



Cynthia Burrows, Ph.D.

University of Utah, Department of Chemistry

“Single-Molecule Studies of Human Telomeric G-Quadruplexes in a Voctoliter Cavity”

Abstract: Human telomeric DNA has tandem repeats of the sequence 5'-TTAGGG terminating with a 3' single-stranded overhang of 100-200 bases. These guanine-rich DNA sequences can fold into tetra-stranded structures, known as G-quadruplexes. The precise fold of the G-quadruplex structure is dictated by the metal ions present, which we have studied through the use of the α -hemolysin ion channel. Being electrophoretically driven into the *cis* side of the α -hemolysin, the hybrid fold (K^+) entered the vestibule leading to current blockages for the duration of the time the DNA resided in the vestibule. Due to the polymorphic nature of the hybrid folds, the recorded current signatures could be correlated to the major structural topologies that exist for this fold in solution (e.g., hybrid-1, hybrid-2, and triplex). The hybrid folds were not capable of traversing to the *trans* side of the nanopore, while the triplex could achieve translocation. Secondly, oxidative damage to the telomeric sequence is proposed to contribute to telomere shortening, dysfunction and cell aging. Locations of the oxidative damages have different effects on the G-quadruplex folding that produced significant changes in their nanopore behavior. Placement of the guanine oxidation product, 8-oxoguanosine (OG), in a top or bottom tetrad results in destabilization of that layer, whereas the presence of OG in a middle tetrad leads to complete unfolding of the G-quadruplex. These behaviors were determined by their translocation times, which correlated with the folding free energy.

Brief Bio: Dr. Cynthia J. Burrows is Distinguished Professor of Chemistry at the University of Utah and presently Chair of the Department of Chemistry. She was raised in St. Paul, Minnesota and Boulder, Colorado. Her early training was in physical organic chemistry with Prof. Stan Cristol at the University of Colorado (B. A. 1975) and Prof. Barry Carpenter at Cornell University (Ph.D., 1982), followed by a NSF-CNRS postdoctoral fellowship in the laboratory of Prof. Jean-Marie Lehn, Université Louis Pasteur, Strasbourg (1981-83). From 1983-1995, she held the positions of Assistant through Full Professor of Chemistry at the State University of New York at

Stony Brook, before returning to the West to take a position at the University of Utah in Salt Lake City in 1995.

Prof. Burrows has been a member of numerous editorial boards and review panels; from 2001–2013, she served as Senior Editor of the *Journal of Organic Chemistry*. She is a past recipient of the Robert Parry Teaching Award and in 2011 of the University Distinguished Teaching Award; her research was recently recognized with the ACS Utah Award, ACS Cope Scholar Award, and the University of Utah's Distinguished Creative and Scholarly Research Award. In 2009, she was inducted into the American Academy of Arts and Sciences, and in 2013 she was appointed the inaugural holder of the Thatcher Presidential Endowed Chair of Biological Chemistry.