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Complex dynamics of genomic sites in the nucleus of live cells

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The DNA in a human cell is ~3 meters long. It is dynamic and yet is well organized. What are the mechanisms that organizes the chromatin and chromosomes in the nucleus?

Using dynamic methods in live cells, we identified a mechanism that maintains the genome organization in the nucleus. We claim that lamin A forms chromatin loops by lamin A dimers (or oligomers) thereby restricting the chromatin dynamics significantly. This can explain the maintenance of chromosome territories in the nucleus.

We use advanced methods for studying the dynamics of chromatin and proteins in the nucleus. These methods are based on measuring the signal and fluctuations of fluorescent molecules and the use of biophysical models based on Smoluchowski equation and modified diffusion equations. It allowed us to identify that ~50% of a crucial protein named lamin A is bound to the chromatin everywhere in the nucleus interior.

Specific sites along the chromatin commonly exhibit anomalous diffusion (alpha in the range of 0.4-0.7). When lamin A is eliminated, the diffusion dramatically changes to normal diffusion, which is difficult to understand. By analyzing the diffusion in specific time-windows, we show that the dynamics of the genomic sites is bi-modal; they are normally constrained and exhibit anomalous diffusion, except for short time-windows where they super-diffuse.

By using single-molecule methods including tethered particle motion (TPM) and atomic force microscopy (AFM) we show the type of bonds formed by lamin A and demonstrate the actual bonding that lamin A forms on the DNA.

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