solution. Nor is there, as yet, any reason to modify the statement of this temporarily assumed relationship; for one fact, and an unavoidable fact, spoils the value of the experiment from this point of view. The theoretical value required by the relation, 1·50, was almost attained in the experiment, but this was in the first five minutes, when the value rose to 1·40. After this the value has steadily fallen until in forty minutes it has reached a value as low as that reached by the nerve in Experiment V (·6 per cent. NaCl) in a time four times as great.

*Immersion in a dilute solution increases the value of the 'injury current' as long as the immersion leaves the concentration of the 'internal solution' of the nerve fairly intact: but prolonged immersion rapidly dilutes this internal solution and diminishes the value of the injury current, and the more dilute the experimental solution, the more rapid and the more final is this diminution.*

Such considerations as these may serve to justify the course adopted in the experiments of the next section, for the results of which a real quantitative value is claimed. In these experiments the time of immersion adopted is of five minutes duration, and no attention is paid to modifications produced by a more prolonged immersion than this.

Since in this section alone the effects of prolonged immersion are studied, it seems better to include here a few experiments which completely shew the similarity in action upon the injury current of dilute solutions of the following electrolytes :—

Sodium chloride. (Already given in Experiment IIA).
Caustic soda.
Hydrochloric acid.
Potassium chloride.

## EXPERIMENT VI

### SCIATIC NERVE OF CAT

Piece of Nerve 5 centimetres long. Experimental solution used ·372 grammes per cent. KCl.

| | | Potential Differences | |
|---|---|---|---|
| | | × $10^{-3}$ Daniell | In terms of the original value as unity |
| | Nerve upon removal ... ... ... | 19·5 | 1·00 |
| (5) | After 5 min. in ·372 per cent. KCl. ... | 22·4 | 1·15 |
| (10) | Another 5 min. in ·372 per cent. KCl. ... | 20·1 | 1·02 |
| (15) | ,, ,, ,, ,, ... | 18·0 | 0·92 |
| (20) | ,, ,, ,, ,, ... | 15·3 | 0.78 |
| (25) | ,, ,, ,, ,, ... | 13·2 | 0·68 |
| (30) | ,, ,, ,, ,, ... | 10·0 | 0·51 |
| (35) | ,, ,, ,, ,, ... | 9·2 | 0.47 |
| (40) | ,, ,, ,, ,, ... | 6·6 | 0·34 |
| (45) | ,, ,, ,, ,, ... | 5·8 | 0·30 |
| (50) | ,, ,, ,, ,, ... | 4·8 | 0·24 |
| | After 10 min. in tap water ... ... ... | 4·0 | 0·20 |

This nerve was removed immediately after the death of the animal. The second sciatic nerve was, as a contrast (see below), removed one-and-a-half hours after death, and similarly examined.

### THE SECOND NERVE

| | | Potential Differences |
|---|---|---|
| | Nerve upon removal ... ... ... | 9·8 × $10^{-3}$ Daniell |
| | After 5 min. in ·372 per cent. KCl. ... | 13·7 |
| (5) | Another 5 min. in ·372 per cent. KCl. ... | 15·0 |
| (10) | ,, ,, ,, ,, ... | 19·5 |
| (15) | ,, ,, ,, ,, ... | 17·4 |
| (20) | ,, ,, ,, ,, ... | 17·0 |
| (25) | ,, ,, ,, ,, ... | 14·2 |
| (30) | ,, ,, ,, ,, ... | 10·5 |

## EXPERIMENT VII

### Sciatic Nerve of Cat

(*a*) Piece of Nerve 5 centimetres long. Experimental solution used for immersion of nerve ·025 of NaOH. Nerve removed immediately after the death of the animal.

| | Potential Differences | |
|---|---|---|
| | $\times 10^{-3}$ Daniell | In terms of the original value as unity |
| Nerve upon removal ... ... ... | 23·0 | 1·00 |
| (5) After 5 min. in ·025 per cent. NaOH ... | 23·9 | **1·04** |
| (10) Another 5 min. in ·025 per cent. NaOH ... | 26·7 | 1·16 |
| (15) ” ” ” ” ” ... | 22·1 | 0·96 |
| (20) ” ” ” ” ” ... | 21·2 | 0·92 |
| (25) ” ” ” ” ” ... | 17·0 | 0·74 |
| (30) ” ” ” ” ” ... | 9·2 | 0·40 |
| (35) ” ” ” ” ” ... | 6·8 | 0·34 |

(*b*) The other nerve of the same animal removed one hour after death of the animal—

| | Potential Differences | | |
|---|---|---|---|
| | $\times 10^{-3}$ Daniell | In terms of the original value as unity | In terms of the original value of the first nerve as unity |
| Nerve upon removal ... ... ... | 14·4 | 1·00 | 0·62 |
| (5) After 5 min. in ·025 per cent. NaOH ... | 23·9 | 1·66 | **1·04** |
| (10) Another 5 min. in ·025 per cent. NaOH ... | 24·6 | 1·70 | 1·07 |
| (15) ” ” ” ” ” ... | 22 1 | 1·54 | 0·96 |
| (20) ” ” ” ” ” ... | 21·2 | 1·47 | 0·92 |
| (25) ” ” ” ” ” ... | 16·1 | 1·12 | 0·70 |
| (30) ” ” ” ” ” ... | 9·9 | 0·68 | 0·43 |

## EXPERIMENT VIII

### Sciatic Nerve of Cat

(*a*) Piece of Nerve 5 centimetres long. Experimental solution used for immersion of the nerve ·02 per cent. HCl. First nerve examined immediately after death of the animal—

| | Potential Differences | |
|---|---|---|
| | × 10—3 Daniell | In terms of the original value as unity |
| Nerve on removal ... ... ... | 17·7 | 1·00 |
| (5) After 5 min. in ·02 per cent. HCl ... | 25·9 | **1·46** |
| (10) Another 5 min. in ·02 per cent HCl ... | 21·1 | 1·19 |
| (15) „ „ „ „ ... | 19·5 | 1·10 |
| (20) „ „ „ „ ... | 17·2 | 0·97 |
| (25) „ „ „ „ ... | 14·5 | 0·82 |
| (30) „ „ „ „ ... | 6·9 | 0·39 |

(*b*) The second nerve removed one hour after death—

| | Potential Differences | | |
|---|---|---|---|
| | × 10—3 Daniell | In terms of the original value as unity | In terms of the original value of the first nerve as unity |
| Nerve on removal ... ... ... | 12·4 | 1·00 | 0·70 |
| (5) After 5 min. in ·02 per cent. HCl ... | 25·9 | 2·09 | **1·46** |
| (10) Another 5 min. in ·02 per cent. HCl ... | 22·4 | 1·80 | 1·26 |
| (15) „ „ „ „ ... | 19·8 | 1·59 | 1·12 |
| (20) „ „ „ „ ... | 18·5 | 1·49 | 1·04 |
| (25) „ „ „ „ ... | 13·2 | 1·06 | 0·75 |
| (30) „ „ „ „ ... | 5·3 | 0·43 | 0·30 |

Modification in the injury 'current' (P.D.) produced by immersion of the nerve in dilute solutions of electrolytes.

| | EXPERIMENT II (A)<br>·45 per cent. NaCl | EXPERIMENT VII<br>·372 per cent. KCl | EXPERIMENT VI<br>·025 per cent. NaOH | EXPERIMENT VIII<br>·02 per cent. HCl |
|---|---|---|---|---|
| Nerve at once ... ... | 1·00 | 1·00 | 1·00 | 1·00 |
| After 5 min. immersion ... | 1·40 | 1·15 | 1·04 | 1·46 |
| ,, 10 ,, ,, ... | 1·37 | 1·02 | 1·16 | 1·19 |
| ,, 15 ,, ,, ... | 1·20 | 0·92 | 0·96 | 1·10 |
| ,, 20 ,, ,, ... | 1·09 | 0·78 | 0·92 | 0·97 |
| ,, 25 ,, ,, ... | 0·79 | 0·68 | 0·74 | 0·82 |
| ,, 30 ,, ,, ... | 0·60 | 0·51 | 0·40 | 0·39 |

From the curves in figure B, or from the numbers in the table, it is possible to appreciate the close similarity in effects of all these dilute solutions of electrolytes. This is the more remarkable if one considers that there is every reason to suppose that a better selection of corresponding concentrations of these different electrolytes would have led to a closer correspondence still. The curves are very similar, and are quite unlike the curves obtained from concentrated solutions as is seen from the curves of figure A. It is also obvious that they form evidence strengthening the conclusion already arrived at, that real attempts to quantitatively estimate the modification produced by immersion in a solution of electrolytes had better be limited to a study of the results of the first five minutes' immersion.

The details of these experiments bears witness also to another very interesting fact which is brought out by the contrasted examination of nerves removed at different periods after the death of the animal.

*For a very considerable interval after the death of the animal the nerves are practically unaltered by the changes which immediately follow death, as far at least as the characteristics of structure are concerned which give rise to the injury current, except in one particular.*

The outer solution of the nerve is synonymous with the lymph of the tisssue; and the nerves examined (the sciatic nerves) lie, while in the body, imbedded in great muscular masses. From these muscles carbonic acid and other disintegration products are continually being cast off, which, during life, are removed by the circulating blood, but after death accumulate locally in the lymph of the part in which they are formed. The outer solution of the nerve is therefore being gradually altered after the death of the animal by the concentration in it of electrolytes derived in the first place from the surrounding muscles.* Such a concentration of the outer solution leads to a diminution in the injury current, and nerves removed from the body even five minutes after death exhibit a diminution in the demonstrable injury current, and from this cause.

When the nerves are immersed for a short time in a solution which successfully replaces the 'external solution' originally present, they are then in a more standard condition for comparison than when the variable 'external solution' remains. A comparison under such circumstances gives more reliable information as to the condition of the other factors necessary to the manifestation of the injury current, *e.g.*, the tubular membrane and the enclosed 'internal solution.'

### DATA FROM EXPERIMENTS VII AND VIII

| | Experiment VII. ·025 per cent. NaOH | | Experiment VIII. ·02 per cent. HCl | |
|---|---|---|---|---|
| | First nerve removed at once | Second nerve removed in 1 hour | First nerve removed at once | Second nerve removed in 1 hour |
| Potential Difference | 23·0 | 14·4 | 17·7 | 12·4 |
| After successive immersions in their respective solutions. (1) | 23·9 | 23·9 | 25·9 | 25·9 |
| (2) | 26·7 | 24·6 | 21·1 | 22·4 |
| (3) | 22·1 | 22·1 | 19·5 | 19·8 |
| (4) | 21·2 | 21·2 | 17·2 | 18·5 |
| (5) | 17·0 | 16·1 | 14·5 | 13·2 |
| (6) | 9·2 | 9·9 | 6·9 | 5·3 |

In each of these experiments it is obvious that whereas a great difference exists between the nerve removed at once and that removed an hour later, when first examined: *yet the first immersion has in either case placed the two nerves upon an absolute equality*, which is maintained throughout their subsequent history.

It is worthy of note that the first beneficent effect of immersion is produced alike by dilute solutions of acid or of alkali, the following experiment will shew, too, that there is no particular virtue in the fact that these solutions are dilute.

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* See Waller, *Animal Electricity*, p. 56

## EXPERIMENT IX

### Sciatic Nerve of Cat

Piece of Nerve 5 centimetres long. Experimental solution used : ·25 per cent. NaOH.

| First Nerve removed at once | | Second Nerve removed in one hour |
|---|---|---|
| Potential difference of the nerve upon removal ... | 20·1 × $10^{-3}$ D. | 10·6 × $10^{-3}$ D. |
| (5) After 5 minutes in ·25 per cent. NaOH ... | 9·0 „ | 8·2 „ |
| (10) Another „ „ „ ... | 3·4 „ | 5·2 „ |
| (15) „ „ „ „ ... | 2·1 „ | 2·1 „ |
| (20) „ „ „ „ ... | 1·6 „ | 1·8 „ |

In this experiment the same fact is seen elicited by a solution which has the typical effect of a concentrated solution. Nor is this revelation of the still pristine vigour of the nerve limited to the action of acids and alkalies, it may be observed more or less completely in the case of the action of any solution of electrolytes. A reference to the data of Experiment VI will show the same influence at work, as revealed (at a longer interval after death) by the solution of a neutral salt (KCl). In the next section the influence of this factor is seen in the data obtained from every solution of electrolytes used : the preliminary difference is there seen as the result of a stay of only five minutes longer in the body, and its removal is seen as a consequence of immersion in many different solutions.

In all the experiments previously quoted, the experimental solutions into which the nerve was placed have been of the temperature of the room. In the succeeding section care has been taken that in every case the solution used should be at the same temperature, 18° C., and that this should be maintained constant. In an examination of a process presumably dependent upon a diffusion process, the precaution of maintaining a constant temperature is an obvious necessity, the rate of diffusion being notably influenced by temperature. The choice of a standard temperature is more or less a matter of convenience, and the most convenient, from the point of view of physical measurements, is the temperature chosen. This standard temperature was not, however, chosen at once, since in the case of mammalian nerve certain other considerations are of value. The nerve removed rapidly from the animal is already at a temperature of 38° C. approximately, therefore scruples which dictate a study of, what is called, nerve in a normal condition point to the selection of this temperature for the examination of the nerve. One scruple of this kind, more definite than the remainder, is strongly in favour of such a course, namely, that which is affected by the condition of the myelin sheath.

A temperature of 38° C. is not, however, so easily maintained as a temperature of 18° C., it is also a temperature at which the rate of decline of the injury current is very great, as would the rate of any process of diffusion also be. In an attempt to study the quantitative effect of immersion in various solutions, this declining value of the original phenomenon has to be borne in mind as carefully as in the case of any of the other measurements undertaken previously. Nor can this source of error be as easily dealt with as in the case of the examination of the distribution potential (see previous section on 'current of injury'). In that case the error was eliminated by taking two sets of measurements in a regular order. In this case no such method is applicable, since, as has been clearly stated, even a short immersion in any solution (which is not the 'isotonic' one) leaves a fractional, but still important, effect behind it upon the concentration of the 'internal' as well as of the 'external' solution of the nerve. At first this point was not as clearly recognized as now, and experiments were made by the author in which immersions in the experimental solution were alternated with immersions in an isotonic solution: such experiments, although of some interest, have no quantitative importance, and have the disadvantage of appearing to correct an error which they largely leave unmodified, or only modify it in a new and undesirable fashion.

The decline of the injury current is, therefore, an important consideration, and is most satisfactorily dealt with by immersions in solutions at a temperature unfavourable to its marked occurrence.

Data have already been given* from experiments in which the influence of temperature was studied, the data of the following experiment will serve here as an illustration :—

## EXPERIMENT X

### Sciatic Nerve of Cat

| | | |
|---|---|---|
| (*a*) First nerve, removed immediately after death :— | | |
| Potential difference at once ... ... ... | 13·3 | × $10^{-3}$ Daniell |
| After 25 minutes in ·75 per cent. NaCl solution at 17° C. | 12·5 | ,, |
| (*b*) Second nerve, removed immediately after death :— | | |
| Potential difference at once ... ... ... | 13·3 | ,, |
| After 25 minutes in ·75 per cent. NaCl solution at 38° C. | 8·2 | ,, |
| After a subsequent 5 minutes in ·75 per cent. at 17° C. | 8·1 | ,, |

In this experiment the two nerves were fortunately in the same original condition, and the degree of modification by immersion in the same solution at different temperatures is clearly seen. At a temperature of 38° C. the decline in the injury current is 39 per cent. of the original, at 17° C. the decline is only 6 per cent. in the same interval of time.

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* J. S. Macdonald, *Preliminary Communication*, *Proc. Roy. Soc.*, 67, 321.

There is, however, another fact to consider, namely, that if at any time the temperature of the nerve could be suddenly changed from 38° C. to 17° C., the value of the injury current (as determined by a diffusion process) would be found to be quite different, without there being any intervening differential rate of decline to consider. In view of such consideration it will be seen that in the second part of the experiment the temperature of the nerve, which had been for twenty-five minutes at 38° C., was changed to 17° C. without producing any alteration in the low value due to more rapid decline through the preceding twenty-five minutes. The result of this secondary modification in this experiment is also of interest from another point of view. A differential modification of the temperature of the 'internal' and 'external' solutions of the nerve might be of importance. Taking the main characteristic of the physical structure of nerve to be the separation of its solutions by tubular membranes, such a characteristic might conceivably be a factor determining that the temperature of the 'external solution' should be more readily capable of modification than that of the 'internal solution.' Such a differential modification would alone account for great modification of the injury current, and is probably accountable for differences observed in the nerve injury current at very different temperatures of the air. It is satisfactory, therefore, to note that the modification produced in five minutes must have, in view of the result obtained, equally affected all the factors in the production of the injury current. For had the cooling affected only the external solution, the injury current would have been increased. Immersion in a solution at a temperature of 18° C. is therefore convenient, and also five minutes is an adequate time in which to bring the whole nerve approximately to this temperature.

## QUANTITATIVE COMPARISONS

### Experimental Procedure

Non-polarizable electrodes, having been prepared, were placed in position 2·5 centimetres apart.

A cat having been killed, a piece of one sciatic nerve, 5 centimetres long, was immediately removed.

The potential difference was measured between the upper cross section and a point on the longitudinal surface 2·5 centimetres distant.

The nerve was then immersed in the solution which had been previously prepared and brought to a temperature of 18° C. The nerve was left in this for five minutes exactly timed. During the immersion the vessel containing the solution was frequently shaken. The quantity of the solution used was always the same, 200 cc.

At the end of five minutes the nerve was removed. This was accomplished by seizing its lower end, which is always easily identified, in fine pointed forceps.

The nerve was placed upon a sheet of filter paper, which was then folded upon it. Complete drying was obtained by rolling the nerve and longitudinally compressing it between finger and thumb in the fold of filter paper. This drying operation was repeated three times, a dry place in the filter paper being used each time.

The potential difference was then again measured.

When the second sciatic nerve of the same animal was used, a routine method was followed. As soon as the first nerve had been placed in the prepared solution the second was immediately removed, examined, and placed in a separate vessel of solution just as the time approached for the final examination of the first nerve. In this the examinations and immersions of the two nerves were made to alternate, and consequently only a small interval of time elapsed between the removal of the two nerves. Even this slight difference was not, however, without its consequence (for reasons, see previous section), and accordingly in all the experiments quoted such nerves are always marked '(2)' to distinguish them from the nerves prepared first, which are marked '(1).'

The confidence placed in a single examination of the potential difference between the upper cross section and the mid-point of the nerve was the outcome of the experiments performed in the first section of this paper. In the curves of that section it will be noticed that the main variations in the value of the potential difference take place in the first two centimetres, and are unimportant at a greater distance.

The solutions were made up with pure chemicals dissolved in distilled water.

Great care was taken to insulate all the conducting paths used in the measurements taken, with the intention of making the results obtained as reliable as possible. For the same reason the drying of the nerve was always complete, and the attempt at drying the nerve after immersion in a solution was always carried to a point when the nerve left no further visible trace of moisture upon the filter paper used.

The measurement of potential difference was always accomplished by the usual compensation method. A large (quart) Daniell cell being carefully made up each morning for experiments carried out in the afternoon.

All the figures given are the result of quite separate experiments, in each of which an initial value and a final value for the potential difference having been obtained, before and after immersion, the nerve was thrown away.

In all cases the nerves used were, as stated above, the sciatic nerves of cats.

## TABLE OF EXPERIMENTS

| | Concentration of the Solution Used | | Potential Difference | | | Number of Experiment |
|---|---|---|---|---|---|---|
| | (1) In grammes per cent. | (2) In gram-molecular per litre | (1) Initial Value × 10−3 Daniell | (2) Final Value × 10−3 Daniell | (3) Final value in terms of the initial value as unity | |
| Solutions of Hydrochloric acid HCl | ·2 | $\frac{1}{18·2}$ | 13·46 | 4·22 | 0·31 | **Experiment I** (1) |
| | ·1 | $\frac{1}{36·3}$ | 13·99 | 8·71 | 0·62 | „ **II** (1) |
| | ·025 | $\frac{1}{145·2}$ | 15·84 | 19·27 | 1·21 | „ **III** (1) |
| | ·0125 | $\frac{1}{290·4}$ | 18·48 | 28·25 | 1·51 | „ **IV** (1) |
| Ammonium Chloride $NH_4Cl$ | 5·35 | 1 | 14·52 | 0·66 | ·045 | **Experiment V** (1) |
| | 5·35 | 1 | 18·74 | 1·92 | ·102 | „ **VI** (1) |
| | 2·67 | $\frac{1}{2}$ | 15·05 | 4·89 | ·325 | „ **VII** (2) |
| | 2·67 | $\frac{1}{2}$ | 17·16 | 5·68 | ·330 | „ **VIII** (2) |
| | 1·33 | $\frac{1}{4}$ | 14·52 | 9·50 | ·654 | „ **IX** (1) |
| | 0·67 | $\frac{1}{8}$ | 13·73 | 12·14 | ·884 | „ **X** (2) |

## TABLE OF EXPERIMENTS—*continued*

| | CONCENTRATION OF THE SOLUTION USED | | POTENTIAL DIFFERENCE | | | Number of Experiment |
|---|---|---|---|---|---|---|
| | (1) In grammes per cent. | (2) In gram-molecular per litre | (1) Initial Value x $10^{-3}$ Daniell | (2) Final Value x $10^{-3}$ Daniell | (3) Final value in terms of the initial value as unity | |
| Lithium Chloride LiCl | 4·25 | 1 | 19·67 | 5·28 | 0·268 | Experiment XI (1) |
| | 2·12 | ½ | 20·72 | 12·28 | 0·593 | ,, XII (1) |
| | 1·06 | ¼ | 19·11 | 17·42 | 0·911 | ,, XIII (2) |
| | 0·53 | ⅛ | 15·58 | 19·01 | 1·220 | ,, XIV (2) |
| Calcium Chloride ½ ($CaCl_2$) | 5·55 | 1 | 19·44 | 6·88 | ·354 | Experiment XV (1) |
| | 2·77 | ½ | 19·27 | 12·49 | ·648 | ,, XVI (1) |
| | 1·39 | ¼ | 21·00 | 18·40 | ·876 | ,, XVII (1) |
| Barium Chloride ½ ($BaCl_2$) | 10·4* | 1 | 17·69 | 4·36 | ·245 | Experiment XVIII (1) |
| | 5·2 | ½ | 13·60 | 6·73 | ·495 | ,, XIX (2) |
| | 2·6 | ¼ | 18·22 | 12·67 | ·695 | ,, XX (1) |
| | 1·3 | ⅛ | 13·20 | 12·54 | ·950 | ,, XXI (2) |
| Sodium Chloride NaCl. | 5·85 | 1 | 20·59 | 2·77 | ·135 | Experiment XXII (1) |
| | 2·92 | ½ | 17·16 | 5·28 | ·308 | ,, XXIII (1) |
| | 2·92 | ½ | 17·42 | 5·03 | ·289 | ,, XXIV (1) |
| | 1·46 | ¼ | 20·59 | 13·73 | ·666 | ,, XXV (1) |
| | 1·46 | ¼ | 16·63 | 9·77 | ·588 | ,, XXVI (2) |
| | 0·73 | ⅛ | 16·63 | 15·04 | ·904 | ,, XXVII (1) |
| Potassium Chloride† KCl. | 7·45 | 1 | 14·52 | 1·59 | ·109 | (1) |
| | 3·72 | ½ | 24·29 | 9·90 | ·407 | (1) |
| | 1·86 | ¼ | 14·78 | 9·50 | ·640 | (1) |

* Including Water of Crystallization, total weight, 12·2 grammes per cent.

† Potassium Chloride Solutions will be found later treated as a special case, the experiment given here are taken from experiments given later.

In this table are collected the results of twenty-eight experiments in which should be found data sufficient to test any presumed relationship existing between the effects of immersing the nerve in different concentrations of the same electrolyte, and also of different electrolytes. The immersions have been in solutions of seven electrolytes, all chlorides—

Hydrochloric acid,
Ammonium chloride,
Lithium chloride,
Calcium chloride,
Barium chloride,
Sodium chloride,
Potassium chloride.

It is of interest to commence with an examination of the relationship which we preliminarily tested, namely, a variation inversely as the concentration : and also with solutions of hydrochloric acid, for in their case the real relationship, as will subsequently be seen, is most obvious and convincing.

The concentration of hydrochloric acid made use of are evidently capable of producing a wide range of effects. Solutions of ·025 and ·013 grammes per cent. produce, and in the right relative degree, the typical effects of dilute solutions, increasing the injury current. Solutions of ·1 and ·2 per cent. produce the typical effects of concentrated solutions, diminishing the injury current, and also in the right relative degree. If in addition to this conformity to the general statement, they also conform to the assumed arithmetical relation ; then the value of 'x' in each of the following cases should be the same :—

Experiment I— $x = \cdot 2 \times \cdot 31 = \cdot 62$
Experiment II— $x = \cdot 1 \times \cdot 62 = \cdot 62$
Experiment III— $x = \cdot 025 \times 1 \cdot 21 = \cdot 30$
Experiment IV— $x = \cdot 0125 \times 1 \cdot 51 = \cdot 19$

In the first two of these experiments the value for 'x' is the same, and therefore, for these two cases, and presumably for intervening examples, it might be said that the potential difference varies inversely with the strength of the experimental solution. But when we turn to the remaining experiments (III and IV) we find that such a relation no longer exists, as is also the case with similar solutions of NaCl, *i.e.*, those which also cause an increase in the value of the injury current.

Faced with such a fact, it is natural to enquire the reason which induced us to seek for, and to appreciate when found, the existence of this inverse relationship of the value of the injury current to that of the experimental solution. The reason undoubtedly was based upon the opinion that the injury current was caused by an inequality in the 'internal' and 'external' solutions of the nerve, and might therefore be expected to depend upon the ratio existing between them, *e.g.* :—

$$\frac{\text{Internal solution}}{\text{External solution}}$$

But such an expectation is not based upon a knowledge of the value of the potential difference to be obtained from such arrangements of solutions, which varies not directly with this ratio but with its logarithm; although for a short range the two methods of variation might agree, and a too limited examination might lead to the inference that the more simply relation was in existence.

Let us therefore take the ratios discovered in these four experiments (Experiment I, ·31; Experiment II, ·62; Experiment III, 1·21; Experiment IV, 1·51) to exist between the final and initial values of the potential difference, and examine not these figures themselves, but the numbers of which they are the logarithms.

Experiment I— 0·31 = log. 2
Experiment II— 0·62 = log. 4·2
Experiment III— 1·21 = log. 16·2
Experiment IV— 1·51 = log. 32·5

Such a collection of figures becomes of immediate interest when it is appreciated that the concentrations of the experimental solutions used in these experiments bear the following ratios to one another:—

| Experiment I | Experiment II | Experiment III | Experiment IV |
|---|---|---|---|
| 32 | 16 | 4 | 2 |

it is at once realized that a definite relation has been discovered which unites together completely the very different effects of the solutions of hydrochloric acid used in these experiments.

Final potential difference = initial potential difference × log. $\frac{k}{n}$; where 'k' is a constant for all the experiments, and 'n' is the concentration of the solution in gram-molecules per litre—

$$E_\omega = E_\alpha \log. \frac{k}{n}$$

Needless to say, such a formulated expression of opinion can be readily tested by the use of the data from each of the four experiments, and that in each case the use of these data should lead to the discovery of the same value for 'k.'

### Experiment I

$$13{\cdot}46 \times \log.\,(18{\cdot}2,\, k) = 4{\cdot}22$$
$$\log.\,(18{\cdot}2,\, k) = {\cdot}31 \quad = \log.\ 2$$
$$\therefore\ k = \frac{2}{18{\cdot}2} = {\cdot}11$$

### Experiment II

$$13{\cdot}99 \quad \log.\,(36{\cdot}3,\, k) = 8{\cdot}71$$
$$\log.\,(36{\cdot}3,\, k) = {\cdot}62 \quad = \log.\ 4{\cdot}16$$
$$\therefore\ k = \frac{4{\cdot}16}{36{\cdot}3} = {\cdot}11$$

### Experiment III

$$15{\cdot}84 \times \log.\,(145{\cdot}2,\, k) = 19{\cdot}27$$
$$\log.\,(145{\cdot}2,\, k) = 1{\cdot}21 \quad = \log.\ 16{\cdot}2$$
$$\therefore\ k = \frac{16{\cdot}2}{145{\cdot}2} = {\cdot}11$$

### Experiment IV

$$18{\cdot}48\ \log.\,(290{\cdot}4,\, k) = 28{\cdot}25$$
$$\log.\,(290{\cdot}4,\, k) = 1{\cdot}51 = \log.\ 32{\cdot}5$$
$$\therefore\ k = \frac{32{\cdot}5}{290{\cdot}4} = {\cdot}11$$

'k' therefore is in reality a constant, and the law which unites the effects of solutions of hydrochloric acid is simple, and is—

$$E_{\omega} = E_{\alpha}\ \log.\ \frac{{\cdot}11}{n}$$

The discovery of such a 'concentration law' has two important results. The first of these is undoubtedly the strong confirmation of the value of the line of reasoning which led to its discovery, namely, that based primarily upon the opinion that the source of E.M.F. of the injury current is due to a difference between the solutions in contact with the electrodes, such as may be described as a solution 'concentration cell.' The second is the strong indication that valuable information is to be obtained from the observed effects of solutions of other electrolytes; if attention is paid to the numbers of which the ratios between the final and the initial potential difference are the logarithms, and not to these ratios themselves. The value of such an indication is seen by a consideration of the experiments given in the preceding table.

Taking the data from this table, let us arrange them in a manner which will test the hypothesis, that the law discovered for hydrochloric acid solutions is not peculiar to it, but is common to all solutions of electrolytes.

$$\frac{E\omega}{E\alpha} = \log. \frac{k}{n}$$

The number, which is the logarithm of the ratio between the final and initial value of the potential difference, is always equal to a constant 'k' divided by the concentration of the experimental solution expressed in gram molecules per litre.

To test such an opinion it is only necessary to obtain the ratio $\frac{E\omega}{E\alpha}$; to find the number of which this value is the logarithm; and to multiply the value thus found by 'n' the concentration.

$$\text{Since } \frac{k}{n} \times n = k.$$

Found in this way, the value 'k' should be constant for each electrolyte.

The following tables of data provide the briefest method of describing the results of this test of the hypothesis.

### Solutions of Ammonium Chloride

| Number of Experiment | $\frac{E\omega}{E\alpha}$ | $\frac{k}{n}$ | n | Therefore k is equal to |
|---|---|---|---|---|
| **Experiment V** ... ... | ·045 = log. | 1·10 | 1 | 1·10 |
| „ **VI** ... ... | ·102 = „ | 1·26 | 1 | 1·26 |
| „ **VII** ... ... | ·325 = „ | 2·11 | $\frac{1}{2}$ | 1·05 |
| „ **VIII** ... ... | ·330 = „ | 2·14 | $\frac{1}{2}$ | 1·07 |
| „ **IX** ... ... | ·654 = „ | 4·51 | $\frac{1}{4}$ | 1·13 |
| „ **X** ... ... | ·884 = „ | 7·66 | $\frac{1}{8}$ | 0·96 |

$$\therefore \frac{E\omega}{E\alpha} = \log. \frac{1}{n} \text{ (approx.)}$$

## Solutions of Lithium Chloride

| Number of Experiment | $\frac{E\omega}{E\alpha}$ | $\frac{k}{n}$ | n | Therefore k is equal to |
|---|---|---|---|---|
| **Experiment XI** ... ... | 0·268 = log. | 1·85 | 1 | 1·85 |
| „ **XII** ... ... | 0·593 = „ | 3·92 | $\frac{1}{2}$ | 1·96 |
| „ **XIII** ... ... | 0·911 = „ | 8·15 | $\frac{1}{4}$ | 2·07 |
| „ **XIV** ... ... | 1·220 = „ | 16·60 | $\frac{1}{8}$ | 2·20 |

$$\therefore \frac{E\omega}{E\alpha} = \log. \frac{2}{n} \text{ (approx.)}$$

## Solutions of Calcium Chloride

| Number of Experiment | $\frac{E\omega}{E\alpha}$ | $\frac{k}{n}$ | n | Therefore k is equal to |
|---|---|---|---|---|
| **Experiment XV** ... ... | 0·354 = log. | 2·26 | 1 | 2·26 |
| „ **XVI** ... ... | 0·648 = „ | 4·45 | $\frac{1}{2}$ | 2·23 |
| „ **XVII** ... | 0·876 = „ | 7·52 | $\frac{1}{4}$ | 1·98 |

$$\therefore \frac{E\omega}{E\alpha} = \log. \frac{2}{n} \text{ (approx.)}$$

## Solutions of Barium Chloride

| Number of Experiment | $\frac{E\omega}{E\alpha}$ | $\frac{k}{n}$ | n | Therefore k is equal to |
|---|---|---|---|---|
| **Experiment XVIII** ... | 0·245 = log. | 1·76 | 1 | 1·76 |
| „ **XIX** ... ... | 0·495 = „ | 3·13 | ½ | 1·57 |
| „ **XX** ... ... | 0·695 = „ | 4·96 | ¼ | 1·24 |
| „ **XXI** ... ... | 0·950 = „ | 8·91 | ⅛ | 1·14 |

$$\therefore \frac{E\omega}{E\alpha} = \log. \frac{1\cdot5}{n} \text{ (approx).}$$

## Solutions of Sodium Chloride

| Number of Experiment | $\frac{E\omega}{E\alpha}$ | $\frac{k}{n}$ | n | Therefore k is equal to |
|---|---|---|---|---|
| **Experiment XXII** ... | 0·135 = log. | 1·36 | 1 | 1·36 |
| „ **XXIII** ... | 0·308 = „ | 2·03 | ½ | 1·01 |
| „ **XXIV** ... | 0·289 = „ | 1·95 | ½ | 0·97 |
| „ **XXV** ... | 0·666 = „ | 4·63 | ¼ | 1·16 |
| „ **XXVI** ... | 0·588 = „ | 3·88 | ¼ | 0·97 |
| „ **XXVII** ... | 0·904 = „ | 8·01 | ⅛ | 1·00 |

$$\therefore \frac{E\omega}{E\alpha} = \log. \frac{1}{n} \text{ (approx.)}$$

SOLUTIONS OF POTASSIUM CHLORIDE

| Number of Experiment | $\frac{E\omega}{E\alpha}$ | $\frac{k}{n}$ | n | Therefore k is equal to |
|---|---|---|---|---|
| **Experiment** (a) ... | 0·109 = log. | 1·28 | 1 | 1·28 |
| „ (b) ... | 0·407 = „ | 2·55 | $\frac{1}{2}$ | 1·27 |
| „ (c) ... | 0·640 = „ | 4·40 | $\frac{1}{4}$ | 1·10 |

$$\therefore \frac{E\omega}{E\alpha} = \log. \frac{1}{n} \text{ (approx.)}$$

It may truly be said that the data from these experiments, arranged in this manner, need little commentary.

The tale which they tell is evidently a simple one, each electrolyte relating its not very different variant.

All these electrolytes, NaCl, KCl, $BaCl_2$, $CaCl_2$, LiCl, $NH_4$ Cl, produce an effect upon the value of the injury current which is mainly dependent upon their concentration; and the effects of different concentrations are in each case united by a simple law which is apparently different for different electrolytes.

The general form of the law is constant throughout the series—

$$\frac{E\omega}{E\alpha} = \log. \frac{k}{n}$$

it would seem, however, that there is a value of 'k' proper to each electrolyte. The determination, therefore, of this value in each case becomes a matter of importance.

The experiments, the records of which are briefly given in the data of the tabulated lists below, were performed to determine in the case of each electrolyte this value 'k'; it being considered temporarily of greater interest to devote time and material to this cause than to the further exploration of the action of other electrolytes. The electrolytes already examined, although all belonging to the same group, chlorides, are sufficiently well known to have materially different influences upon biological phenomena, to make even their agreement in this manner an anomaly difficult of explanation upon any other than purely physical lines. Besides, the same general statement has been found possible as a description of the action of a quite different substance NaOH,* although in this case the form of the concentration law has not yet been determined.

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* See preliminary communication, *Proc. Roy. Soc.*, *p.* 67

Each line in the lists given below represents the data obtained from a separate experiment performed as before, each upon a different sciatic nerve (cat). The solution used was in every case of the concentration of one equivalent gramme molecule per litre ; as will be seen, a large number of separate experiments were performed with such a solution of each of the electrolytes in question.

In the case of each electrolyte, one of the experiments given below has been already quoted. Every such experiment is marked with an asterisk, and numbered as previously.

### Experiments Performed with the Normal Solution of NaCl

(5·85 grammes per cent.)

(Concentration $n = 1 \quad \therefore \frac{k}{n} = k$)

| Number of Experiment | Potential Difference $\times 10^{-3}$ Daniell | | Ratio $\frac{E\omega}{E\alpha}$ | k |
|---|---|---|---|---|
| | Initial $E\alpha$ | Final $E\omega$ | | |
| * Experiment XXII (1) ... | 20·59 | 2·77 | ·135 = log. | 1·36 |
| ,, XXVIII (1) ... | 19·40 | 3·04 | ·156 = ,, | 1·43 |
| ,, XXIX (1) ... | 18·22 | 3·17 | ·174 = ,, | 1·49 |
| ,, XXX (2) ... | 17·16 | 3·04 | ·178 = ,, | 1·50 |
| ,, XXXI (1) ... | 16·37 | 3·17 | ·193 = ,, | 1·56 |
| ,, XXXII (1) ... | 15·05 | 1·72 | ·114 = ,, | 1·30 |
| ,, XXXIII (2) ... | 14·92 | 2·51 | ·168 = ,, | 1·48 |
| ,, XXXIV (1) ... | 10·03 | 0·92 | ·092 = ,, | 1·24 |
| Average of eight experiments ... | 16·47 | 2·54 | ·157 = log. | 1·42 |

$\therefore E\omega = E\alpha$ log. 1·42

## EXPERIMENTS WITH THE NORMAL SOLUTION OF KCl

(7·45 grammes per cent.)

| Number of Experiments | Potential Difference × $10^{-3}$ Daniell | | Ratio $\frac{E_\omega}{E_\alpha}$ | k |
|---|---|---|---|---|
| | Initial $E_\omega$ | Final $E_\alpha$ | | |
| **Experiment XXXV** (1) ... | 20·33 | 2·11 | ·104 = log. | 1·27 |
| „ **XXXVI** (2) ... | 19·27 | 2·38 | ·123 = „ | 1·33 |
| „ **XXXVII** (1) ... | 17·16 | 1·32 | ·080 = „ | 1·21 |
| „ **XXXVIII** (1) ... | 15·84 | 1·58 | ·100 = „ | 1·26 |
| „ **XXXIX** (2) ... | 15·71 | 2·11 | ·134 = „ | 1·36 |
| „ **XL** (1) ... | 15·05 | 1·72 | ·114 = „ | 1·30 |
| „ **XLI** (2) ... | 15·05 | 1·58 | ·105 = „ | 1·27 |
| „ **XLII** (2) ... | 15·18 | 2·11 | ·138 = „ | 1·37 |
| * „ **XLIII** (1) ... | 14·52 | 1·59 | ·109 = „ | 1·28 |
| „ **XLIV** (2) ... | 11·88 | 1·32 | ·111 = „ | 1·29 |
| Average of ten experiments ... ... | 16·08 | 1·78 | ·112 = log. | 1·30 |

$\therefore E_\omega = E_\alpha \log. 1{\cdot}30$

## NORMAL SOLUTION OF LiCl

(4·25 grammes per cent)

| Number of Experiment | Potential Difference $\times 10^{-3}$ Daniell |  | Ratio $\frac{E\omega}{E\alpha}$ | k |
|---|---|---|---|---|
|  | Initial $E\alpha$ | Final $E\omega$ |  |  |
| **Experiment XI** (1) ... | 19·67 | 5·28 | ·268 = log. | 1·85 |
| ,, **XLV** (1) ... | 17·82 | 6·07 | ·340 = ,, | 2·19 |
| ,, **XLVI** (2) ... | 16·10 | 4·22 | ·262 = ,, | 1·83 |
| ,, **XLVII** (1) ... | 14·52 | 3·70 | ·255 = ,, | 1·80 |
| ,, **XLVIII** (2) ... | 12·66 | 3·83 | ·302 = ,, | 2·00 |
| Average of five experiments ... | 16·15 | 4·62 | ·285 = log. | 1·93 |

$$\therefore E\omega = E\alpha \log. 1{\cdot}93$$

### NORMAL SOLUTION OF $NH_4Cl$.

(5·35 grammes per cent)

| Number of Experiment | Potential Difference × 10−3 Daniell | | Ratio | k |
|---|---|---|---|---|
| | Initial $E\alpha$ | Final $E\omega$ | $\frac{E\omega}{E\alpha}$ | |
| Experiment XLIX (1) ... | 23·23 | 2·90 | ·125 = log. | 1·33 |
| ,, L (2) ... | 20·33 | 1·85 | ·090 = ,, | 1·23 |
| ,, LI (2) ... | 18·74 | 2·38 | ·127 = ,, | 1·34 |
| ,, LII (1) ... | 18·61 | 1·85 | ·099 = ,, | 1·25 |
| ,, LIII (1) ... | 17·16 | 1·58 | ·092 = ,, | 1·23 |
| ,, LIV (2) ... | 16·90 | 1·45 | ·086 = ,, | 1·22 |
| ,, LV (1) ... | 16·76 | 1·45 | ·086 = ,, | 1·22 |
| ,, LVI (2) ... | 15·84 | 1·19 | ·075 = ,, | 1·19 |
| ,, LVII (1) ... | 15·05 | 0·79 | ·052 = ,, | 1·13 |
| * ,, V (1) ... | 14·52 | 0·66 | ·045 = ,, | 1·10 |
| ,, LVIII (2) ... | 12·94 | 0.79 | ·061 = ,, | 1·15 |
| Average of eleven experiments ... | 17·40 | 1·57 | ·084 = log. | 1·22 |

$\therefore E\omega = E\alpha$ log. 1·22

## NORMAL SOLUTION OF $\frac{1}{2}$ ($BaCl_2$)

(10·4 grammes per cent.)

12·2 grammes per cent. of the crystalline salt

| Number of Experiment | Potential Difference $\times 10^{-3}$ Daniell | | Ratio $\frac{E\omega}{E\alpha}$ | k |
|---|---|---|---|---|
| | Initial $E\alpha$ | Final $E\omega$ | | |
| **Experiment LIX** (1) ... | 19·01 | 3·96 | ·208 = log. | 1·61 |
| ,, **LX** (1) ... | 17·95 | 4·49 | ·250 = ,, | 1·78 |
| * ,, **XVIII** (1) ... | 17·69 | 4·36 | ·245 = ,, | 1·76 |
| ,, **LXI** (1) ... | 16·90 | 3·17 | ·187 = ,, | 1·54 |
| ,, **LXII** (2) ... | 16·76 | 4·49 | ·267 = ,, | 1·85 |
| ,, **LXIII** (2) ... | 16·10 | 3·96 | ·246 = ,, | 1·76 |
| ,, **LXIV** (2) ... | 13·46 | 3·56 | ·268 = ,, | 1·85 |
| ,, **LXV** (1) ... | 12·67 | 2·64 | ·208 = ,, | 1·62 |
| ,, **LXVI** (2) ... | 11·88 | 3·17 | ·266 = ,, | 1·84 |
| Average of nine experiments ... | 15·62 | 3·75 | ·238 = log. | 1·73 |

$\therefore$ $E\omega = E\alpha$ log. 17·3

## Normal Solution of $\frac{1}{2}$ ($MgCl_2$)

(4·75 grammes per cent.)

10·15 grammes per cent. of the crystalline salt

| Number of Experiment | Potential Difference x 10—3 Daniell | | Ratio $\frac{E\omega}{E\alpha}$ | k |
|---|---|---|---|---|
| | Initial $E\alpha$ | Final $E\omega$ | | |
| **Experiment LXVII** (1) ... | 22·18 | 6·60 | ·297 = log. | 1·97 |
| ,, **LXVIII** (2) ... | 20·20 | 6·07 | ·300 = ,, | 2·00 |
| ,, **LXIX** (1) ... | 19·80 | 5·28 | ·266 = ,, | 1·84 |
| ,, **LXX** (2) ... | 18·22 | 5·41 | ·296 = ,, | 1·98 |
| ,, **LXXI** (1) ... | 17·69 | 4·49 | ·246 = ,, | 1·76 |
| ,, **LXXII** (2) ... | 17·42 | 5·02 | ·288 = ,, | 1·94 |
| ,, **LXXIII** (1) ... | 16·50 | 5·02 | ·304 = ,, | 2·01 |
| ,, **LXXIV** (1) ... | 15·31 | 4·75 | ·310 = ,, | 2·04 |
| ,, **LXXV** (2) ... | 14·52 | 4·22 | ·290 = ,, | 1·95 |
| ,, **LXXVI** (1) ... | 14·12 | 2·64 | ·187 = ,, | 1·54 |
| ,, **LXXVII** (2) ... | 12·67 | 3·04 | ·240 = ,, | 1·74 |
| Average of eleven experiments ... | 17·15 | 4·78 | ·275 = log. | 1·89 |

$\therefore E\omega = E\alpha$ log. 1·89

### NORMAL SOLUTION OF $\frac{1}{2}$ ($CaCl_2$)

(5·55 grammes per cent. of anhydrous salt)

| Number of Experiment | Potential Difference × 10−3 Daniell | | Ratio $\frac{E\omega}{E\alpha}$ | k |
|---|---|---|---|---|
| | Initial $E\alpha$ | Final $E\omega$ | | |
| * **Experiment XV** (1) … | 19·44 | 6·88 | ·354 = log. | 2·26 |
| ,, **LXXVIII** (1) … | 18·48 | 6·34 | ·343 = ,, | 2·20 |
| ,, **LXXIX** (2) … | 15·05 | 5·28 | ·351 = ,, | 2·24 |
| ,, **XC** (2) … | 13·73 | 5·28 | ·384 = ,, | 2·42 |
| ,, **XCI** (1) … | 12·94 | 3·96 | ·306 = ,, | 2·02 |
| Average of five experiments … | 15·93 | 5·55 | ·348 = log. | 2·23 |

$\therefore E\omega = E\alpha \log. 2{\cdot}23$

## SUMMARY OF PRECEDING RESULTS

| The average result of an immersion of five minutes duration in a normal (1 gramme equivalent molecule per litre) solution of | Is to give a new value to the 'injury current,' which can be expressed as being equal to the initial value multiplied by the following factor | This factor can be expressed also in the form given below |
|---|---|---|
| NaCl | ·151 | log. 1·42 |
| KCl | ·112 | ,, 1·30 |
| LiCl | ·285 | ,, 1·93 |
| $NH_4$ Cl | ·084 | ,, 1·22 |
| $\frac{1}{2}$ ($BaCl_2$) | ·238 | ,, 1·73 |
| $\frac{1}{2}$ ($MgCl_2$) | ·275 | ,, 1·89 |
| $\frac{1}{2}$ ($CaCl_2$) | ·348 | ,, 2·23 |

Assuming it to have been proved, that in the case of each electrolyte there is a concentration law' uniting the effects of solutions of this electrolyte in every possible concentration upon the value of the injury current, and that this law is always of the general form—

$$E\omega = E\alpha \log.\frac{k}{n},$$

where 'n' is the concentration: then in the case of each electrolyte given above we have a different value for the constant 'k.'

Since, in the preceding experiments, $n = 1 \quad \therefore \log.\frac{k}{n} = \log. k.$

| | | |
|---|---|---|
| $\therefore$ **NaCl** | ... | **k** = 1·42 |
| **KCl** | ... | **k** = 1·30 |
| **LiCl** | ... | **k** = 1·93 |
| **$NH_4Cl$** | .. | **k** = 1·22 |
| $\frac{1}{2}$ (**$BaCl_2$**) | ... | **k** = 1·73 |
| $\frac{1}{2}$ (**$MgCl_2$**) | ... | **k** = 1·89 |
| $\frac{1}{2}$ (**$CaCl_2$**) | ... | **k** = 2·32 |

The 'concentration law' is evidently not greatly different in the case of these different electrolytes, the value of the constant 'k' varying with each electrolyte to a not very remarkable extent. It will be seen that an allowance made for the influence of an important factor, not yet considered, brings even these differences approximately to naught, and the action of the different electrolytes within the bounds of a law common to them all.

If the action of all these solutions is a purely physical one and dependent upon their electrical properties alone, then we have hitherto been assessing the concentration of the different solutions at a mistaken value. The salt which is in solution as such, and is not dissociated by the fact of solution, is of no account from the purely electrical point of view, consisting, as it does, of neutral molecules. We are alone concerned with the other moiety of the salt, which has been dissociated by the fact of solution into positively and negatively charged particles, hydrolysed into 'ions.' Such a reflection discovers for us a method of regarding the so-called 'equivalent' solutions of electrolytes (used in the experiments of the preceding section) in which they are seen as no longer equivalent, and which points to the necessity of still further checking the results obtained by their use. The concentrations of the solutions used have yet to be brought to a common standard in terms of the dissociated ions contained in them, before the results are made strictly comparable.

'The degree of dissociation of a substance in a solution is equal to the ratio of the equivalent conductivity of that solution to its equivalent conductivity at infinite dilution.'[1] Fortunately, tabulated lists of such equivalent conductivities obtained by the experimental work of many investigators, have been prepared by FITZPATRICK,[2] to which we may conveniently refer (the same lists are also found as an appendix to WHETHAMS' *Solution and Electrolysis*). From these lists the following data have been collected and used in the determination of the dissociation constants :—

| Electrolyte | Molecular conductivity of the 'equivalent' solution | Molecular conductivity at infinite dilution | Dissociation constant |
|---|---|---|---|
| NaCl | 695 | 1024 | ·68 |
| KCl | 919 | 1216 | ·75 |
| $NH_4$ Cl | 907 | 1215 | ·75 |
| $\frac{1}{2}$ ( $BaCl_2$ ) | 658 | 1144 | ·58 |
| $\frac{1}{2}$ ( $MgCl_2$ ) | 631* | 1070* | ·59 |
| $\frac{1}{2}$ ( $CaCl_2$ ) | 633 | 1043 | ·60 |
| LiCl | 591 | 965 | ·61 |

The normal solution of NaCl therefore used in the experiments of the preceding section, did not, as we have formerly represented it, contain one equivalent gramme molecule per litre of important material, but only ·68 of this.

The value of 'k' obtained from the result, $\frac{k}{n} = 1{\cdot}42$, is not $k = 1{\cdot}42$, since 'n' is not equal to 1, but to ·68,

$$\therefore k = 1{\cdot}42 \times {\cdot}68$$
$$= {\cdot}97$$

The values of 'k' obtained for each of the other electrolytes has similarly to be corrected by the use of the dissociation constants given above, the results of this correction are given on following page.

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[1] Le Blanc, *Electro-chemistry*, 87, transl.

[2] *British Association Reports*, 1893.

| Electrolyte | Dissociation constant | Corrected value of k |
|---|---|---|
| NaCl | ·68 | 1·42 x ·68 = 0·97 |
| KCl | ·75 | 1·30 x ·75 = 0·95 |
| $NH_4$ Cl | ·75 | 1·22 x ·75 = 0·92 |
| $\frac{1}{2}$ ($BaCl_2$) | ·58 | 1·73 x ·58 = 1·00 |
| $\frac{1}{2}$ ($MgCl_2$) | ·59 | 1·89 x ·59 = 1·11 |
| $\frac{1}{2}$ ($CaCl_2$) | ·60 | 2·23 x ·60 = 1·34 |
| LiCl | ·61 | 1·93 x ·61 = 1·17 |

In this list there is little need to call attention to the extreme similarity in action upon the injury current of the solutions of these electrolytes. Their action is not only similar in a general sense, but in an exact quantitative sense ; in each case that action following a general law

$$E\omega = E\alpha \log. \frac{1}{n}$$

It may be said that this is only approximately general, the approximation is, however, sufficiently close—

| Electrolyte | Concentration Law |
|---|---|
| NaCl | $\frac{E\alpha}{E\omega} = \log. \frac{\cdot 97}{n}$ |
| KCl | ,, = ,, $\frac{\cdot 95}{n}$ |
| $NH_4$ Cl | ,, = ,, $\frac{\cdot 92}{n}$ |
| $\frac{1}{2}$ ($BaCl_2$) | ,, = ,, $\frac{1 \cdot 00}{n}$ |
| $\frac{1}{2}$ ($MgCl_2$) | ,, = ,, $\frac{1 \cdot 11}{n}$ |
| $\frac{1}{2}$ ($CaCl_2$) | ,, = ,, $\frac{1 \cdot 34}{n}$ |
| LiCl | ,, = ,, $\frac{1 \cdot 17}{n}$ |

The approximation is sufficiently close to point to a very definite moral ; namely, that the actions of all these solutions are in very definite agreement, and depend upon a property common to them all.

The property can also be assigned definitely as attributable to the dissociated moiety of these electrolytes, to the electrically charged ions contained in these solutions ; since it is obviously dependent upon the number of ions present.

Further, there remains the remarkable fact, not yet commented upon, that the form of the law determines one concentration which should reduce the potential difference to zero : and that this particular concentration, since log. $1 = 0$, is $n = 1$.

A solution of concentration $n = 1$, one equivalent gramme molecule per litre of dissociated electrolyte should cause the injury current to vanish. Such a necessity logically carries us to an extraordinary conclusion, when attention is paid to the main contention which we have attempted to establish : namely, that the current of injury is due to the inequality between the 'external' and 'internal' solution of the nerve. For equality of these two solutions is the condition essential to the elimination of the injury current ; and it must be admitted that, with the figure just given, equality is reached at an extraordinary concentration of the 'external solution.'

Such a conclusion necessitates a very rigid examination of the 'concentration law,' and this seems best performed by an exhaustive examination of the action of one of those electrolytes over a wide range of concentration.

There does not seem to be any great advantage obtainable from the choice of a special electrolyte, the action of all so far being similar. For this examination KCl has been chosen thus at random.

# SOLUTIONS OF POTASSIUM CHLORIDE

## SPECIAL EXAMINATION OF THE ACTION OF SOLUTIONS OF POTASSIUM CHLORIDE

The action of solutions of the concentration of one gramme equivalent molecule per litre (7·45 grammes per cent.) has already been completely examined (see p. 316), the average result being

$$E\omega = E\alpha \overset{*}{\log} 1{\cdot}42.$$

This relation differently expressed being

$$E\omega = E\alpha \log \frac{{\cdot}97}{n}$$

where 'n' represents the concentration in gramme molecules per litre of the dissociated portion of electrolyte (·68).

The following results, with this, cover an examination of a sufficiently wide range of concentrations, from 7·45 grammes per cent. to 0·18 grammes per cent.

The experimental method followed is precisely that previously detailed, and each observation recorded is from an individual sciatic nerve (cat) used for this observation (injury current before and after immersion in the given solution) and for no other.

### KCL (3·72 GRAMMES PER CENT.)

($\frac{1}{2}$ gramme equivalent molecule per litre.)

| Number of Experiment | Potential Difference × 10−3 Daniell | | Ratio $\frac{E\omega}{E\alpha}$ | $\frac{k}{n}$ |
|---|---|---|---|---|
| | Before Immersion $E\alpha$ | After Immersion $E\omega$ | | |
| **Experiment XCII** (1) ... | 24·29 | 9·90 | ·408 = log. | 2·56 |
| ,, **XCIII** (2) ... | 17·29 | 8.45 | ·489 = ,, | 3·08 |
| ,, **XCIV** (1) ... | 17·16 | 5·68 | ·331 = ,, | 2·14 |
| ,, **XCV** (2) ... | 14·78 | 5 02 | ·339 = ,, | 2·19 |
| ,, **XCVI** (1) ... | 14·52 | 6·60 | ·454 = ,, | 2·85 |
| ,, **XCVII** (2) ... | 13 60 | 6·46 | ·475 = ,, | 2·99 |
| ,, **XCVIII** (1) ... | 18·88 | 9·00 | ·479 = ,, | 3·01 |
| ,, **XCIX** (2) ... | 16·37 | 7·79 | ·475 = ,, | 2·99 |
| ,, **C** (1) ... | 18·22 | 8·18 | ·449 = ,, | 2·81 |
| ,, **CI** (2) ... | 19·27 | 9·37 | ·486 = ,, | 3·06 |
| Average of ten experiments ... ... | 17·44 | 7·65 | ·438 = log. | 2·74 |
| Average of five experiments marked (1) | 18·61 | 7·87 | ·423 = ,, | 2·65 |
| Average of five experiments marked (2) | 16·26 | 7·48 | ·460 = ,, | 2·89 |

## KCl (1·86 GRAMMES PER CENT.)

(¼ gramme equivalent molecule per litre)

| Number of Experiment | Potential Difference × $10^{-3}$ Daniell | | Ratio $\frac{E\omega}{E\alpha}$ | $\frac{k}{n}$ |
|---|---|---|---|---|
| | Before Immersion $E\alpha$ | After Immersion $E\omega$ | | |
| Experiment CII (1) ... | 22·18 | 11·15 | ·503 = log. | 3·19 |
| ,, CIII (2) ... | 21·38 | 10·96 | ·512 = ,, | 3·24 |
| ,, CIV (1) ... | 17·42 | 9·77 | ·561 = ,, | 3·64 |
| ,, CV (1) ... | 22·18 | 12·94 | ·583 = ,, | 3·83 |
| ,, CVI (2) ... | 16·90 | 12·14 | ·718 = ,, | 5·23 |
| ,, CVII (1) ... | 19·01 | 9·50 | ·500 = ,, | 3·16 |
| ,, CVIII (2) ... | 16·90 | 10·82 | ·640 = ,, | 4·37 |
| ,, CIX (1) ... | 14·78 | 9·50 | ·643 = ,, | 4·40 |
| ,, CX (2) ... | 15·05 | 10·82 | ·718 = ,, | 5·23 |
| ,, CXI (1) ... | 13·46 | 9·24 | ·686 = ,, | 4·86 |
| ,, CXII (2) ... | 13·20 | 8·45 | ·640 = ,, | 4·37 |
| Average of eleven experiments ... | 17·40 | 10·48 | ·610 = log. | 4·14 |
| Average of six experiments marked (1) | 18·17 | 10·35 | ·569 = ,, | 3·71 |
| Average of five experiments marked (2) | 16·68 | 10·64 | ·638 = ,, | 4·35 |

### KCl (1·49 GRAMMES PER CENT.)

($\frac{1}{5}$ gramme equivalent molecule per litre.)

| Number of Experiment | Potential Difference × 10$^{-3}$ Daniell | | Ratio $\frac{E\omega}{E\alpha}$ | $\frac{k}{n}$ |
|---|---|---|---|---|
| | Before Immersion $E\alpha$ | After Immersion $E\omega$ | | |
| **Experiment CXIII** (1) ... | 15·05 | 10·56 | ·701 = log. | 5·03 |
| „ **CXIV** (2) ... | 13·20 | 9·11 | ·690 = „ | 4·90 |
| „ **CXV** (1) ... | 22·70 | 15·58 | ·686 = „ | 4·86 |
| „ **CXVI** (2) ... | 17·42 | 12·14 | ·697 = „ | 4·98 |
| „ **CXVII** (1) ... | 19·54 | 14·78 | ·756 = „ | 5·71 |
| „ **CXVIII** (2) ... | 18·48 | 13·20 | ·714 = „ | 5·18 |
| „ **CXIX** (1) ... | 18·48 | 10·56 | ·571 = „ | 3·73 |
| „ **CXX** (2) ... | 20·06 | 12·14 | ·605 = „ | 4·03 |
| Average of eight experiments ... | 18·11 | 12·26 | ·677 = log. | 4·76 |
| Average of four experiments marked (1) | 18·94 | 12·87 | ·679 = „ | 4·78 |
| Average of four experiments marked (2) | 17·29 | 11·65 | ·674 = „ | 4·73 |

## KCl (·745 GRAMMES PER CENT.)

($\frac{1}{10}$ gramme equivalent molecule per litre.)

| Number of Experiment | Potential Difference x 10—3 Daniell | | Ratio $\frac{E\omega}{E\alpha}$ | $\frac{k}{n}$ |
|---|---|---|---|---|
| | Before Immersion $E\alpha$ | After Immersion $E\omega$ | | |
| **Experiment CXXI** (1) ... | 18·74 | 20·20 | 1·078 = log. | 11·97 |
| „ **CXXII** (2) ... | 16·10 | 16·63 | 1·033 = „ | 10·79 |
| „ **CXXIII** (1) ... | 21·38 | 19·93 | 0·932 = „ | 8·55 |
| „ **CXXIV** (2) ... | 17·42 | 18·22 | 1·046 = „ | 11·12 |
| „ **CXXV** (1) ... | 15·58 | 16·24 | 1·042 = „ | 11·02 |
| „ **CXXVI** (2) ... | 13·20 | 17·95 | 1·359 = „ | 22·86 |
| „ **CXXVII** (1) ... | 20·20 | 17·42 | 0·862 = „ | 7·28 |
| „ **CXXVIII** (2) ... | 17·42 | 18·74 | 1·076 = „ | 11·92 |
| „ **CXXIX** (1) ... | 18·22 | 16·63 | 0·913 = „ | 8·19 |
| „ **CXXX** (2) ... | 15·05 | 17·16 | 1·140 = „ | 13·81 |
| „ **CXXXI** (1) ... | 26·66 | 22·18 | 0·832 = „ | 6·79 |
| „ **CXXXII** (2) ... | 21·91 | 25·08 | 1·145 = „ | 13·97 |
| „ **CXXXIII** (1) ... | 15·84 | 17·95 | 1·133 = „ | 13·59 |
| „ **CXXXIV** (2) ... | 15·05 | 17·69 | 1·175 = „ | 14·97 |
| „ **CXXXV** (1) ... | 15·05 | 17·69 | 1·175 = „ | 14·97 |
| „ **CXXXVI** (2) ... | 17·69 | 16·63 | 0·940 = „ | 8·71 |
| „ **CXXXVII** (1) ... | 16·90 | 14·78 | 0·874 = „ | 7·48 |
| „ **CXXXVIII** (2) ... | 15·84 | 14·78 | 0·933 = „ | 8·57 |
| „ **CXXXIX** (1) ... | 15·31 | 14·52 | 0·948 = „ | 8·87 |
| „ **CXL** (2) ... | 15·84 | 16·37 | 1·033 = „ | 10·79 |
| Average of twenty experiments ... | 17·47 | 17·84 | 1·021 = log. | 10·5 |
| Average of ten experiments marked (1) | 18·39 | 17·75 | 0·965 = „ | 9·23 |
| Average of ten experiments marked (2) | 16·55 | 17·93 | 1·083 = „ | 12·11 |

So far as the examination of the action of solutions of potassium chloride has been carried, the 'concentration law,' as determined in the preceding sections, holds good, and serves to combine the results obtained. The range of concentrations examined has been, it will be acknowledged, fairly extensive, from 7.45 grammes per cent. to 0·745 grammes per cent. *The whole range of concentrations used, with the exception of the last example, however, is above that of the isotonic solution.*

In the following table the average results of these experiments with different concentrations of potassium chloride solution are arranged. The comparison, so facilitated, will be found to amply vindicate the truth of the 'concentration law.'

AVERAGE RESULTS TABULATED

| CONCENTRATION OF THE SOLUTION | | The dissociation constant at this concentration | The Ratio between the Final and Initial Potential Differences | The general 'Concentration Law' as defined by the data from each special case (value of 'n' corrected by the use of the dissociation constant) |
|---|---|---|---|---|
| In grammes per cent. | In gramme equivalent molecules per litre | | | |
| (*a*) 7·45 | 1 | ·68 | log. 1·30 | $\frac{E\omega}{E\alpha} = \log. \frac{·97}{n}$ |
| (*b*) 3·72 | $\frac{1}{2}$ | ·78 | ,, 2·74 | ,, = ,, $\frac{1·07}{n}$ |
| (*c*) 1·86 | $\frac{1}{4}$ | ·85 | ,, 4·14 | ,, = ,, $\frac{·85}{n}$ |
| (*d*) 1·86 | $\frac{1}{5}$ | ·85 | ,, 4·76 | ,, = ,, $\frac{·82}{n}$ |
| (*e*) 0·745 | $\frac{1}{10}$ | ·86 | ,, 10·50 | ,, = ,, $\frac{·91}{n}$ |

The general agreement is shown by the last column of the preceding table. It will be seen to be in marked contrast to the results obtained from the action of solutions much below the 'isotonic solution' in concentration, as shewn by the experiments collected in the following tables. A glance at the ·745 KCl table will show how great the individual exceptions are which are found at this concentration. The truth of the law is here only indicated by an appeal to the average result obtained : which is, however, conclusive. Such an appeal to an average is only of value when no liberty is retained to eliminate undesirable cases from the list, and this method has been strictly followed in the ·745 table. It has also been strictly adhered to in tabulating the results obtained with solutions still more dilute than the isotonic, the results of which are given in the two following tables.

## KCl (0·372 GRAMMES PER CENT.)

($\frac{1}{20}$ gramme equivalent molecule per litre)

| Number of Experiment | $E\alpha$ × $10^{-3}$ Daniell | $E\omega$ × $10^{-3}$ Daniell | $\frac{E\omega}{E\alpha}$ |
|---|---|---|---|
| Experiment CXL (1) ... | 15·84 | 17·42 | 1·09 |
| ,, CXLI (2) ... | 13·46 | 14·78 | 1·09 |
| ,, CXLII (1) ... | 23·76 | 24·42 | 1·03 |
| ,, CXLIII (2) ... | 24·02 | 24·02 | 1·00 |
| ,, CXLIV (1) ... | 17·42 | 19·01 | 1·09 |
| ,, CXLV (2) ... | 15·51 | 16·37 | 1·06 |
| ,, CXLVI (1) ... | 18·22 | 19·14 | 1·05 |
| ,, CXLVII (2) ... | 13·86 | 15·05 | 1·09 |
| ,, CXLVIII (1) ... | 19·01 | 20·46 | 1·08 |
| ,, CXLIX (2) ... | 16·10 | 17·42 | 1·08 |
| ,, CL (1) ... | 21·52 | 19·54 | 0·91 |
| ,, CLI (2) ... | 16·37 | 18·48 | 1·13 |
| ,, CLII (1) ... | 21·91 | 21·91 | 1·00 |
| ,, CLIII (2) ... | 19·54 | 21·65 | 1·11 |
| ,, CLIV (1) ... | 17·42 | 19·54 | 1·12 |
| ,, CLV (2) ... | 17·42 | 19·27 | 1·11 |
| ,, CLVI (1) ... | 17·42 | 18·74 | 1·08 |
| ,, CLVII (2) ... | 16·63 | 19·80 | 1·19 |
| ,, CLVIII (1) ... | 17·69 | 15·84 | 0·89 |
| ,, CLIX (2) ... | 16·63 | 16·63 | 1·00 |
| Average of twenty experiments ... | 17·99 | 18·98 | 1·055 = log. 11·4 |
| Average of ten experiments, marked (1) | 19·02 | 19·60 | 1·030 = ,, 10·8 |
| Average of ten experiments, marked (2) | 17·00 | 18·35 | 1·079 = ,, 12·0 |

## KCL (0·186 GRAMMES PER CENT.)

($\frac{1}{40}$ gramme equivalent molecule per litre).

| Number of Experiment | $E_{\alpha}$ × 10−3 Daniell | × 10−3 Daniell $E_{\omega}$ | $\frac{E_{\omega}}{E_{\alpha}}$ |
|---|---|---|---|
| **Experiment CLX** (1) ... | 19·80 | 23·50 | 1·19 |
| ,, **CLXI** (2) ... | 19·27 | 22·44 | 1·16 |
| ,, **CLXII** (1) ... | 19·27 | 21·12 | 1·10 |
| ,, **CLXIII** (2) ... | 17·16 | 21·65 | 1·26 |
| ,, **CLXIV** (1) ... | 22·18 | 23·76 | 1·07 |
| ,, **CLXV** (2) ... | 17·16 | 22·18 | 1·29 |
| ,, **CLXVI** (1) ... | 20·06 | 20·59 | 1·02 |
| ,, **CLXVII** (2) ... | 17·95 | 20·06 | 1·12 |
| ,, **CLXVIII** (1) ... | 17·95 | 18·74 | 1·04 |
| ,, **CLXIX** (2) ... | 17·69 | 20·33 | 1·15 |
| ,, **CLXX** (1) ... | 17·95 | 19·54 | 1·09 |
| ,, **CLXXI** (2) ... | 17·16 | 19·01 | 1·11 |
| ,, **CLXXII** (1) ... | 21·65 | 25·08 | 1·16 |
| ,, **CLXXIII** (2) ... | 19·01 | 21·91 | 1·15 |
| ,, **CLXXIV** (1) ... | 19·54 | 21·12 | 1·08 |
| ,, **CLXXV** (2) ... | 18·22 | 23·76 | 1·30 |
| ,, **CLXXVI** (1) ... | 18·22 | 22·97 | 1·26 |
| ,, **CLXXVII** (2) ... | 14·52 | 24·02 | 1·65 |
| ,, **CLXXVIII** (1) ... | 16·90 | 21·91 | 1·29 |
| ,, **CLXXIX** (2) ... | 14·52 | 20·33 | 1·40 |
| Average of twenty experiments ... | 18·11 | 21·70 | 1·198 = log. 16 |
| Average of ten experiments marked (1)... | 19·35 | 21·80 | 1·129 = ,, 13·5 |
| Average of ten experiments marked (2)... | 17·26 | 21·56 | 1·249 = ,, 17·8 |

An examination of the experimental observations tabulated in the two last tables establishes some confidence in the average uniformity of action of the two solutions upon the injury current of nerve. Either solution may be truly said to produce an effect characteristic to itself and different from that produced by solutions of different concentration.

The results obtained are not, however, as great as was anticipated from the point of view justified by the examination of solutions of greater concentration, namely, that the results of all solutions of KCl could be summed up in a universally applicable 'concentration law,'

$$\frac{E\omega}{E\alpha} = \log \frac{1}{n} \text{ (approx.)}$$

Thus in the case of solutions of ·372 grammes per cent. KCl, the concentration in gramme molecules per litre, n, is equal to $\frac{1}{20}$. The dissociation constant at this concentration is ·9. The concentration of the dissociated moiety of the KCl is nearly that of the total KCl present,

$$\frac{\cdot 9}{20}$$

$$\therefore \frac{E\omega}{E\alpha} = \log \frac{1}{\frac{\cdot 9}{20}}$$

$$= \log.\ 22{\cdot}\dot{2}\dot{2}$$

$$E\omega = 1{\cdot}345 \times E\alpha$$

But the actual result of the experiments was not this; the final value was smaller than such anticipation suggested, and was

$$E\omega = 1{\cdot}055 \times E\alpha$$
$$\text{or } E\omega = E\alpha \log.\ 11{\cdot}4$$

Similarly, in the case of ·186 grammes per cent. solutions of KCl ($\frac{1}{40}$ gram. mol.), the anticipation of the general law is not fulfilled; is, indeed, further from attainment than in the last case.

Thus the dissociation constant at this concentration is ·93 (approx.)

$$n = \frac{\cdot 93}{40}$$

$$\therefore E\omega = E\alpha \log.\ \frac{1}{\frac{\cdot 93}{40}}$$

$$= E\alpha \log.\ 43$$

$$= E\alpha \times 1{\cdot}63$$

Whereas the result actually obtained was—

$$E\omega = E\alpha \times 1{\cdot}20$$
$$E\omega = E\alpha \log.\ 16.$$

Nor is this the most severe way in which the difference between anticipation and reality could be described. An examination of the first of these two tables will show that in this series of experiments the anticipated result was not even once approached; that in the second table the anticipated result was only once obtained, and then in an experiment upon a 'second nerve' (Experiment CLXXVII). The universality of the general 'concentration law' has, therefore, broken down, while still the general statements made as to the graduated effects of solutions of different concentration are unaffected, as will be seen from the collection of the results in the following table:—

### SOLUTIONS OF POTASSIUM CHLORIDE

| Concentration in grammes per cent. | Number of Sciatic Nerves examined | Average initial Potential Difference | Average final Potential Difference | The Final Value expressed in terms of the Initial Value as unity |
|---|---|---|---|---|
| 7·45 | 10 | ·0160 Daniell | ·0018 Daniell | 0·11 |
| 3·72 | 10 | ·0174 ,, | ·0076 ,, | 0·44 |
| 1·86 | 11 | ·0174 ,, | ·0105 ,, | 0·60 |
| 1·49 | 8 | ·0181 ,, | ·0123 ,, | 0·68 |
| 0·75 | 20 | ·0175 ,, | ·0179 ,, | 1·02 |
| 0·37 | 20 | ·0180 ,, | ·0190 ,, | 1·06 |
| 0·19 | 20 | ·0181 ,, | ·0217 ,, | 1·20 |

It has been pointed out (p. 325) that the 'concentration law' has an interest of much greater magnitude than that given to it by the fact, that it successfully describes the effects of solutions within a wide range of concentrations.

*It has a value which is given to it by its own form.* The form is, in the first place, a confirmation of the position which has been maintained in this paper as regards the method of production of the injury current. In the second place, the actual numerical values of the expressions contained in this law have a very great interest; for no matter what the explanation of the quantitative relation discovered between the results of immersion in solutions of varied concentration, whether it is the one here taken or some other, the expression $E\alpha = E\omega \log. \frac{1}{n}$ gives rise intrinsically to a most important question.

*This expression* (*since log.* $1 = 0$) *predicts a value for the solution, an immersion in which should reduce the value of the injury current to zero; and the prediction is a very* *remarkable one.* For the value of the predicted concentration is one gramme equivalent molecule (dissociated) per litre, and is, therefore, very great; being that of a solution capable of exerting an osmotic pressure ten times greater than that of ordinary 'normal saline' solution.

If, therefore, the theory here maintained is the true one, if the injury current is due to the contrast between internal and external solution, if also the electrolytes of this internal solution are not very different from the chlorides examined; then the concentration law, as found, points to the existence of a solution of this extraordinary concentration within the axis cylinders of the nerve fibres.

If on the other hand, the theory now maintained and supported by so much circumstantial evidence is false; then, if still the 'concentration law' holds good, *an explanation has to be found for this relationship explanatory of another indication which it holds forth, namely, that a solution of greater concentration still must reverse the direction of the injury current.*

For take the expression $E_{\omega} = E_{\alpha} \log \frac{k}{n}$; in this expression when 'n' is greater than 'k,' then $\log \frac{k}{n}$ becomes negative, and with it necessarily also the value of $E_{\omega}$, the final potential difference after immersion.

In illustration of this necessity the following experiments with solutions of NaOH are given. The data given are the results of experiments upon sciatic nerves (cats) exactly similar to the preceding ones, and like them shewing the effect of immersions of five minutes duration.

SOLUTIONS OF NaOH

| Number of Experiment | Concentration of the Solution in grammes per cent. | Initial Potential Difference × 10—3 Daniell | Final Potential Difference × 10—3 Daniell | Final Value expressed in terms of the Initial Value as unity |
|---|---|---|---|---|
| * (1) ... | 0·025 | 23·0 | +23·9 | +1·04 |
| Experiment CLXXX (2) ... | 0·063 | 13·2 | +20·1 | +1·60 |
| ,, CLXXXI (1) ... | 0·125 | 13·2 | +15·0 | +1·14 |
| * (1) ... | 0·250 | 20·1 | + 9·0 | +0·45 |
| ,, CLXXXII (1) ... | 0·500 | 20·9 | + 1·9 | +0·09 |
| ,, CLXXXIII (2) ... | 1·000 | 20·3 | — 1·3 | —0·06 |
| ,, CLXXXIV (1) ... | 1·000 | 13·3 | — 2·3 | —0·16 |

* Experiments previously quoted on pages 298, 302

I have shewn previously* that the results of more prolonged immersions in solutions of NaOH follow the same law (general statement) as that followed by the results of such electrolytes as NaCl, KCl, HCl. The experiments given above are the only ones which I have performed with immersions of short duration, and are given without exception. If attention is paid to the ratios in the last column, then, the first experiment excepted, the experimental results form an excellent series of values declining to a complete reversal. If attention is paid to the final differences of potential alone then there is no exception, and such a course is justified by the data and observations of page 300. Exception or not, the fact of the reversal is definite, and is confirmed by repetition.

The form, therefore, of the 'concentration law' is of the utmost importance. Is it to be considered as unfavourably affected by the failure to bring within its limits the results of experiments with solutions of ·37 and ·19 grammes per cent. potassium chloride? Without hesitation one answers that it is not, and this answer is based upon evidence already exhibited in this paper. *In the first place*, consider the curves of fig. A, page 292, and the experiments from which they were drawn, which shew the anomalous effect of solutions less concentrated than the 'isotonic' solution. The same anomaly has undoubtedly here presented itself in this attempt at quantitative comparison.

The evidence of those earlier experiments is, however, decisive in its indication that the anomalous variation is secondary to a primary normal variation capable of anticipation upon the lines there indicated and now more definitely formulated in the 'concentration law.' The considerations there advanced in explanation of this secondary anomaly may be summarized in the statement—*that the decline of the injury current is more rapid in solutions below the 'isotonic' solution in concentration, because the diffusion of electrolytes out of the axis cylinders of the nerve is more complete.* The decline in this case is, as was then shewn, a real one, and is in contrast to the apparent decline which is experienced in concentrated solutions.

It has been previously asserted (page 303) that the final value after immersion should be compared, not to the initial value, but to the value as affected by the normal decline, and that there is no means of doing this. The necessity for such a correction is greater still when it is acknowledged that the experimental modifications used are inevitably themselves productive of variations in this rate of decline.

The error cannot therefore be allowed for, and necessarily limits the possible range of experiment: for its mode of action is capable of prediction, but not its quantitative value. That the error has been met with in these experiments with dilute solutions is a fact to be recognized, and regretted, but in no way can it be allowed to detract from the value of the remaining experiments.

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* Preliminary communication, *Proceedings Royal Society*, vol. 67, p. 322.

*In the second place*, the results obtained by the immersion of nerves in hydrochloric acid (page 309) strongly reinforce such a line of argument. In that instance the widest range of effects, from extreme increase to extreme decrease of the injury current, was obtained by the use of a set of solutions all much more dilute than the 'isotonic' solution. All these solutions practically formed 'vacua' into which the electrolytes of the nerve diffused with great rapidity, the limit to the extent being determined by the time of immersion and being practically the same in each case.

In this case the effect of the error is not obvious, because it is always maximal and the same in the results of every solution used. It is not obvious until the actual quantities in the 'concentration law' for hydrochloric acid solution is examined.

$$\frac{E\omega}{E\alpha} = \log. \frac{\cdot 1}{n}$$

The value of k in this example is minimal. One of the reasons which contributes to this diminution is the factor capable of definite anticipation, namely, the dilution of the 'internal solution' of the nerve by rapid diffusion processes.

The form of the 'concentration law' is always the same; conclusions deducible from its form, such as the possibility of reversing the direction of the injury current are, therefore, inevitable. The actual value of the constant 'k' which it contains

$$\frac{E\omega}{E\alpha} = \log. \frac{k}{n}$$

is the same for a very great range of concentrations, and is only varied by conditions which change permanently the value of the source of the injury current. *The meaning of this value* 'k' *is fixed by the form of the law, when* k = n *the injury current vanishes;* 'k' *therefore is the concentration of the solution, an immersion in which will reduce the value of the injury source to zero, and necessarily is different for different conditions of the nerve.*

The particular value of 'k,' which is of the greatest interest, is the value which is true for the effects of immersion in solutions which produce the least permanent effect upon the conditions of the nerve, that is for the value obtained by experiments with solutions as near the 'isotonic' solution in concentration as possible. The range of concentration, which is suggested as being most worthy of accurate experiment, is from one-fifth to one-tenth gramme molecule per litre of the chloride solutions which have been examined.

From this point of view the following series of experiments with one-eighth gramme molecule KCl seem worthy of especial attention.

In order that the real quantitative value of these results may be of permanent interest, they also are given as they were taken in succession, and are given, without exception, from a series of experiments performed one after another in the course of three days. It will be seen that the initial values are greater than usual, a fact which is probably explainable in terms of the temperature of the air in which the observations were made, 23·5° C (July 16, 1901). The solutions were, of course, kept at the standard temperature of 18° C, but the actual measurements were necessarily affected by the temperature of the electrodes and of the moist chamber which were at the temperature of the room.

This average initial value, greater than usual, has induced me to withhold these experiments from their proper place amidst those previously given; where, had it been possible, I would have preferred to have produced tables in which the experiments were in each case so many and so distributed over different periods of the year (different room temperatures) that the average initial value observed should have been in each case the same. For then the average final values can be expressed in terms of the general average initial value.

### KCl (·93 GRAMMES PER CENT.)

($\frac{1}{8}$ gramme equivalent molecule per litre)

| Number of Experiment | $E\alpha$ | $E\omega$ | $\frac{E\omega}{E\alpha}$ | $\frac{k}{n}$ |
|---|---|---|---|---|
| **Experiment CLXXXV** (1) ... | 22·44 | 20·59 | 0·917 = log. | 8·27 |
| ,, **CLXXXVI** (1) ... | 21·91 | 21·12 | 0·964 = ,, | 9·20 |
| ,, **CLXXXVII** (1) ... | 21·91 | 20·59 | 0·940 = ,, | 8·71 |
| ,, **CLXXXVIII** (1) ... | 21·91 | 19·54 | 0·892 = ,, | 7·80 |
| ,, **CLXXXIX** (1) ... | 22·70 | 23·22 | 1·023 = ,, | 10·55 |
| ,, **CXC** (1) ... | 22·57 | 20·33 | 0·900 = ,, | 8·00 |
| ,, **CXCI** (1) ... | 26·66 | 24·29 | 0·911 = ,, | 8·15 |
| Average of seven experiments all upon nerves marked (1) ... ... | 22·87 | 21·38 | 0·935 = log. | 8·61 |

$$E\omega = E\alpha \log. 8{\cdot}61.$$

From this case then

$$\frac{k}{n} = 8{\cdot}61$$

and, since $n = \frac{1}{8} \times {\cdot}85$, the dissociation factor at this concentration being ·85, therefore

$$k = \frac{8{\cdot}61}{8} \times {\cdot}85$$
$$= {\cdot}91$$

and the 'concentration law,' judged from this instance, is

$$E\omega = E\alpha \log. \frac{{\cdot}91}{n}$$

The concentration of the solution, therefore, which is indicated by this result as likely to annul the injury current, is ·91 gramme molecule (dissociated) per litre of potassium chloride, that is a solution of approximately 10 grammes per cent. of KCl.

Contrast such a result, which is in complete agreement with those obtained from the majority of the examples previously given, with the conclusion to be derived from an examination of the 'concentration law' for a range of extremely dilute solutions, ·2 grammes per cent. KCl, etc. There, judging from the example given on page 332, the 'concentration law' is

$$\mathrm{E}\omega = \mathrm{E}\alpha \log.\ 16$$

$$n = \tfrac{1}{40} \times {\cdot}94$$

$$\therefore \mathrm{E}\omega = \mathrm{E}\alpha \log.\ \frac{{\cdot}37}{n}$$

The concentration of the annulling solution here indicated is ·37 gramme molecules (dissociated) per litre of potassium chloride, that is a solution of approximately 3·5 grammes per cent of KCl.

Why should a nerve, which has been immersed for five minutes in an almost 'isotonic' solution, be so repeatedly drawn into prophecying the annihilation of this phenomenon of the injury current as the result of an immersion of similar duration in 10 grammes per cent. KCl, and a reversal of the phenomenon as the result of immersion in solutions stronger than this: whereas a nerve which has been immersed for five minutes in a very dilute solution, far below the concentration of the isotonic solution, prophesies a similar doom for itself when less stringent measures are used against it, namely, when it is immersed in 4 grammes per cent. KCl ?

The answer, suggested by many facts exhibited in this research, and also by its absolute inherent probability, is that the reason is to be found in the removal of electrolytes from the nerve. A removal which has permanently diminished the value of the structures giving rise to the injury current, and 'weakened the nerve' by diluting the internal solutions of the axis cylinders.

# THE CONDUCTIVITY OF THE INTERNAL SOLUTION

If, as has been assumed in the previous section, the immersion of a nerve in solutions approximately isotonic with 'normal saline,' and in solutions slightly more concentrated than this, does not affect to any appreciable extent the pre-existing concentration of the internal solutions ; it should be possible by measurements of the conductivity before and after the immersion to calculate the amount of this which is due to the 'internal solution.'

The data from the following two experiments may serve this purpose in a preliminary fashion, sufficing until they can, as is intended, be repeated with solutions of other concentrations.

The first experiment given below, A, serves to shew that a nerve which has been immersed in a ·745 grammes per cent. solution of potassium chloride is practically unaltered, as far as its conductivity is concerned, by the immersion ; just as in the last section it was shewn that it is unaltered as far as the difference of potential between its longitudinal surface and cross section is concerned.

The experiment is produced mainly so that it may be seen that the basis of the calculation made upon data of the subsequent experiment, B, is not very far from accuracy. This basis being the assumption that the conductivity of the external solution pre-existent upon the nerve is practically that of a ·745 grammes per cent. solution of potassium chloride.

## Experiment A

Sciatic Nerve of cat immediately removed from the animal after death.

The following measurements were made before and after immersion of the nerve in ·745 per cent. KCl ($\frac{1}{10}$ normal solution). for five minutes, at 18° C. :—

| Before | | After | |
|---|---|---|---|
| Weight | ·200 grammes [*] | Weight | ·201 grammes [*] |
| Length | 4·7 centimetres | Length | 4·6 centimetres |
| Resistance | 20,500 ohms | Resistance | 20,100 ohms |

---

[*] The treatment to which these nerves were subjected was exactly the same as that dealt out to the nerves used in the experiments of the preceding section : the time of immersion, the temperature of the solution, the method of subsequent drying of the nerve in filter paper, etc.

The attempt was always made in the subsequent drying of the nerve to regain after immersion the original condition of the nerve, as far as the presence of surface moisture is concerned. To succeed in this attempt it was considered necessary to deliberately dry the nerve, even at the apparent risk of injuring it, until it no longer left any damp mark upon the filter paper.

The minuteness of the alteration in weight recorded in experiments A and B is taken as evidence of this attempt.

The point is not unimportant, since the fact which it establishes is of interest from the point of view that the external solution is a 'short circuiting solution.' The fact may be stated as follows :—

The bulk of the pre-existent external solution, unlike its conductivity, was not affected in these experiments.

From these data the 'specific resistance' in each case can be calculated (for method see p. 260) and is—

| Before | After |
|---|---|
| 186 ohms | 190 ohms |

corresponding to a 'specific conductivity' in each case respectively of 50·7 and 50·2, expressed in the usual units.

The alteration in the specific conductivity is therefore extremely small, and may, for the purposes of calculation from the data of the next experiment, be neglected.

## EXPERIMENT B

Sciatic Nerve of cat immediately removed from the animal after death.

Measurements taken before and after immersion in a 1·49 grammes per cent. solution of potassium chloride ($\frac{1}{5}$ normal solution), for five minutes, at 18° C.

| Before | | After | |
|---|---|---|---|
| Weight ... | ·2035 grammes | Weight ... | ·1995 grammes |
| Length ... | 5 centimetres | Length ... | 5 centimetres |
| Resistance ... | 22,276 ohms | Resistance ... | 20,500 ohms |
| Specific resistance | 181 ohms | Specific resistance | 164 ohms |
| Specific conductivity | 52·7 in terms of mercury at 18° C × $10^{-8}$ | Specific conductivity | 58·1 in terms of mercury at 18° C × $10^{-8}$ |

In this experiment there is a considerable alteration in the 'specific conductivity.' This increase is also not to be explained by the addition of a new cylindrical covering of solution in excess of its pre-exisistent one, since the weight has diminished by 4 milligrammes, most probably by the abstraction of water from the internal solution.*

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* Preliminary Communication, *Proceedings Royal Society*; 67, 317.

From this fact and from the following considerations an attempt is made to deduce the conductivity of the internal solution.

In the first place, it is assumed that an 'external solution' of the conductivity of ·745 grammes per cent. KCl has been replaced by a similar bulk of a solution of 1·490 per cent. KCl, an assumption which is justified by the regularity of the results obtained in the preceding section of this paper.

In the second place, the alteration in weight is taken as too small to affect the result.

It may, therefore, be considered that the following equations represent the conditions present :—

(1) The conductivity as measured before immersion. = { The conductivity of the pre-existent 'external solution,' having the same specific conductivity as one-tenth normal solution of KCl.
+
The conductivity of the internal solution. }

(2) The conductivity as measured after immersion. = { The conductivity of a solution of one-fifth normal KCl, having the same spatial distribution as the pre-existent 'external solution.'
+
The conductivity of the internal solution. }

But these equations are simplified by the fact that the specific conductivities of one-tenth and one-fifth the normal KCl solution are known and are to one another practically as 1 is to 2.

Therefore,

$$(1) \quad 52{\cdot}7 = C_e + C_i$$
$$(2) \quad 58{\cdot}1 = 2\,C_e + C_i$$

where $C_e$ is the conductivity of the 'external solution' and $C_i$ is the conductivity of the 'internal solution,'

$$\therefore \text{ by subtracting (1) trom (2)}$$
$$C_e = 5{\cdot}4$$

That is to say, that the conductivity due to the pre-existent external solution is practically one-tenth of the total conductivity of the nerve.

*As a corollary it follows that the conductivity of the axis cylinders accounts for nine-tenths of the total conductivity of the nerve.*

In the sciatic nerve of the cat only one-third of the total area of the nerve is taken up by the circular bundles of nerve fibres. This figure was obtained by casting the enlarged shadow of a cross section upon a screen, drawing over the shadow, cutting up and weighing the paper.

Let us, as a concession, admit that one-half of the space is so taken up.

In the nerve bundle only one-third of the space is taken up by the axis cylinders of the nerve fibres. This figure was found by the examination of an enlarged microphotograph of a cross section of a fasciculus of nerve fibres.*

On this computation only one-sixth of the total cross section of the nerve consists of cross sections of axis cyclinders.

Let us, as a further concession, admit that the axis cylinders form one-fifth of the total bulk of the nerve.

*Therefore, we find ourselves to have come to the opinion that structures occupying only one-fifth of the bulk of the nerve account for nine-tenths of its electrical conductivity.*

The amount of water in the nerve is not more than two-thirds of its weight. All the electrolytes which can conduct an electrical current are in solution in this water.

Let us suppose the water to be uniformly distributed throughout the nerve trunk, to be all free to take electrolytes into solution, and admit that two-thirds of the mass of the axis cylinders consists of solutions of electrolytes.

Then it follows that solutions occupying only two-fifteenths—

$$\frac{2}{3} \times \frac{1}{5} \quad \text{or} \quad \frac{2}{15}\text{ths}$$

of the total bulk of the nerve account for nine-tenths of its conductivity.

Truly, although the total conductivity of the nerve is small, the specific conductivity of these solutions in the axis cylinders of the nerve must be very great.

The specific conductivity of nerve = 50 ... ($\text{Hg.} \times 10^{-8}$).

$$50 \times \frac{9}{10} = 45$$

The specific conductivity of solutions occupying only 2-15ths of the space, and accounting for a conductivity of 45 is equal to

$$4 \times \frac{15}{2} \text{ or } 340 \text{ (approx.)}$$

*That is to say, upon this computation, that the solutions of the axis cylinder have a conductivity as great as that of a 2·6 grammes per cent. solution of KCl.*

These figures are large. They are not so large as an admission of any, even of the necessary, imagination might have made them. They are too small to explain the facts of the previous section, but even in this form they are large enough to provide a basis for criticism of the 'apparently' concentrated solutions of the axis cylinder.

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* This figure was determined by the examination of a square area of the drawing in Böhm Davidoff and Huber ; p. 143.

# GENERAL CONCLUSIONS

It is impossible, in considering the electrical phenomena accompanying manifestations of change in the body, to neglect the primary importance of processes of diffusion in their production : and in no case is such a statement more apposite than when it is brought to bear upon electrical phenomena determined by injury. For the quantitative distribution of electrolytes in the tissues is notoriously by no means uniform, and the tendency to uniformity which follows injury is necessarily the cause of their redistribution.

It, therefore, follows that in the case of any remarkable electrical phenomenon, attributable to 'injury,' the part taken in its production by this redistribution of electrolytes must *necessarily* be examined. Where this enquiry has not been elaborately made, there is reason to undertake it, even if some other cause has, upon apparently adequate grounds, been previously assigned to the phenomenon.

When, as in the case of the injury current of nerve, the pursuit of the cause has been abandoned, and an agreement has been come to, to cover the abandonment by a phrase ; then, such a course can only be justified upon the grounds that the phenomenon is of very minor importance, and is better disregarded whilst more fundamental facts are being observed and investigated.

In the case of the injury current of nerve the abandonment has been definite, the justification has not been pleaded ; since under whatever phrases the phenomenon and its causation have been concealed, it is a matter of common opinion that this phenomenon may be a crude, stationary, and therefore useful, instance of the travelling phenomenon of the nervous impulse.

The lack of justification is not only made evident by such an important consideration, but even better so by another still more important one ; for the evidence is by no means conclusive, is even fallacious when apparently most definite, which has been used to prove that the injury current is not the outcome of conditions pre-existing in the nerve fibre.

As long as it remains possible to regard this phenomenon as due to previously existent structures newly arranged in regard to one another by the process of injury ; so long must it be regarded as probably a most important guide to the differences of structure between the component parts of the nerve ; since such differences can be estimated by use of the electrical phenomenon as an index, and the new arrangement consequent upon injury is capable of being directly studied.

There is no justification, therefore, for an abandonment of the enquiry into the causation of this phenomenon.

There is one 'pre-existent structure' of the nerve which necessarily plays an important part, namely, the barrier (or barriers) which previously to the occurrence of 'injury' had maintained separate and distinct from one another the different structures of the nerve.

There is another 'pre-existent structure' also of undoubted importance in determining the value and direction of the phenomenon, namely, the solution which bathes the outer surfaces of the nerve fibres.

The value of this last factor has been studied in this paper, and it has in this research been definitely proved to have a value which is only and completely given to it by the fact that it is a solution of electrolytes : a value which may be altered in a precise and quantitative manner by modifications of the electrolytes which it contains; these modifications adding to it, subtracting from it, and even reversing it.

The strength of the solution, as it exists upon the nerve removed from a living animal or immediately after death (before the stoppage of the circulation has had time to lead to local modifications in the lymph), is that of the ordinary 'normal saline' solution; that is to say it is 'entirely pre-existent :' modifications occurring later are only sources of error in the estimation of its importance.

The remaining structure upon which the injury current depends, the 'internal solution' of the nerve, as necessarily owes all its importance and value to the fact that it is a solution of electrolytes ; and it is, as such, capable of modification by the addition or subtraction of electrolytes.

The decision as to its 'pre-existent' or 'newly acquired' importance, as determining the value of the injury current, lies entirely in the answer to this question.

*Are the electrolytes in this solution, which render its value (as a solution) different from that of the external 'normal saline,' pre-existent; or are they newly contributed by chemical change, the secondary consequence of injury?*

It is considered that this question is best approached in the following way.

A study of the polarization phenomena of nerve has led to an appreciation of the fact, that the greater part of the conductivity of the nerve is due to the internal solutions of the axis cylinders.

If this greater conductivity means a greater specific conductivity of these solutions, then the injury current is explained in terms entirely of pre-existent structures. If it does not, but means a greater volume of 'normal saline' solution within the axis cylinder than outside of it in the nerve trunk, then the axis cylinder solutions form by far the greatest mass of conducting structure in the nerve.

Changes in the specific conductivity of this mass, such as would follow the addition of electrolytes by chemical change affecting each unit of it, and subsequent to injury, must necessarily add considerably to the general conductivity of the nerve.

There is, however, no evidence that the conductivity of the nerve is affected by injury other than such as is adequately explained by the destruction of 'membranes,' structures which are characterized by low specific conductivity. There is, therefore, no evidence of the addition of electrolytes to the internal solution, nor even of the addition of electrolytes to localized portions of this solution. There is, therefore, no evidence that secondary chemical change takes any part in the development of the injury current.

There is, on the contrary, evidence that all the conductivity of nerve is adequately explained by the presence of its inorganic salts, and, therefore, that all the electrolytes of normal nerve are inorganic salts. The electrical phenomena of nerve, if such evidence is considered as conclusive, depends entirely upon the inorganic salts which it contains.

If it is proven that the injury current is due to a 'pre-existent' differential distribution of electrolytes, and that all the electrolytes it contains are its inorganic salts, then the injury current becomes disappointingly a guide to nothing more than the differential distribution of inorganic salts in the nerve.

The disappointment is modified, however, when the extraordinary nature of the differential distribution, as indicated by this phenomemon, is realized. For the indication it gives is, that there is to be found within the axis cylinders a solution of extraordinary concentration; a possibility itself intrinsically of great interest.

When such a discovery is considered solely from the point of view of the previously determined facts of the conductivity of nerve, and the secondary consequences of conduction by a nerve (the electrotonic phenomena), then it appears at once as the necessary corollary to such facts. Indeed, the probable occurrence of such a differential distribution of electrical conductors within the nerve, as indicated by these facts, has often been considered, even if no definite limits have been given to the speculation. The results of other methods of investigation used by physiologists may be said to have determined the expectation of such a condition, which expectation these results have amply justified.

When such a differential distribution is, however, considered from another side, there is a very grave difficulty in accepting its possibility. For such a concentrated solution placed within the cell of an osmometer, separated only by a semi-permeable membrane from the dilute 'normal saline,' would be found capable of giving rise to a pressure of many atmospheres inside the cell. There is no knowledge available to decide the possible magnitude of the strain, which the extremely minute capillary tubes, in which we may presume this solution lies, would stand; but it is, in ignorance, inconceivable that they should stand such a strain as this.

On the other hand, there is reason to believe that in such capillary tubes the expected osmotic pressure may not arise, although highly concentrated solutions are present. Thus, there is the fact that fibrillar structures may actually concentrate within their pores solutions in which they are immersed, so that the pores finally contain solutions much more concentrated than the 'mother' solution surrounding the fibrillar structure. Such a fact is extremely suggestive when the extremely fine nature of the interspaces which lie between the fibrillae of the axis cylinder is considered. It is more suggestive still when the possibility of regarding the fibrillae as themselves tubular is taken into account.

Accepting all that is taken as known of the minute microscopical structure of the axis cylinder of the nerve: then there is no inherent improbability in the supposition that the inorganic salts of the nerve might there be held enchained in a highly concentrated solution free to move parallel to, but not at right angles to and away from the fibrillae.

Granting such a possibility, we are, however, faced by the important corollary that such concentrations are indeed enchained there, and are, therefore, unable to exert an osmotic pressure, or by diffusing away give rise to electrical phenomena. To explain, in the presence of such an hypothesis, diffusion processes consequent upon injury, it seems necessary to invent a phenomenon really secondary to the injury, involving new conditions of the fibrillar structure.

To invent such a phenomenon is as culpable as the invention of a chemical change, and the necessity for doing so is equivalent to the necessity for abandoning this supposition.

On no lines known, therefore, can we explain how we could place and retain in, and subsequently allow to diffuse away from the axis cylinders, a highly concentrated solution of electrolytes. But the physical capabilities of such a position, in the longitudinal pores of capillary tubules so minute, are unknown, and beyond the reach of investigation.

Granted strong presumptive evidence of the presence of a highly concentrated solution, and of the possibility of its diffusing away from it subsequently to an 'injury,' it is essential first to criticize severely the nature of the evidence.

Granted that the evidence is found satisfactory, then the question of possibilities may be with greater advantage discussed; since such a case might in itself light up possibilities.

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