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Precise genome-wide mapping of single nucleosomes and linkers in vivo

n eukaryotes, nucleosomes are the basic units of DNA packaging. Micrococcal nuclease (MNase) digestion followed by sequencing (MNase-seq) is the most used method of mapping nucleosomes. Unfortunately, MNase digests different sequences with different rates, and nucleosome maps are affected by the degree of digestion. Moreover, other proteins also offer protection against MNase and can be mistaken for nucleosomes in MNase-seq experiments. To eliminate the biases introduced by MNase, we have developed a chemical cleavage method that allows us to precisely map both single nucleosomes and linkers with very high accuracy genome-wide in budding yeast. We confirm that S. cerevisiae promoters are sites of strong nucleosome depletion but attribute the putative nucleosome depletion seen at termination sites to MNase bias. Our nucleosome mapping data has the highest resolution among the currently available techniques, and this accuracy allows us to distinguish alternative rotational positions that nucleosomes occupy in different cells. Furthermore, we show that linker DNA has quantized lengths for individual genes. By comparing our nucleosome dyad positioning maps to existing genomic and transcriptomic data, we evaluate the contributions of sequence, transcription, histone H1 and the H2A.Z variant in defining the chromatin landscape. We show that DNA sequence has a very limited effect on establishing the nucleosome organization as observed in vivo. Moreover, we find that the degree of gene compaction, measured by the spacing between neighboring nucleosomes, correlates with the transcription level, amount of histone H1 bound to the gene, and the amount of H2A.Z variant that is incorporated in the nucleosomes closest to the gene promoter ("+1 nucleosomes"). Furthermore, we present a biophysical model based on simple physical principles, which shows that steric exclusion between neighboring nucleosomes suffices to explain the salient features of nucleosome positioning and the complex nucleosome phasing pattern that is observed near the gene ends.

Biography

Razvan Chereji holds a PhD degree in physics from Rutgers University and currently, he is a research fellow at the National Institute of Child Health and Human Development, NIH. He studies physical models that describe the chromatin organization, its dynamics, and the interactions between DNA and DNA-binding proteins, including histones, transcription factors, polymerases and chromatin remodelers.

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