Equilibrium and non-equilibrium fluctuations at the single molecule level: from free-energy measurements to inference

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Optical tweezers allow the measurement of fluctuations at the nano-scale, in particular fluctuations in the end-to-end distance of single bio-molecules. This kind of experiments, at the interface between biology, chemistry and physics offer the possibility of testing recent results in non-equilibrium statistical physics and applying them in high-resolution measurement of intra and inter-molecular interactions. Thermal fluctuations play a prominent role in these experiments and fluctuation spectra yield valuable information. However fluctuation spectra can be easily distorted by unavoidable instrumental effects[1]. I will show how, once instrumental effects are correctly taken into account, equilibrium fluctuations in the end-to-end distance of a single molecule allow for a precise measurement of its entropic elastic response and of its folding kinetics. I will then describe non-equilibrium experiments in which optical tweezers perform work on a tethered molecule, forcing its unfolding. The statistics of the work necessary to unfold the molecule, collected in repeated cycles, allow us to measure the equilibrium folding free energy from non-equilibrium pulling experiments via the so-called fluctuation relations[2] (FR). In the last part of the talk I will move the discussion to a more general level and will present a tentative but general strategy to use FRs in measurements, which we call an *inference* via the FR, inspired by our recent work on FRs in dual-trap setups[3]. Our starting point will be the following: the violation of FRs is itself an important information since it hints that we are probably missing some contribution to the entropy production. Can the extent of this violation tell us something about the missing entropy? Can we extract meaningful quantitative information from such violation? These questions are particularly interesting if a "hidden" entropy source is not directly measurable. This situation is found in many experiments, e.g. in systems with hidden degrees of freedom[4], systems with incomplete detection[5] and systems with more than one configurational variables[3].

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