Stretching biomolecules: a (non-equilibrium) statistical mechanics perspective

In recent years, single-molecule experimental techniques, such as atomic force microscopy (AFM) or laser optical tweezers (LOT) have been used to look into the elasticity of proteins and nucleic acids. The biomolecule is typically pulled from one end while the other is kept fixed, and either its length or the applied force is controlled. The typical outcome of these experiments is a force-extension curve (FEC), which gives the force needed to stretch the biomolecule as a function of its length.

To be specific, first we focus on modular proteins, which are composed of several identical domains. Their FEC shows a sawtooth behaviour under length-control: the unfolding of the different units that constitute the polyprotein is accompanied by a drop of the force. Moreover, the force at which the unfolding takes place, increases with the stretching rate. On the other hand, there are also protein domains that are composed of several stable structural units or “unfoldons”. The unfolding pathway is defined as the order and the way in which these “unfoldons” unravel, and it depends on the pulling speed. Consistently with the physical intuition, the weakest unfoldon opens first at low pulling rates. However, at higher rates, no longer is the weakest unit but the pulled one that unfolds first.

In this talk, we discuss how some key aspects of these pulling experiments can be understood by using a (non-equilibrium) statistical mechanics approach. Basically, the extension of each unit is assumed to follow an overdamped Langevin equation. First, for the analysis of the FEC, the units are independent except for the global constraint given by the length-control condition. Second, we study the unfolding pathway by taking into account the spatial structure of the molecule, which introduces crucial additional couplings among the units.

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