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A Biographical Memoir by

GEORGE ADELMAN AND BARRY SMITH

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BY GEORGE ADELMAN AND BARRY SMITH

FRANCIS O. SCHMITT was one of the founders of two interdisciplinary life science fields that were to become of ever-greater importance in the latter part of the twentieth century. One of these is biophysics, which he helped to define in the 1930s by his revolutionary physical studies of the fine structure and molecular properties of proteins (such as collagen and neurofilaments), of cells (such as neurons and glia), and of tissues (such as connective tissue and muscle). The other is neuroscience, which he launched in the 1960s with his Neuroscience Research Program. By dint of his broad and forward-looking vision, his unflagging vigor, and his boundless enthusiasm, Schmitt managed to bring together colleagues from diverse disciplines and stimulate their highly productive interactions in the study of the nervous system. Thus he changed the lives and careers of many scientists, some of them young and others not so young.

Schmitt was born in St. Louis in 1903, the son of second-generation German immigrants and the grandson of a Lutheran pastor. Raised by hard-working, enlightened parents, Frank took an early interest in science, and at age twelve, he signed up for the scientific curriculum at the recently founded, progressive Grover Cleveland High School.

By the time he was sixteen, he was enrolled in St. Louis's Washington University as a premedical student, since his father had set a career as a physician or surgeon as Frank's professional goal. Inspired by one of his professors, the cytologist Caswell Grave, Frank carried out a research project in his senior undergraduate year on the coordination and regulation of ciliary movement in a mollusk. The results of this study produced Frank's first publication, on which Grave was listed as a coauthor.

Having received his B.A. in 1924, Frank moved on to Washington University's School of Medicine, after spending the summer, at Grave's suggestion, taking the physiology course at Woods Hole Biological Laboratory. There he met physiologist Robert Chambers, who took young Frank under his wing and published a joint paper with him on fluid crystals and meristematic growth. This paper presaged Frank's future, lifelong interest in molecular structure and function in biology. Woods Hole had opened up new vistas and opportunities for Frank and convinced him, notwithstanding his father's plans, that seeking a career in clinical medicine would be the wrong choice. An encounter with Joseph Erlanger, head of the Department of Physiology at the medical school, led Erlanger to propose that Frank work toward a Ph.D. in physiology under Erlanger's direction, rather than seek an M.D. Frank eagerly accepted this offer and became Erlanger's only graduate student at the time.

The physical and chemical basis of the nerve impulse was the focus of Erlanger's research program, which he carried out in collaboration with two colleagues, the pharmacologist Herbert Gasser and the physiologist George Bishop. Thus, as a beginning graduate student at the start of his research career, Frank happened to fall in with a group of pioneering neurophysiologists. They were engaged in groundbreaking work on the nerve fiber and its then still mysterious action potential, using the recently developed techniques of X-ray diffraction, polarization optics, and electronic display of electrophysiological recordings. Scanning the scientific horizon with what he later called his biological radar, Frank locked onto the cell membrane, whose structure Harvey White was studying in a laboratory next to Frank's as another critical aspect of the conundrum of the nerve impulse. So he collaborated with White in a study of kidney membrane function in the mud puppy, *Necturus maculosus*, and presently published two jointly authored papers on this work. Frank's doctoral dissertation was entitled "The Conduction of the Impulse Through Cold-Blooded Heart Muscle Locally Altered." He defended it successfully on May 21, 1927, on the day Charles Lindbergh landed in Paris.

After being awarded a National Research Council Fellowship, Schmitt spent the years 1927-29 doing postdoctoral studies in California, England, and Germany. He first went to Berkeley to work with the physical chemist G. N. Lewis on the effect of ultrasonic waves on the speed of chemical reactions and of electric currents on the stability of monomolecular lipid films. He continued his investigations of lipid films with Sir Jack Drummond in the Biochemistry Department at University College, London, and he finally went to the Kaiser-Wilhelm Institutes for Biology (in Berlin) and for Medical Research (in Heidelberg) to study the metabolism of nerve fibers with Otto Warburg and with Otto Meyerhof, respectively.

After his two postdoctoral Wanderjahre, Frank returned to Washington University in 1930 as an assistant professor of zoology and established his own highly productive research program devoted to topics ranging from surface chemistry and neurochemistry through ultrastructure of cell components to embryology. In this program, he collaborated with his younger brother, Otto Schmitt, a brilliant engineer, in the development of highly innovative instrumentation techniques. He also came to be regarded as an excellent teacher, who took a great personal interest in his students and rose through the academic ranks to full professor and eventually to department head.

In 1941, by which time Frank had published nearly 100 papers reporting the results of his highly fruitful and diverse investigations, he left St. Louis to accept an invitation of MIT President Karl Compton to become head of the MIT Department of Biology and Biological Engineering. With a prescient vision of the future of twentieth-century life science research, Frank emphasized the molecular approach to biology in his leadership of the department and in his own research, thus assuring that the 1940s and 1950s would become flourishing and exciting times for the life sciences at MIT. World War II had just begun when Frank arrived at MIT, and the work he and his colleagues were doing on collagen had direct application to the treatment of burns and was of great practical importance for the war effort. But the contributions of Frank's research group transcended the merely practical and deepened our fundamental understanding of macromolecular biological fibers. For instance, in collaboration with Jerome Gross and John Highberger, Frank undertook a systematic analysis of the in vitro reconstitution of cross-striated fibrils from solutions of purified collagen molecules. These experiments demonstrated that various supramolecular forms of collagen can be reconstituted by self-assembly, and this led both to the determination of the dimensions of the collagen molecule (tropocollagen) and the quarter-stagger hypothesis, which accounted for the observed axial periodicity of the molecule. Frank and his colleagues Albert E. Rubin, D. Pfahl, P. T. Speakman, and Peter F. Davidson went on to isolate and determine the primary structure of the noncollagen-like peptides (teleopeptides) at either end of the collagen molecule, which make it immunogenic and which are critical factors in fibrinogenesis, as well as in pathophysiology.

There were also important advances in the techniques of electron microscopy that emerged from Frank's MIT laboratory. With his students Cecil Hall and Marie Jakus, Frank pioneered the use of heavy metal stains in electron microscopy and published some of the earliest electronmicrographs of striated muscle fibers, correlating these data with those obtained by Richard Bear from X-ray diffraction analyses, while H. Latta and F. Hartman invented the glass knife for cutting ultra-thin sections. These technical advances allowed Jakus and Hall to examine the ultrastructure of isolated and purified actin and myosin molecules, as well as their interactions and polymerization, and allowed Hall to study the conversion of fibrinogen to fibrin and the fine structure of catalase at a resolution of 15A. Moreover, in Frank's laboratory during that period, Jean Hanson and Hugh Huxley developed their sliding filament model of muscle fiber contraction, James Robertson his unit membrane model, and Betty Geren her "jelly roll" model of myelin assembly.

Frank's great talents as a theoretician and a hands-on bench scientist combined with his energy and enthusiasm for inspiring (and finding support for) collaborative interdisciplinary efforts of colleagues, played no small part in the many achievements of the biology department he founded. He turned it into an exciting place, because he generated an ambiance sizzling with ideas and enthusiasm. As one of his colleagues put it, working with Frank was like trying to take a drink from a fire hydrant. His appointment as MIT's second institute professor in 1955 allowed him to relinquish the administrative responsibilities of department head and to pursue any scientific project he desired.

Acutely aware that the division of science into disciplinary pigeonholes was an arbitrary administrative artifice, Frank was convinced that it did great harm by creating barriers for heuristically fertile communication. In particular, he fervently believed in the need for a cross-disciplinary perspective in order to find physical solutions to biological problems, and thus he became a leader in the effort to broaden and reformulate the nascent interdisciplinary field of biophysics. In 1955 the National Institutes of Health officially recognized that field by establishing a Biophysics Study Section with Frank as its first chairman. To limn the contours and define the content of biophysics, Frank organized a four-week-long conference in the summer of 1958, the Intensive Study Program in Biophysics, held at the University of Colorado in Boulder. Some 200 biologists, chemists, physicists, psychologists, and engineers came to Boulder to attend formal and informal lectures, seminars, and discussions on subjects ranging from the molecules of life to whole organisms. The published proceedings of that conference, *Biophysical Science: A Study Program,* provided a conceptual foundation and research agenda for the new field. The success of this experiment on the cross-disciplinary exchange of information, for which Frank's involvement in planning and implementation had been the crucial factor, made so strong an impression on him that he would use this model again to assist in the birth of neuroscience.

As the years went by, the nervous system came to dominate Frank's theoretical and practical research interests to an ever greater degree. In the late 1930s, continuing the work he had begun as a graduate student under Erlanger and Gasser in St. Louis, Frank pioneered the use of the giant axon of the squid for the study of the action potential and nerve impulse conduction. The British zoologist John Z. Young, whom he met while doing postgraduate work at

Woods Hole, had introduced him to the squid axon preparation. Most of Frank's initial work on the giant axon was done with the modestly sized squid, *Loligo pealii*, which is abundant in the Atlantic waters off Cape Cod. But in the late 1950s, while visiting the Chilean Marine Biology Station at Viña del Mar, Frank encountered the elephant of the squids, *Dosidicus gigas*, whose axons reach diameters of up to 4 mm, in the Pacific waters of the Humboldt Current. This preparation allowed Frank and his team—stateside as well as Chilean investigators—to study the chemical constituents of the axoplasm, as well as axonal flow and transport, in individual nerve fibers.

Frank's preeminent motivation for studying nerve cells was to fathom the function of the human brain and, ultimately, nature's deepest mystery, the mind. Towards that goal, invertebrate nervous systems such as that of the squid were good objects on which to start. Yet, they are only a start, because what Frank wanted to know was not merely how the human brain senses the world and produces appropriate motor responses to it, which is what the squid brain does too, but he reached out for understanding mental functions such as memories, thoughts, and emotions, of which squid brains are unlikely to be capable. Drawing on his earlier experience with the Biophysics Study Program and fully aware of recent advances in disciplines cognate to neurobiology, Frank decided that the time was ripe for creating a basis for a novel multidisciplinary approach to the questions of how nervous systems mediate behavior and how mind is instantiated in the brain. To get started on this novel approach, Frank organized two seminar series at MIT in 1960 and 1961, which brought together people who were interested in bridging the gap between physical, chemical, and structural studies of the brain on one hand and behavioral, psychological, and psychiatric studies on the other.

The overview of what was happening at that time in brain research and cognate fields provided by these discussions was published by MIT Press in 1962.

Convinced of the practicability of the interdisciplinary neurobiological research program he had in mind, Frank invited a small international group of eminent scientists representing diverse physical and biological disciplines, and who he knew shared his interests, to a meeting in New York City in February 1962. At this gathering, Frank proposed that to create a basis for the effective pursuit of the Promethean quest for understanding the mind/brain, it would be necessary to create an organization dedicated to that goal, similar to the Biophysical Study Program, which had defined the new biophysics. The attendees at that meeting agreed to form the governing board of an organization that they named (on Frank's recommendation) the Neurosciences Research Program (NRP), and which Frank had arranged to be housed at the American Academy of Arts and Sciences in Brookline, Massachusetts.

Thus, at the age of fifty-nine Frank embarked on another major project. He set the course for the NRP that it followed for the next twenty years: to promote interdisciplinary attacks on neuroscientific problems, to organize interdisciplinary conference and comprehensive study programs, and to proselytize notable senior and promising junior scientists representing diverse disciplines. The NRP's publication program included a series of monographs, which disseminated concepts developed at NRP conferences, and the massive records of four intensive Neuroscience Study Programs held, like their predecessor Biophysics Study Programs, during the summer in Boulder.

It is fair to say that the NRP did create the basis for the modern vanguard field of neuroscience as a unitary discipline that seeks to understand how the nervous system and its apogee, the brain, work to produce behavior, thus laying the groundwork for the eventual establishment of the Society for Neuroscience. It hardly can be a coincidence that of the first twelve presidents of that society, ten were or had been members of the NRP governing board, and that, of the more than 2,500 people who took part in the NRP's programs during the twenty years that Frank had been the NRP's spiritus rector, many later became the leading lights of neuroscience.

Frank Schmitt was that rare combination of theoretician, experimentalist, leader, organizer, and motivator. He was not only a great scientist but also an admirable person. He was devoted to his wife Barbara (a professional-class pianist) and to his daughter Marion and his sons David and Robert. Love of music and religion were both important parts of Frank's world. Although born and raised in the Lutheran faith, he became an active communicant of the Congregational Church and sought to reconcile science and religion in a rational framework. Towards that end, he brought theologians and scientists together to try to harmonize subjective tenets of faith with objective scientific findings. His deep interest in how the brain works to produce the mind was energized by his desire to understand human spirit and soul. Neuroscience, to whose development he contributed so much, continues to move ahead rapidly. Frank would surely be glad to see all this progress and would probably remark, as he often did, "You ain't seen nuthin' yet!"

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