MECHANICAL UNFOLDING OF A SIMPLE MODEL PROTEIN GOES BEYOND THE REACH OF ONE-DIMENSIONAL DESCRIPTIONS

Rafael Tapia-Rojo[1], **Sergio Arregui**[1], **Juan José Mazo**[2] **and Fernando Falo**[1]

[1] *Instituto de Biocomputación y Física de Sistemas Complejos and Departamento de Materia Condensada, Universidad de Zaragoza, 50009 Zaragoza, Spain*
[2] *Instituto de Ciencia de Materiales de Aragón and Departamento de Física de la Materia Condensada, CSIC-Universidad de Zaragoza, 50009 Zaragoza, Spain*
E-mail: Rafa.T.Rojo@gmail.com

The characterization of the free energy landscape (FEL) of biomolecules has become one of the key problems in biophysics, as it allows to shed light both on their structural properties and biological function. Nonetheless, due to the great complexity of the problem, a description along a single reaction coordinate is typically considered, both in experimental and computational applications. In this work [1], we study computationally the mechanical denaturation of coarse-grained protein $BLN - 46$ [2] by analyzing its Langevin-integrated trajectories through two different approaches, which allow a comparison between the conclusions yielded by each. First, we build one dimensional free-energy profiles along two appropriate reaction coordinates. Second, we describe the configurational space of the system by using Markov-Model methods [3] and decipher the unfolding paths by applying transition-path theory [3].

Opposed to the one-dimensional profiles, the Markov description depicts a complex scenario, where unfolding takes place through more than a single pathway. In addition, the mechanical intermediate suggested in the one-dimensional profiles is found to have little role in the actual unfolding process. In this sense, we find that, even for such a simple system, one-dimensional descriptions might drive to misleading conclusions. Even more, we also suggest a rigorous analysis protocol that allows to detect systematically every macrostate visited by the molecule, defining also the routes that connect two sets of states, namely the native and stretched.

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