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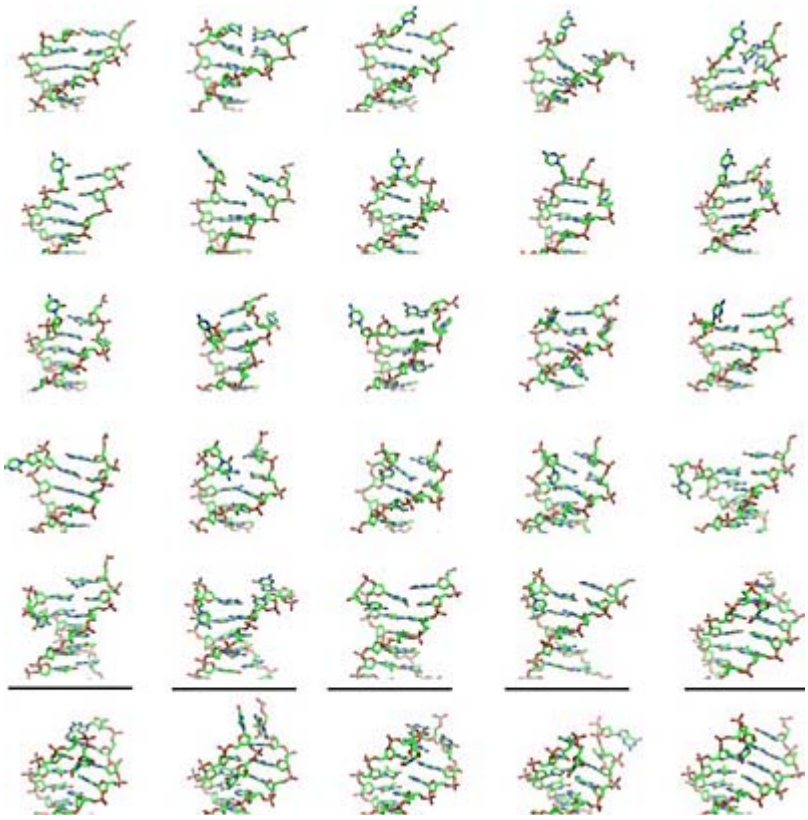
First High-res Observations of Unfolding DNA Produced using Mare Nostrum Supercomputer



From left to right and up to down, DNA structure movements that provide an idea about the mechanism by which DNA starts to unfold. *Courtesy of A. Pérez*

Separation of two DNA strands occurs in millionths of a second. Consequently, it is extremely difficult to study this phenomenon experimentally, and researchers must rely on computational simulations. However, after four years of fine-tuning an effective physical model and massive use of the supercomputer Mare Nostrum, researchers at IRB Barcelona and the Barcelona Supercomputing Center (BSC) have managed to produce the first realistic simulation of DNA opening at high resolution.

The scientists, Modesto Orozco, group leader of the Molecular Modelling and Bioinformatics Group at IRB Barcelona, Full Professor of Biochemistry and Molecular Biology at the University of Barcelona and director of the Life Sciences Deptment at the BSC, and Alberto Pérez, "Juan de la Cierva" researcher at BSC, currently at the University of California, San Francisco, publish their findings in the international chemistry journal *Angewandte Chemie*.

Alberto Pérez explains that "many of the functions of DNA come about when its two strands separate, when, for example, it has to replicate during cell division or in repair processes. With this study, we propose a mechanism for this process which, in turn, will lead to new experiments for its final corroboration."

The researchers have studied a small DNA fragment of 12 base pairs (the human genome has about 3,000 million base pairs), and have obtained 10 million structural snapshots of how DNA unfolds. In this process, they have revealed the two main ways by which the natural folded structure move to an unfolded state.

"This project", explains Orozco, "is part of a greater objective of the lab: to attempt to understand the changes that the DNA structure undergoes in biological processes that occur within the cell, such as the expression and repression of genes or DNA replication and transcription."

DNA holds the genetic information of living organisms and its double helical structure was discovered more than 50 years ago by Watson and Crick. DNA and the proteins that modify it are the most important therapeutic targets in several pathologies, and particularly in cancer. The work performed at IRB Barcelona provides a detailed view of the mechanism through which one of the most crucial processes in DNA occurs, and opens up new prospects regarding the connection between physical properties, functionality and pharmacological effect. The final objective is to achieve new breakthroughs that turn DNA into a universal pharmacological target.

Citation: "Real-time Atomistic Description of DNA Unfolding." Alberto Pérez and Modesto Orozco. *Angewandte Chemie* (2010). doi: 10.1002/ange.201000593. *Angewandte Chemie* - International Edition (2010) doi: 10.1002/anie.201000593