A Hundred Years Ago:

Julius Bernstein (1839-1917) Formulates His "Membrane Theory"

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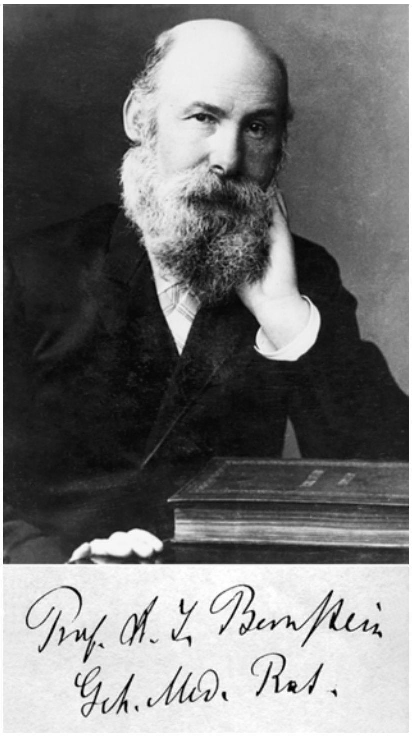
"The electrical currents observed in many living organs of animals and plants have been the objects of much research. We detect such currents in muscles, nerves, secretory glands, and electric organs of fish as well as in plant tissue (…) It seems likely that all these currents have a similar, if not the same basis, and that their strength and potency depends on the structural conditions and chemical composition of the cells making up each organ."



Such were the ambitious words of Julius Bernstein one hundred years ago, at the very beginning of his "Investigations into the Thermodynamics of Bioelectrical Currents", in which he suggested a new "membrane theory" (Bernstein 1902). He started with the assumption that muscle and nerve fibers are enveloped by isolating boundary shells that are permeable only to specific ions. Bernstein primarily considered K^+ diffusing in the direction of the concentration gradient into the extracellular medium. As negative ions -- in particular, phosphates -- apparently could not follow this same course, Bernstein argued that an electrical potential builds up across the semipermeable membrane, which would impede further outflow of potassium. This potential corresponded exactly to the "resting current", which was clearly measurable with the methods available at the time. Furthermore, Bernstein postulated that an excitation of the fibers would lead to a brief loss of the selective membrane permeability, thereby eliciting "action currents" and a “negative variation” in the potential. Bernstein’s findings and interpretations led to a paradigm shift in the understanding and further investigation of bioelectrical processes. Fifty years later, these studies would lead to the ionic theory of neuronal excitation and culminate in the identification of ion channels in cell membranes.

Family Background and Scientific Career

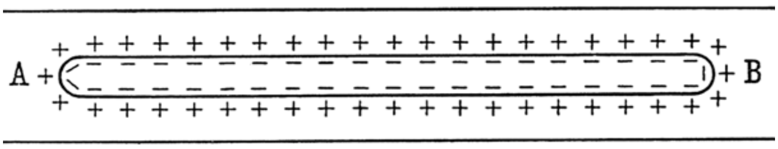
Julius Bernstein came from a very progressive, liberal family in Berlin. His father Aaron Bernstein (born 1812 in Danzig, died 1884 in Berlin-Lichterfelde) was a co-founder of the "Berliner Jüdische Reformgemeinde" in 1845 [Berlin Congregation of Reform Judaism] and participated in the German Revolution of 1848 as a politician and journalist. Among other works, he published popular scientific articles, which were later collected and published in book form under the title of "Naturwissenschaftliche Volksbücher" [Scientific Popular Books], which received widespread distribution. In 1849, he founded the "Urwähler-Zeitung", a newspaper that was banned in 1853, but reappeared under the name of "Volks-Zeitung" to become Berlin’s newspaper with the highest circulation by 1861 (Schoeps 1992). The famous social democratic politician and theoretician Eduard Bernstein (1850-1932) was a nephew of Aaron Bernstein and hence a cousin of Julius Bernstein.

Julius Bernstein was the oldest of seven children. He attended "Gymnasium" [high school] in the Berlin district of Neu-Cölln. Already during his school days he enjoyed access to the laboratories of the Physiological Institute at the University of Berlin, which was headed by the famed electrophysiologist Emil du Bois-Reymond (1818-1896). In 1858, Bernstein began the study of medicine in Breslau. He transferred to Berlin in 1860, finishing a doctoral thesis under the supervision of du Bois-Reymond on invertebrate muscle physiology in 1862. Two years later, Bernstein began his university career as an assistant to the famous physicist and sensory physiologist Hermann von Helmholtz (1821-1894) in Heidelberg. He qualified as a university lecturer in 1865, was elevated to an associate professorship in 1869, and appointed interim head of the Heidelberg Institute in 1871 after Helmholtz left to take up the Chair of Physics at the University of Berlin. During his tenure in Heidelberg, Bernstein’s research results won him immediate acclaim. By constructing his own differential rheotome ("current slicer") he explored the amplitude, time course, and conduction velocity of the negative variation (or "action current", respectively) in frog nerve (Bernstein 1868). In modern terminology, his study was in effect the first exact description of the nerve action potential (see the detailed account by Schuetze 1983).

After a short interlude in Berlin, Bernstein was appointed Chair for Physiology at the University of Halle an der Saale. Eight years later (1881) he moved into a new institute building that had been equipped according to his wishes. There he engaged in teaching and research for nearly forty years until becoming professor emeritus in 1911. In 1875 he became a member of the "Deutsche Akademie der Naturforscher Leopoldina". He was dean of the medical faculty nine times, based on a rotation schedule, and was elected Rector of the University for the academic year 1890/91. The portrait photograph shown in **Fig. 1** was presumably taken during his time as Rector.

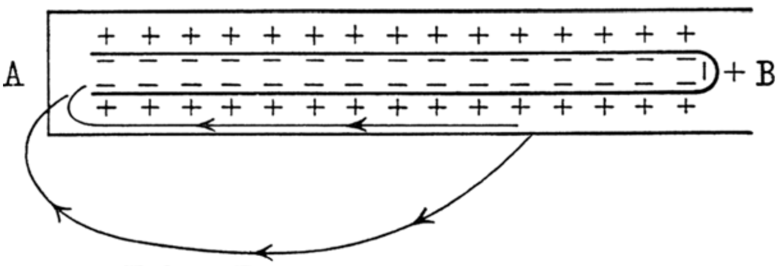
The Development of Bernstein's Membrane Theory

Fig. 32 a.



Unverletzte Faser mit elektrischer Doppelschicht, stromlos.

Fig. 32 b.



Verletzte Faser mit elektrischer Doppelschicht, Längsquerschnittstrom.

Bernstein's biophysical studies at the beginning of the 20th century conclude a long series of controversies and attempts to explain the phenomena of bioelectricity (see also Bernstein 1912; Lenoir 1987; Florey 1992). In experiments on cross-sectioned, resting frog muscle done more than 60 years earlier, the Italian physicist Carlo Matteucci (1811-1868) had observed an outward current flow from the area of the cut (i.e., from inside) to the undamaged muscle surface (outside). In the mid-nineteenth century, Bernstein's mentor du Bois-Reymond was the first to discover action currents in activated muscles and nerves; with constantly improved techniques he observed a temporary decrease in the injury current described by Matteucci, which he termed "negative variation". The causes of the injury current and the negative variation , however, remained the subject of heated debate for decades. Ludimar Hermann (1838-1914), one of Bernstein's childhood friends and also a student of du Bois-Reymond, proposed his "Kernleitertheorie" (core conductor theory) in 1898, which assumes that nerve and muscle fibers contain a highly conductive core surrounded by a non-conducting boundary shell. In this theory, stimulation produces action currents that polarize small regions of the boundary shell; this successively activates adjacent regions of the fiber through electrical induction ("Hermannsche Strömchen-Theorie"; now known as local-circuit theory of electrical propagation). The source of the local excitation was attributed to explosive chemical reactions in the fiber core, thus representing sudden changes (alterations) of metabolism ("alteration theory").

Bernstein (1902) reached a different conclusion by studying the temperature dependence of the resting current in frog muscle and nerve: "One can…with some certainty conclude that a chemical process cannot at all serve as the direct energy source for the electrical energy of muscle current." According to his interpretation, his results indicated that pre-existing electrolytes in the fiber give rise to the resting current and its negative variation.

His theory was based on two assumptions: (i) Following the reasoning of Walther Nernst in 1888/1889 about diffusion potentials of chemical substances at different concentrations, Bernstein treated muscles and nerves as chains of concentration circuits ("Konzentrationsketten"). He used the equations first developed by Nernst to predict the electrical potentials resulting from concentration gradients and compared these with the "resting currents" that he had measured in nerve and muscle. He found that the two matched sufficiently. (ii) At almost the same time as Nernst published his results, the physical chemist Wilhelm Ostwald (1853-1932) suggested that the electrical potential at (artificial) semipermeable membranes was due to their selective permeability to ions ("ion sieve"). Bernstein applied these ideas to muscle and nerve fibers, treating the non-conducting fiber shell as a semipermeable membrane. In 1902, he writes: “A second assumption [*in addition to the validity of the Nernst equations*] concerning the composition of the concentration chain in muscle is that the electrical potential of the lesioned muscle is caused by the electrolytes, in particular by inorganic salts such as K_2HPO_4, already contained in the undamaged muscle fiber. Let us imagine that these electrolytes diffuse unhindered from the axial cross section of the fibrils into the surrounding fluid, while they are prevented from diffusing through the longitudinal section by an intact sarcoplasmalemma which is impermeable to one kind of ion such as the anion (PO_4^- etc.) to a greater or lesser degree. Then an electrical double layer would emerge at the surface of the fibril, with negative charges towards the inside and positive charges towards the outside. Indeed, this electrical double layer must also exist in the undamaged fiber, but would become apparent only in response to lesion or stimulation (negative variation). This assumption would imply a theory of preexistence; as the semipermeable membrane plays an essential role in this theory, I will succinctly call it 'Membrane Theory'.” Later, in his monograph "Elektrobiologie" (1912), Bernstein illustrated the main tenet of his 1902 article using two schematic drawings (see **Fig. 2**). Forty to fifty years were to pass before new, intracellular measuring techniques and the radioisotope method were to modify and expand upon Bernstein’s “Membrane Theory” and ultimately usher in another paradigm change in the study of bioelectricity -- a development vividly described, among others, by two of its chief protagonists, Katz (1966) and Huxley (1995).

Epilogue

In 1917, Julius Bernstein died in Halle at the age of 78 -- esteemed by colleagues and friends as a researcher, professor, and "Geheimer Medizinalrat". His collaborator von Tschermak (1919) called him "a true paragon of a German scholar". Three editions of Bernstein’s Textbook of

Physiology acquainted several generations of medical students with modern (that is, contemporary) concepts of physiology. His publications, foremost his "Membrane Theory" of 1902, belong to the cornerstones of neurobiology and cell physiology and are still cited even in current textbooks. The Physiology Institute of the University of Halle was renamed for its founder at its centennial in 1981, and is now known as the "Julius-Bernstein-Institut für Physiologie".

The sources available to us give no indication of anti-Jewish prejudice or discrimination against Julius Bernstein. There were, however, some obstacles because of his Jewish religious background which had to be overcome before he could take up his position in Halle; a university statute allowed only Protestants to be hired at the "Martin-Luther-Universität" (Zett 1983). Also Catholics needed to gain a special dispensation to obtain an academic position in Halle (Kaiser and Völker 1983).

A different fate awaited Bernstein’s eldest son, the prominent mathematician and statistician Felix Bernstein (1878-1956), in Göttingen. After World War I he became "Reichskommissar für Anleihen" (High Commissioner of Government Bonds) in Berlin; in the 1920s he was a respected professor and consultant. After the rise to power of the Nazis, he was dismissed from his position in Göttingen in 1934 while on a lecture tour in the USA. He remained in the U.S. in exile and died in Zurich in 1956.

Acknowledgements

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"Martin-Luther-Universität Halle" for providing helpful information and access to source material.

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Figure Legends

Fig. 1: Julius Bernstein, portrait from ca. 1890; at this time Bernstein was Rector of the University of Halle (printed by permission from university archives Halle, Repro 40, BI 18). Bernstein's autograph is from a letter written in 1910 (UA Halle, P.A. 4431).

Fig. 2: Schematized drawing of the "electrical double layer" at the surface of a muscle fiber (**AB**) that was used by Bernstein to discuss the essential features of his "Membrane Theory" of 1902. *Top (Fig. 32a)*: intact fiber, in which no current flow was measurable. *Below (Fig. 32b)*: fiber injured on the left (i.e., cross-sectioned at **A)**; now the "negative charges towards the inside and the positive charges towards the outside (...) become apparent" (reproduced from Bernstein, 1912).