The Neuron Doctrine, the Mind, and the Arctic

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THE LATE 19TH century and early 20th century represent an era of significant progress and important discoveries. Explorers of unknown continents interacted with pioneers of neuroscience, including the founders of the neuron doctrine, which asserted that nerve tissue was composed of individual cells that were genetic, anatomic, functional, and trophic units. Fridtiof Nansen (1861–1930), an arctic explorer and a cofounder of the neuron doctrine, knew Sigmund Freud (1856–1939), a neuroscientist and the founder of psychoanalysis, as well as Harvey Cushing (1869–1939), the father of modern neurosurgery. This is an account of the evolution of the neuron doctrine at a time of great explorers and scientists, with insight into their common interests and interactions on scientific and social levels. (Neurosurgery 47:1381–1389, 2000)

Key words: Explorers, Neuron doctrine, Neuroscience

The classic "neuron theory" or "neuron doctrine," which was introduced at the end of the 19th century, asserts that nerve tissue, like other tissues, is composed of individual cells, which are genetic, anatomic, functional, and trophic units (2). The neuron (a nerve cell with its processes) is the structural unit of nervous tissue, and the neurons are the only elements in the nervous system that conduct nervous impulses. The dendrites and soma are receptive, that is, they are acted on by impulses from other neurons, whereas the axon transmits impulses arising in the neuron to its terminals ("dynamic polarization" of the neuron). The other types of cells, i.e., the various glial types, the ependyma, the neuroepithelium of the choroid plexus, and connective tissue cells, serve other functions. This classic neuron doctrine has been a central feature in our interpretation of the nervous system and has proved very useful as a working hypothesis.

For several decades, the proponents of the neuron doctrine were opposed by other researchers (often called "reticularists") who maintained, largely on the basis of silver-impregnated specimens, that there was continuity between nerve cells through fine fibrils; according to the neuron doctrine, the termination of an axon on a cell is a mere contact. The controversy was definitively settled in favor of the neuron theory by electron microscopic studies.

In 1906, Camillo Golgi from Italy and Santiago Ramón y Cajal from Spain were jointly awarded the Nobel Prize for physiology and medicine. Cajal was rewarded for developing the neuron doctrine, which we argue was also pioneered by others, including the arctic explorer Fridtiof Nansen and the psychoanalyst Sigmund Freud. The following is an account of the development of the neuron doctrine, with special emphasis on the interaction between famous explorers and neuroscientists. A century ago, the social and scientific interactions among all of these explorers must have yielded fascinating discussions on topics of geography, politics, and medicine. Through their introductions to heads of universities and heads of state, individuals now perceived to be from disparate worlds came to know one another.

THE NEURON

Christian Ehrenberg (1833) is credited with being the first to recognize the nerve cell as the important element of the nervous system, but Robert Remak (1838) provided its first accurate description (16). Rudolph Wagner (1852), using the teasing needle for dissection, observed that, of the many nerve cell processes that arise in the nerve cell, only one continues as a nerve fiber. Shortly thereafter, Remak observed a similar condition existing in the motor cells of the gray matter of the anterior horn of the spinal cord of oxen. Otto Deiters (1865), still relying on very primitive dissection methods but using human specimens, observed that only one of the many branches of the nerve cell remains undivided. He named this long, uniform-caliber process the axis cylinder. He designated the shorter branching cell extensions as the protoplasmic processes. At that time, the prevailing opinion was that of Joseph von Gerlach (1858). He assumed that contiguous processes of neighboring cells were fused to yield a reticulum of delicate fibers, i.e., a meshwork characteristic of the gray matter. He further assumed that the minute cell processes that form this reticulum rearrange and recollect themselves to give rise to nerve fibers that, after emerging from the gray substance, take the form of nerves. In accordance with this view, it was also thought that this "nerve fiber reticulum" represented mainly the terminal sensory branches, which, after fusing with the protoplasmic processes of neighboring motor cells, permitted a direct flow of sensory impulses to the motor cells. These views, however, were soon abandoned as better methods of histological study were developed.

With Camillo Golgi (1883) and his silver chromate method, a new epoch in the understanding of the finer constituents of nervous tissue began (36, 42). This led to the discovery that cells are endowed with short processes that terminate, shortly after their formation, in many end-branches and that many cells are endowed with, among several processes, one that is long and gives rise to collateral processes. Accordingly, Golgi grouped neurons into two categories, which were later designated as Golgi Type I and Type II neurons (16, 17). In the Type I category, he grouped the cell forms that present one long nerve process that, as it proceeds, is converted into a nerve fiber. In the Type II category, he assembled the cell forms that have many short processes that divide into numerous terminal branches. What may be more important is the conclusion he reached, namely that the protoplasmic processes of neighboring cells do not fuse or anastomose with one another. It is this view that led to the abandonment of the concept of von Gerlach and the establishment of the neuron doctrine. Additional proof in support of the newer doctrine was found in the embryological studies of Wilhelm His (1883), who demonstrated that nerve cells display and maintain an independent unit character for varying periods during certain stages of embryonic life. August Forel (1887), using the observation of Bernhard von Gudden on pathological conditions, provided additional evidence that nerve processes of adjacent or remote cells, although in contact with one another, are not in direct continuity (1). Vilhelm von Waldeyer (1891) stated that the nervous system consists of innumerable units that are not connected anatomically. He proposed to call the unit "neuron," from the Greek word for "sinew." Fridtiof Nansen was one of six pioneers whose work he summarized. The remarkable studies of Santiago Ramón y Cajal (1893) supported the theory that the neuron with its several parts (such as the cell body and the processes) constitutes a unit structure. Other important contributors to this theory were the English anatomist and physiologist Edward Schafer, the Hungarian anatomist Michael von Lenhossék, the Swiss physician Albrecht von Kölliker, and Carl Ludwig Schleich, who was a surgeon and anesthetist in Berlin (8, 22, 37, 40). Therefore, it required a half-century to assemble all of the essential data and observations to formulate the hypothesis that is now fully accepted as a working theory, i.e., the neuron doctrine. Our present concept of the organization and function of the nervous system is largely based on this theory (2, 6, 7, 14).

THE RENAISSANCE MAN

In 1882, after returning home to Norway from a voyage to Greenland on the sailing ship *Viking*, Fridtiof Nansen, who was then 21 years of age, was appointed curator of zoology at the Bergen Museum (4, 15) (*Fig. 1*). The director of the museum was Dr. Daniel Danielssen. On the staff was Dr. Gerhard Armauer Hansen, who in 1873 had discovered the species *Mycobacterium leprae* (41). Before Nansen joined the Bergen Museum, Armauer Hansen had been invited by Professor Louis Antoine Ranvier, a nervous system specialist in Paris, to investigate the motor nerves of the leech. Armauer Hansen observed that these nerves divided without anastomosing with the muscles and terminated in a triangular thickening (1881). This early observation of discontinuity in the peripheral nervous system probably inspired Nansen in his research on the nervous system of marine invertebrates. Nansen finished his first scientific report on the nervous system of the myzostome in 1885, followed by articles on *Myxine glutinosa* (3, 25, 26).

In 1886, Nansen left Bergen for continental Europe, to study the silver chromate staining method of Professor Camillo Golgi in Pavia. He later commented, "Never in my life had I imagined it was possible to prepare such elegant to distinct nerve sections" (21, p 46). Nansen became the first to apply Golgi's method to invertebrates, including ascidians and lancelets. He also visited Professor Anton Dohrn in Naples, where he became familiar with the new Zeiss opochromatic (color-corrected) microscope. Nansen's findings were published in Norwegian by the Bergen Museum during the summer of 1886 and were given wider circulation by a translation in a well-known English scientific journal (27). Nansen announced that, "Anastomoses or unions between the different ganglion (nerve) cells, I have been unable to demonstrate with certainty" (21, p 53; 40, p 122).

Unknown to Nansen at that time, Wilhelm His, a Swiss embryologist, had discovered that, during early stages of development in human embryos, nerve cells were definitely not in contact, which led His to similar views. Nansen was

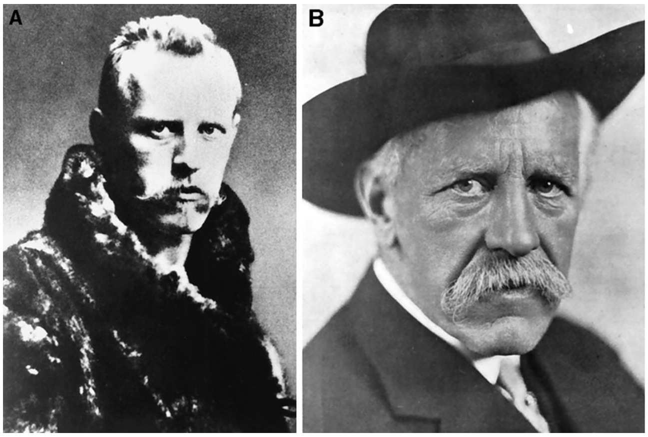
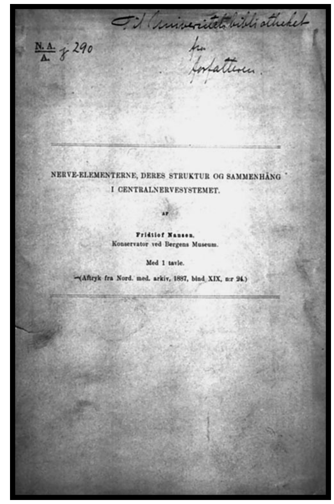


FIGURE 1. Fridtiof Nansen, the arctic explorer in the 1880s (*A*) and the humanitarian and statesman in 1928 (*B*) (courtesy of the Fram Museum, Oslo, Norway).



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NERVE-ELEMENTERNE, DERES STRUKTUR OG SAMMENHÄNG I CENTRALNERVESYSTEMET.

AF

Fridtiof Nansen,
Konservator ved Bergens Museum.

Med 1 tavle.

(Aftryk fra Nord. med. arkiv, 1887, bind XIX, n:r 24.)

FIGURE 2. Nansen's doctoral dissertation (1887), dedicated by the author (courtesy of the National Library, Haandskriftavdelingen, Oslo, Norway).

also unfamiliar with the work of August Forel, a Swiss psychiatrist, who observed that degeneration in the nervous system did not spread but was bounded by the limits of the cell, which led him also to deny continuity. From different perspectives, Forel, His, and Nansen had each launched onslaughts on the orthodox reticular theory, becoming cofounders of the modern view of the nervous system. Nansen's English translation was published in September 1886, followed by His' report on the subject in October 1886 and Forel's work in January 1887. By being the first to see his text in print, Nansen secured priority in establishing the neuron doctrine (22). Several articles followed, addressing a variety of topics such as vertebrate hermaphroditism, plants, and drift-ice (5, 31, 32, 34).

In August 1887, Nansen published a German translation of the part of his article on myzostomes that concerned the nervous system, where he reported his original statement that the cellular nerve units were not fused but only touched each other (28, 29). He also declared that all nerve units had membranes, which provided a logical explanation for discontinuity in the nervous system and the independence of the cellular nerve units. Furthermore, Nansen was the first to correctly interpret the phenomenon of "dotted substance." This substance was conventionally observed as spongy material fusing the nerve endings together (19). Nansen found the dotted substance to be the result of cutting sections through nerve bundles where the nerve fibers communicated with each other. "This tangle of the fibers is the true seat of the psyche" (21, p 55; 40, p 124). The dotted substance, which was later called the gray matter in vertebrates and neuropil in invertebrates, was subsequently demonstrated to be the site of synaptic transmission (20).

The reflex arc is the mechanism by which sensory impulses are transmitted to motor nerves to become transformed into physical actions. The reigning view was that the conduction path ran through fusions of the cell bodies in the peripheral nervous system. Nansen drew other conclusions from his model of the independent cellular unit. He proposed instead that the sensory nerves conducted information from the periphery and central nerve cells then relayed the impulses to motor nerves, which in turn activated the muscles (22). Nansen had become the first to provide the correct theoretical explanation, long before the reflex arc in any species had been adequately described.

In December 1887, Nansen published his final comprehensive article by the Bergen Museum, entitled "The Structure and Combination of the Histological Elements of the Central Nervous System" (33). In addition to presenting a revolutionary theory, Nansen had prepared all of the illustrations himself, etching directly from the microscope onto the stone for lithographic reproduction. To present the report for a doctoral degree in Christiania (now Oslo), Nansen produced a shortened translation into Norwegian (30) (*Fig. 2*). On April 28, 1888, exactly 4 days before he was scheduled to depart for Greenland, Nansen underwent the doctoral disputation and defended his thesis in public (21).

The First Opponent, Dr. Axel Holst, attacked Nansen for contradicting the generally accepted theory. Although the Norwegian condensation of Nansen's article had been formally presented, it was the original English version that was actually on trial. What particularly enraged Holst were the central assertion, "we are obliged to abandon the theory of the direct combination between the [nerve] cells," and the footnote, "we cannot change the reality according to our ideas but we can change our ideas according to the reality" (21, p 75). Dr. Holst declared that "one ought to eschew theories until one clearly saw that all the experimental facts were consistent." The Second Opponent, Professor Hjalmar Heiberg, expressed his conviction that "the hypotheses the Candidate had presented will certainly share the fate of so many others: they will be forgotten. The anatomic discoveries, on the other hand, will remain significant" (21, p 75). Nansen had observed that nerve fibers, after entering the spinal cord, bifurcate (like a T-joint) into ascending and descending branches. These fibers are now known as Nansen's fibers. The discovery provided the foundation for an understanding of spinal reflexes. "Direct anastomosis [fusion] between the processes [nerve fibers] . . . does not exist," was his categorical summing up. Therefore, "we are obliged to abandon the theory of the direct combination of the [nerve] cells." This is the original definition of the modern view of the independence of the cellular nerve unit. It was also the first explicit rejection of the reigning network theory. Nansen's concept of the cellular nerve unit as an independent entity provided "a new view" of the function of the nerves and the brain. "According to this view, there could be a localization in the central nerve-system but no isolation. This view will also make up for the function of lost parts" (21, p 56).

Nansen wrote a scientific article on the development of the dolphin, with Professor Gustav Adolph Guldberg in Christiania, before turning his full attention to polar exploration (18). After the dangerous but successful crossing of Greenland on skis, Nansen wrote the book *Eskimoliv* (*Eskimo Life*), which was published in 1891. Two years later, he set sail for the North Pole (9) (*Fig. 3*). After his return from the *Fram* expedition in 1896, an endowed professorship in zoology was established for him at the University of Christiania. When

FIGURE 3. Nansen (and others) and the *Fram* in the Arctic, 1895 (courtesy of the Fram Museum, Oslo, Norway).

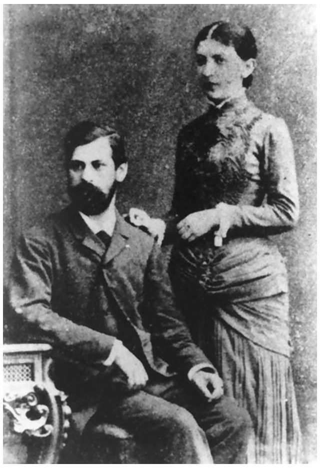


FIGURE 4. Sigmund Freud and his fiancée Martha Bernays, 1885 (reprinted with permission from, Jones E: *The Life and Works of Sigmund Freud.* New York, Basic Books, 1953 [23]).

Armauer Hansen urged him to return to the central nervous system, Nansen replied, "If only I were there again, but it will have to wait a little" (21, p 370). Nansen then hurried off on a lecture tour of the United States. At the White House in Washington, he was received by President William McKinley; this was followed by a reception at the Arlington Hotel, where he met the future President Theodore (Teddy) Roosevelt (21).

In 1906, Camillo Golgi and Santiago Ramón y Cajal were jointly awarded the Nobel Prize for physiology and medicine. It recognized their work in Nansen's field of neurobiology. Cajal was rewarded for developing the now generally accepted neuron doctrine, in the early development of which Nansen had so notably played his part two decades earlier.

Meanwhile, Nansen's interests shifted from zoology to physical oceanography; in 1908, his status was changed to professor of oceanography. As Nansen grew older, he became more interested in relations between individuals and nations. The founder of the "evil empire," Vladimir Ilyich Lenin, who used and manipulated Nansen, wrote in 1919, "You are an educated man, Mr. Nansen, you know perfectly well that every war and every truce is politics. This means you have linked the 'humanitarian' with the 'political.' You have lumped them together" (21, p 488). Nansen's role as a statesman and humanitarian culminated with the Nobel Prize award for peace in 1922, in recognition of his famine relief work in Russia and his development of the concept of refugee status. Nansen, who may equally have deserved the Nobel Prize in medicine, commented:

> To me, the Peace Prize is strange and incomprehensible, since I was forced by chance into this work, which was not mine at all. My scientific work has convinced me that everything goes in cycles, in waves; it is my consolation, even if the periods of decay can be long, and the wave troughs deep, a crest comes again, if only one can wait . . . even after the twilight of the Gods there is another world (21, p 532).

Nansen died in 1930, at 68 years of age.

THE FOUNDER OF PSYCHOANALYSIS

Sigmund Freud (*Fig. 4*) entered medical school in Vienna in 1873, at 17 years of age. As a student, he studied nerve cells and fibers in primitive fish (*Petromyzon*) and crayfish, under Professor Ernst Brücke (40). This led to his first scientific reports (in 1877 and 1878), in which he concluded that Reissner's cells "are nothing else than spinal ganglion cells which, in those low vertebrates, where the migration of the embryonic neural tube to the periphery is not yet completed, remain within the spinal cord" (40, p 69). With these articles, Freud helped pave the way for the neuron doctrine, conceiving the nerve cells and fibrils to be one morphological and physiological unit (11).

Within 1 year after the crayfish article was published, Freud delivered a lecture to the local psychiatric society, which was published in 1884 as *The Structure of the Elements of the Nervous System.* His views on the relationship between nerve structure and nerve function are summarized in the following passage:

> If we assume that the fibrils of the nerve have the significance of isolated paths of conduction, then we should have to say that the pathways which in the nerve are separate are confluent in the nerve cell: then the nerve cell becomes the 'beginning' of all those nerve fibers anatomically connected with it . . . . I do not know if the existing material suffices to decide the problem, so important for physiology. If this assumption could be established it would take us a good step further in the physiology of the nerve elements: we could imagine that a stimulus of a certain strength might break down the isolation of the fibrils so that the nerve as a unit conducts the excitation, and so on (40, pp 72–73).

Freud received his M.D. degree in Vienna in 1881. Although he appeared to be ready for a career in laboratory investigation into the histological features of nerve cells, his prospects for an academic position were poor, because Brücke had not one but two heirs-apparent, namely Siegmund Exner and Ernst von Fleishl-Marxow, both of whom were relatively young and very able. In 1882, Brücke advised Freud, in view of Freud's "bad financial position," to "abandon his theoretical career" (40, p 75). Freud seems to have accepted this advice without discussion; he immediately became a junior resident physician in the main general hospital in Vienna. There he began specialization in neurological disorders and, under Theodor Meynert, he pursued microscopic studies of nerve tracts in the human brain, especially the hindbrain (medulla oblongata).

In 1885, Freud submitted his application for the position of *privatdozent,* which was essential for continuing his professional and academic career. The research accomplishments described in his application included his microscopic studies of nerve cells under Brücke and of nerve tracts in the medulla under Meynert and clinical studies of a case of cerebral hemorrhage. He had also initiated experiments on the behavioral effects of cocaine, including on himself. He was successful in his application and in obtaining, in the same year, a travel grant to study in Paris under the great neurologist Jean Charcot (40).

For the next several years, he was absorbed in his work in clinical neurology. His earlier microscopic work, especially on the origin of dorsal root fibers, was often referenced by later workers whose studies led to the neuron doctrine. In 1891, the same year in which the neuron doctrine was promulgated, he published a book on aphasia. From that time he moved step by step toward his theory of psychoanalysis, through his studies of hysteria (1895), dreams (1899), and sexuality (1905).

It might be assumed that during this period he turned his back on the studies of the nerve cell; for example, the subject of the neuron doctrine receives no mention in his autobiography. But the influence of his early neuroanatomic training was not dismissed so easily. In 1895, Freud attempted to provide a mechanistic basis for his emerging psychological concepts by writing *Project for a Scientific Psychology*, drawing on everything he had learned regarding nerve cells and brain structure from Brücke and Meynert, as well as the work leading to the neuron doctrine. His hope, which seems to be traced directly back to Brücke's vow in the 1840s, was to define how nerve cells and their mechanistic states of energy could generate quantitatively determined psychical processes. After several months of feverish effort, he abandoned the project in despair; it was not published during his lifetime. However, he never abandoned his ambition to establish a scientific psychology. In contrast to Nansen, Freud narrowly missed world fame in early life by not pursuing his thoughts to their logical conclusion (40). Looking back, Freud wrote, in 1935:

> Although we lived in very limited circumstances, my father insisted that, in my choice of a profession, I should follow my own inclinations. Neither at that time, nor indeed in my late life, did I feel any particular predilection for the career of a physician. I was moved, rather, by a sort of curiosity, which was, however, directed more towards human concerns than towards natural objects; nor had I recognized the importance of observation as one of the best means of gratifying it. At the same time, the theories of Darwin, which were then of topical interest, strongly attracted me, for they held out hopes of an extraordinary advance in our understanding of the world; and it was hearing Goethe's beautiful essay on Nature read aloud at a popular lecture just before I left school that decided me to become a medical student (38, p 502).

WHEN GREAT MINDS MEET

The end of the 19th century and the beginning of the 20th century represented an era of significant scientific progress and important discoveries. It is probably no coincidence that some of the outstanding pioneers in these advances were acquainted with each other. The pioneer Norwegian neurosurgeon Vilhelm Magnus (1871–1929) studied medicine at the Royal Frederik University in Christiania with the Norwegian explorer Roald Amundsen (1872–1928), who abandoned medicine for arctic ventures (10). Amundsen's mentor was Fridtiof Nansen (1861–1930), who interacted with Sigmund Freud (1856–1939) and the Swedish explorer of Central Asia Sven Hedin (1865–1952), who in turn established a close friendship with Harvey Cushing (1869–1939).

In 1887, Fridtiof Nansen wrote, about Sigmund Freud:

> Freud (1882) does not seem to have paid any special attention to the structure of the dotted substance. The relation of the ganglion cells to the nerve tubes, he supposes to be the same in invertebrates as in vertebrates, and he believes to a certain extent at all events, in a direct origin: he expresses himself, however, very indistinctly on this subject (40, pp 60–61).

In Vienna in 1898, Sigmund Freud was reading Nansen's book *Farthest North* (35) and commented that he himself could make good use of Nansen's dreams, which were absolutely obvious from his book. Freud stated that "his psychological condition is quite simply typical of those who try something new with confidence, and in a round about way, probably discover something new, and not so much as he imagined. I know from my own experience" (21, p 377).

In 1891, Vilhelm von Waldeyer, who introduced the term *neuron*, wrote of Nansen that "he knew how to handle the microscope as well as an ice ax and snow shoes" (21, p 218). At the time of his departure for the North Pole in 1893, Nansen was presented with the latest volume of *Biologische Untersuchungen* by the Swedish anatomist Professor Gustaf Retzius (1842–1919). It was dedicated to "my friend Fridtiof Nansen, the bold and distinguished explorer of the central nervous system and the polar regions." Retzius made important contributions to studies of the nerve cell, and he is regarded as one of the key participants in the emergence of the neuron doctrine (39, 40).

Sven Hedin, who later became a famous explorer, met Nansen in Stockholm in 1887 and found him "really a thoroughly unusual apparition" (21, p 61). Hedin and Nansen had much in common and became good friends.

In the spring of 1929, by coincidence, both Hedin and Nansen visited Harvey Cushing in Boston (12, 21, 24). Hedin had been referred from Beijing by Cushing's former pupil Georges Shaltenbrand, because of a suspected cervical tumor. Hedin traveled from China to Boston accompanied by his sister Alma and expedition physician David Hummel. The distinguished patient was cleared after 5 days in the hospital. Cushing found Hedin, with his broad interest in literature, art, and exploration, to be one of the most stimulating men he had ever encountered. A few months later, Cushing visited Hedin in Stockholm (*Fig. 5*).

FIGURE 5. Harvey Cushing (*left*) with Sven Hedin (*center*) and Einar Key (*right*) in Stockholm, 1929 (reprinted from, Ljunggren B: Harvey Cushing and Sven Hedin. Surg Neurol 17:165–171, 1982 [24], with permission from Elsevier Science).

During his visit, Cushing admired an early 15th century surgical manuscript by John of Arderne at the Royal Library in Stockholm. This 3-meter-long parchment roll, containing hand-colored depictions of human diseases and their treatments, had been presented to Erik of Pomerania, King of Denmark, Norway, and Sweden, as a gift from his wife, Queen Filippa (24). Hedin had the parchment roll copied by the Swedish artist Carl Olausson and presented it to Cushing the following Christmas (*Fig. 6*). Cushing responded:

FIGURE 6. John of Arderne manuscript *Practica Magistri Johannis Ardeni de Newark: De Arte Phisical & de Cirurgia*, 1412 (courtesy of the Yale Historical Library, New Haven, CT).

> Dear Sven: The marvelous copy of the Arderne MS that you have had made for me in celebration, I presume of the operation I did not perform on your spinal marrow, has come just in time for Christmas. And such a present! . . . which will always remain far the most precious item in my library, doubly precious not only in its intrinsic value but because of its association for me with you and your sisters (12, p 582).

For the first few months of 1929, Fridtiof Nansen was in the United States on a lecture tour, attempting to raise money for an Arctic airship flight (21). While in Boston, Nansen met with Cushing and Professor Arnold Carl Klebs (1870–1943), one of Cushing's close long-time friends (13). He was the son of the famous Swiss bacteriologist Edwin Klebs who, with Loeffler, discovered the diphtheria bacillus in 1884. At a subsequent dinner in Klebs' house in Nyon, Switzerland, Nansen and Cushing signed their names on a wooden panel (*Fig. 7*), which is now displayed in the Historical Library at Yale University.

After his visit to Boston, Nansen sent Cushing his then 40-year-old articles on neuroscience. Cushing wrote a letter of appreciation on November 27, 1929 (*Fig. 8*). A few months later, Nansen died as a result of a heart attack.

THE NEURON DOCTRINE TODAY

We may conclude that much of the classic neuron doctrine has stood the test of time. It has served well as the theoretical basis for the great advances in our current understanding of the cellular basis of nervous system function. Few theories in science have met such demanding tests, for so many years, with such obvious success.

The classic neuron doctrine expressed the widest possible range of cellular properties, including structure, function, metabolism, and development. Future research may establish the neuron as a basic information-processing unit (40). The present understanding of neural networks represents a view of nervous organization that mirrors that of Golgi, i.e., the view that the complex interconnectedness of networks is more important than the details of neuronal structure and function. An exciting challenge for the future is to incorporate real neuron properties into these networks. If this could lead to a better understanding of the biological basis of human thought, it would certainly have won the approval of the explorers and pioneers of the neuron doctrine.

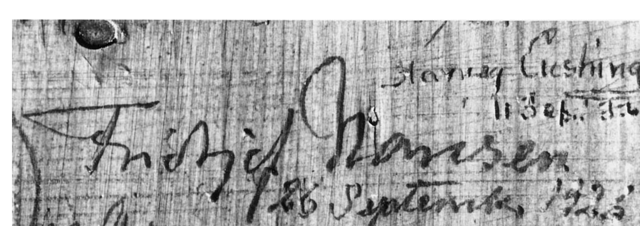
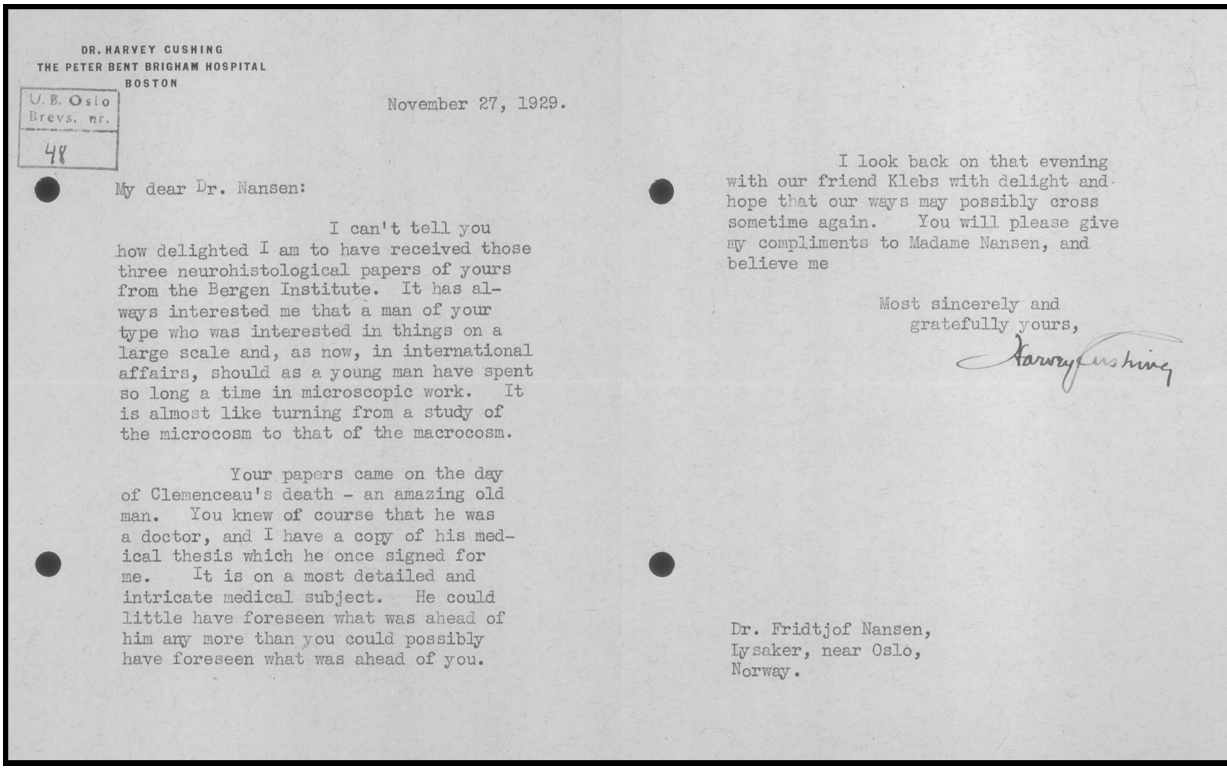


FIGURE 7. Nansen's and Cushing's signatures on the wooden board from the door frame at the home of Arnold Klebs, 1929 (courtesy of the Yale Historical Library, New Haven, CT).



DR. HARVEY CUSHING
THE PETER BENT BRIGHAM HOSPITAL
BOSTON

U. B. Oslo
Brevs. nr.
48

November 27, 1929.

My dear Dr. Nansen:

I can't tell you how delighted I am to have received those three neurohistological papers of yours from the Bergen Institute. It has always interested me that a man of your type who was interested in things on a large scale and, as now, in international affairs, should as a young man have spent so long a time in microscopic work. It is almost like turning from a study of the microcosm to that of the macrocosm.

Your papers came on the day of Clemenceau's death - an amazing old man. You knew of course that he was a doctor, and I have a copy of his medical thesis which he once signed for me. It is on a most detailed and intricate medical subject. He could little have foreseen what was ahead of him any more than you could possibly have foreseen what was ahead of you.

I look back on that evening with our friend Klebs with delight and hope that our ways may possibly cross sometime again. You will please give my compliments to Madame Nansen, and believe me

Most sincerely and
gratefully yours,
Harvey Cushing

Dr. Fridtjof Nansen,
Lysaker, near Oslo,
Norway.

FIGURE 8. Cushing's letter to Nansen, 1929 (courtesy of the National Library, Haandskriftavdelingen, Oslo, Norway).

Here, silent, speak the great of other years,
the story of their steep ascent from the
unknown to the known, erring perchance
in their best endeavor, succeeding often,
where to their fellows they seemed most to fail;
Here, the distilled wisdom of the years, the
slow deposit of knowledge gained and writ
by weak, yet valorous men, who shirked not
the difficult emprize;
Here is offered you the record of their days
and deeds, their struggles to attain that
light which God sheds on the mind of man,
and which we know as Truth.
Unshared must be their genius; it was their
own; but you, be you but brave and diligent,
may freely take and know the rich companionship
of others' ordered thought.

Lines written by George Stewart, carved over the fireplace in the Historical Library of the Yale University School of Medicine, 1941.

Se tu sarai solo tu sarai tutto tuo
(If thou art alone, thou wilt be wholly thyself)

Epigram (Leonardo da Vinci), over the mirror in Arnold Klebs' library, Yale University School of Medicine.

ACKNOWLEDGMENTS

This article is dedicated to Professor Emeritus Hirotaro Narabayashi, a true friend and pioneer neuroscientist who guided so many of us through the intricate and fascinating world of neurons, and to Professor M. Gazi Yaşargil, NEUROSURGERY's "Man of the Century," who taught us the spirit of innovation and exploration.

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COMMENTS

A good history is like a woven tapestry. The base is a strong fabric, and woven throughout are the panels that elucidate the story to be presented. Most tapestries lack the basic construction or the woven patterns are blurred, so that one loses the theme or is unable to trace the story. That is certainly not the case here. For a fundamental concept of the neurosciences, namely the neuron theory, an intricate history of important discoveries, as well as the personalities behind them, is presented. And what personalities they are, including an Arctic explorer who later earns a Nobel Prize and along the way writes several brilliant articles on the neuron theory. Threaded through the tapestry are personalities such as Freud, Klebs, Lenin, and Cushing, among many others. To provide additional depth, the authors have added many personal details of how these critical personalities interacted. The end result includes a founder of modern neurosurgery, the founder of psychoanalysis, and an early Arctic explorer, Nobel Laureate, and cofounder of the neuron theory, all elegantly woven into a wonderful tapestry of incredible depth and richness.

James T. Goodrich
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This remarkable article describes some of the most interesting persons in the 19th century and is highly enjoyable reading. Commenting on a previous article by Fodstad et al. (1), I wrote that some German neuroanatomists consider Fridtiof Nansen to be an important contributor to the development of the neuron hypothesis. The authors obviously already had the documentation for that idea, and the present article proves that Nansen not only contributed to the development of the hypothesis but was the first to publish experimental evidence in its favor. It is, however, important to emphasize the fact that the hypothesis was probably developed with the contributions of several distinguished scientists, including Wilhelm His, August Forel, and Santiago Ramón y Cajal. Considering Cajal's monumental work, there seems to be no doubt that he deserved the Nobel Prize in physiology and medicine that he received in 1906.

Several of the most distinguished scientists in the 19th century seem to have been renaissance persons, receiving and understanding information from other sciences and culture and incorporating this information into their scientific work. There may be reasons to think that many of us today have orientations that are too narrow. The deadly storm of information within our own field makes it difficult to take time to study and relate other sciences, history, culture, and art. In this respect, I think that both the renaissance men of the 19th century and the present editor of *Neurosurgery* would agree with Henrik Ibsen, who recommends going to the heights to obtain a panoramic perspective on life. From the last verse of "On the Moors" (2):

I'm clad now in steel, I follow full-shod
the high-country summons to wander
I've lived out life on the low land clod;
up here on the heights there is freedom and God,
the rest are groping down yonder.

Iver A. Langmoen
Stockholm, Sweden

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This historical article presents new and interesting facts regarding both the history of neuroscience and the history of exploration. The individuals involved are fascinating contributors to both areas, and the article nicely chronicles a time of intense excitement. From the standpoint of the history of medicine, this article also demonstrates how often scientific "role hybrids" are in positions to make major advances in scientific knowledge and shifts in previously accepted paradigms.

Edward R. Laws, Jr.
Charlottesville, Virginia

Fodstad et al. have brought to our attention the admirable life of Fridtiof Nansen, who was not only an arctic explorer of world renown but also a cofounder of the neuron doctrine. He was on friendly terms with both Freud and Cushing. This communication is successful in demonstrating the interactions of great scientists and explorers on intellectual and social levels.

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