Mechanics, thermodynamics, and kinetics of ligand binding to biopolymers

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Ligands binding to polymers regulate polymer functions by changing their physical and chemical properties. This ligand regulation plays a key role in many biological processes. We propose here a model to explain the mechanical, thermodynamic, and kinetic properties of the process of binding of small ligands to long biopolymers. These properties can now be measured at the single molecule level using force spectroscopy techniques. Our model performs an effective decomposition of the ligand-polymer system on its covered and uncovered regions, showing that the elastic properties of the ligand-polymer depend explicitly on the ligand coverage of the polymer (i.e., the fraction of the polymer covered by the ligand). The equilibrium coverage that minimizes the free energy of the ligand-polymer system is computed as a function of the applied force. We show how ligands tune the mechanical properties of a polymer, in particular its length and stiffness, in a force dependent manner. In addition, it is shown how ligand binding can be regulated applying mechanical tension on the polymer. Moreover, the binding kinetics study shows that, in the case where the ligand binds and organizes the polymer in different modes, the binding process can present transient shortening or lengthening of the polymer, caused by changes in the relative coverage by the different ligand modes. Our model will be useful to understand ligand-binding regulation of biological processes, such as the metabolism of nucleic acid. In particular, this model allows estimating the coverage fraction and the ligand mode characteristics from the force extension curves of a ligand-polymer system. We illustrate the power of the method based in this model with the analysis of experimental results of Human mitochondria SSB (HmtSSB) binding to single stranded DNA (ssDNA), which has allowed to characterize the binding modes and coverage of HmtSSB-ssDNA complexes in several configurations, including ssDNA generated during DNA replication.

[l] J. Jarillo, et al., PlosOne **12**, e0174830 (2017).

[2] J.A. Morín, et al., Submitted (2017).