A BRIEF HISTORY OF ELECTROPHYSIOLOGY AND IT'S TECHNIQUES

FOREWORD

During almost three decades of teaching and research at the School of Medicine of the UPR, I collected copious notes on one of my favorite subjects: the history of electrophysiology. Knowledge of history is essential for the full and proper understanding of any facet of human activity, and that of science in particular, as science is a cummulative subject *par excellence.* "Indeed, if we wish to know how and why a particular theory or technique emerged at a given moment we should first know the old theories and techniques that were replaced by the new ones. The best way to understand the new, or the present, is in terms of the old, and this is precisely how history operates as Isaac Asimov emphasized in his book 'Adding a Dimension', "There is no discovery in science, however revolutionary, however sparkling with insight, that does not arise out of what went before".

It can be argued, that by accelerating the flow of time in our imagination, it may be possible to anticipate the future. This is so, although the capacity of extrapolating the present is not a gift evenly distributed among men. It is highly developed in some individuals such a Jules Verne and Arthur Clarke, to mention only two well-known writers, famous for the accuracy of their long-range high technology forecasts.

It should be noted here that one of the most prominent German electrophysiologists Julius Bernstein, was endowed with forecasting powers similar to those of Verne and Clarke. Indeed, in a book written in the first decade of the 20th Century, published in 1912, he predicted the use of Braun's cathode ray tube as an ideal friction and inertia free display device for the recording of fast electrophysiological events. The Braun's tube which at the turn of the century was only a simple gadget, has evolved into an essential component of most experimental set-up systems in any science. In fact the Braun's tube has become the most important component of the cathode ray oscilloscope, computers, scanning and video monitors etc.

Thinking that my notes on the history of electrophysiology might be of interest not only to graduate students but to all who use electricity in electrical techniques for biological and medical applications, I decided to publish them after a certain amount of processing. However, I soon realized that trasforming my notes into a book would involve extensive rewriting that would interfere with other projects. Then the idea was born to publish our work as a series of separate sections. We are grateful to the Editor of this Journal, Dr. Rafael Villavicencio, for giving us the opportunity to see our material in this feuilletonesque format.

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SECTION I

Static or Frictional Electricity and the Discovery of Direct Current

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Electrophysiology and the branch of physical sciences known as electricity have a common ancestry. Both were born at the end of the 18th Century as the result of a controversy between two Italian scholars, Luigi Galvani and Alessandro Volta, on the nature of the interactions between metals and muscles.

Electrical phenomena, particularly the atmospheric ones, had been witnessed by our pre-human forbears, but until the year 1800 only one type of electricity had been available for experimentation, that called static or frictional; i.e. the electrical phenomena which appear as the result of rubbing non-conductive materials (or insulators) such as glass, amber, resin, sealing-wax, etc. against other insulating materials: silk, wool, or a cat skin. The fact that, as a result of rubbing them, those materials acquired the property of attracting small particles had kindled the curiosity of many keen intellects.

Thales, the pre-socratic Greek philosopher who lived in the 6th Century B.C, in Miletus, a city in Asia Minor, is attributed with the above observation; however, the first recorded description of this phenomenon was made by Theophrastus [372-287 B.C,] who described it in his treatise on gems. Long before this curious property of amber was observed, another force capable of exerting attraction at-a-distance was known: magnetism first noticed in magnetite or loadstone, an iron oxide mineral that was used to develop the magnetic compass, making long distance navigation possible. However, the existence of two forces sharing an apparently common feature, that of acting from a distance, confused rather than helped some authors who wrote commenting about materials that they had never seen or handled. Two notable exceptions were Jerome Cardan [1501-1576] and William Gilbert of Colchester [1540-1603].

Cardan separated fact from fiction and emphasized the differences between the attraction exerted by rubbed amber and the loadstone. Gilbert, physician to Queen Elizabeth I, wrote a magistral treatise entitled De Magnete published in 1600 (1). It has been argued that De Magnete did not contain any original material and that its only merit was that of collecting and passing to posterity the verifiable portions of knowledge on magnetism accumulated up to the turn of the 17th Century. However, Gilbert introduced a number of basic ideas that 400 years later still provide a significant part of the conceptual framework we utilize whenever we work with, or think of, magnets. He separated, precisely, once and for ever, electricity from magnetism. To do so he needed a word to qualify the phenomena associated with the rubbing of amber, since no such term was available in Elizabethan English, he had to invent one.

Gilbert looked for a generic word that would embrace all substances which upon rubbing, behave like amber and he called them "electric", as opposed to other substances which do not develop such power and he called them "anelectric" or "non-electric", all terms derived from the Greek word for amber *(elektron)*. Gilbert's most important contribution to science is his theory of terrestrial magnetism, based on observations made on a model of our planet that he fashioned by shaping a loadstone into a sphere (called by him *terrela* or "little earth"). In addition, the use of the terrela as a substitute for reality, was, probably the first application of a physical model in scientific research; followed about 100 years later by Galileo's use of the movement of bodies placed on inclined planes as a model for free fall. By exploring the surface of the terrela with a magnetized needle Gilbert was able to visualize the earth as a huge magnet with the two poles, North and South, in their approximate positions. Also, he used the terrela to explain the magnetic dip.

In 1660 the first frictional electrostatic generator, a machine capable of producing large amounts of static electricity,was built by Otto von Guericke [1602-1686] for the purpose of saving the experimenters the effort of constantly rubbing bars of different materials. von Guericke, a physicist who was the Burgomaster of Magdeburg for 35 years, is remembered in Physics for his work on Pneumatics and for his skills as an instrument maker. A few years before he produced his electrostatic generator he designed a very efficient vacuum pump that was used in the famous experiment known as the *Hemispheres of Magdeburg*, dramatized by Albert Dürer in a not less famous engraving.

Also in mid-18th Century, a way to condense and store static electricity became available for experimentation.

This was the Kleistran, also known as the Leyden bottle, invented independently and almost simultaneously in 1745-1746 by Ewald Jurgen von Kleist, Dean of Kamin Cathedral , in Pomerania, near Leipzig, and by Peter van Musschenbroeck [1692-1761] Professor of Natural Philosophy in Leyden. This contraption, which today we describe as a capacitor or condenser, consists of a glass bottle or jar, filled with either metal shot or leaves of copper or gold foil (or even plain water in its first versions), the outside of the bottle was wrapped in foil, and a metal rod, passing through the cork, communicated the inside of the bottle with the outside. The jar was charged by holding it by the outer metal foil and touching the end of the rod to a piece of glass or other material which had acquired an electric charge as a result of rubbing. This operation could be repeated an many times and, as a consequence, the amount of charge which could be accumulated or condensed into it could be very large, (hence the name condenser, first used in this sense by Volta).

The jar was discharged by joining the metal rod to the outer foil by a conductor, a metal or a living being. The discharge was accompanied by a spark and a painful shock if the conductor happens to be an animal or a human. 'Trics' and demonstrations using static electricity were regarded, both in France and Britain, as a form of entertainment similar to modern 'magicians'. Indeed, the Court of King Louis XV of France retained the services of an official "electrician", the Abbé Jean-Antoine Nollet [1700-1770], a professor of Experimental Physics at the University of Navarre. In addition to serving as tutor to the *dauphin,* Nollet staged and directed "electric" shows. Thus, on one occasion, the Abbot arranged seven hundred monks in a circle, each monk joined to his two neighbors by short lengths of iron wire. Then he interposed between two monks a fully charged Leyden jar. And when the circuit was closed, and the electricity condensed in the bottle was discharged and allowed to flow through the human chain, all the monks jumped up in pain with the precision and synchrony of a highly trained *corps de ballet,* to the amazement of the King, his court and the progress of Science. However, no information has reached us regarding the incidence of cardiac fibrillation among the performers.

Other experiments made possible by the availability of electrostatic generators and Leyden jars, included the electrification of whole human beings standing on an insulating platform or suspended from the ceiling by a silk harness. Their hair would stand up and emit sparks when the spectators came close to them. Although the motivation of these performers was not strictly scientific their desire to add new acts to their repertoire led them to incessant experimentation, in the course of which they made interesting observations and discoveries and deserve to be mentioned. Gray [1696-1736] was the first to demonstrate that the electric charge generated at one point spreads throughout the entire body or even to other bodies if a proper pathway is available. Charles Dufay [1698-1739] was the first one to suggest the existence of two kinds of electricity that he called vitreous and resinous. The former occurring most often when glass is rubbed, whereas the latter is commonly associated with amber and other resins. In addition, he observed that a body charged with vitreous electricity will repel all other bodies with the same electricity while it would attract bodies of different charge.

Benjamin Franklin

No matter how brief and elementary, any discussion of the early ideas on electricity would be incomplete without making due reference to the life and work of the American statesman, inventor and scientist Benjamin Franklin [1706-1790] one of the founding fathers of the USA, and regarded by many as the founder of modern electrical science. Franklin was born in Boston, the 10th of the 17 children of a soap and candle maker. His formal education ended when he was 10 and at the age of 12 he was apprenticed to one of his brothers, a printer, with whom he learned this trade. After working in London as a printer for almost two years, he settled in Philadelphia as a printer and publisher. Besides publishing periodicals that included the *Pennsylvania Gazette* and the *Poor Richard's Almanack,* he was the official printer of paper money for the American colonies and was extremely active in community affairs. Among his contributions are the foundation of an Academy that would evolve into the University of Pennsylvania; a public library, improvement of the fire department and being the postmaster general of the USA. In 1748 he gave up the management of his publications to devote himself to science. Franklin's scientific interests ranged from Oceanography to Botany, but as many other Natural Philosophers of that time, he found electricity particularly challenging and interesting.

In 1751, Franklin published a book entitled *Experiments and Observations on Electricity* (2). This book, as others of the same period, was a collection of letters written by Franklin to his friend Peter Collinson F.R.S. [1694-1768], a successful textile manufacturer in England and a competent and respected amateur botanist. Collinson was instrumental in stimulating Franklin's interest in electricity by maintaining an uninterrupted correspondence with him on this subject, and providing him with materials for his experiments when needed.

Also, by communicating to the Royal Society the letters in which Franklin described his experiments, results and his interpretations, he became well known in all the learned circles of Europe. Franklin's main purpose in his book *Experiments and Observations* was to postulate a unifying theory that would account for all the experiments involving electricity, and as Gilbert had done before, he began by dividing all materials into two classes: electric or non-conductors, and non-electric or conductors.

Franklin developed the idea of conservation of charge. For him the electricity stored in the Leyden jar represented not a net increase in charge, but rather the fact that electrical charges ever present in the jar, had been separated and were ready to snap back together again when the inside of the bottle and the outside foil were connected by a conductor. He also demonstrated the equal and opposite nature of the charges on either side of the glass, or in his own words, that "the Leyden bottle has no more electrical fire in it when electrified than before", and further demonstrated that the energy of the bottle resided in the glass. According to this, the one electrified body has an excess of fluid and its partner an equal deficit, which led him to introduce the terms positive and negative electricity, as used today. There is not, in principle, any great difference between the one-fluid and the two-fluid theory (as a negative wealth may equally well be called a debt) but Franklin's treatment clarified the whole subject. Franklin also invented a modified version of the Leyden jar, called the magic square or plate, which was nothing else than a plane condenser. It consisted of a sheet of window glass, set in a wooden frame, between two thin plates of lead. This device, sometimes known as "Franklin's panel" accumulated electricity just as the Leyden jar.

Nevertheless, Franklin is most widely known as the man who established the electrical nature of lightning and designed the first effective lightning conductor or lightning rod. The fact that lightning and the sparks produced by the electrostatic generators had something in common had been casually conjectured before, but it was Franklin who first went into the matter systematically, giving a list of twelve particulars in which the electrical fluid resembles lightning. Thus, Franklin wrote on November 7th 1749, "Electrical fluid agrees with lightning in these particulars: 1) giving light 2) color of the light 3) crooked direction 4) swift motion 5) being conducted by metals 6) crack or noise in exploding 7) subsisting in water or ice 8) rending bodies it passes through 9) destroying animals 10) melting metals 11) firing inflammable substances 12) sulphurous smell. The electric fluid is attracted by points we do not know whether this property is in lightning. But since they agree in all the particulars wherein we can already compare them is it not probable they agree likewise in this? Let the experiment be made", Franklin concluded.

He had observed that pointed bodies connected to ground rapidly discharge electrified bodies in their vicinity, and this observation led him to propose the form of lightning rod with which his name is associated. "Would not-he asks-these pointed rods probably draw the electrical fire silently out of a cloud before it... strikes?". He also suggested an experiment in which a man standing on an insulating block in a sentry box in a high building, should draw sparks from thunder clouds by means of a pointed rod, an experiment which, following his proposal was successfully carried out in France.

The experiment with the kite, (not less suicidal than the one above) which has always been the one achievement generally associated with his name, was performed by Franklin in Philadelphia. The kite was flown on a twine which, when wetted by the rain, became a conductor-fortunately for the experimenter, not a very good one. The twine was separated from the hand by a silk ribbon. With his knuckles Franklin drew sparks from a key attached to the twine. Although this experiment was a confirmation of what had already been established, it has represented Franklin in the popular mind in the same manner that Newton is symbolized by a falling apple. Franklin is most widely known as the man who established the electrical nature of lightning and designed the first effective lightning conductor or lightning rod.

However, all the experiments performed with static electricity, no matter how amusing, impressive, or dangerous they were, did not lead to the understanding of the nature and properties of electricity, mainly because static electricity could be tamed only in part. It could be generated and stored, but its discharge or dissipation was always instantaneous: as a flash or a spark. Electricity did not become available for experimentation until the invention of the electric pile or battery by Volta in 1800, which was sparked by a notorious controversy between him and his fellow countryman Galvani.

The Galvani-Volta Controversy

Since the first experiments with electrostatic machines and storing devices it was known that the discharge of static electricity could induce muscle contractions. Indeed, as early as 1747, Antoine Louis quoted by Dibner (1952), showed that paralytic muscles would twitch when a Leyden jar was discharged through them. However, the same discharge was ineffective on atrophied muscles. It was Luigi, also known as Aloisii, Galvani [1737-1798] who first systematically investigated the effects of electricity on muscle. Galvani was born, lived and died in Bologna. (Fig. 1) He attended the University of his hometown where he first studied Theology, but soon he switched to Medicine. In 1762, after having worked on the avian kidney and auditory organs he began to lecture in Medicine. In 1775 he was appointed Professor of Anatomy and later also Professor of Gynaecology.

In 1773 Galvani was already working on frog muscle and had begun to study the stimulation of the 'muscle moving', or motor nerves that he discussed in a lecture entitled *Sul moto musculare nelle rane* (Concerning muscle movement in the frog) delivered that year, However, at the time of this lecture he had worked only with mechanical stimulation. It was on November 6, 1780, while experimenting with one of the electrostatic generators designed by Otto von Guericke [1602-1686] when Galvani observed that strong muscular contractions occurred in frog legs, when their lumbar nerves were touched lightly with the tip of a dissecting scalpel. He soon noticed that the contractions occurred simultaneously with the electric sparks produced by the generator, and only when the experimenter held the scalpel by the conducting part of the blade and not by its insulated handle. This observation, often described as Galvani's first experiment, was remarkable because of the lack of a direct connection between the electrostatic generator and the frog preparations which were some distance away. Galvani dedicated the rest of his life to the investigation of this puzzling phenomenon, using mostly frog nerves and muscles. His initial objective was to study under what conditions the twitches of the frog legs occurred without being in direct communication with the source of electricity.

Figure 1. Luigi Galvani (1737-1798)

Although rarely recognized as such, one can characterize Galvani's first experiment as one of telestimulation by electromagnetic (EM) induction. Each spark produced in the electrostatic generator is accompanied by the emission of a burst of EM radiation, mainly in the radiofrequency range. These waves in turn induce oscillations in the body of the researcher holding the scalpel, who acts as a human antenna. Unless the researcher is well grounded, the currents induced in his body by the EM radiation would flow through the scalpel into the frog tissues which being wet offered a lower resistance to ground. Thus, the motor nerve fibers are stimulated and the leg mucles will contract.

In experiments performed in his garden during a thunderstorm, Galvani discovered that the natural electrical discharges, lightning, would induce strong muscle twitches in frog preparations hanging from a metal rail. He interpreted this observation as a confirmation of Benjamin Franklin's ideas and experimental results on the identity of atmospheric and frictional electricity exemplified in his Philadelphia experiment with the kite. However, Galvani went about these experiments rather cautiously, since he knew that the Swedish physicist George Wilhelm Richmann [1711-1753] had been struck and killed by lighting in St. Petersburg in July 1753 while attempting to confirm, once more, Franklin's hypothesis on the nature of lightning. A faulty and imperfectly grounded apparatus was blamed for the accident.

A related series of experiments known collectively, as Galvani's second experiment, culminated in the development of a simple but extremely useful electrophysiological instrument, a stimulator known ever since as Galvani's forceps. This device consists of two pieces of different metals, most often copper and zinc, soldered together at one end while the two free opposite ends are shaped in the fashion of a pincer or forceps. When the tips of the forceps are applied to the living tissue the nerve fibers are stimulated, due to the fact that the electrode potential of the two metals are different (copper and zinc). This difference acts as an electromotive force which will move electrically charged particles, ions and electrons. The current stimulates the nerve fibers which happen to be between the two points or forceps.

The Galvanic forceps were actually suggested by a fortuitous observation. For some reason Galvani had hung several skinned frogs on brass hooks from an iron rail in his garden. He noticed that when a frog happened to contact the iron its muscles would twitch strongly. He first assumed that the contractions might be due to atmospheric influences. But he discarded this possibility by repeating the experiments with the same results, both when the skies were clear, and indoors, whenever the leg muscles were connected to the lumbar nerves by two dissimilar metals. Galvani found that the strength of the contractions depended on the choice of the two metals that had to be in contact with each other, as well as with the frog tissue, the muscle on one side and the nerve on the other. He eventually found that weak contractions could also be elicited when a bridge made of a single metal was interposed between the nerve and the muscle. He also verified that the discharge of a Leyden jar exerted similar effects on muscle.

Galvani might have concluded from these experiments that electricity had a stimulating action on muscles and be contented with that. But somehow the idea flashed in his mind that the relationship between electricity and muscle was of a much more fundamental nature. Indeed, he reasoned that electricity had a powerful effect on muscles because the muscles themselves contained electricity. The existence of the so-called animal electricity had been formally proposed. The theory he developed to explain his observations was rather convoluted and certainly went well beyond the bare facts. He claimed that two types of electricity are inherent to animal tissues, but are maintained in strict separation: one type in the nerves, the other in the muscles. He compared the nerves to the rods of the Leyden jars. The muscles would be the bottles themselves. When nerves and muscles were joined by the bimetallic device electricity would be discharged and, as a result, the muscles would twitch.

Galvani reported his collected experiments in his major work *De viribus electricitatis in motu musculari commentarius* (Comments on electrical effects on muscle movement) which appeared as volume VII of the Proceedings of the Institute and Academy for Science and Arts in Bologna in 1791. The ideas described in this book brought him under the fire of Volta [1745-1827], another natural philosopher with a keen interest in electricity, to which he devoted his entire life. He became famous since his first invention: the electrophorus, a device which could produce large amounts of electricity and was used to charge Leyden jars. Another of his inventions was the condensing electroscope; an instrument which could detect very small electrical charges.

In 1791, when Volta became acquainted with Galvani's results and interpretations, he vigorously rejected those hypotheses and devoted himself to perform electrophysiological experiments. He easily confirmed that electricity stimulates muscle, but he guessed that the key to the interpretation of Galvani's experiments lay in the bimetallic junction. He reasoned that each metal would possess a characteristic amount of electricity (thus anticipating the concept of electrode potentials) and concluded that if two pieces of dissimilar metals are joined together at one end while their opposite ends contact a wet surface, electricity would flow between them, stimulating any muscles in its path, in much the same manner as the discharge of a Leyden jar (Fig. 2). With his electroscope Volta was able to detect an electrical difference between the copper and the zinc of Galvani's forceps. In addition, he proved that such difference would stimulate tissues. He did so by holding one of the arms of the forceps in his mouth while touching a corner of his eye with the other; a sensation of light was the result. But he firmly denied the existence of the animal electricity that Galvani had proposed.

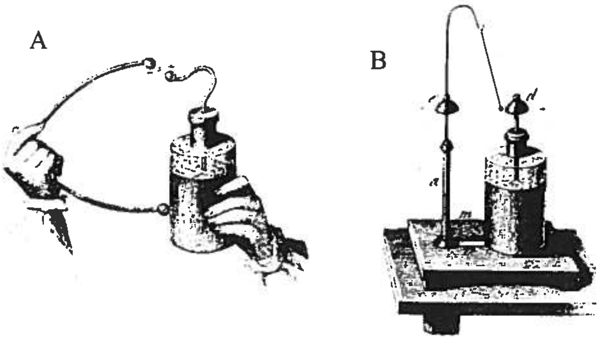

Figure 2. Two ways of discharging a leyden jar

Count Alessandro Giuseppe Volta, a brilliant scholar, Professor of Physics at Pavia, Fellow of the Royal Society of London, corresponding member of the French Academy, with wide contacts in the learned circles of Europe, was easily the winner of the dispute over his provincial opponent. He proved his contention by inventing an apparatus that the world would know as the voltaic battery or pile, due to the way it was constructed (Fig. 3). This consisted of alternating discs of copper and zinc separated by pieces of board or cloth wetted in brine. An electric current would flow through a wire connected to a sequence of discs starting with copper and ending with zinc. For the first time a device that could produce an uninterrupted flow of electricity, rather than brief sparks, was available for experimentation. This was, without doubt, one of the most important technological advances in the history of mankind. The invention of the

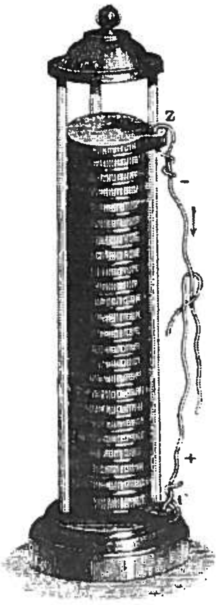

Figure 3. The Voltaic pile or battery

voltaic battery was followed by the development of many other types, more powerful, efficient and reliable which were known by the names of their inventors: Daniell, Bunsen, Leclanche, etc...

His controversy with Volta ended bitterly for Galvani, who spent the last years of his life in misery as a consequence of his defeat. Yet, before Galvani's death an anonymous tract was published describing how a frog muscle could be stimulated in the absence of any metallic instruments by touching the muscle to the sectioned spinal cord. Historians have speculated that such publication was authored or co-authored by Galvani. In addition, the last years of Galvani's life were shadowed by overpowering political events. Napoleon Bonaparte, greatly admired by Volta, occupied Northern Italy in 1796 and founded the Cis-Alpine Republic that included Galvani's home town of Bologna, which had previously belonged to the ecclesiastic state. Galvani refused to swear the Oath of Allegiance to the new constitution and was consequently deprived of all his offices. Although his friends, in particular Professor Aldrini, achieved his reinstatement, which was to be effective on January 1st, 1799, Galvani died on December 4th, 1798 at the age of 61. Not until 43 years after his death, in 1841, were his collected works published by the Academy of Science of Bologna.

References

1. De Magnete G. Dover Publications, New York 1600.
2. Franklin B. Experiments and Observations on Electricity, 1751.