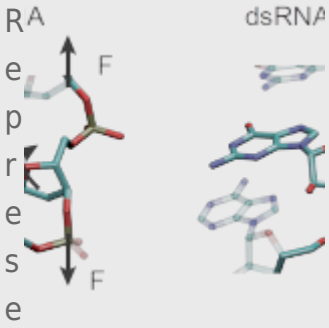
Solving the Mystery of the Strikingly Different Mechanical Response of Nucleic Acids



Representation of two base-pair steps to highlight the different orientation of the sugar with respect to the phosphate backbone of dsDNA (Left) and dsRNA (Right). The extra hydroxyl group in the ribose – the dsRNA sugar – changes its stereochemistry and is ultimately responsible for the opposite twist-stretch coupling.

Article: published in Proceedings of the National Academy of Sciences by J. G. Vilhena, and Ruben Perez, IFIMAC researchers and members of the Department of Theoretical Condensed Matter Physics.

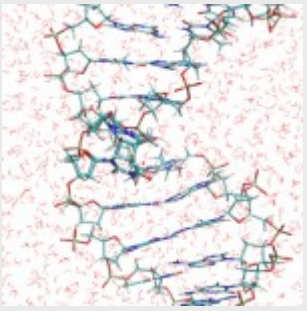
The mechanical properties of nucleic acids (NAs) regulate multiple biological processes ranging from complex chromosome packing to replication of a plasmid. In vivo, NAs are not typically found in their relaxed forms. Instead, in the biological processes in which they take part, proteins wrap, bend, stretch, and twist double-stranded DNA (dsDNA) and double-stranded RNA (dsRNA) molecules. In spite of sharing a common double helix structure, single-molecule experiments have reported puzzling differences between their mechanical properties. dsRNA has a threefold softer stretching constant. More strikingly, dsDNA overwinds when stretched while dsRNA displays the expected unwinding response.

Understanding how a force induces changes in the structure of NAs at the atomic level is a challenge. In a recent publication in the Proceedings of the National Academy of Sciences (PNAS), researchers from the National Center for Biotechnology (CNB-CSIC) and from IFIMAC have used all-atom, microsecond-long molecular dynamics (MD) simulations to unveil the atomic-scale origin of the marked difference in the stretching response of dsRNA and dsDNA, their opposite twist-stretch coupling, and its nontrivial force dependence. They have implemented a new constant-force protocol, that closely mimics the single-molecule experiments, in order to simulate the structure of dsDNA and dsRNA subjected to stretching forces up to 20 pN. This methodology allows a direct determination of all of the elastic constants through the response of the average elongation, the average twist, and the coupling of their fluctuations to the applied force. A hierarchical analysis of these simulations sheds light into the physical mechanisms that control the mechanical response. The lower dsRNA stretching resistance is linked to its more open structure, whereas the opposite twist-stretch coupling of both molecules is due to the very different evolution of the molecules' interstrand distance with the stretching force. A reduction of this distance leads to overwinding in dsDNA. In contrast, dsRNA is not able to reduce its interstrand distance and can only elongate by unwinding. The analysis of the parameters that characterize locally the double helix shows a direct correlation between the interstrand distance and the slide, the displacement of two consecutive base pairs in the plane perpendicular to the helical axis. In turn, the different behavior of the slide parameter of dsDNA and dsRNA can be traced down to the most fundamental difference between these two molecules: the extra hydroxyl group in the dsRNA sugar that connects the nitrogenous bases to the phosphate backbone. The comprehensive atomic-scale understanding of the mechanical response of NAs achieved in this study highlights MD simulations as a powerful tool to unveil the connection between forces and structure of NAs and, possibly, to gain insight into the associated changes in their biological functionality. [Full article]

References

Alberto Marin-Gonzalez, Jose Guilherme Vilhena, Rubén Pérez, and Fernando Moreno-Herrero. Understanding the mechanical response of double-stranded DNA and RNA under constant stretching forces using all-atom molecular dynamics. PNAS, (2017).

Computational Simulation of Photochemical Reactions in DNA



The figure shows a fragment of DNA, with the thymine dimer in the middle, sorrounded by the water molecules of the solvent.

Article: published in The Journal of Physical Chemistry Letters by Jesús I. Mendieta-Moreno and José Ortega, IFIMAC researchers and members of the Department of Theoretical Condensed Matter Physics.

The photostability of DNA is a key property for life. It is well-known that the absorption of ultraviolet (UV) radiation may result in harmful genetic lesions that affect DNA replication and transcription, ultimately causing mutations, cancer, and/or cell death. Luckily for us, cellular DNA presents remarkable stability against this photodamage: the huge majority of the absorbed photons are transformed into heat, which is transferred to the solvent without causing any lesion.

The most frequent DNA photolesion produced by sunlight is the cyclobutane thymine dimer (CTD) that is characterized by the formation of two covalent bonds between adjacent thymine bases (see Figure). In a recent collaboration, led by an IFIMAC group and published in the The Journal of Physical Chemistry Letters, this photochemical reaction has been simulated at the atomic level. The results reveal how the structure and dynamics of the DNA double-helix drastically reduce the probability of photolesion, thus protecting the integrity of the genetic code. The results also highlight the importance of properly taken into account the biomolecular environment for the study of photochemical reactions in biomolecules.

Quantum Mechanics and Molecular Mechanics

Theoretical analysis of photochemical reactions in biomolecules is a very challenging problem that requires mixing different theoretical and computational strategies. In this work, a hybrid quantum mechanics / molecular mechanics (QM/MM) method, recently developed by the authors, was used to explore the conformational and dynamical properties of the system. This method presents a very good balance between accuracy

and computational efficiency, a very important property to study complex biomolecular systems. Moreover, non-adiabatic QM/MM molecular dynamics simulations were performed to study the dynamics of photo-excited DNA and analyze the atomic mechanisms of the reaction. [Full article]
Also read on UAM Gazette.

Building Nano-Lenses Based on DNA Origami Structures

When: Friday, 20 November (2015), 12:00h
Place: Departamento de Física de la Materia Condensada, Facultad Ciencias, Module 3, Seminar Room (5th Floor).
Speaker: Guillermo Acuña, TU Braunschweig, Institute of Physical and Theoretical Chemistry, Hans-Sommer-Str. 10, Braunschweig, Germany.
Abstract:

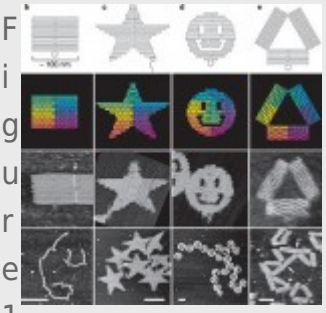
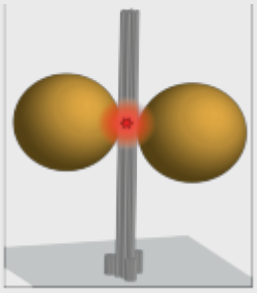


Figure 1.

In this presentation, we will show how the DNA-Origami technique [1] (Figure 1.) can be introduced for plasmonic and photonic applications. Firstly, we employ DNA-Origami as a platform where metallic nanoparticles as well as single organic fluorophores can be organized with nanometer precision in three dimensions. With these hybrid structures we initially study the nanoparticle-fluorophore interaction in terms of the distance-dependent fluorescence quenching [2] and angular dependence around the nanoparticle [3]. Based on these findings, we build highly efficient nano-lenses (Figure 2.) based on 100 nm gold dimers [4] which are able to strongly focus light into the sub-wavelength region where the fluorophore is positioned and produce a fluorescence enhancement of more than two orders of magnitude [5].

Figure 2. 

Using this highly confined excitation field we were able to perform single molecule measurements in solution at concentrations as high as 25µM in the biologically relevant range. Additionally, we report on a controlled increment of the radiative rate of organic dyes in the vicinity of gold nanoparticles with the consequent increment in the number of total emitted photons [6,7].

References

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