Cooperative force-extension behavior of bistable polymer molecules: a statistical mechanics approach

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Since the last decades, scientists can manipulate single polymer molecules. This amazing possibility allows the direct measure of very small forces and displacements, opening the way for studying the statistical mechanics of small systems. In many cases in which the thermodynamic limit is not satisfied, different macroscopic boundary conditions (i.e. constant-force or constant-displacement) may yield to different force-displacement curves. This point has a crucial impact on many experimental results [1].

Such an impact is shown to be extremely suggestive when dealing with bistable molecules, composed of a series combination of domains that can exhibit transitions between two stable states. This scenario leads from a cooperative to non-cooperative force-extension behavior of the molecule, depending on its size and the specific boundary conditions [2]. In particular, I will show that for short molecules, the domain response is non-cooperative and originates the typical "sawtooth" force-extension curve, as observed for the titin protein. On the other hand, upon increasing molecule length, the response of each domain is cooperative and results in a "plateau-like" curve, as observed for the dextran polysaccharide. Our theoretical framework provides a unified picture for such apparently contrasting experimental situations.

Finally, I will discuss the cooperative behavior of a system composed of a parallel combination of bistable domains that share two rigid points. As an important biophysical application, I will focus on the role of SNARE proteins in neurotransmission. These proteins can perform synchronized and explosive conformational changes, triggering the neurotransmission process in a millisecond time-scale. By means of a kinetic model that retains the biophysical key properties of the SNAREs bistability, we studied their stochastic dynamics and predicted the existence of a minimum time-fusion as a function of the number of SNAREs involved. We found that $N = 5 \pm 1$ is the optimal number of SNAREs required to catalyze fusion within 0.1 milliseconds [3]. This optimum is due to the intrinsic bistabilty of SNAREs and can be one of the major physiological principle governing the quick timescale of neurotransmitter release.

[1] F. Manca, S. Giordano, P. L. Palla, R. Zucca, F. Cleri, L. Colombo, *Elasticity of flexible and semi-flexible polymers with extensible bonds in the Gibbs and Helmholtz ensembles*, J. Chem. Phys. 136, 154906 (2012).
[2] F. Manca, S. Giordano, P. L. Palla, F. Cleri, L. Colombo, *Two-state theory of single-molecule stretching experiments*, Phys. Rev. E 87, 032705 (2013).
[3] F. Manca, F. Pincet, L. Truskinovsky, J.E. Rothman, L. Foret, M. Caruel, *Optimal number of SNARE proteins for fast neurotransmetter release*, to be submitted in PNAS.