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Roles of Electrostricted and Structural Hydration in Modified DNA Duplex Stability

Abstract: The global stability of DNA molecules depends on base stacking, base-pairing, ionic and hydration contributions. To understand the mechanisms that govern the many biological roles of nucleic acids, it is essential to have a complete physical description of the folding/unfolding of nucleic acids, including ion and water binding. To investigate the role of water in the stability and melting behavior of DNA structures, we use biophysical techniques such as differential scanning calorimetry (DSC), density and temperature-dependence UV spectroscopy to measure complete thermodynamic profiles for the unfolding of DNA hairpins and duplexes containing chemical modifications or adducts. The favorable folding of a DNA duplex (negative ΔG) results from a compensation between a favorable ΔH and unfavorable $T\Delta S$ terms. DSC and UV melting curves of DNA duplexes as a function of salt and osmolyte concentrations show ion and water release. Therefore, the favorable folding of each DNA molecule results from the formation of base-pair stacks and uptake of both counterions and water molecules. Furthermore, the comparison of the signs of $\Delta\Delta G^{\circ}$ (or $\Delta\Delta H$-$\Delta(T\Delta S)$ compensation) with $\Delta\Delta V$ of the Hess cycles for pairs of duplexes with and without a chemical modification (bulge, mismatch or adduct), indicates the type of hydration of the particular chemical modification: similar signs indicate electrostricted hydration while opposite signs indicate structural hydration. The main conclusion is that incorporating stabilizing chemical modifications in DNA is accompanied by an immobilization of electrostricted water while the destabilizing modification immobilize structural water.

Bio: Luis Marky received his Ph.D. in chemistry from Rutgers University. From 1987 to 1997, he was a member of the faculty in the Department of Chemistry at New York University. He joined the Department of Pharmaceutical Sciences at UNMC as a Professor in July of 1997. Dr. Marky is involved in the mentoring of young scientists with different backgrounds from high school students to postdoctoral/research associate fellows, ~80 young scientists. In 2006, he was the recipient of the "Outstanding Faculty Mentor of Graduate Students Award" at UNMC. He was a member of the Minority Affairs Committee (MAC now called CID) of the Biophysical Society (2002-2016 and Chair 2009-2012). Dr. Marky teaches and coordinates several courses at UNMC, which includes Pharmaceutical Biochemistry, Quantitative Pharmaceutical Sciences, Physical Pharmacy and Biophysical Chemistry. He was a Fulbright Scholar in 1998 and President of the UNMC Faculty Senate in 2010-11. Dr. Marky is interested in the role of the molecular forces and hydration in the folding/unfolding of proteins and nucleic acids and their association with ligands. He is currently working on the targeting of unusual DNA structures and of mRNA with partially complementary strands and on the interaction of oligonucleotides with polycationic micelles for cellular delivery purposes. He has had continuous funding from NIH and/or NSF since 1988; he has published nearly 160 articles with an average of 80 citations per article and has presented over 100 lectures throughout the world and ~300 abstracts at national and international conferences. He has been named a 2009-Distinguished Scientist and the 2015 "Research Leadership Award" at UNMC. He has been a rotating program director in the Molecular Biophysics Cluster of the Division of Molecular and Cellular Biosciences at the National Science Foundation (2013-2015).