Nanobiological Computational Microscopy: DNA Oxidation Damage, Lipid Bilayer Hydration, and Transmembrane Nanojet Transport

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Gaining insights into the nature of physical, chemical, and biological systems of highly reduced sizes, and developing experimental and theoretical methodologies aimed at probing, manipulating and controlling them on the atomic and molecular level, are among the major challenges of current research. Computationally-based theoretical modeling and simulations play an increasingly important role in modern condensed matter physics, chemistry, materials science, and biology. In particular, such studies, that may be called "computational microscopies", serve as tools of discovery allowing explorations of complex phenomena with refined resolution in space and time [1].

All living organisms store the information necessary to maintain life in their DNA. Any process that damages DNA and causes loss or corruption of that information jeopardizes the viability of the organism. One-electron oxidation is such a process. Loss of an electron (ionization) from DNA generates an electron hole (radical cation), located primarily on its nucleobases, that migrates reversibly through duplex DNA until it is trapped in an irreversible chemical reaction. In the first part of this lecture we address through the use of large-scale coupled first-principles quantum and classical molecular dynamics simulations, in conjunction with laboratory experiments, three central features of one-electron oxidation of DNA [2]: i) migration of the radical cation away from its generation site, occurring via an ion-gated mechanism ; ii) electronic and structural factors that determine at which nucleobase irreversible reaction occurs; iii) atomic level analysis of the chemical mechanisms for reaction of nucleobase radical cations, resulting in mutagenetic damage.

In the second part of the lecture we discuss structural, dynamical, and rheological properties of water at the hydration interfacial region of a lipid bilayer membrane (DPPC), and describe recent large-scale molecular dynamics simulations of trans-membrane transport processes investigated with the use of molecular dynamics simulations of nanojet injection through lipid bilayer membranes, illustrating membrane puncture and subsequent self-healing processes.

1. U. Landman, "Materials by Numbers: Computations as Tools of Discovery", Proc. Nat. Acad. Sci. (USA) 102, 6671 (2005).
2. S. Kanvah, J. Joseph, G. B. Schuster, R.N. Barnett, C.L. Cleveland, U. Landman "Oxidation of DNA: Damage to Nucleobases", Acct. Chem. Res. 43, 280 (2010).

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