Abstract

Macromolecule Dynamics: from a Coarse Grain Approach to Continuum Modeling

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In this talk I consider reduced molecular dynamics simulations and a relevant coarse-grained continuum modeling. A Gó-like model (3) and a morphological descriptor (7) for the Maltose Binding Protein (MBP) are set up and their dynamical response tested.

First the focus is on the phenomenology of the transport of the molecule across a nanopore, a process usually named ‘translocation’. This part of the work is motivated by recent experiments on voltage-driven translocation of MBP, (8, 9). The effect of denaturation, namely of the degree of ‘compactness’ of the macromolecule, on the transport is investigated. Numerical results are qualitatively in compliance with the outcome of experiments and are able to reproduce a non-trivial set of phenomena, from short to long channel blockades Fig. 1 and, to some extent, bumping effects, (2).

Customarily, physical and chemical processes are summarized in low-dimensional mathematical models where only the evolution of a few order parameters is retained as it is deemed exhaustive for the complete dynamics of the system, see for example (5). In this perspective, the simplified approach discussed allows a statistical mechanical interpretation in terms of first passage time statistics of biased random walkers, (1, 10). Accordingly, umbrella sampling simulations are performed to obtain a 1D free-energy profile in a meaningful reaction coordinate that will be exploited in the mentioned theoretical framework.

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Figure 1: Stalls snapshots during translocation of a folded MBP.
Moreover, since continuum models have been just challenged, in the second part of the talk I enrich the standard 1D continuum interpretation by selecting an additional order parameter (a morphological descriptor) to take into account shape variations of the molecule while undergoing standard dynamics such as thermalization, mechanical stretching and translocation. A second-rank tensor is selected to this purpose, as suggested in (4). However, mechanics of complex materials (6) is here taken into account. Indeed a macromolecule is suitably described by such a framework: its elementary material points can be seen as the granules within a material element belonging to a granular body. The latter set is naturally embedded into the class of complex materials. Here the protein is thus thought to constitute the inner micro-structure of as a single isolated material element, without neighboring fellows. Consequently, the evolution equation for the morphological descriptor reads simply as, (11):

$$\dot{\nu} = -z_a$$

where $\nu$ is the morphological descriptor tensor and $z_a$ the inner self-action. The latter accounts for the interactions amid constituents of the macromolecule. Its identification at continuum level from information on the interactions in the discrete molecular structure is obtained by following a suggestion in (7) used for granular materials but valid in a wide range of phenomena. Essentially, the idea is to use at molecular level Cauchy-Born rule, assuming that at least portions of the molecule itself deform homogeneously. Here the whole molecule is assumed to deform this way along mechanical stretching and translocations in long pores. As we will see, such a definition poses some limitations to the suitability of the descriptor outside the homogeneous-deformation condition, while it allows a proper representation of the protein shape in constrained dynamics, Fig. 2. Therefore additional empirical definitions of the self action are compared and discussed.

Figure 2: Snapshot of molecule MBP and relevant morphological ellipsoid during a simulation of mechanical pulling.
References


