From fibers to the sea of nucleosomes

From fibers to the sea of nucleosomes: Computer simulations of the regulation of the spatial structure of Mbp chromatin domains in the nucleus

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In Short

- In the nucleus DNA forms a bead-on-a-string like structure termed chromatin
- The structure of chromatin is important for gene regulation and dysregulation.
- Computer simulations elucidate the difference between different chromatin in different organisms and cells.
- Computer simulations help to understand the interplay of the spatial structure of chromatin and the activation and repression of gene clusters.

In the nucleus of eukaryotes DNA is wrapped around proteins forming cylindrical units called nucleosomes. Nucleosomes are connected by linker DNA and form a bead-on-a-string like structure termed chromatin. Chromatin is the main constituent of the chromosomes. In vitro chromatin is observed as a fiber with a diameter of 30 nm. In vivo different structures are observed depending on the organism, the differentiation and the cell state. This structure is important for gene regulation. In order to understand the folding in the nucleus in computer simulations the crowding condition must be included. These will help to understand the difference between in vitro and in vivo structures as well as differences in chromatin structure in different parts of the cell nucleus with different density. The positions of the nucleosomes on the DNA and binding of special proteins like CTCF or cohesin are important factors for controlling gene activity. Computer simulations including these elements help understanding the mechanisms. Data from computer simulations will be compared with experimental data. In this project the nucleosomes are modelled by cylindrical units connected by springs describing the linker DNA. Applying Monte Carlo methods configurations are sampled. In first test runs changes of chromatin structure depending of the density was observed (Figure **??**). The simulation results will help to understand the biological meaning of observations of experimental techniques as e.g. chromosome conformation capture techniques. In order to understand changes between healthy and malign cells we plan to research contact probabilities between transcription factors bound to enhancers and promoters. This knowledge is a key for the understanding of the regulation of the spatial structure of the nucleus which is important for the comprehension of gene regulation and deregulation.

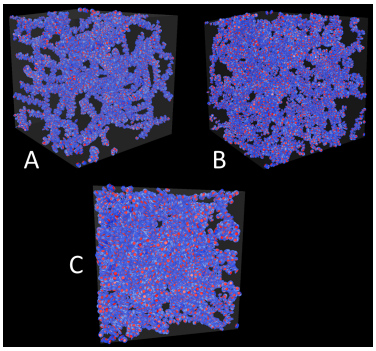

***Figure 1:** Visualization of configurations from test simulations of 8000 nucleosomes with CL geometry in different box sizes modelling different nucleosome densities (A, B, C). The fiber dissolves with increasing density but is still visible (Zülske, Groß, Wedemann unpublished).*

WWW

http://bioinformatics.fh-stralsund.de

More Information

[1] R. Stehr, N. Kepper, K. Rippe, G. Wedemann, *Biophys. J.* **95**, 3677-3691 (2008). doi:10.1529/biophysj.107.120543

[2] O. Müller et al, *Biophys. J* **107**,2141-2150 (2014). doi:10.1016/j.bpj.2014.09.026

[3] Diermeier et al., *Genome Biology* **107**,15:536 (2014). doi:10.1186/s13059-014-0536-6

[4] Teif et al., *Journal of Physics: Condensed Matter* **27**, 064110 (2015). doi:10.1088/0953-8984/27/6/064110

Project Partners

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