Dennis A. Dougherty

Professor Dennis A. Dougherty received his B.S. and M.S. degrees from Bucknell University in 1974. He did his doctoral research at Princeton University with Kurt Mislow and a year of post-doctoral studies with Jerome Berson at Yale University. Dougherty joined the faculty in the Division of Chemistry and Chemical Engineering at the California Institute of Technology in 1979, where he is now the George Grant Hoag Professor of Chemistry.

Dougherty is perhaps best known for development of the cation-π interaction, a novel but potent binding interaction between molecules that plays a central role in establishing protein structures and in modulating drug-receptor interactions. The fundamental nature of the interaction was established through extensive theoretical and model studies by the Dougherty group. Dougherty also established the prevalence of the cation-π interaction in biological systems, and it is now recognized to be important in a wide range biological processes.

More recently, Dougherty has addressed molecular neurobiology, applying the mindset and tools of physical organic chemistry to the complex proteins of neuroscience – the molecules of memory, thought, and sensory perception; of Alzheimer's, Parkinson's, and schizophrenia. Target receptors include the nicotinic acetylcholine receptor, the 5-HT_3 (serotonin) receptor, and the D2 dopamine receptor. Through these efforts, Dougherty has produced fundamental insights into drug-receptor interactions, including cation-π interactions.

Dougherty is a member of the National Academy of Sciences and a fellow of the American Association for the Advancement of Science and the American Academy of Arts and Science. He has been recognized with a number of awards, including the ACS James Flack Norris Award for Physical Organic Chemistry, the AstraZeneca Excellence in Chemistry Award, the Arthur C. Cope Scholar Award, and has been recognized as a Javits Neuroscience Investigator by NIH. He is also the co-author, with Professor Eric Anslyn, of the influential textbook, *Modern Physical Organic Chemistry.*

Chemistry on the Brain, Part I: Understanding the Nicotine Receptor

Monday, September 20, 3:00 pm
LHSC – UH Auditorium A (Room B3-246)

The human brain is the most complex object known to man. It presents daunting challenges at all levels, from the anatomical, to the cellular, to the molecular. Our work seeks to provide a chemical-scale understanding of the molecules of memory, thought, and sensory perception; of Alzheimer's, Parkinson's, and schizophrenia. An area of particular interest has been the chemistry of nicotine addiction. The initial chemical event of nicotine addiction involves nicotine binding to and activating acetylcholine (ACh) receptors in the brain. Using the mindset and methodologies of physical organic chemistry, we have probed these complex membrane proteins with a precision and subtlety normally associated with small molecule studies. We have established that the cation-π interaction plays a pivotal role in promoting the high potency of nicotine in the brain, leading to its addictive properties. We have also discovered key hydrogen bonding interactions that uniquely contribute to the binding of nicotine to ACh receptors. These chemical studies provide a high-precision structural model for the interaction of potent drugs at brain receptors.

The Cation-π Interaction: A New View of Benzene, Phenylalanine, Tyrosine, and Tryptophan

Tuesday, September 21, 3:00 pm
LHSC – UH Auditorium A (Room B3-246)

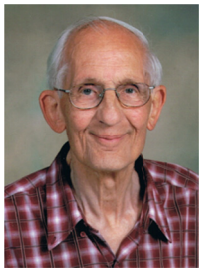
The cation-π interaction is an underappreciated but universally employed noncovalent interaction between any positive charge and the face of a simple π system such as benzene or ethylene. Gas phase studies establish the considerable strength of the interaction and the primarily electrostatic nature of its origin. Using designed and synthesized cyclophane receptors, the ability of the cation-π interaction to act as a potent force for binding organic molecules in water has been established. The pervasive role of the cation-π interaction in biology has been established through an extensive survey of the structural data bases and detailed analyses of a number of systems. These studies establish the cation-π interaction as a pervasive force in structural biology, molecular recognition, and catalysis.

Chemistry on the Brain, Part II: Chemical-Scale Studies of Neuroreceptors and Ion Channels

Wednesday, September 22, 11:00 am
LHSC – UH Auditorium A (Room B3-246)

The complex membrane proteins of the mammalian nervous system present special challenges to the experimentalist. We have developed a powerful and general methodology to incorporate unnatural amino acids into neuroreceptors and ion channels site-specifically. When combined with the remarkable sensitivity of electrophysiology, this approach enables chemical-scale studies of the proteins of neuroscience. Along with describing the methodology in some detail, we will describe biophysical studies enabled by it, including applications to a range of neuroreceptors and ion channels. In particular, we will describe new insights in the function of G protein-coupled receptors (GPCR), the largest class of membrane proteins in humans and the most prominent target of the pharmaceutical industry.

Fred L.M. Pattison



Born in Scotland, where he received his early education, he attended the University of Cambridge in 1941 for undergraduate work in Natural Sciences, followed by a Ph.D. in Organic Chemistry. After spending a year at Dalhousie University as Lecturer, he joined Western as Assistant Professor in 1948.

Fred established a Ph.D. program in the department, and his research on biologically active organic fluorine compounds produced many scientific papers, garnered the award of an Sc.D. by the University of Cambridge, and resulted in the publication of a book, *Toxic Aliphatic Fluorine Compounds*. In 1959, he became Professor and Head of the Department, and he presided over the expansion of the department and its move to new facilities.

In 1965, Fred decided on a career change, and at the age of 42, he enrolled at Western as a first-year medical student. After completing his M.D. four years later, he interned at St. Joseph's Hospital in London and served for a year as resident in the Family Practice Program. As well, he was enrolled in a diploma course in venereology at the University of Liverpool. During 1971-73, Fred followed up a long-standing interest in the people of Canada's North by working with the International Grenfell Association. He provided solo medical care to about 6,000 people scattered along 120 miles of the Atlantic coast of Newfoundland.

Fred returned to London in 1973, when he joined Western's student health service, holding the position of Director at his formal retirement in 1988. During the same period he was clinical assistant professor in the Faculty of Medicine, giving instruction in venereology, and director of the Middlesex-London Sexually Transmitted Disease Clinic.

On his retirement, Fred was able to resume his connection with the Chemistry Department with the rank of Professor Emeritus. Fred passed away in August of 2010. In view of his long service and many contributions to chemistry and medicine at Western, it is entirely fitting that the department dedicate a lecture series bearing his name.

Contact Information

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Fred Pattison Senior Lectureships

1992	Sir Derek Barton, Texas A & M University
1993	Barry Trost, Stanford University
1995	Stephen J. Benkovic, Penn State University
1996	Steven V. Ley, University of Cambridge
1997	Anthony J. Kirby, University of Cambridge
1998	Larry E. Overman, Univ. of California, Irvine
1999	Sir Fraser Stoddart, Northwestern University
2000	Dennis Curran, University of Pittsburgh
2001	Joseph Lambert, Northwestern University
2002	Anthony Barrett, Imperial College
2003	Richard Wolfenden, UNC Chapel Hill
2004	Victor Snieckus, Queen's University
2005	Lutz F. Tietze, Georg-August University, Göttingen
2006	Juan C. (Tito) Scaiano, University of Ottawa
2007	François Diederich, ETH Zürich
2008	Erik J. Sorensen, Princeton University
2009	Chad A. Merkin, Northwestern University

Light snacks and refreshments will be served 15 minutes prior to each lecture.

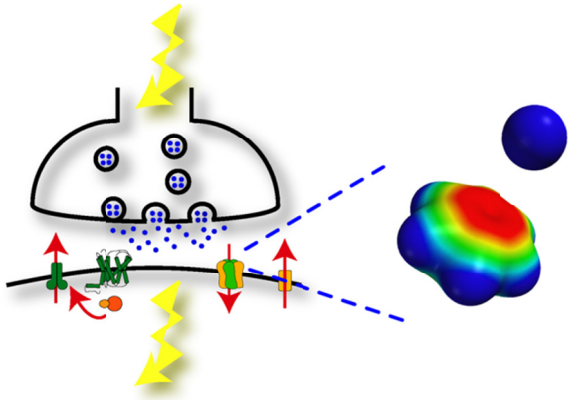
If you require this information in an alternate format, or if any other arrangements can make this event more accessible to you, please contact us.

The Department of Chemistry
presents the
2010 Fred Pattison Senior Lecturer

Dennis A. Dougherty

George Grant Hoag Professor of Chemistry

California Institute of Technology



A three-part lecture series
September 20–22, 2010

London Health Sciences Centre
University Hospital, Auditorium A

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