Biophysical Reviews' "Meet the Editors Series"—a profile of Wilma K. Olson

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Abstract

As one of the five Executive Editors of Biophysical Reviews I have been asked to provide this short biographical sketch for the readers of the journal. I have been a member of the Editorial Board since the inception of the journal in 2008 and an Executive Editor since 2014. I hold a B.S. degree in Chemistry from the University of Delaware and a Ph.D. in Physical Chemistry from Stanford University. Except for a year as a Damon Runyon Postdoctoral Fellow at Columbia University, I have spent my entire professional career at Rutgers, the State University of New Jersey, where I am currently the Mary I. Bunting Professor of Chemistry and Chemical Biology. I served for many years as Founding Director of the Rutgers University Center for Molecular Biophysics and Biophysical Chemistry, and have trained undergraduate, graduate, and postdoctoral students from a variety of academic disciplines.

In addition to my work with Biophysical Reviews, I have served as an Associate Editor of Annual Reviews of Biophysics and Biomolecular Structure as well as a member of the Editorial Boards of leading journals in our field, such as Biophysical Chemistry, Biophysical Journal, Biopolymers, and Journal of Biological Chemistry. I am a past President of the Biophysical Society and a past Vice President and Council Member of the International Union for Pure and

Applied Biophysics. I have also served on the NIH National Advisory General Medical Sciences Council and the Howard Hughes Medical Institute Scientific Review Board, and have helped to organize scientific conferences and workshops, such as the Conversations in the Discipline Biomolecular Stereodynamics, Biopolymers Gordon Conference, Biophysical Society Thematic Meetings, and Isaac Newton Institute Programme on Topological Dynamics.

My research involves the development and application of new computational and theoretical approaches to analyze, model, and interpret the biophysical properties and interactions of nucleic acids. I am especially grateful for the recognition of my research by scientific colleagues. I have been fortunate to hold Alfred P. Sloan and John Simon Guggenheim Fellowships, a U.S. Public Health Service Research Career Development Award, a National Institute of General Medical Sciences MERIT Award, and a Biophysical Society National Award for Excellence and Leadership in Biophysics. I am also an elected fellow of the American Association for the Advancement of Science, American Physical Society, and Biophysical Society.

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Contributions to biophysics

I have long been interested in the role that chemical architecture plays in determining the conformation, properties, and interactions of nucleic acids and for many years have focused on deciphering the energetic and spatial codes embedded in

the nucleotides found in high-resolution DNA and RNA structures and on studying the effects of this information on the biophysical properties of linear and supercoiled molecules. My early work (Olson and Flory 1972) pioneered conformational analyses and computer modeling of DNA and RNA before the development of nucleic acid structural biology and the advent of routine biomolecular simulations. I developed virtual bond treatments of the polynucleotide backbone that accounted for physical properties of long single-stranded chains (Olson 1975) and identified energetically feasible double-helical structures, including a novel double helix (Olson 1977) with vertically inclined base pairs that subsequently surfaced in crystal structures of DNA bound to the TATA-box binding protein (see Fig. 1). My treatment of nucleic acid conformational energy, particularly the successful simulation of the deformations (pseudorotation) of the sugar ring (Olson and Sussman 1982), was a forerunner of, and basis for, the force fields now routinely used to refine and simulate nucleic acid structures and interactions. My virtual bond scheme (Olson 1980) is commonly implemented in descriptions of high-resolution RNA structures.

My research group is unique in having adapted approaches from a variety of disciplines to address open questions concerning spatially constrained DNA molecules. Our

adaptation of B-spline mathematical functions from engineering design to represent the double helical axis (see Fig. 1) led to the first successful computer simulations of the large-scale folding of supercoiled DNA (Hao and Olson 1989). Subsequent extension of Fourier sampling techniques from applied physics (Zhang et al. 1994) and finite element analyses from mechanical engineering to DNA (Yang et al. 1993) made it possible to incorporate protein and sequence effects in the treatment of DNA minicircles. Further development of a base-pair level theory of DNA mechanics (Coleman et al. 2003) allowed us to explore the influence of sequence at the level of single nucleotides on the global equilibrium configurations (Todolli et al. 2017) and the low-frequency normal modes of DNA chains subject to ring closure, forced extension, and ligand-induced structural perturbations (Matsumoto et al. 2005).

Extension of the virtual-bond representation of single-stranded polynucleotides to the treatment of successive base pairs in double-helical DNA allowed our group to explore the effects of intrinsic nucleotide structure and deformability on the global properties of linear chains (Maroun and Olson 1988) and to use this theory to interpret as well as suggest experiments (Gorin et al. 1995). We were the first to demonstrate how sequence-dependent bending of neighboring base pairs

Fig. 1 Gallery of schematic and molecular images illustrating: (left) a virtual bond scheme used in early treatments of the nucleic acid backbone (Olson and Flory 1972), a novel “vertical” double helix found upon reorienting the base side groups (Olson 1976), and a minimum-energy configuration of a thin DNA rod obtained using a B-spline approximation

(Hao and Olson 1989); (right) rigid-body parameters (Lu and Olson 2003) used to take account of known structural features of successive base pairs in treatments of deformable, protein-free (Czapla et al. 2006) and protein-decorated DNA (Kulaeva et al. 2012)

influences the conformation of the DNA chain as a whole and how small perturbations of local geometry and local structural fluctuations translate into large-scale effects at the macromolecular level (Olson et al. 1993). We also extracted, from the fluctuations and correlations of structural parameters in high-resolution DNA-protein complexes, a widely used set of sequence-dependent elastic potentials that capture the intrinsic structure, deformability, and coupled motions of paired bases and base-pair steps (Olson et al. 1998). Our group has continued to update these potentials as the library of high-resolution DNA structures grows and to show how these knowledge-based “rules” account for sequence-dependent features of DNA, such as the positioning of nucleosomes on arbitrary base sequences (Balasubramanian et al. 2009).

Possibly the best known aspect of our group’s work is the set of structural parameters that we developed to specify the arrangements of bases and base-pairs in double-helical structures (see Fig. 1). Our analysis of the conflicting interpretations of early high-resolution nucleic acid structures (Lu and Olson 1999) led to the establishment of a standard reference frame for the description of base-pair geometry (Olson et al. 2001) and the creation of the now widely used 3DNA suite of programs for the analysis, rebuilding, and visualization of three-dimensional nucleic acid structures (Lu and Olson 2003; Li et al. 2019). Our studies have uncovered novel conformational markers of protein- and drug-induced transitions of the double helix (Tolstorukov et al. 2007). These findings add a new dimension to literal analyses of genomic sequences (see Fig. 1), illustrating how well-known sequence-dependent features of double-helical DNA, such as intrinsic curvature, can account for the large-scale properties of the chain (Czapla et al. 2006). Our latest analysis software for dissecting the spatial structures of RNA and DNA (Lu et al. 2015) is proving useful in the identification of noncanonically paired bases and unusual conformational motifs in large, folded nucleic acid structures (Olson et al. 2019).

Our group’s base-pair-level treatments of spatially constrained DNA molecules have provided new understanding of large protein-DNA assemblies and the communication among the various molecular species involved in the regulation of transcription (Todolli et al. 2017). Our studies of Lac repressor-mediated looping have identified conditions, later confirmed experimentally, under which the tetrameric protein assembly adopts an extended conformation (Swigon et al. 2006) and have shown how nonspecific, architectural proteins influence DNA chain closure (Czapla et al. 2013) and become site-specific upon loop formation (Wei et al. 2014). The correspondence between the predicted and observed rates of communication between regulatory elements on chromatin constructs point to the essential role of the histone tails (Kulaeva et al. 2012) and the spacing of nucleosomes (Nizovtseva et al. 2017) in these processes (see Fig. 1).

Our group is continuing to establish methodologies to model long, protein-decorated DNA chains at a “realistic” level and to characterize the topology of the simulated structures. Given the similar roles played by the nucleosomes in chromatin and the base pairs in DNA, we are using knowledge about the spatial arrangements of interacting nucleosomes to study regularly repeating chromatin fibers (Clauvelin et al. 2015). Our team is also devising new methods to decipher how the pieces of the ribosome fold and fit together in what is still an immense, inscrutable 3D puzzle.

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