

Unveiling Chromatin Fiber Condensation Through Many-Body Nucleosome Interactions

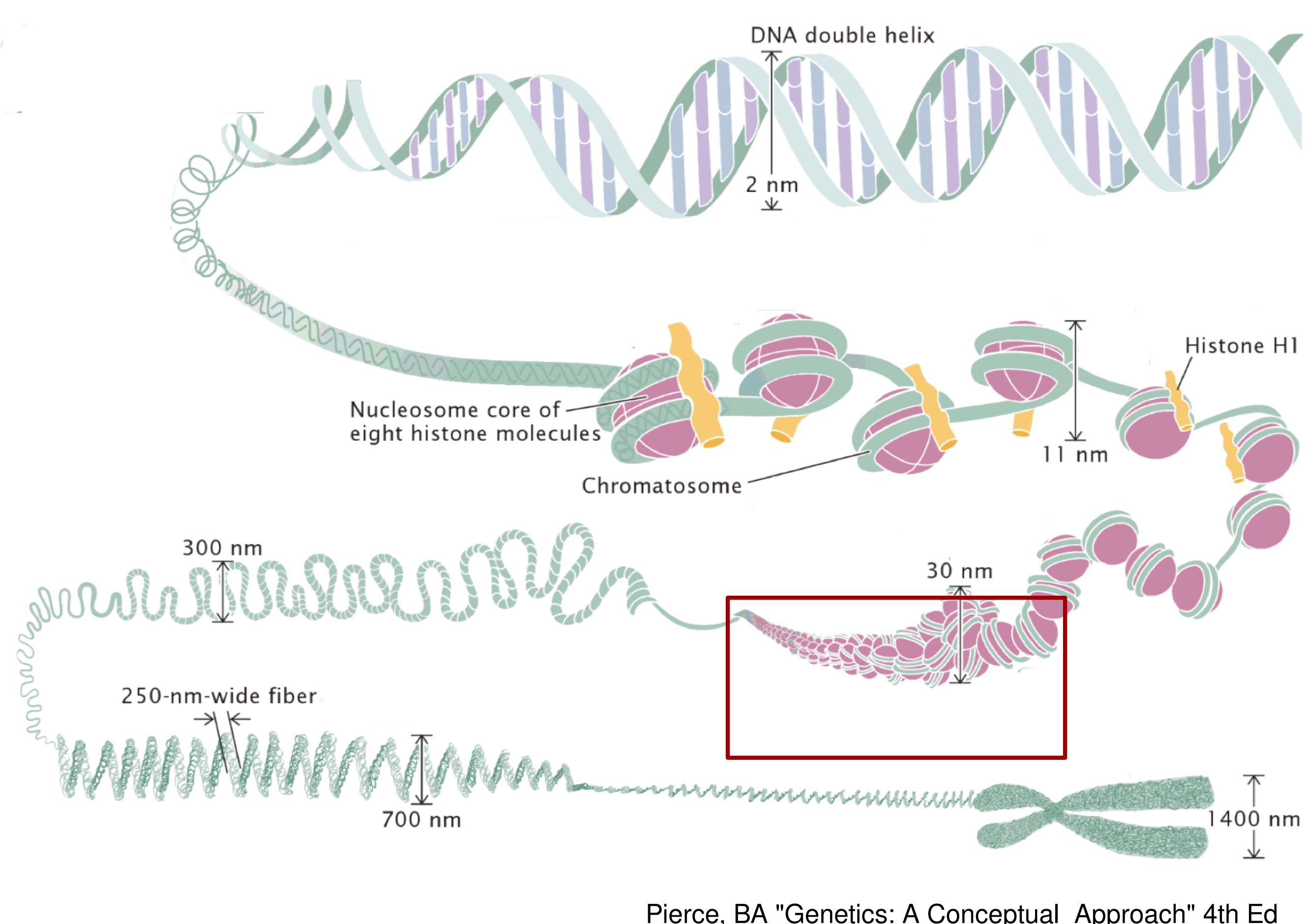
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Abstract

Chromatin, a fiber comprised of DNA and DNA-binding proteins (histones), has a dynamic and poorly understood structure. The structure of chromatin is related to vital cellular processes like DNA transcription, replication, and repair through epigenomic regulation. Through X-ray crystallography the largest stable unit of the chromatin fiber has been determined to be the nucleosome. The nucleosome and its energetics and dynamic modes have been the subject of a number of coarse-grained simulation studies. Building upon these coarse-grained nucleosome simulations, we have developed a novel chromatin model to solve the structure-function problem of chromatin. We have validated our bottom-up model to experimental data to prove that it can reproduce structural properties of chromatin. Here, we uncover a structural motif of chromatin that we can use to construct and predict the structure of entire chromosomes.

The Problem: The Structure Of Chromatin



Why should we care about the structure of chromatin?

The underlying DNA is accessed more readily when the chromatin structure is more open.

There are chemical modifications that occur to the histones (sometimes single residue modifications) that incur an opening of chromatin structure.

Similarly, there are modifications that can close the structure of chromatin.

If a section of chromatin is "incorrectly" closed/opened, it can have catastrophic consequences.

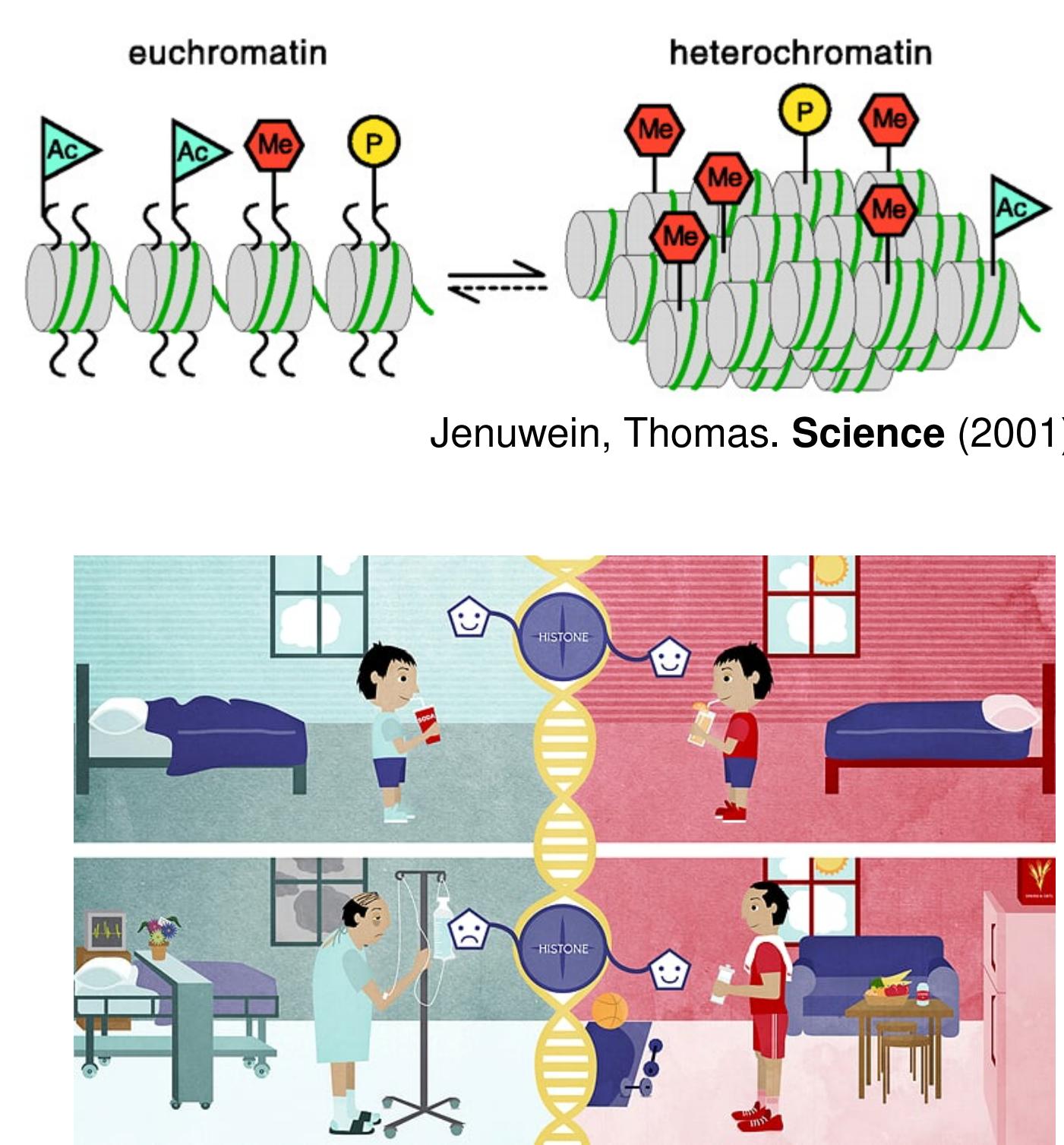
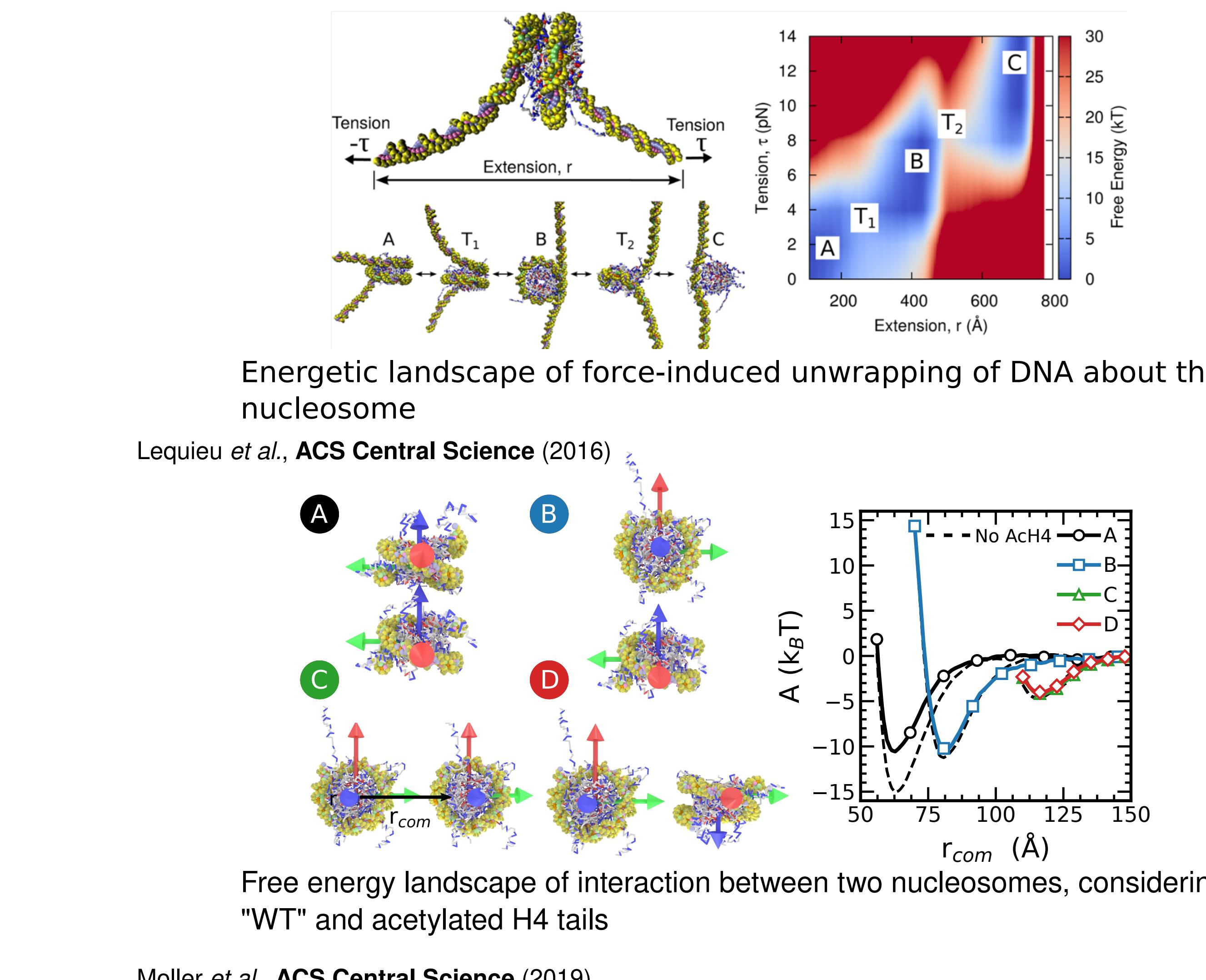


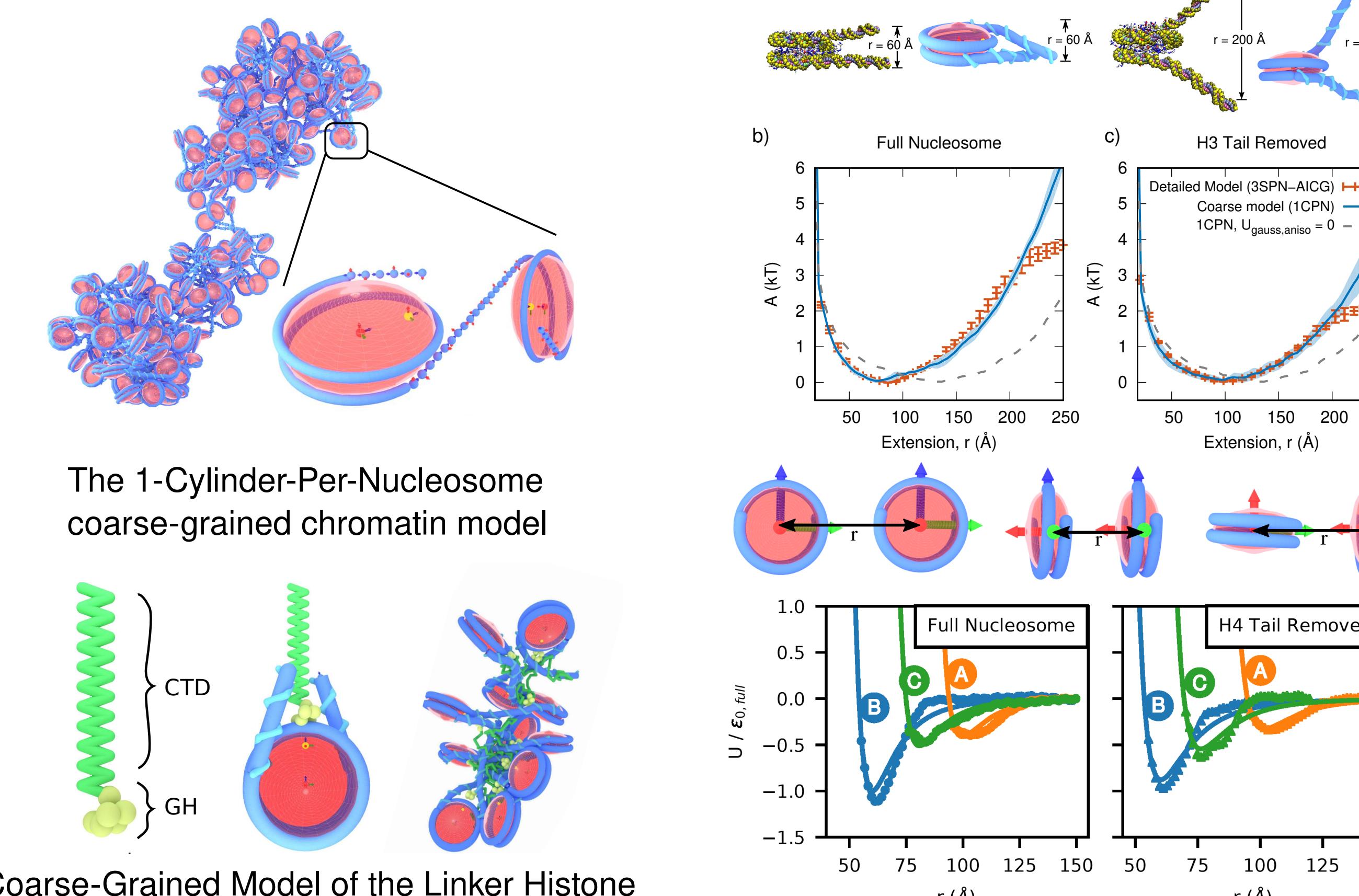
Photo Cred: Ottawa Hospital Research Institute

Molecular Dynamics Simulations of Nucleosomes

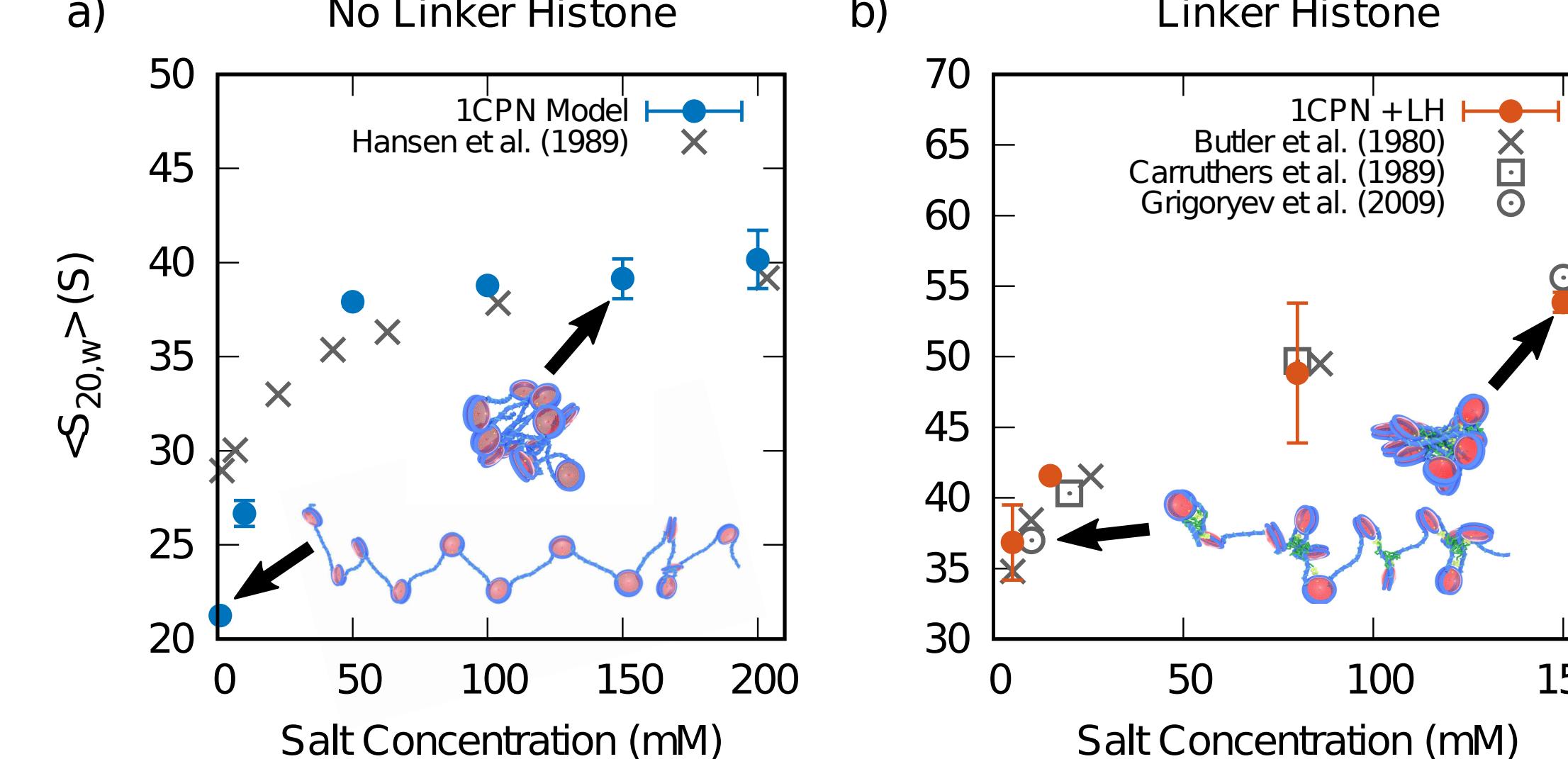


Moller et al., ACS Central Science (2019)

The 1CPN Model of Chromatin



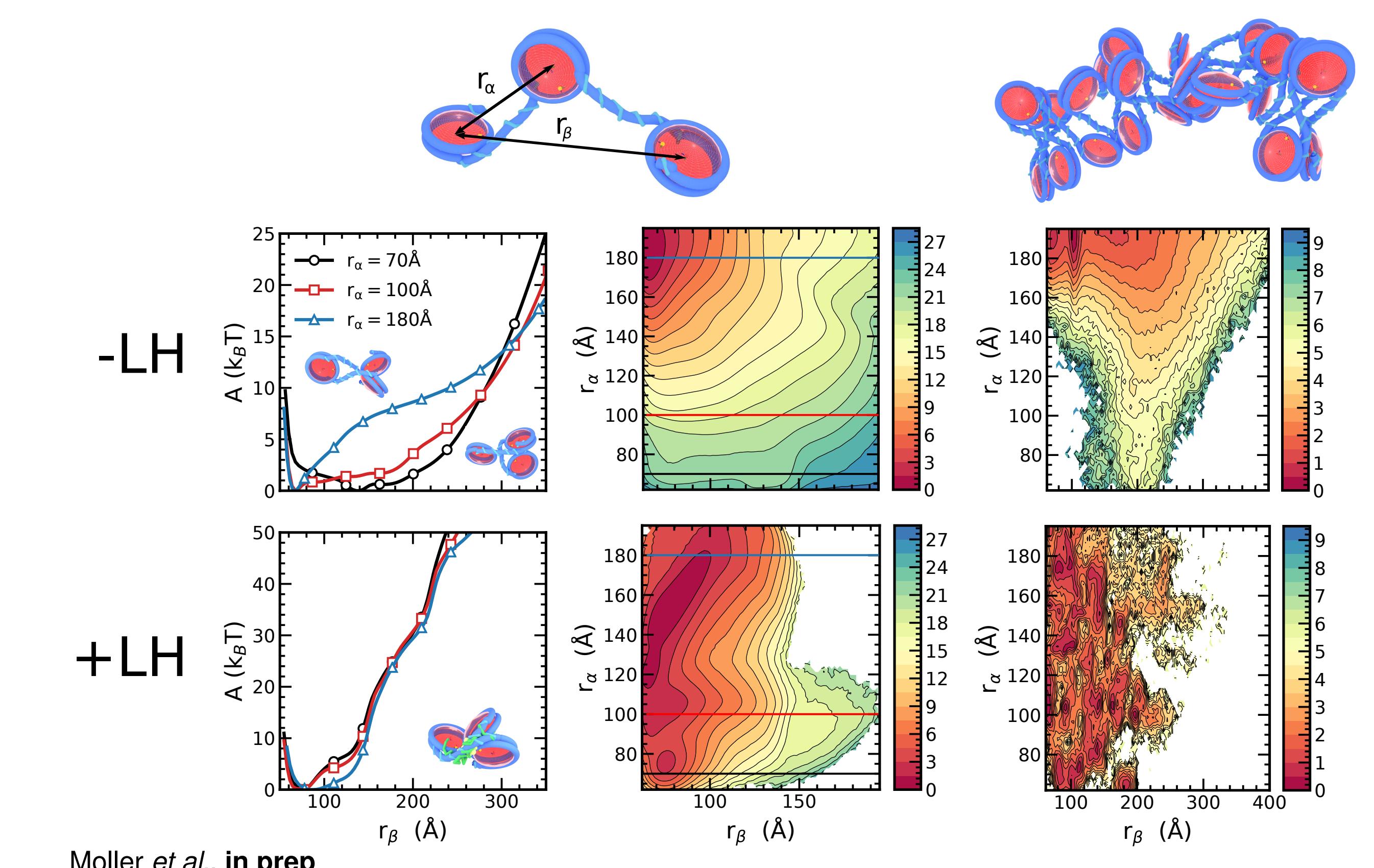
Coarse-Grained Model of the Linker Histone



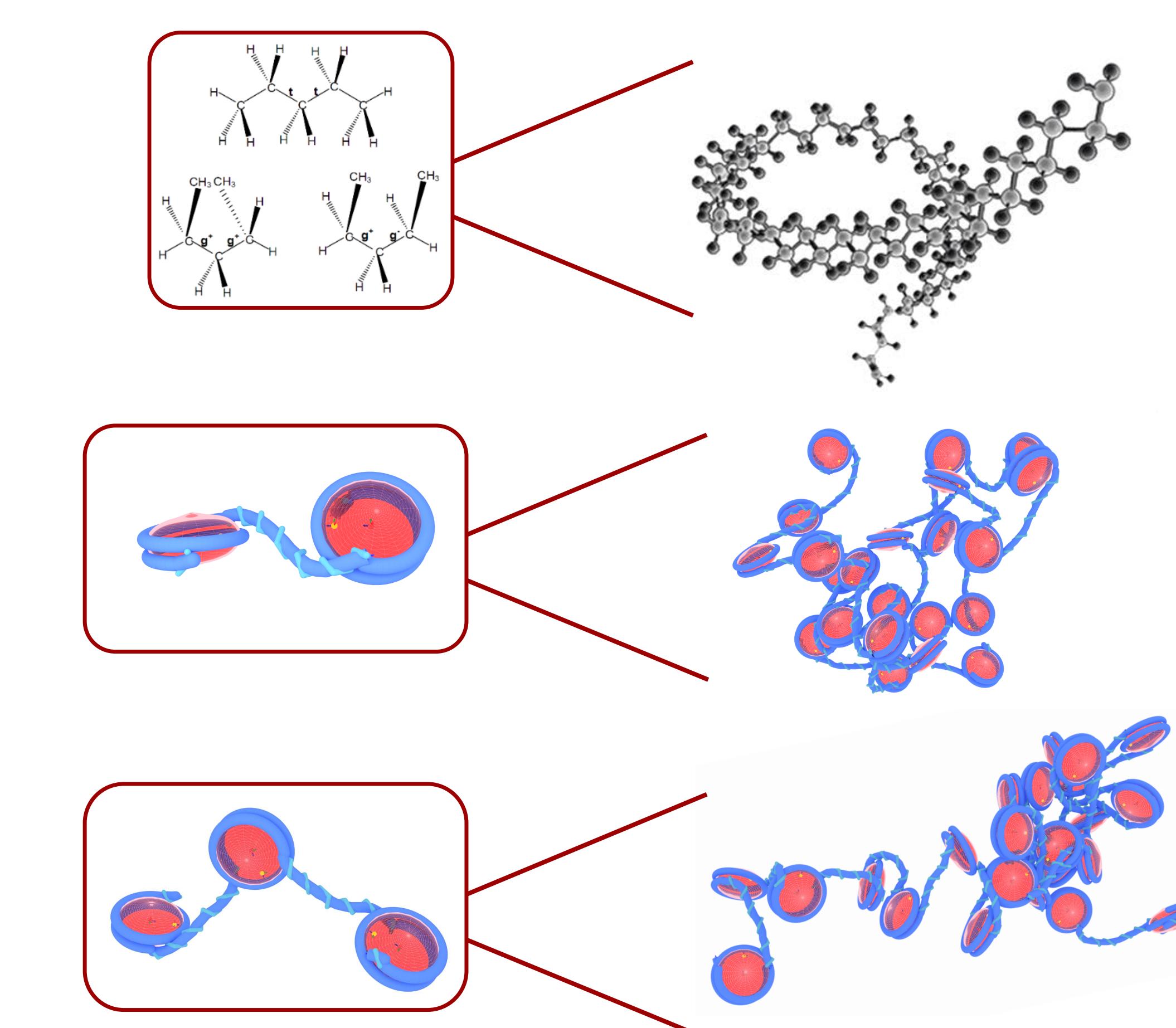
Lequieu et al., JCP in press.

Building the Chromatin Fiber

Through free energy methods, we uncover the repeating tri-nucleosome motif to describe the structure of the chromatin fiber



We can use the probabilities from the tri-nucleosome results to construct fibers and show that a trinucleosome motif is able to help us quickly generate large chains, similar to Flory's Rotational-Isomeric-State model



Flory, P. J. "Statistical Mechanics of Chain Molecules" 1969

