Special Colloquium

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The physics of chromosomes: from DNA loops to nucleus-scale structures

Monday, February 6, 2017

4:00 pm—5:15 pm

145 Goodwin Hall

Human chromosomes in a cell's nucleus have long been thought to behave like encapsulated random polymers. Recent experiments, however, have shown that chromosomes organize into well-defined three-dimensional structures thereby controlling the cell's state. The very presence of such structures implies existence of yet unknown physical interactions that define the free energy of chromosomes in a cell's nucleus and govern the free-energy change during processes such as cell development and cancer. Using high-through put molecular dynamics simulations and single-molecule experiments, we determined the free energy landscape of the fundamental structural unit of chromosome organization—a nucleosome, which is a fragment of DNA wrapped around a protein core. At a single nucleosome level, we found the nucleotide sequence of DNA and its CpG methylation to uniquely determine the orientation of the DNA loop with respect to the protein core, offering a simple physical mechanism of controlling DNA accessibility to DNA reader machinery. At a multi-nucleosome level, we found the AT content of the DNA sequence and the methylation of either DNA or the nucleosome proteins to govern association of nucleosomes into clusters. Overall, our findings suggest that intrinsic properties of DNA may play a considerable role in defining the free energy landscape and the nucleus-scale organization of chromosomes.