**Rouse polymer dynamics in viscoelastic media**

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**Recommended with a commentary by Michael Tamm, Moscow State University**

The last years have seen a significant advance in experimental techniques allowing to study the properties of the chromosome packing in the living prokaryotic and eukaryotic cells, both from static (FISH and Hi-C experiments) and dynamic (single particle tracking using fluorescent markers) point of view. These advances have led to plethora of theoretical works trying to make sense of the structure and dynamics of chromosome matter from the point of view of polymer physics.

From the perspective of conformational statistics, there have been a lot of renewed interest in the study of the so-called crumpled or fractal globule state of polymer chains, as well as annealed randomly branched polymer conformations and conformations stabilized with thermoreversible saturating bonds; all of these models are presumed to be candidates for the description of the chromosome conformations within living cells under some conditions.

Making sense of the chromosome dynamics, in turn, requires understanding how it is influenced by variety of complex factors, including molecular crowding, role of entanglements in the chromatin (or genophore in the case of prokaryots), non-Gaussian statistics of the chromatin chain, and active forces present in living cells. One of the important aspects of the problem is to understand how the polymer dynamics is influenced by the fact that surrounding medium is itself viscoelastic. Indeed, there is strong experimental evidence that a test particle put, for example, into a cytoplasm of a living cell exhibits fractal Brownian dynamics with mean-square displacement $\left\langle x^2(t)\right\rangle$ proportional to $t^\alpha$ with $\alpha < 1$ rather than $\alpha = 1$ as in usual Brownian motion.

The most basic formulation of the problem of polymer in viscoelastic media is to study the dynamics of a simplest Rouse model of polymer chain coupled with correlated noise, i.e., to consider fractional Langevin equation of the form

$$\int_0^t K_\alpha\left(t-t'\right)\frac{\partial x(t',s)}{\partial t'}dt' = \frac{\partial^2 x(t,s)}{\partial s^2} + \xi_\alpha(t,s) \tag{1}$$

where $x(t,s)$ is a monomer displacement as a function of time $t$ and coordinate along the polymer chain $s$, the memory kernel $K_\alpha(t) = A(2-\alpha)(1-\alpha)|t|^{-\alpha}$, and $\xi_\alpha$ is a fractal Brownian noise, i.e. Gaussian noise with correlation functions of the form

$$\langle\xi_\alpha(t,s)\rangle = 0;\ \ \langle\xi_\alpha(t,s)\xi_\alpha(t',s')\rangle = kTK_\alpha(t-t')\delta(s-s'), \tag{2}$$

and this particular form of relation between the noise correlations and the memory kernel is dictated by the fluctuation-dissipation theorem (note that $\alpha = 1$ corresponds to the simple white noise and thus to original Rouse model).

In two recent works of A. Spakowitz's group [1, 2] this problem has been studied in remarkable detail. It turns out that the analogue of the Rouse time, i.e. the time at which chain diffuses for a distance equal to its spatial dimension, for viscoelastic case behaves as

$$\tau_\alpha = N^{2/\alpha}\tau_0, \tag{3}$$

where $N$ is the number of monomers in the chain and $\tau_0$ is typical microscopic time; and at times much less than this characteristic time $t \ll \tau_\alpha$ the monomers move subdiffusively $\left\langle x^2(t)\right\rangle \sim t^\beta$ with $\beta = \alpha/2$. In the recent paper [2] the authors, motivated by developments in the experimental techniques, have studied the velocity autocorrellation functions and time-dependent two-point correlations functions of the chain. On the qualitative level, the main results are that autocorrelation function is negative for the non-overlapping time intervals, and decays as a power law with increasing time difference; and that two-point correlation function

$$\frac{\langle x(t,s)x(t+\tau,s+\sigma)\rangle}{\langle x(t,s)\rangle\langle x(t+\tau,s+\sigma)\rangle} \tag{4}$$

is, for a long chain, a function of a single scaling variable $z = \tau\sigma^{-2/\alpha}$ and grows from 0 for small $z$ to 1 for large $z$. Moreover, the authors are able ot obtain many of the interesting correlation functions in close analytical form or in the form of infinite series.

Note, however, that the problem of chromosome dynamics is, of course, far from being sold completely yet: there are several important unsolved questions which still linger. Let us mention a few of them:

- It is not at all clear what is the physical reason which results in the appearance of a fractal Brownian noise of the form (2), most importantly - whether it is caused by the features external to chromatin itself (e.g., molecular crowding in the nucleus/nucleoid) or is the reason somehow connected with the presence of the chromatin chain itself;
- We know for sure from the FISH and Hi-C experiments that chromatin conformations are not Gaussian; it is not clear therefore whether Rouse model itself is applicable (it is definitely not applicable for non-Gaussian equilibrium conformations, but the chromatin is definitely far from equilibrium, where the situation is much less clear);
- Active forces obviously play an important role in chromatin dynamics, so one can expect that to describe the chromatin dynamics properly one should add some (probably, random) active force into (1) on top of the thermal force obeying fluctuation-dissipation theorem; it is known that addition of such an active force even in the most simple form can result in variety of new and counterintuitive phenomena.
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However, this set of new analytical results is, without any doubt, an important addition to our knowledge about the polymer dynamics and will work as a natural reference points for the further advances in the field of chromosome dynamics in partiular, and, more generally, in the study of polymer dynamics in crowded, viscoelastic and active media.

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[1] S.C. Weber, J.A. Theriot, A.J. Spakowitz, Phys. Rev. E, **82**, 011913 (2010).
[2] T.J. Lampo, A.S. Kennard, A.J. Spakowitz, Biophyisical Journal, **110**, 338 (2016).