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Electrochemistry and Neuroscience

Abstract and Keywords

Neurophysiology has long characterized the method of functioning of the nervous system as electrical. This characterization preceded the understanding of the physical sciences with regard to the phenomenon of **electricity** as dependent upon the movement of **electrons** and holes, and the role of the electron in chemistry and **electrochemistry**. The theoretical understanding of the underlying physics behind cell membrane voltages is based upon an 1888 equation, the **Nernst equation**, which was not about electricity at all. This theoretical understanding, from Julius Bernstein in 1902 was not revised when the physical sciences arrived at the description of **cathode rays** as electrons and ionizing **beta radiation**. Consequently, even until the present, neuroscience has struggled with a treatment of electricity that is archaic, a treatment that prevents the understanding of the electrochemical nature of the nervous system, a treatment, which perpetuates the clinical inconsequence of neurological science by preventing the true simulation of the nerve impulse as one involving electrochemistry. In place of this understanding has arisen a form of pseudo-physics that considers the movement of ions in an **electrolytic cell** as I in the equation V=IR instead of R, that invokes obscure entities as **proton pumps** to account for energy transmission in the cell, and that labels this pseudo-explanation as the **chemiosmotic hypothesis**. This suggests that neuroscience's theoretical understanding of electricity is still in the 19th century, and its clinical poverty is a result of this.

List of Key Words
chemiosmotic hypothesis, proton pump, electron, electrochemistry, electricity, beta radiation, Nernst equation, cathode rays, ions, ionic currents

Electrochemistry and Neuroscience

Background

In the mid-18th century Benjamin Franklin noted there appeared to be two types of electrical fluid, which he called positive and negative, and that they would cancel each other out. He also noticed that the charge in atmospheric electricity, lightning, was identical to that produced by rubbing amber and stored in a Leyden jar. In 1791 Luigi Galvani hypothesized the existence of what he called 'animal electricity' as a result of his experiments using Leyden jars on the bodies of small, dead animals, which made their muscles contract as if they were alive. But he also noticed that the muscles would contract even without the intervention of a Leyden jar if mounted a certain way and touched with a scalpel. Alessandro Volta in 1800 announced before the Royal Society that Galvani's 'animal electricity' was actually the reaction between the metals used to mount the animal's parts and the scalpel. He proffered a new apparatus to generate electricity, which depended upon the interaction of the metals, and this became known as a voltaic pile, later to be called a battery. Volta said that animal electricity was nothing more than regular electricity like that which he could produce using his apparatus. This supported the idea that life and animation could be accounted for by appeal to natural processes.

The same year that Volta announced the voltaic pile Anthony Carlisle and William Nicholson used it to decompose water into hydrogen and oxygen. By so doing the two dramatically demonstrated the significance of electricity for chemistry and introduced the notion of polarity to chemistry. What they had created was the first man-made electrolytic cell, a cell to which energy as an electric field from a battery is introduced which causes chemical activity within the cell. In the next ten years Humphry Davy, using electrolysis, was able to isolate and identify six new metal elements. In 1812 Davy gave a lecture at the Royal Institution in London at which Michael Faraday was in attendance. Faraday was so impressed that he avidly pursued his own studies into the phenomena of electricity, light, chemistry, and magnetism.

In the 19th century the study of the restorative effects of electrical stimulation upon the living, human body became widely taken up using voltaic piles. Prior to this experimenters like Franklin had resorted to the use of stored charge in a Leyden jar. Franklin had concluded that the claims for any restorative effects were overstated, and that the pain from the shocking far outweighed any negligible benefits produced. The level of knowledge of electricity at this time did not allow for the understanding that the electricity from a Leyden jar was of a high voltage while that which came from a battery could be of a much lower voltage while allowing for the production of a greater amount of the electrical fluid. What the experimenters looked for was muscle contraction and this could be produced less painfully using a battery. Luigi Galvani and later his nephew Giovanni Aldini believed that the recently drowned could be restored to life using electricity, and conducted tests in northern Italy in the early 19th century to verify this. Such investigations of life and nature were, at the time, known as *natural philosophie*, a term, which was later, replaced with the word 'science.' It was talk of these experiments which prompted Mary Shelley to write her novel *Frankenstein* in 1813 while vacationing in the north of Italy because of a bet with her husband, Percy Shelley. The bet was over who could write a more horrifying story.

In 1823 Andre-Marie Ampere developed a theory relating electricity to magnetism, proposing that the movement of very small electrical charges causes magnetism. In 1908 the International Conference on Electrical Units and Standards adopted the *ampere* as the rate of flow of these small electrical charges, known subsequently as electrons. But in 1831 Michael Faraday and Joseph Henry discovered that electricity could be produced by changes in a magnetic field. This form of electricity became known as *faradic current*, in contrast with *galvanic current*, which was the type of electricity that came from a battery and was intimately associated with chemistry. The former type of current later was referred to as *alternating current* (AC) while the latter became known as *direct current* (DC). In 1833, in correspondence with William Whewell, Faraday introduced the terms *electrode*, *anode*, *ion*, *cathode*, *anode*, *cation*, and *electrolysis*. In that same year he introduced what became known as the law of electrolysis which held that the amount of substance decomposed by an electric current was proportional to the length in time and magnitude of the electric current producing electrolysis. Length in time and magnitude of flow of electrical charges carried by electrons are what amperes concern themselves with. Yet none of these terms were used in discussions of faradic current which was used mostly to create motors and generators through the use of changing magnetic fields and conductors passing through the lines of force of those fields. Alternating current did not have chemical effects but was used mostly for the transduction of mechanical energy, that energy needed to move conductors through magnetic fields. Having found that a magnetic field could affect the polarization of light, Faraday proposed in 1846 that light might be waves in the lines of force in electromagnetism. This marked the first attempt to understand light in terms of electromagnetism.

In 1843 Emil Heinrich du Bois-Reymond by touching an electrode to a nerve and making a muscle jump demonstrated that electricity was used by the nervous system to communicate between different parts of the body. Although this was similar to what Galvani had done fifty years earlier, this time it was in a living creature. This was followed in 1849 by Rudolph von Kolliker's finding that the nerve fibers electrified by Bois-Reymond were the extension of nerve cells. In 1852 Hermann von Helmholtz became the first to discover the speed of transmission of a nerve impulse in a frog's nerve cell. That the speed of the impulse was slower than that of electricity through a wire introduced some complications to the idea that the nerves functioned strictly electrically. As will be seen below, what happened to resolve these complications was the resort, in 1902, by Julius Bernstein to fluid dynamics and thermodynamics to account for this difference in conduction velocity.

In 1855 Guillaume Duchenne, for whom Duchenne's muscular dystrophy is named, recommended that AC was preferable to DC for electrical stimulation since it was not characterized by the skin blistering and pitting that resulted when DC was used to make muscles contract. Muscle contraction, whether in live or dead subjects, was taken as the indication of nerve simulation. Strong contraction was easier to achieve with AC than with DC without attendant skin problems. Duchenne, the father of electrotherapy, did not have the knowledge to understand the difference between the two sorts of current, but the physical scientists did not either. His decision was made on the basis of the effects of the two currents on the patient's skin and the ease of use for the therapist. The use of direct current exposed the skin to ionizing radiation, later known as beta radiation or electron flow, and this is what caused the blistering and pitting that made the use of DC in electrotherapy undesirable. Yet this sort of radiation is also what made direct current have its chemical effect, something which could not be achieved with alternating current. The electrotherapists of the time did not know the difference between voltage transmission and electrochemistry, and how each made the muscle contract in a different way. What they did notice, however, was that muscle contractions triggered with AC were far stronger than those triggered by DC, even on weak muscle, and that AC did not have to be repeatedly turned off and on for each new contraction, as was the case with DC.

The limits of understanding of the nature of electricity characterized the contribution in 1870 of two German physiologists, Edouard Hitzig and Gustav Theodor Fritsch who introduced the study of the brain by electrical stimulation. Patricia Churchland writes of their work, "The first well-designed and significant studies on the nervous system using electrical stimulation were undertaken by two German physiologists...and the method has been of enormous and enduring importance" [1986] Given that knowledge of electricity at the time was so rudimentary, it is suggested that such 'enormous and enduring importance,' whatever it may have been, is related to the enduring clinical irrelevance of electrotherapy. This position will be developed below.

The Relation Between the Electron and Chemistry

During the 1870s Hermann von Helmholtz and others wondered about the possibility of atoms of electricity, and agreed, by 1881, that electric charges in atoms were divided into definite, integral portions, suggesting that there is a smallest unit of electricity. This was reminiscent of Andre-Marie Ampere's 1823 hypothesis about magnetism being due to small electrical charges. Helmholtz was able to detect the passing of nerve impulses in the body and timed their speed, but he did not associate them with electrons or anything like electrons even though they were detectable as electrical. Electronic treatments of the phenomenon of electricity would not become commonplace for almost another quarter century.

In 1881 English physicist George Stoney named the hypothesized particle, the smallest unit of electricity, the *electron* after having coined it in 1874 to stand for his estimate of the unit of charge of Hemholtz's hypothesized atom of electricity. Thinking about the subject of regular atoms, in 1875, James Clerk Maxwell noted that atoms have a structure far more complex than rigid bodies, the rigid bodies of Newtonian classical mechanics. It was Maxwell's later mathematization of the fields of force of Faraday, self-admittedly weak in mathematics and more visually oriented, that provided the unification of optics and magnetism. Almost twenty years later, in 1898, J.J.Thomson discovered the electron a year after Heinrich Lorentz calculated the theoretical mass/charge ratio of an electron by studying the deflection of cathode rays in a magnetic field.

Electrons were first understood as cathode rays and not particles. Cathode rays were emitted by the cathodic electrode into the air when a high voltage was placed across a gap between two electrodes. The rays behaved similarly to light, though the ground electrode took up most of them. The broadcast of cathode rays soon lead to experimentation with what became known later as radio. Advances in the understanding of electromagnetism were driven by hypothesizations of people like Emil Wiechert, a German physicist, who predicted that there existed particles in atoms between 2000 and 4000 times lighter than the hydrogen atom, although these were not yet known to be the same as cathode rays. It would not be until the second decade of the 20th century that the role and place of the electron in the atom would begin to be understood. In 1895 Jean-Baptiste Perrin showed that cathode rays deposit a negative charge where they impact, and thought that this refuted the idea of Heinrich Hertz that cathode rays were waves and instead supported the idea that they were particles. The duality of electrons as particles would later become a foundation of quantum mechanical theorization for, as it turned out, whether electrons could be thought of as one or the other depended upon the procedure used to detect them.

> Until the very last years of the nineteenth century, most if not all physicists who believed in the reality of atoms shared Maxwell's

> view that these particles remain unbroken and unworn...It is true that many of these same physicists (Maxwell among them) were convinced that something had to rattle inside the atom in order to explain atomic spectra. Therefore, while there was a need for a picture of the atom as a body with structure, this did not mean (so it seemed) that one could take the atom apart. However, in 1899, two years after his discovery of the electron, Joseph John Thomson announced that the atom had been split: 'Electrification [that is, ionization] essentially involves the splitting of the atom, a part of the mass of the atom getting free and becoming detached from the original atom. (Pais, 1982)

And with this the electromagnetism was related to chemistry in a theoretical way, unlike the empirical observations of the physical chemists who studied the use of electrolysis to isolate chemical elements. This theorization was to lead to the refinement of the periodic table of the elements in terms of an atomic nucleus and the 'shells' of electrons around it in the 1920s, and, in the next decade, to the understanding of ionic and covalent chemical bonding, things dependent upon these electrons.

In 1902 Julius Bernstein hypothesized that the nerve cell should have a detectable voltage across its membrane if it were to function electrically, a widespread belief in neurophysiology. Like Duchenne, Hitzig and Fritsch, Bernstein knew nothing about the phenomenon of electricity involving the movement of electrons and holes, and the role of the electron in chemistry. The role of the electron in chemical bonding and the arrangement of the periodic table of the elements would not be articulated until the late 1920s and Linus Pauling's work in the 1930s. Instead early electrophysiologists tried to understand electricity in terms of ions and ion movement since Ohm's law, V=IR, was a law for fluid motion. It was believed by neurophysiologists that the electrical fluid could include ions, charged particles, carried along by fluid, in the hopes that this would account for why electrical impulses detected in the body by people like Helmholtz were slower than those in wires. In *Principles of Neural Science* John Koester writes:

> In 1902 Julius Bernstein used the Nernst equation as the theoretical framework on which to develop the hypothesis that the resting potential of neurons is based on the selective permeability of the membrane to K+ [potassium ions]. Bernstein's idea could not be tested quantitatively until the 1940's, when techniques for intracellular recording were developed, and voltage potentials were found across the membranes of cells.(1991).

When these potentials were found it was automatically assumed that the metaphysical framework for them in the Nernst equation was confirmed, that is, these potentials were due to concentration gradients of ions across the cell membrane. The 1888 equation of Walter Nernst was not about electricity however. There is not a single electrical term in it.

What Nernst was dealing with was the thermodynamic, entropic pressure figured to cause two separate concentrations of an ion to mingle so that the concentration gradient between the two solutions would approach the value of one. The terms in the equation are limited to the temperature in degrees Kelvin, the Faraday constant, the gas constant, a term for the sign of the valence of the ion, and the two concentrations of ion expressed as absolute values. Nernst, because he was dealing with ions and pressure, called this pressure a voltage, which is, in the world of electricity, an electrical pressure acting to drive charge carried by electrons. Nernst's voltage was not an electrical pressure, it was an entropic pressure. That electricity wass still thought of as a fluid and Nernst's model dealt with with ions in solution, did not make Nernst's voltage and electrical voltage as electricity was later understood.

But JuliusBernstein arrogated it as an electrical equation, and from that time until the present it has been taken to define the cell membrane potential. Nernst's equation came at a time when there was increasing acceptance amongst chemists that things such as ions and molecules and atoms were real things with shapes rather than hypothetical entities for theoretical physicists. But his equation did not deal with these issues. The only thing electromagnetic about the Nernst equation is the sign for valence; the equation was a mathematical construct and had nothing to do with measurement. "The post-Maxwell, pre-Einstein attitude [about electricity and electromagnetism] which eventually became preponderant was that electrodynamics is Maxwell's equations plus a specification of the charge and current densities contained in these equations plus a conjecture of the nature of the aether."(Pais, 1982) And the Nernst equation, which was devised in that period, had nothing to say about any of these things.

Modern Understanding of Electrochemistry

The standard electrochemical model invokes oxidation-reduction reactions. These are reactions in which electrons are transferred from one place to another. In this model are shown two beakers. In one beaker is found a reducing agent, and in the other an oxidizing agent. The two beakers are connected by a wire along which electrons travel from the beaker with the reducing agent to the beaker with the oxidizing agent. These electrons are made available by oxidative reactions in the reducing agent. The essence of oxidation-reduction is the rate of movement of electrons, the I in Ohm's law V=IR.

In the beaker with the reducing agent oxidation takes place liberating electrons which travel along the wire to the beaker with the oxidizing agent, triggering reduction reactions there. Rather than two beakers, consider now the one in which the oxidative [catabolic, corrosive, cathodic] reactions are taking place is a battery. From the chemical reactions that take place in this beaker the derivation of electrons is possible, and these electrons are introduced to the beaker by a wire, and it is then, consequently, an electrolytic cell, a cell to which energy is introduced. The energy comes in the form of the electrons which introduce an electrical field from the battery. When the beaker is empty, or filled with pure water, an insulator, the movement of electrons from the battery's cathode, the source of electrons and the site of the oxidation taking place, is only possible at high voltages. This is what cathode rays are, high energy electrons, electrons moving under great pressure.

For electrochemical purposes, the amount of voltage needed to drive these electrons is excessive unless there is also what is called a *salt bridge*, and this is the placing of ions in the second beaker's pure water solution to reduce the resistance so that

V doesn’t have to be so high in V=IR for there to be an I, the movement of electrons. A salt bridge is a membrane through which ions may move from one beaker to the other, in the classical, electrochemical model involving two beakers; or gas or ions in solution in the electromagnetic/battery model. In the case of the electrochemical model the membrane is much like that of a biological cell. The movement of electrons over this bridge from chemical reactions outside the biological cell to inside the cell is facilitated by a lower value for R made possible by the movement of ions across the cell’s membrane What is of importance is that there be a measurable pressure from one side of the membrane to the other, for without V there can be no I no matter what the value for R is.

The neuron is treated as an electrolytic cell. That it does not have a wire connecting it to a battery does not remove it from the world of electrochemistry or from electromagnetic analysis. John Koester, in his essay "Membrane Potential" in *Principles of Neural Science* (1991, p.82) writes:

> "In an ionic solution electrical current is carried by ions - both anions and cations. By convention, the direction of current flow is defined as the direction of *net* movement of *positive* charge. Thus, in an ionic solution cations move in the same direction as the current, and anions move in the opposite direction."

What Koester is saying is that cations are drawn to the anode, and anions to the cathode. The anode is where the electrons are introduced, by means of the ionic solution, from the battery. And in this solution the electrons cause electrolysis/hydrolysis. The latter is the breakdown of water into oxygen and hydrogen, with the hydrogen drawn to the anode and the oxygen drawn to the cathode. In the two beaker electrochemical model the anode is the beaker in which the reduction takes place, and reduction involves the bonding of hydrogen to carbon. This is organic chemistry, the same upon which all of terrestrial life is based.

Koester and all of neuroscience regards, mistakenly, the current flow as the movement of the ions when, in physics, the movement of the ions is R and not I in V=IR. It is I that is the current flow, the movement of electrons. Neurophysiologists think that bio-electricity is different from that of the physicists, not involving the movement of electrons, yet rely upon the idea that current flow is dependent upon the net movement of positive charge, as the electrochemist’s would admit. But the electrochemist would insist that current flow is still electron flow, and that the movement of those electrons is indeed dependent upon the movement of positive charge carried by cations moving across a salt bridge [a beaker with ionic solution], but that the two are not the same. Dependence is not identity; the movement of electrons is not the movement of ions in solution. The latter is R, the former is I.

The salt bridge which is composed of the movable ions provides a much lower resistance and thus assures that voltage need not be great, but the movement of these ions is not I. The ions do indeed act as a carrier, introducing a needed value for R that is an important part of any electron movement, but must be distinguished from the thing carried, and that is electrons or chemical energy. Attempts to model the current flow of the nerve impulse based upon consideration of ion movement are, at best, only half correct, and miss what electrons are doing. If the biological cell’s membrane provides the salt bridge, then the movement of cations into the cell from electrical pressure is the result of increased negative charge and reduction reactions there made possible by extracellular chemical reactions like digestion. In a similar dynamic, mitochondrial respiration in the cell's cytoplasm triggers reduction reactions in the nucleus and ribosomes. The implication is that a voltage can be measured from the cytoplasm to the inside of the nucleus and some cellular organelles.

Electrons are things whose existence is problematic; they do not exist until they are measured. Quantum measurement does not imply the use of measuring instruments. Quantum measurement is the interface of the quantum world with its *imaginary numbers* and the chemical Newtonian world in which atoms and molecules have three-dimensional shapes and cells have key-like receptors. Measurement is the residue of negative electrical charge left by a cathode ray striking a surface seen as the phosphorescing on the screen of a cathode ray tube. Another example would be the movement of cations across the membrane of a biological cell to its anodic interior just as if the electrons were being introduced to the cell from the anode of a battery. What is seen is the movement of ions, and this movement is accounted for by the hypothesization of electron movement. No one has ever seen an electron, merely its effects.

Since what is involved is the hypothesization of the movement of electrons, Ohm's law is pertinent. In Ohm's law [V=IR] the rate of movement of electrons, amperes, is I, and the movement of ions is R. This is explained by Richard Feynman as follows:

> Suppose we have a gas in a vessel in which there are also some ions - atoms or molecules with a net electric charge. . . . If two opposite walls of the container are metallic plates, we can connect them to the terminals of a battery and thereby produce an electric field in the gas. The electric field will result in a force on the ions, so they will begin to drift toward one or the other of the plates. An electric current will be induced, and the gas with its ions will behave like a resistor. (1961-63)

The electric field is introduced from an external source, a battery, or a beaker in which oxidation acts as a reducing agent. Its introduction is I. The R is provided by ion movement like calcium in solution. This is not lightning; this is life. Life involves the capture and use of energy by chemistry, at a low voltage. If V is small and there is to be any I, the movement of chemical energy or electrons, then R must be small. This is accomplished by oxidation-reduction reactions facilitated by salt bridges across cell membranes. The more cations in solution the smaller the R, to a point.

Surprisingly, although I may be measurable in view of known effects of hypothesized electrons on instrumentation, R must be assumed when not measurable. And it is not measurable when permeability of a membrane to ion passage is considered, as in the case of the biological cell. This is unlike the measurement of resistance in an electric circuit which is easily determined using an ohmmeter. The measurement of an ohmmeter requires some input, however, unlike the measurement of a voltmeter or an ammeter, which uses some of the energy of the circuit being measured.

This account of electrochemistry and its dependence upon electron and ion movement conflicts with the generally-accepted, neurophysiological model of bio- or neuro-electricity. The latter model forsakes electrons on the notion that any sort of electron movement is dependent upon conduction and the presence of wires which are not found in biological cells or neurons. This latter model treats the movement of ions as I and not as R, and suggests that free electrons do not exist in the body. This model conflicts then with the known fact of chemistry that all chemical reactions are either endothermic or exothermic, and therefore involve the movement of electrons since it is electrons which are chemical energy As will be seen below the movement of ions is tied instead to the rundown of concentration gradients and the action of proton pumps rather than the movement of electrons facilitated by a diminished R through the action of a salt bridge.

The Neurophysiological Model of Bioelectricity and Its Deviation from Electrochemistry

Bertil Hille writes: "Much of what we know about ionic channels was deduced from electrical measurements...The biophysical method fosters sensitive and extensive electrical measurements and leads to detailed kinetic descriptions," and "...cares less about the chemistry of the structures involved than about the dynamic and equilibrium properties they exhibit."(1991) Given that what is claimed to be known about the role of ionic channels was deduced from electrical measurements without understanding of the nature of electricity, it is no wonder that the 'biophysical method…cares less about the chemistry of the structures involved." This despite the claim that the nervous system is or could be electrochemical. Deduction of this sort in which there is a gap in theoretical understanding, is useless if not misleading. In the field of neuroscience, as will be discussed below, the misconceptions of early neurophysiologists as to the nature of electricity have been perpetuated by dedication to historical traditions.

The Nernst/Bernstein theoretical framework for cell membrane voltages caught on and has endured into the 21st century, demonstrating the overriding influence of historical traditions in the field of neurophysiology. Bert Sakmann won the Nobel Prize in physiology in 1991 for his development of patch clamping. Patch clamping allowed for the extremely fine study of cellular electrical functioning through the divination of the meaning of electrical measurements.

When a nerve impulse passes there is a change in cell membrane voltage that heralds its passing. A patch clamp allows for the introduction of electrical charge carried by electrons so that the wave of changing voltage of a nerve impulse is stopped, with the voltage remaining constant. Those who work with patch clamping assert that they are determining the amperage of the ionic current this way, the amperage of R. What they believe is I, the movement of electrons, is, for them, the movement of ions which have the equivalent energy value of electrons, what is termed a 'proton current'. Sakmann stated in an interview in 1994 that "It's very difficult to explain how the current is carried by ions and not by electrons. The way the cell signals and how messages are sent by action potentials or impulses that travel down the axon is hard for people to grasp."(Bass, 1994) Sakmann (Bass, 1994) states: "Membrane potentials are the means by which cells communicate with each other...the requirements for signaling in the nervous system." The motor neurons, types of cell which send signals to the muscle to contract, "...generate action potentials that travel along the nerve...it's all done electrically." Given that, it would seem that the neuroscientific understanding of electricity is badly in need of amendation.

For the physicist, the electric fluid itself became the electron's movement, for the neurophysiologist it remained the ion. In 1952 Alan Hodgkin and Andrew Huxley formulated the modern theory of the excitation of nerves based upon the movement of sodium and potassium ions through ion channels. The detection of voltage changes as a nerve impulse passed suggested to them that these changes were the artifact of ion movement through membrane channels. The voltage, a Nernst voltage, was still tied to the un-chemical, un-electrical ion concentration gradient. Voltage change was associated with the movement of ions up or down the gradient. Electrical excitation of the nerve fiber by voltage transmission was thought to simulate the voltage change analogously, and trigger the movement of ions across the membrane. This bit of circularity held then that not only was the membrane voltage fully dependent upon the ion concentration gradient, but also the voltage could be changed independently of that gradient, thereby triggering changes in the gradient. Such a bit of circularity was possible only in a theoretical construct which sought to render the Nernst equation an electrical equation, and could do so only by taking liberties with the definition of electricity.

Bertil Hille (1991) states that:

> Electrical phenomena arise whenever charges of opposite sign are separated or can move independently. Any net flow of charges is called a CURRENT, and Ionic fluxes are electric currents...

Here Hille is claiming that the movement of ions in an electrolytic cell is not R, it is I. John Eccles, who, with Alan Hodgkin and Andrew Huxley, received a Nobel Prize in 1963 for what became known as the ionic channel school of nerve impulse propagation, in his *The Understanding of the Brain* (1973), wrote, "No engineer could design or imagine anything so beautiful and efficient and effective as a nerve impulse and the communication that it gives along nerve fibers, and so from one nerve cell to others." Sakmann (1994) states, when asked what the channels look like,

> A funnel and a gate large enough to pass one ion at a time...at least this is one theory. The actual mechanism remains a mystery.

In a spinal nerve fiber these ion channels are in the Schwann cell myelin and occur at the Ranvier nodes. Attempts to account how nerve impulses in myelinated fibers travel more swiftly than on non-myelinated nerve fibers touched off years of research which sought to make sense of it all by appeal to the equations of electricity. In 1980 in a *Scientific American* article, Pierre Morell and William T. Norton report in their essay "Myelin" that "...the mechanism by which Myelin facilitates conduction has no exact analogy in electrical circuitry." Below it will be seen that in the attempt to create a more 'exact analogy in electrical circuitry' neuroscientific dogma again takes liberties with the known physics of electricity.

The equations of electrical circuitry are resorted to extensively by John Koester (1991) in his authoritative "Passive Membrane Properties of the Neuron." "A simple mathematical model derived from electrical circuits is helpful for describing the three critical features used by the nerve cell for electrical signaling - the ion channels, the concentration gradients of relevant ions, and the ability of the membrane to store charge."

The claim is that the stored charge is that held by ions, usually cations, and that unbalanced proton/neutron combinations in such ions are equivalent to electrons. "An Equivalent Circuit Model of the Membrane Includes: Batteries, Conductors, a Capacitor, and a Current Generator." (1991) The suggestion here is that the battery is not a current generator.

Koester speaks of 'ionic batteries' and how the charge separation behind the [Nernst] voltage is due to density differences of ions on either side of a membrane, or Q in the equation V=Q/C where C is the capacitance of the membrane. This is the Nernst voltage expressed in electrical terms instead of thermodynamic ones, unlike in the original Nernst equation which was not about electricity. The stored charge, however, is the charge carried by one or more pairs of neutron and proton per atom unbalanced by an electron, as in an ion of hydrogen. The stored charge, according to this model, is not due to electrons although it has the same properties as electrons.

How the current generator differs from a battery is not stated, although the generation of current is associated with a change in membrane voltage, ΔV. The relation is expressed as follows, "When current flows into or out of a cell through ion channels in the membrane, the membrane voltage always changes more slowly than the current." (Koester, 1991) In Nernst the voltage was tied to the concentration gradient, was calculated and not measured, and therefore changed simultaneously with changes in the gradient. Koester seeks to account for deviations in measurement from calculation by introducing capacitors and RC time circuits in order to explain this delay. He writes, "The cell membrane is represented by a capacitor (C) in parallel with a resistor (R)." The currents are described as "C*apacitative membrane current*(s)...carried by ions that change the net charge stored on the membrane." But the net charge stored on the membrane, in this model, is not distinguished at all from the charge carried by the ions. It has no existence apart from that charge carried in the ion. Electrons are not permitted to occur freely in the body.

Koester speaks of membrane resistance, cytoplasmic resistance, and axoplasmic resistance, and sees the myelin as both a capacitor and an insulator, though, in electrical circuitry the two are not the same. That the axoplasm could be treated as a resistor in a membrane 'equivalent circuit' despite its intricate architecture involving microfilaments, microtubules, vesicles of acetylcholine, and neurofilaments, suggests something is amiss in the model. This is detectible in the discussion of resistance. "The greater the length of the cytoplasmic core, the greater the resistance, because ions experience more collisions as they flow down the length of the dendrite." (Koester, 1991) In his diagram he notes how, for all practical purposes, the axon and dendrite are similar in his 'electrical equivalent circuit,' so that the cytoplasmic core and the axoplasmic core can be said to serve equivalent functions. Yet in other diagrams the ion flow along the nerve fiber is depicted as transmembranal and not longitudinal or 'down the length of the [axon],' at all. So in this case the length of the cytoplasmic or axoplasmic core should not result at all in increased resistance to trans-membranal flow. These difficulties are not addressed in the model and need not be since the model has already been awarded a Nobel Prize and has been removed from question or criticism.

Resistance down the axon which connects two segments of membrane, each composed of a resistor (r_m) and a capacitor connected in parallel, is called axial resistance (r_a). Total axial resistance (R_a) is the sum of the numerous segments of axoplasm connecting the many r_m's and membrane capacitors connected in parallel. As the axoplasm is lengthened R_a increases but not r_m, apparently. Longitudinal and axial movement of ions in this model is considered so analogous to electron movement that the equations of electricity are treated as still valid for fluid dynamics if the fluid carries ions.

The treatment of the axoplasm as a resistor in an 'equivalent circuit' rather than a conductor of sorts, expressed by Koester (1991) in his "Passive Membrane Properties of the Neuron," has its precedent in the work of Eccles, Hodgkin, and Huxley almost forty years earlier. Koester (1991) writes:

> Rapid propagation of the action potential is functionally important, and two distinct mechanisms have evolved to increase it. One adaptive strategy is to increase conduction velocity by *increasing the diameter of the axon core*. Because the axial resistance (r_a) decreases in proportion to the square of the axon diameter, while the capacitance per unit length of the axon (c_m) increases in direct proportion to diameter, the net effect of an increase in diameter is a decrease in $r_a c_m$. This adaptation has been carried to its extreme in the giant axon of the squid..

John Eccles (1973) implies that the structure of the nerve fiber is not at all important to the way it works naturally, that the contents of the axon could be considered as a resistor, where a resistor is seen as an impediment to flow rather than a requirement for flow, and something that can be dispensed with entirely in the attempt to show that the favored model was confirmed. In other words making r_a equal to zero eliminated consideration of RC time factors, and the two conductors (cytoplasm/axoplasm and extracellular fluid) would carry voltage changes introduced from an electrode along the membrane as fast as regular electricity, something which nature seems to have overlooked in the evolution of nervous systems in its pursuit of speedier nerve impulse propagation. Eccles writes:

> The content of the axon has the consistency of jelly, and for most purposes you can substitute an appropriate salt solution without deteriorating impulse conduction by the fiber. For example Baker and Shaw were able to squeeze out the contents of the squid giant axon with an open end by a kind of microroller, leaving a collapsed, flattened axon that appeared destroyed. Yet when they reinflated it by an appropriate salt solution, a potassium salt, the fiber was restored and conducted well for hours.

That Eccles and the ionic channel school though it was valid to alter the nerve fiber drastically so that confirming measurements of the model could be obtained suggests some blurring of the digital with the analog. Koester (1991), in his"Voltage-Gated Ion Channels and the Generation of the Action Potential," writes:

> In its most basic form a change in membrane potential involves the flow of ionic current through membrane channels, which leads to a change in the net charge stored on the membrane. This process does not require a

> change in intracellular ionic concentrations, and in general such changes are negligible.

Yet that flows of ions into the cell as an impulse passes can fail to have no more than a negligible effect on concentrations there, is a notion that is in conflict with the foundation of modern understanding of electrical readings. That foundation is the Bernstein hypothesis and its reliance upon Nernst to account for those readings in terms of ion concentration gradients. The Nernst equation suggests that voltage changes from negative to positive as a nerve impulse passes herald significant ion concentration changes. The Nernst foundation is not, however, questioned by neuroscientists like Koester who, on the one hand, assert its relevance, and on the other, as above, dismiss it as negligible. It would seem more likely, and be in accordance with the conservation of energy, if the mass of the ions that moved was equivalent to the mass of electrons that were moving. That way few ions would have to move for great movements of electrical charge carried by electrons, the former being several thousand times greater than the latter. But this account is ruled out by neurophysiological dogma which does not allow for free electrons in the body despite that without the movement and sharing of electrons there can be no chemical reactions.

Electrochemistry suggests that it is not the movement of ions that changes the net charge, but instead the two are related as R and I in Ohm's law. Change in net charge due to I is facilitated by ion movement (R) across a salt bridge or membrane ion channel. But it is not ***caused*** by that ion movement. That ion movement is the smaller R which makes possible the electron movement at a lower V then would otherwise be needed.

Those who work with patch clamping in tinkering with this net charge and its changes as an impulse passes insist what they are measuring in amperes is capacitative membrane current said to be carried by ions behaving analogously to electrons. This sort of current, according to Koester, is said to differ from 'ionic current' in that, despite the fact that both types of current are allegedly carried by ions and treated as I in Ohm's law, ionic current is flow of cations into and out of the cell as 'leakiness' while capacitative membrane current I can apparently flow either way and effects the net charge stored on the membrane. "The sum of these two components is the total membrane current." (Koester, 1991)

Since what is measured is measurable in amperes, then the patch clampers are missing entirely the movement of electrons, I, confusing R with I and entirely overlooking the movement of electrons longitudinally down the nerve fiber as they accelerate from one node to another. This misunderstanding as to what is being measured suggests that neuroscientists are getting only half the picture of the nature of the nerve impulse, and the half they are missing is the half which deals with the reduction triggered by electrons liberated by an oxidative reaction in the beaker of the reducing agent, whether that beaker is the gut or the respiration of a mitochondria.

Further Problems with Traditional Views of Neuro-electricity

Hille (1991) writes,

> One can draw an analogy between Ohm's law for electrical flow and the rule for flow of liquids in narrow tubes" and "In this heroic time of what can

> be called classical biophysics (1935-1952) the membrane ionic theory of excitation was transformed from untested hypothesis to established fact...The story illustrates the tremendous power of purely electrical measurements in testing Bernstein's membrane hypothesis.

The misunderstanding of the nature of electricity suggests that the testing of Bernstein's membrane hypothesis was certainly not rigorous. And that it made the move from 'untested hypothesis to established fact' is a claim that is certainly not incontrovertible.

The Nernst potential deals with states in which there is no flow between the two concentrations. Of the changing of membrane voltages accompanying the passage of a nerve impulse Hille (1991) writes, "...[the] simplifying rule of equilibrium cannot be applied, and the derivation must make assumptions about the structure of the channel," i.e., about the values to be assigned to the permeability of the channels (rm) so that restrictions to ion flow could be treated as the R in Ohm's law. John Koester (1991) in his "Membrane Potential" shows a graph of cell membrane potentials versus potassium ion concentration gradients. It is seen that measured membrane potentials deviate quite significantly from the potentials predicted by Nernst, with the two slopes intersecting once and otherwise diverging, especially at low concentration gradients. Rather than question the validity of Bernstein's hypothesis or reconsider his understanding of electricity, Koester makes the claim that this divergence is due to the presence of still other 'species' of ions. He then goes on to describe how the Goldman equation helps to account for this mathematically.

The Goldman equation purports to combine Nernst voltages with Ohm's law, and seeks to give Nernst's mathematics some empirical content; it is used to make theory and fact, calculation and measurement, fit more closely. Koester points out how this is done by *assuming* values for permeability (r_m) that vary for each 'species' of ion. These values are not measured or calculated, they are assumed so that the mathematics more closely approximate the measurements. These assumptions are necessary if electron movement or I, is to be discarded as irrelevant for biology, and to be replaced by ion current which formerly was R. The assumptions become the new R, resistance to fluid flow in small tubes. And these assumptions are at the heart of selective voltage gating, a concept which is still not fully articulated and the understanding of whose mechanism is still considered by some neuroscientists as the holy grail of neurophysiology. Yet this phenomenon is more easily explainable if the ability of a channel to pass ions, or membrane permeability, is not something that must be assumed, something different from the actual movement of those ions. That is, if membrane permeability and the movement of ions are considered the same thing, rm, rather than the movement of ions being considered I.

The historical failure to understand the nature of electricity as an electronic phenomenon, and the role of polarity in electrochemistry and in electrolytic cells, still shows up dramatically in measurement techniques used in neuroscience and cell biology. For the sake of measurement of neuron membrane voltages, the ground is placed externally to the cell. Hille claims this is because the cell is treated as an electrolytic cell. An electrolytic cell is one to which energy is introduced from an external source, e.g., a battery. In the standard electrochemical model the battery was the reducing agent in which oxidation occurred, liberating electrons made available at the anode which triggered reduction reactions. What this suggests is that the ground electrode, when measuring cell membrane voltages and treating the neuron as an electrolytic cell, should actually be located intracellularly and not extracellularly, since this is where reduction reactions take place. In addition, according to electrochemistry and Koester above, the movement of cations is in the direction of current flow , and this is toward the anode. The movement of sodium, potassium, and calcium, and so on, is into the cell from the extracellular space when a nerve impulse passes or when, for example, the apical hypha in a cell triggers growth of the cell through internal reduction reactions. But the persuasive power of historical traditions in the field of neurophysiology is so great that the theoretical foundations for the cell membrane voltage were never revised with the advance of the understanding of electricity that took place in the physical sciences. Choice of location for the ground electrode in neuroscience could only have been dictated by the necessity of agreeing in sign with voltages from Nernst, for if the ground were placed internally to the cell the sign would be the opposite of that called for by Nernst.

In the late 1940s two schools of thought contested the issue of the nature of the nerve impulse as revealed by the measurements made possible during the 1940's. Bertil Hille (1991) calls these two schools the ionic channel school and the epiphenomenalist school. The beliefs of the ionic channel school have been presented. For the epiphenomenalist school Hille (1991) writes, "...propagation of the nervous impulse was a chemical reaction confined to axoplasm and the action potential was only an epiphenomenon - the membrane reporting secondarily on interesting disturbances propagating chemically within the cell." That the propagation of these 'interesting disturbances' could involve electrochemistry may have been something conceivable to the epiphenomenalists. It was totally ruled out by a theoretical foundation which treated the Nernst equation as an electrical one, and which viewed the axoplasm as a resistor, ra, in an equivalent circuit rather than a substance embodying an organic semi-conductor in the form of a mircrotubule.

Franklin Harold in his 2001 *The Way of the Cell* writes,

> The two major pathways that generate and regenerate ATP are called oxidative phosphorylation and photophosphorylation, driven by respiration and light absorption respectively....Just how ATP is produced remained mysterious for many years, until it was discovered that the process is at bottom electrical.

But not, apparently electrochemical or involving the movement of electrons. Harold (2001) writes,

> Both the respiratory chain..., and the analogous photosynthetic cascade, generate a current of protons across the membrane in which these protons are inserted. These currents power ATP synthesis, and also serve directly for certain [cellular] work functions. We can thus think of ATP and the proton current (more precisely the proton potential) as alternative and incontrovertible energy currencies.

Biology still holds to the idea that electricity can be the movement of protons, that protons are a chemical energy 'currency,' and that electrons and protons are so analogous that they are mutually substitutable as chemical energy. Yet the standard electrochemical model treats the movement of proton-neutron pairs that are cations as the result of the presence of an electrical field in the electrolytic cell introduced by a battery, and not the result of the action of what has become known as a proton pump. Resort to such artifices obscures the role of electrons and electrochemistry in cellular energy transactions.

In 1978 Peter Mitchell received a Nobel in chemistry for his study of biological energy transfer. Of Peter Mitchell's award Harold (2001) writes,

> In Mitchell's view, then, the coupling of electron respiratory transfer to ATP synthesis is effected not by a chemical interaction but by a circulation of protons across the membrane. What that proton current does is quite analogous to the role of the electron current in coupling a flashlight battery to the bulb.

But the 'circulation of protons across the membrane', is in no way 'analogous to the role of the electron current in coupling a flashlight battery to the bulb.' The electron current powering a flashlight battery is the result of a chemical interaction in the battery. There are no two ways about it. For the circulation of these protons is R in Ohm's law, not I; and ohms are not analogous to amperes even though they may be necessary for amperes to flow at a low voltage.

In *fauna* or multicellular organisms with nervous systems, the oxidative or battery-like catabolic reaction that makes available the electrical field causing the protons to move is both gastrulation and the respiration of the organism. This source of chemical energy supplements that from mitochondrial 'respiration' in the cell. Such digestive and respiration reactions liberate electrons, and it is these electrons or cathode rays or beta radiation which, as I in V=IR, trigger the movement of the protons/ions as R. In electrochemistry this dynamic is known as an oxidation/reduction reaction, one involving the tunneling of electrons through a barrier across which a voltage may be measured. In the case of an electrolytic, biological cell, that barrier is the cell membrane. A voltage is measurable across this membrane, with the ground in the cell and the cathodic electrode in the acidic corrosion in the stomach; I is the movement of electrons; and R is the movement of ions, the most common of which are the calcium and potassium ions necessary for many aspects of intra- and extra-cellular functioning. The idea that a proton pump is involved obscures the role of the electron, quantum mechanics, in biology. Yet this is the now widely accepted chemiosmotic hypothesis which, because of its irrelevance to reality, has never been refuted.

Harold (2001) writes,

> Publication of the chemiosmotic hypothesis touched off a vigorous, sometimes acrimonious controversy over fundamental principles as well as experimental data; this continued for some fifteen years, subsiding only after the award of the 1978 Nobel Prize in chemistry to Peter Mitchell. By then the hypothesis had been as rigorously scrutinized as any proposition in biology and judged to be essentially correct.

The fifteen years of that controversy started with the award to Eccles et al. in '63 for an explanation of the nerve impulse that hypothesized a sodium pump, later called a proton pump by Mitchell. It should be pointed out that, as Dr. Harold notes, the controversy subsided, but was not settled, with the award of the Nobel Prize. The Karolinska Institute was merely reaffirming its choice in 1963 and perpetuating the obscurantism of the ionic channel model.

The limitations of the ionic channel model of nerve impulse propagation are especially stark when the idea of the information processing role of the nervous system is considered. Koester (1991) writes in his "Passive Membrane Properties of the Neuron" that "During signaling the rate of change in the membrane potential, which is important in determining the rate of information transfer within a neuron, is critically dependent on membrane capacitance." How, given the ionic channel model of the nerve impulse, can meaningful information for the cell and the synapse be encoded and transmitted by the harnessing of entropic pressure? Sakmann (Bass, 1994) writes, "Information is not contained in one action potential, but in the different rates or frequencies at which they transmit. This is called *frequency encoding*, but how it actually works is a complete mystery." The doctrine is that by varying the rate of meaningless impulses made possible by voltage gating, membrane capacitance, and the entropic rundown and re-establishment of ion concentration gradients by means of an hypothesized proton pump, these impulses are somehow imbued with meaning for the central nervous system. How this meaning is decoded by the cell or the synapse is necessarily a mystery too. Frequency encoding has been used by those working with radio for over a century, long before the position of the electron in the atom and its role in chemistry was understood. FM radio uses this principle and there is nothing mysterious about it. An electrochemical version of this information processing would assign meaning to each and every single action potential on the basis of the chemical reaction resulting from the arrival or departure of electrical charge carried by electrons and holes, and the movement of ions like those of calcium which have long been known to be necessary catalysts for many intra- and extra-cellular functions.

The Clinical Consequences of Inability to Simulate the Nerve Impulse Using Electrochemistry

The effect of institutionalization of a model of the nerve impulse and of the cell membrane voltage according to Nernst was not limited to obscuring the electrochemical nature of the nervous system. This institutionalization also guaranteed that the nerve impulse or action potential could not be simulated, primarily because there was no practical way to trigger the movement of ions back and forth across the cell membrane by the use of an artificial proton pump. The idea that 'shocking' or 'electrically stimulating' the nerve with a jolt of AC voltage was an adequate simulation of a nerve impulse because a muscle contraction would follow has its roots in the failure to appreciate the difference between voltage transmission and electrochemistry, between AC and DC. This failure of appreciation can be traced at least to the time of Hitzig and Fritsch in the 1870s. Voltage transmission is no substitute for amperage. That is why electrotherapy using AC or *faradic* current has never had any muscle building effect, no matter how intense the contractions, and is not used by NASA or any professional athletes or body builders.

Of his neurological instruction in 1938 at Columbia University Lewis Thomas (1983) writes:

> The making of a neurological diagnosis was itself a kind of game. All you needed to play were three implements, a rubber hammer for eliciting reflexes over tendons and muscles, a pin for testing pain receptors, and a wisp of cotton for testing light touch...
> ...Neurology had always been an entirely descriptive branch of medicine...there was nothing much to be done for therapy because of so little understanding of how the structures really worked.

This state of affairs was not at all later altered despite the 1953 claims of Eccles *et al*. that the nerve impulse had been precisely and correctly modeled. In 1983, five years after Peter Mitchell's Nobel Prize for his work explicating the role of cellular energy transfer, and twenty years after Eccles, Hodgkin and Huxley received the Nobel Prize for their 'correct' model of the nerve impulse, Nobel laureate Sir Peter Medawar, in his essay "Osler's Razor" (1983), wrote, "Neurology today is very like medicine in general fifty to a hundred years ago, in its preoccupation with interpretation and diagnosis and the relative backwardness of treatment."[1991] In this regard the observations of Lewis Thomas about his medical education in the 1930s, a half century before Medawar's essay, are illustrative:

> ...the purpose of the curriculum was, if anything, even more conservative than thirty years earlier. It was to teach the recognition of disease entities, their classification, their signs, symptoms, and laboratory manifestations, and how to make accurate diagnoses. The treatment of disease was the most minor part of the curriculum, almost left out altogether...Nor do I remember much talk about treating diseases at any time in the four years of medical school except by the surgeons, and most of their discussions dealt with the management of injuries, the drainage or removal of infected organs and tissues, and, to a very limited extent, the excision of cancers...The medicine we were trained to practice was, essentially Osler's medicine...[1983]

Osler's medicine was the medicine of William Osler who, in the 1890's, created the school of 'therapeutic nihilism' at Johns Hopkins University. The school asserted that the first duty of the physician was not to cause any harm, after a two thousand year old dictum of Hippocrates who recognized that intervention by physicians usually resulted in greater problems, and that if left alone the patient frequently recovered anyway. Because little or nothing could be done at that time by any physician or surgeon besides set broken bones, amputate limbs, and excise tumors, the school was known as the school of therapeutic nihilism. It was in the pseudo-scientific atmosphere of this environment that a neurophysiology arose in the first decade of the 20th century that could be considered scientific despite the fact that it had no clinical relevance. Indeed, this even became one of its strengths. The reason there was so little understanding of how the structure worked was laid to blame at the complexity of the material rather than the inadequacy of the hypotheses which routinely misinterpreted readings and measurements. It was discipline-wide reverence for foundation figures and the judgment of the Karolinska Institute that served to perpetuate the patina of scientificity for a neurophysiology that and biology that tossed about the term 'energy' yet betrayed not the slightest understanding that chemical energy was electrons, that had not the slightest justification for the investigation of electrochemistry as one way to treat trophoneurotic disorders such like sarcopenia, disuse muscle atrophy or the degeneration of aging.

Electrochemistry suggests that the only way to simulate the nerve impulse and to supplement cellular energy production and capture is to introduce a pulsed, on/off electrical field with the anode of the direct current at the site of the peripheral, chemical synapses. Investigation of the field of the electrochemical stimulation of muscle reveals that this approach to the building of muscle is as unlikely now as it was a century ago because of historical prejudices that continue. The continuing irrelevance of academic neuroscience to the clinic can be seen in the words, again, of Sakmann (Bass, 1994) who, reflecting on his long career in neuroscience and Nobel-winning contributions states,

> Now that I think I understand the neuromuscular synapse, I am curious to know more whether similar principles govern synapses in the central nervous system. When I began working again in this area, one of the most surprising things was how little had changed. People are asking the same questions I was confronting twenty years ago.

Summary and Conclusion

Neuroscience is hobbled by a deviation from the physical sciences which took place in the first part of the 20th century when those same physical sciences started to rally around the newly discovered sub-atomic particles, in particular, the electron. Although the biological and neurosciences took advantage of technological changes to study in greater detail the function and structure of the cell and the nervous system, archaic treatments of electricity as a phenomenon involving the movement of ions prevented the mining of the potential of electrochemistry for clinical treatment of maladies which today are still untreatable for the most part. These sorts of maladies are the chronic and degenerative ones for which Western medicine is notoriously deficient with its focus on acute problems.

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