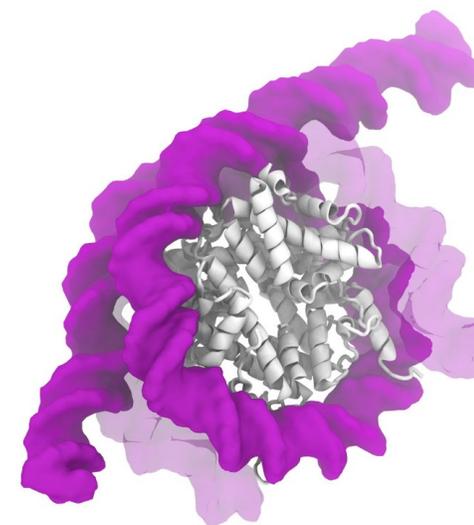




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A nucleosome particle before and in the process of spontaneous unwrapping. White and purple represent the histone protein core and DNA, respectively. DNA's initial conformation is semitransparent; the unwrapped one is opaque.

DNA “BREATHING” CAPTURED IN ALL-ATOM DETAIL

Research Challenge

Cell stores DNA packaged with proteins into nucleosomes. The genetic material must be unpackaged and the nucleosomes disrupted in order for essential biological processes such as transcription to occur. Experiments have identified important determinants of nucleosome stability. Through simulations the team aims to observe atomistic detail of spontaneous and reversible unraveling of nucleosome particles, also known as “DNA breathing.” Reaching the timescale and statistics needed to characterize this process with confidence presents a significant challenge.

Methods & Codes

The team performs explicit-solvent all-atom molecular dynamics (MD) simulations of a set of individual nucleosomes in varying ionic conditions, DNA sequences, and DNA length surrounding the protein core using the latest version of NAMD2 package. Simulated shifting of several protein residues away from the DNA initiates a stepwise mechanism of nucleosomal DNA detachment and unwrapping.

Why Blue Waters

Computational study of the fine details of DNA–histone interactions require explicit-solvent all-atom MD simulations to accurately characterize the surrounding ionic environment. The long timescale needed to observe spontaneous DNA detachment makes such MD simulations computationally demanding. The large number of XK nodes equipped with graphics processing unit accelerators and connected via the fast Gemini interconnect makes Blue Waters one of the best publicly available resources for performing simulations of DNA–protein and DNA–DNA interactions in atomistic detail.

Results & Impact

Computations predict spontaneous and reversible detachment of the outer stretches of nucleosomal DNA under high ionic strength. The likelihood of such DNA breathing events correlates with the coarse-grained (CG) content of the nucleosomal DNA, with higher CG content being associated with more stable nucleosomes. Motion of conserved histone residues orchestrates a stepwise character of the DNA detachment. Adenine–thymine-rich segments of DNA form less stable nucleosomes and may signal the start of transcription.