New and Notable

The Great Hunt For Extra Compliance

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Every field has skeletons in their closet. One of the skeletons of single molecule biophysics is the persistence length of short DNA molecules. Loosely speaking, the persistence length, P, is a statement about the elasticity of a polymer; an infinitely stiff polymer has an infinite P. Knowledge of the persistence length of DNA and RNA is essential to design and interpret single-molecule experiments. Two models of polymer elasticity constitute the theoretical bedrock of the field: the freely-jointed chain and the wormlike chain (WLC). In this issue, Seol et al. (1) extend the classic WLC model in a way that will be immediately useful to experimentalists working on a multitude of systems.

The story starts in the early 1990s, when it became possible to experimentally characterize the elasticity of single DNA molecules. In 1994, Bustamante et al. (2) reported that force extension curves of λ-DNA beautifully fit the WLC model. Despite λ-DNA having a finite length (97 kb) and clearly not being an ideal polymer, a continuum elastic theory such as the WLC captured its elasticity surprisingly well. Right from the beginning, however, it was apparent that we should not expect the WLC to faithfully represent all DNAs in all situations. Even in the first article there were hints of the stretchable solid regime at forces above ~10 pN, and at even higher forces the DNA suddenly overstretched (3), another clear departure from the WLC model.

Nonetheless, one thing was sacred: the persistence length of DNA. The persistence length certainly did depend on ionic strength, pH, and intercalators (3–5), but incoming graduate students were told that P captured an intrinsic property of DNA and did not depend on the polymer's length. Most practitioners suspected that this was not true, since the concept of a persistence length becomes ill-defined when the polymer is not much longer than P. Moreover, many experimental studies of short pieces of DNA revealed that it was more compliant than predicted from the classic WLC parameterized with the canonical value of P, 50 nm.

What we did not know was how P depends on the contour length, and when we need to explicitly incorporate finite L effects in our models and experiments. This is what makes the finite-WLC of Seol et al. so useful—this extension of the classic WLC includes three effects critical to experiments: the finite length of the chain, rotational fluctuations of the bead, and the boundary conditions at the polymer's anchor points.

As described by Seol et al., there are two equivalent ways of applying the finite-WLC to force-extension curves. Experimental data can be fit directly to the finite-WLC, or the data can be fit to the classic WLC, and all the complexity can be dealt with by correcting P for the effects discussed above. The former approach is conceptually more elegant, and the latter approach is mathematically simpler and is easy to plug into existing data-processing scripts.

Out of curiosity, I compared the performance of the classic WLC to the finite-WLC using some single-molecule RNA unfolding data (6), and I found that the finite-WLC does rather well. The article of Seol et al. contains extensive experimental results that establish the performance of their finite-WLC.

Is the finite-WLC the end of the story? Fortunately not—a multitude of essential biological processes take place on length scales far below one persistence length, and we are only beginning to understand the intricacies of DNA and RNA elasticity on short and very short scales. Nonetheless, the finite-WLC gives us a glimpse of what future models of DNA elasticity will look like. Not only that, but Seol et al. also gives us a blueprint for constructing elasticity models for specific experimental geometries and length scales.

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