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Studying chromatin structure and dynamics through single particle tracking and stochastic motion analysis

Eldad Kepten, Physics Department & Institute of Nanotechnology
Bar Ilan University, Ramat Gan, Israel

The Eukaryotic cell's nucleus is a dense and complex space. The expression of genetic functions is controlled through the interaction of numerous proteins, complexes, RNA and DNA. Historically it was believed that the nucleus has no underlying order and resembles a "spaghetti bowl" of long protein covered DNA chains called chromosomes. In recent years it has become apparent that the nucleus has order on all length scales and this order is actually connected to the function of the various genetic circuits. Chromosomes are segregated into separate territories, show non-random folding and various regions can be silenced or activated according to their structural state. Despite these recent advancements we are still largely in the dark regarding the nuclear environment.

The connection between structure and dynamics is fundamental in physics. In the sub-cellular environment, the common mode of motion is that of random walks. Theoretical development has shown that the character of a random walk is greatly shaped by the controlling process. Examples are CTRW, fractional Brownian motion or an obstructed landscape which give rise to anomalous diffusion, but differ in their other stochastic characteristics.

In order to shed light on the submicron mechanisms behind chromatin (DNA) dynamics and structure, we measure the *in vivo* stochastic motion of several chromosome loci. Telomeres, centromeres and a gene locus in U2OS cells are tracked during six time orders with the use of fluorescent microscopy and single particle tracking techniques. A simple analysis using the mean square displacement (MSD) shows that the motion is anomalous sub-diffusion with a slight transition towards higher anomalous exponents at longer times. Since anomalous diffusion is common to several mechanisms, all possible in biological context, we analyze the data with more advanced tests that look at more subtle characteristics of the process. We are able to reject binding and obstruction mechanisms, and find evidence of a correlative process. This motion presumably stems from polymer dynamics and a visco-elastic environment.

This talk will be oriented towards physical aspects of the problem and necessary biological background will be covered at the beginning.