

**MEMORIAL RESOLUTION OF THE FACULTY  
OF THE UNIVERSITY OF WISCONSIN-MADISON**

**ON THE DEATH OF PROFESSOR WILLIAM WALLACE CLELAND**

William Wallace Cleland, professor of biochemistry at the University of Wisconsin-Madison, passed away on March 6, 2013 of injuries sustained in an accident.

Professor Cleland preferred to be addressed as “Mo,” and all of his friends knew him by this name. Mo was born to Elizabeth and Ralph E. Cleland in Baltimore, Maryland on January 6, 1930. His family moved to Bloomington, Indiana, where his father served on the faculty and administration of Indiana University. Mo graduated from Oberlin College, AB 1950, and from the University of Wisconsin, MS 1953 and PhD 1955. He served in the Medical Corps of the U.S. Army for two years, and he carried out postdoctoral research under Eugene P. Kennedy at the University of Chicago. He returned to the University of Wisconsin-Madison as assistant professor of biochemistry in 1959 and advanced to professor of biochemistry in 1966. He served as the Marvin J. Johnson Professor of Biochemistry in 1978 and the Steenbock Professor of Chemical Sciences from 1982-2003.

Mo made many influential contributions to enzymology. He brought order into the field of multisubstrate steady-state enzyme kinetics. In 1963, he published a series of three papers on this topic in *Biochimica et Biophysica Acta*; paper I. Nomenclature and rate equations; II. Inhibition: nomenclature and theory; III. Prediction of initial velocity and inhibition patterns by inspection. In this work, Mo derived the basis for Cleland’s rules, which allow one to write the rate equation for a multisubstrate enzyme by inspection of kinetic patterns. In connection with this work, Mo coined the term “ping pong kinetics” for a kinetic pattern implicating a covalently modified enzyme-substrate intermediate. These papers have been widely cited and led to his inclusion among the 300 most-cited scientists in 1978.

Prior to Mo’s report in the early 1960s, proteins were often purified in the presence of mercaptoethanol, which countered the detrimental effects of oxygen. Mercaptoethanol had an unpleasant odor, and two equivalents were required to reduce a disulfide. Mo studied the reducing properties of a number of dithiol compounds and found that dithiothreitol, also known as DTT or Cleland’s Reagent, fitted the bill perfectly. He found DTT to be a water-soluble solid with little odor and a strong reducing agent. Cleland’s Reagent or DTT has been on the shelf in most biochemical laboratories for nearly half a century.

The analyses of bond changes in nonenzymatic chemical reactions often employ kinetic isotope effects (KIEs) because heavy isotopes alter reaction rates, usually with minimal effects on chemical properties. In enzyme studies, such analyses are complicated by noncovalent steps, such as the binding of reactants and release of products, plus conformation changes of the protein. In early collaborations with University of Wisconsin-Madison colleagues Dexter Northrop and Marion O’Leary, Mo undertook to overcome the problems and apply KIEs to analyze chemical mechanisms in enzymes. In the process, Mo invented the equilibrium perturbation method for measuring KIEs. This method was brilliantly conceived and enabled a KIE to be measured at chemical equilibrium in a single experiment.

Mo continued with this work and became a master of enzymatic kinetic isotope effects. He worked to neutralize the masking of chemical steps by the use of alternative substrates to increase ligand dissociation rates, by determining pH-effects in search of conditions where chemical steps limit rates, and by site-directed mutagenesis to decrease rates of chemical steps. When any of these methods worked, KIEs on maximum turnover velocity could be measured.

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Mo extended these methods by employing multiple KIEs to refine structures of transition states and even to distinguish between step-wise and concerted chemical mechanisms.

Mo was elected to the American Academy of Arts and Sciences in 1977 and to the National Academy of Sciences in 1985. He received the Merck Award from the American Society for Biochemistry and Molecular Biology, the Alfred Bader Award in Bioinorganic or Bioorganic Chemistry from the American Chemical Society (ACS), the Repligen Award in the Chemistry of Biological Processes from the Division of Biological Chemistry of the ACS, the Stein and Moore Award from the Protein Society, and the Hilldale Award in the Physical Sciences from the University of Wisconsin-Madison.

Mo enjoyed sailing and ice boating on Lake Mendota and was the commodore of the Mendota Yacht Club in 1966. He was a patron of the arts and was honored last fall as one of a handful of 50-year subscribers to the Madison Symphony Orchestra concert series. He loved the opera and supported Madison Opera as well as opera companies across the United States.

Mo was a world-class philatelist and held leadership positions in the United States Stamp Society, as well as its presidency in 1992. He published more than 300 articles in the *United States Specialist* and the *Canal Zone Philatelist*. He received the Hopkinson Memorial Literature Award in 1986, 2002, and 2006. He received the Smithsonian Institution's Philatelic Achievement Award in 2008. In 2009, the Stamp Society inducted Mo into the United States Stamp Society Hall of Fame.

Mo was a proud and devoted parent, with his former wife Joan Cleland, to daughters Elsa and Erica and grandparent to Max, Finn, and Griffin. He was generous to colleagues everywhere who consulted him on enzyme kinetics, often insisting that he be given no attribution. Postdoctoral students and young faculty members commented on their pleasant experiences with Mo's quick answers to their questions. He was a kind and generous friend to colleagues and collaborators, and a dominant force in mechanistic enzymology.

MEMORIAL COMMITTEE

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