BIOGRAPHICAL MEMOIRS

Laszlo Lorand

March 23, 1923–December 6, 2018
Elected to the NAS, 1987

A Biographical Memoir by Indrani Mukharji

Laszlo Lorand, a distinguished biochemist and professor at Northwestern University, was best known for his landmark discoveries on the mechanism of blood clotting. In post-World War II Hungary while a medical student at the University of Budapest, Lorand was introduced to Nobel laureate Albert Szent-Gyorgyi. In his third year of medical school, Lorand was offered a research position at Albert Szent-Gyorgyi's Institute of Biochemistry at the University of Budapest. It was there that Lorand became fascinated with the phenomenon of blood coagulation after the discovery of a protein that plays a critical role in blood clotting. This discovery by Kalman Laki and Laszlo Lorand in 1948 laid the foundation for the molecular understanding of the clotting of fibrinogen in blood. As a young medical student in Budapest, he watched how a few drops of thrombin added to blood plasma turned it from liquid into solid in a matter of minutes. It became evident that clotting can be lifesaving for wound healing but likely to be deadly for blood circulation. But the precise physiological pathway of the clotting mechanism was not known at the time. Therefore, Lorand decided to pursue research in this field of thrombosis, protein associations, and calcium ions. In doing so, he contributed greatly to the scientific understanding of the coagulation cascade, having migrated from Hungary to England and finally to the United States, driven by his passion for scientific discovery.

Laszlo Lorand was born in Győr, Hungary on March 23, 1923, to Hugo, a physician, and Margaret (Klein) Lorand. During the Nazi occupation of Hungary in World War II,

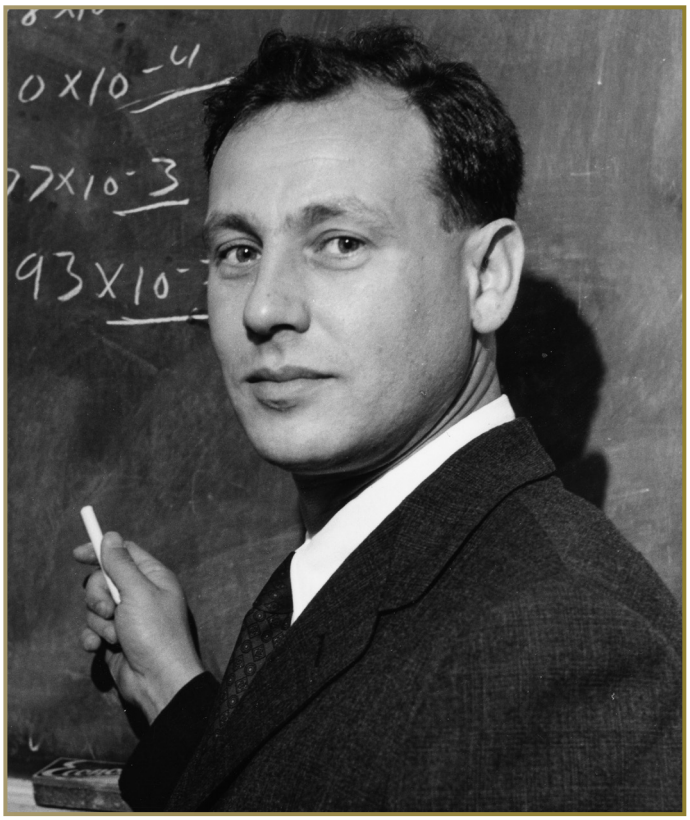

Figure 1 Portrait of Laszlo Lorand at the University of Leeds. *Courtesy Charles Deering McCormick Library of Special Collections and University Archives, Northwestern University Libraries.*

Lorand escaped deportation to Auschwitz by hiding with the help of one of his father's former patients. His family members were sent to concentration camps, and his father died at Auschwitz. After the war, Laszlo entered medical school at the University of Budapest. An introduction to Nobel Prize winner Albert Szent-Gyorgyi in 1946 set the stage for his scientific future. Szent-Gyorgyi was also the honorary president of the Soviet-Hungarian Friendship Society and a member of the Hungarian Parliament. He not only obtained concert and opera tickets for the members of his research team but arranged for them to learn English, something that benefitted Lorand

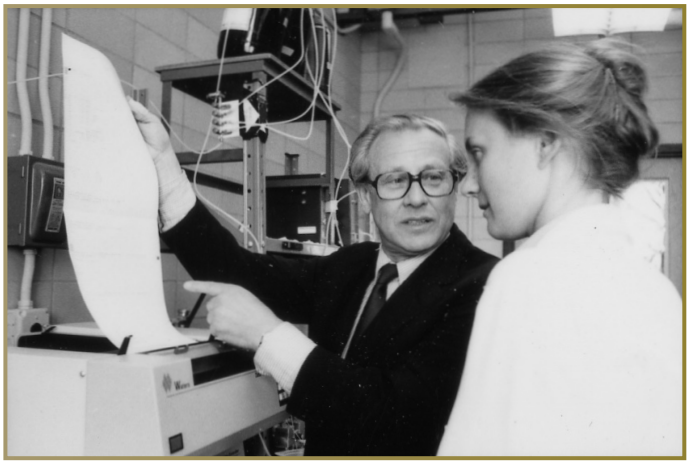

Figure 2 Laszlo Lorand with postdoctoral fellow Margaret Michalski, MD, in May 1984 in his laboratory at Northwestern University's Evanston campus. *Courtesy Charles Deering McCormick Library of Special Collections and University Archives, Northwestern University Libraries.*

a few years later.[11] Research at the Institute of Biochemistry, an intellectual haven of that era, under the mentorship of Szent-Gyorgyi and Kalman Laki led to the discovery of Laki-Lorand factor, which later became known as Factor XIII and led to the molecular understanding of the clotting of fibrinogen in blood. By 1947, Szent-Gyorgyi, Laki, and other eminent scientists began to leave Hungary, which was on the verge of becoming a one-party socialist republic. Szent-Gyorgyi arranged for Laszlo to continue his research in the laboratory of William T. Astbury at the University of Leeds in England. Laszlo finished his medical studies earning the final certificate (*Absolutorium*) in medicine in 1948 from the University of Budapest.[11] Because of the increasingly uncertain political climate in Hungary, Lorand made the difficult decision in December 1948 to leave his widowed mother behind and pursue research at the Department of Biomolecular Structure at the University of Leeds with Astbury.[1]

On the last day of December 1948, Lorand boarded a train bound for Vienna and took on the arduous journey with little money in his pocket and a roast goose and hard salami in one suitcase packed by his mother, who feared that Britain was still suffering food shortages.[1] Postwar austerity in the United Kingdom had made carrying out research quite challenging, with disruptions of electricity and flooding of the laboratories that were housed in residential properties. Lorand's research involved deciphering the molecular mechanism of blood clot formation. He demonstrated that fibrinogen is converted to fibrin, the main component of blood clots, with the concomitant release of smaller peptides through the limited proteolytic action of the enzyme thrombin. The proteolytic activity of thrombin cleaved a small percentage of the fibrinogen from its N-terminal end, thereby producing peptides of unique composition that he termed fibrinopeptides. Subsequent studies showed that fibrin-stabilizing factor, or FXIII, required activation by thrombin and by Ca^{2+} ions to promote clot stabilization, so that in the last stages of the clotting mechanism thrombin has the dual task of converting fibrinogen to fibrin and activating FXIII. Lorand obtained his Ph.D. in biomolecular structure from the University of Leeds in 1952 and with an invitation from the Wayne State University School of Medicine in Detroit, Michigan, landed in the United States the same year. He taught physiology and pharmacology at Wayne State prior to joining Northwestern University in Evanston, Illinois, in 1955.

Early in the 1950s, Laszlo reunited with Szent-Gyorgyi at the Marine Biological Laboratory (MBL) in Woods Hole, Massachusetts, and spent the summer of 1953 doing research there with him. It was at the MBL where he met the love of his life, Joyce Bruner, also a scientist. They were married later that year. Lorand remained a long-time member of the MBL summer research community and a Woods Hole summer resident. He returned to Woods Hole every summer for the rest of his life, studying blood clotting as well as the coagulation cascade in lobsters. Lobster blood is relatively easy to draw for study. Lorand's research showed that transglutamases isolated from vastly different sources are potent blood-clotting enzymes in lobsters.[11] He served on the MBL's board of trustees from 1987 to 1991 and was a faculty member in the MBL physiology course.

Lorand became a naturalized U.S. citizen in 1957 and continued his distinguished scientific career that spanned sixty years at Northwestern University. Lorand was a founding member of the Department of Biochemistry, Molecular Biology, and Cell Biology in the College of Arts and Sciences in 1974 on the main campus of Northwestern University. A recipient of the National Institutes of Health Method to Extend Research in Time (MERIT) Award (1989-1998), Lorand was the first director of the Biochemistry Training Program, funded by the National Institutes of Health (NIH), at Northwestern University. After nearly four decades at the Evanston campus of Northwestern University, Lorand transferred his laboratory in 1993 to the Department of Cell and Molecular Biology at Northwestern's Feinberg School of Medicine in Chicago, Illinois. Soon after, he was made a distinguished investigator at the school's Feinberg Cardiovascular Research Institute. Lorand is credited with helping to strengthen biomedical collaboration across the Evanston and Chicago campuses of Northwestern University, as well as recruiting many prominent scientists to the university.

Lorand was a pioneering scientist in the investigation of the intricate reactions and regulatory mechanisms of blood coagulation, having isolated Factor XIII from human plasma, a transglutaminase that plays a crucial role in normal

hemostasis in the final stages of blood coagulation and the regulation of fibrinolysis by enhancing the stability of blood clot formation. The role of the intrinsic transglutaminase in the calcium-mediated crosslinking of erythrocyte proteins,[2] the identification and characterization of human factor XIII as a fibrin-stabilizing factor,[3] and the elucidation of the structural origins of fibrin clot rheology and those factors that enhance clot rigidity[4] led to the development of clinical treatments for clotting disorders. His lifelong research focused on demonstrating that a large number of important biological processes, such as blood coagulation, skin-barrier formation, hardening of the fertilization envelope, and extracellular-matrix assembly are dependent on the rapid generation of covalent crosslinks between proteins. These reactions are catalyzed by transglutaminases, thereby creating a supramolecular structure with extra rigidity and resistance against proteolytic degradation. Some transglutaminases function as molecular switches in cytoskeletal scaffolding and modulate protein-protein interactions, thereby playing an important role in aging, cataract formation, neurodegenerative diseases, terminal differentiation, apoptosis, and celiac disease, among others.[5] Lorand's research provided insights into the physiology and pathophysiology of members of the transglutaminase family through studies of genetically engineered mouse models and inherited disorders.[6] The analysis of the individual reaction steps and regulatory control mechanisms involved in clot stabilization, which aids in the differential diagnosis of molecular defects of fibrin stabilization,[7] contribute to his repertoire of highly cited published work. The development of a filter paper assay for measuring the activity of transamidating enzymes using radioactive amine substrates proved to be a useful tool for research in the field.[8]

An internationally recognized biochemist known for his landmark discoveries in blood-clotting mechanisms, he was the recipient of numerous awards throughout his career. Elected to the National Academy of Sciences in 1987, Lorand was the author of nearly 200 scientific publications. He was also a fellow of the American Academy of Arts and Sciences elected in 1998, a foreign member of the Hungarian Academy of Sciences, and a trustee of the Marine Biological Laboratory in Woods Hole from 1987–91. Lorand received an honorary doctorate from the University of Illinois in Chicago and an honorary doctor of medicine and surgery from the University of Ferrara, Italy.

Lorand's scientific memberships included the American Society for Biochemistry and Molecular Biology, American Chemical Society, the Biochemical Society (London), American Heart Association, British Society for Cell Biology, International Society of Hematology, International Society on Thrombosis and Haemostasis, American Physiological Society, and Association for Research in Vision and Ophthalmology. He was the co-editor of *Proteolytic Enzymes*, a volume in the scientific series Methods in Enzymology.[9] In 2013, the MBL History and Archives division recorded Lorand discussing his early years at the MBL, the impact that the institution made on his personal and professional lives, and working with Nobel Prize winner Albert Szent-Györgyi.[10] Greater insight into Lorand's work with Szent-Györgyi can be found in his retrospective journal article on Factor XII for the *Journal of Thrombosis and Haemostasis*.[11]

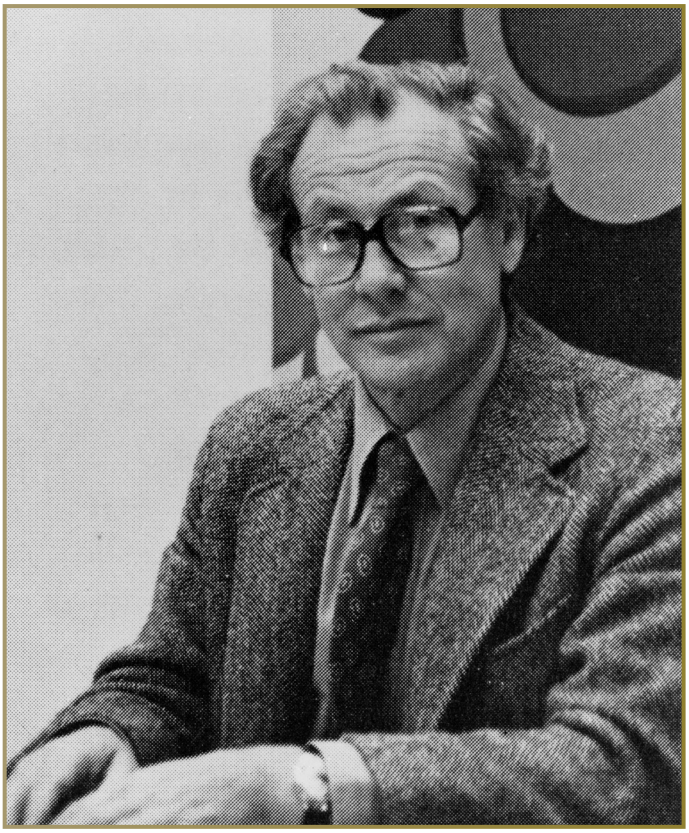

Figure 3 Laszlo Lorand, circa 1970s while he was at Northwestern University's Evanston campus. *Courtesy Charles Deering McCormick Library of Special Collections and University Archives, Northwestern University Libraries.*

Lorand was a highly respected educator and mentor to the students and postdoctoral fellows in his research group. He had a great deal of concern for scientists from foreign countries and cared deeply for them. He set an example of staying fit among his colleagues by playing tennis often during his lunch hour, something he practiced while a medical student at the University of Budapest. Joyce Bruner-Lorand collaborated with her husband on NIH-funded studies at Northwestern for many years and was a coauthor on many of the publications. Lorand's scientific publishing career spanned over seventy years, with his last article accepted for publication shortly before his death. In addition, he was a devoted husband, father, and grandfather and known for complete devotion and dedication to his family.

Laszlo Lorand, professor emeritus of cell and molecular biology, passed away on December 6, 2018, at his home in Glencoe, Illinois, where he had lived for nearly fifty years. The MBL lowered its flag to half-mast in his memory. Lorand was preceded in death by his wife, Joyce Bruner-Lorand, who died in 2010. He is survived by his daughter, Michele Alexandra Lorand, M.D., two grandchildren, and two great-grandchildren.

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