

*Department of Mathematics,
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Informal Seminar on Mathematics and Biochemistry-Biophysics

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Model of Dynamic Single-Molecule Force Spectroscopy That Harnesses Both Loading Rates and Device Stiffness

Abstract:

Single-molecule force spectroscopy experiments involve imposition of controlled forces at the single molecule level and observing the corresponding mechanical behavior of the molecule. The molecular resistance to deformation can be utilized for studying transition pathways of molecules in terms of energy, time scales and even number of transition states. These have found applications in a wide variety of problems, for instance, to understand folding-unfolding dynamics of biomolecules, ligand-receptor binding, transcription of DNA by RNA polymerase, motion of molecular motors to name a few. Existing analyses of force measurements rely heavily on theoretical models for reliable extraction of kinetic and energetic properties. Despite significant advances, there remain gaps in fully exploiting the experiments and their analyses. Specifically, the effect of pulling device stiffness or compliance has not been comprehensively captured. Hence, the best models for extracting molecular parameters can only be applied to measurements obtained from soft pulling devices (e.g., optical tweezers) and result in well-documented discrepancies when applied to stiff devices (e.g., AFM). This restriction makes pulling speed the only control parameter in the experiments, making reliable extraction of molecular properties problematic and prone to error.

Here, we present a one-dimensional analytical model derived from physical principles for extracting the intrinsic rates and activation free energies from rupture force measurements that is applicable to the entire range of pulling speeds and device stiffnesses. The model therefore is not restricted to the analyses of force measurements performed with soft pulling devices only. Further, the model allows better design of experiments that specifically exploits device stiffness as a control parameter in addition to pulling speed for a more reliable estimation of energetic and kinetic parameters. The model also helps explain previous discrepancies noted in rupture forces measured with devices of different effective stiffnesses and provides a framework for modeling other stiffness-related issues in single-molecule force spectroscopy.

Hosts: Li-Tien Cheng and Bo Li

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