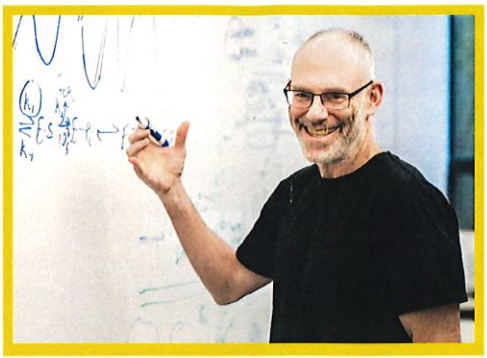
Moses Gomberg Lecture



Daniel Herschlag

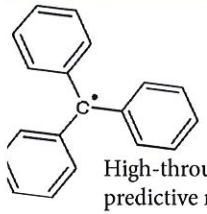
Professor of Biochemistry and (by Courtesy) Chemistry and Chemical Engineering
Stanford University

Bringing Biochemistry into the Genomic Era

December 10, 2018
4-5:30 PM
Chemistry 1640

LSA CHEMISTRY
UNIVERSITY OF MICHIGAN

Daniel Herschlag



Bringing Biochemistry into the Genomic Era

ABSTRACT

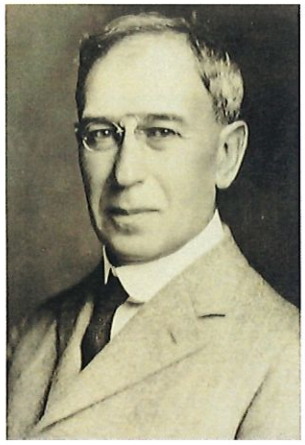
High-throughput and quantitative biochemical approaches will be required to develop predictive models of cell function and regulation, and to understand systems as complex as enzymes. I will describe two such approaches and the insights attained to date. RNA-MaP developed by the Greenleaf lab at Stanford allows us to determine thermodynamic and kinetic rules for RNA binding by RNA binding proteins, and provides testable models for cellular RNA/protein interactions and additional biophysical and evolutionary insights. HT-MEK (High-throughput Mechanistic Enzyme Kinetics), a new microfluidics methodology developed by the Fordyce lab at Stanford, allows us to obtain quantitative kinetic and thermodynamic data for thousands of enzyme variants, in a small fraction of the time and at a minute fraction of the cost of traditional biochemical approaches. Our initial studies on an Alkaline Phosphatase superfamily member provide the first comprehensive functional landscape for an enzyme, delineating function throughout an enzyme scaffold. Studies on this and additional systems are needed to understand enzyme function, to reveal the action of drugs and allosteric effectors, and to develop rules to engineer new enzymes and pathways at will. Most generally, quantitative, high-throughput biochemical methodologies will usher in a post-genomic era in biology that is grounded in biochemical understanding and powered by quantitative physical models.

ABOUT DANIEL HERSCHLAG

Daniel Herschlag, Ph.D., is a Professor of Biochemistry and of Chemistry and Chemical Engineering at Stanford University. The overarching goal of his lab is to understand the chemical and physical principles that
underlie biological processes in order to understand how biology works and how it evolved. His lab has been highly interdisciplinary and collaborative, leading to important discoveries and new directions in enzyme and RNA research, including the RNA Chaperone hypothesis; the evolutionary and mechanistic concept of Catalytic Promiscuity; pioneering genomic studies that revealed the multiplicity of RNA targets of RNA binding proteins; the first smFRET folding and unfolding studies; determination of RNA and protein conformational ensembles; a predictive Reconstitution Model for RNA folding; dissection of the interrelationship between hydrogen bond structure, their environment, and their energetics; and identification of new catalytic mechanisms by enzymes.

Dan has been recognized at Stanford and nationally for his mentoring and is passionate about training the next generation of scientists and science-based thinkers; he created innovative courses and training programs for graduate students, postdocs, and trainees from underrepresented and underprivileged backgrounds while serving as Dean of graduate students and postdocs in the Stanford School of Medicine. Students and postdocs trained from his lab have been highly successful in academic and other leadership positions, and he looks forward to the continued opportunity to address important and exciting biological problems, to participate in and contribute to multidisciplinary research, and to help trainees develop as scientists, citizens, and advocates for reason-based decision making, diversity, and inclusion.

Moses Gomberg



Moses Gomberg was born in Elizabetgrad, Russian Empire in 1866. In 1884, the family emigrated to Chicago where he worked at the Stock Yards while attending Lake High School. In 1886, Moses entered the University of Michigan, where he obtained his B.Sc. in 1890 and his doctorate in 1894 under the supervision of A. B. Prescott. His thesis, titled "Trimethylxanthin and some of its Derivatives," dealt with the derivatization of caffeine and was an extension of Prescott's work. Appointed an instructor in 1893, Gomberg worked at the University of Michigan for the duration of his professional academic career, becoming chair of the Department of Chemistry from 1927 until his retirement in 1936. Dr. Gomberg served as President of the American Chemical Society in 1931. He never married, living with his sister Sophia in Ann Arbor for his adult life.

In 1896–1897 he took a year's leave to work as a postdoctoral researcher with Baeyer and Thiele in Munich and with Victor Meyer in Heidelberg, where he successfully prepared the long-elusive tetraphenylmethane.

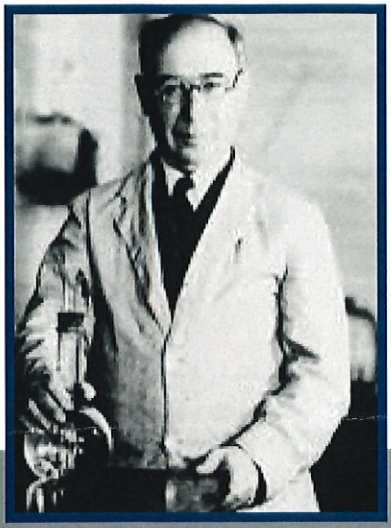
During attempts to prepare the even more sterically congested hydrocarbon hexaphenylethane, he correctly identified the triphenylmethyl radical, the first persistent radical to be discovered, and is thus known as the founder of radical chemistry. The work was later followed up by Wilhelm Schlenk. Gomberg was a mentor to Werner Emmanuel Bachmann who also carried on his work and together they discovered the Gomberg-Bachmann aryl-aryl coupling reaction.

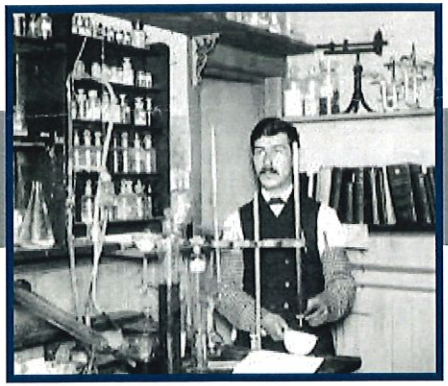
Upon his death in 1947 Moses Gomberg bequeathed his estate to the Chemistry Department of the University of Michigan for the creation of student fellowships. In 2000, the centennial of his paper "Triphenylmethyl, a Case of Trivalent Carbon", a symposium was held in his memory and a plaque was installed in the Chemistry Building at the University of Michigan designating a National Historic Chemical Landmark.

In 1993, the University of Michigan Chemistry Department instituted the Moses Gomberg Lecture series to provide assistant professors an opportunity to invite distinguished scientists to the Chemistry department.

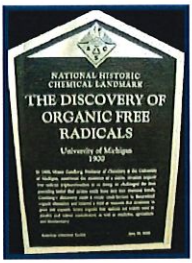
Moses Gomberg Lecture

Gomberg is considered the father of free radical chemistry. He was one of the most eminent organic chemists of his time. In addition, Gomberg worked on applied chemistry and developed solvents for automotive paints, as well as the first antifreeze used in cars. He also served as President of the American Chemical Society (ACS) in 1931. Moses Gomberg retired in 1936 and died on February 12, 1947.





To honor Gomberg's discovery of free organic radicals, the ACS declared the University of Michigan as a "National Historic Chemical Landmark" in 2000.



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