Allegato A PROGETTO Scienza senza Frontiere – Brasile

Name of the doctoral program

Physics

Full degree X Cotutelle X

Title of the research activity

Unfolding and refolding proteins: inferring kinetics from structure using simple statistical physics models

Short description of the research activity

Unfolding and refolding of proteins and other biomolecules can be induced by variations of temperature, denaturant concentration, or applied force. Physical modeling of these phenomena often requires intensive computer simulation of models at different coarse-graining levels, and the availablilty of computational resources limits, often severely, the size of molecules and the time scales that can be investigated.

Here we aim to pursue an alternative, complementary research line, based on extremely simplified (down to binary variables) models from statistical physics, which use the available knowledge of the native structure of the molecules, typically in the form of a contact map. These models have already proven useful and accurate in interpreting experimental results and in describing unfolding and refolding kinetics for several molecules under different conditions, without the need of large computational resources. In particular, we have obtained many results on an Ising-like model proposed by Wako and Saito, and Munoz and Eaton: we have (i) solved exactly the equilibrium thermodynamics [1]; (ii) developed an accurate, semi-analytical approximation for the kinetics [2]; (iii) applied the model to the determination of the pathways of thermal folding and unfolding [7]; (iv) generalized the model to the mechanical unfolding problem [3], and (v) used our generalization to study pathways of mechanical unfolding and refolding [4,5,6], with remarkably good agreement with experimental results.

In the present project we plan to: (1) study the relationship between mechanical unfolding rates (and forces) and structural measures like the contact order, starting from idealized structures and then moving on to real ones, thereby extending to the problem of mechanical unfolding results which are well-established in the thermal case; (2) use residue-specific interactions to approach the protein design problem at the contact map level.

[1] P. Bruscolini and A. Pelizzola, "Exact Solution of the Munoz-Eaton Model for Protein Folding", Phys. Rev.

Lett. 88, 258101 (2002).

[2] M. Zamparo and A. Pelizzola, "Kinetics of the Wako-Saito-Munoz-Eaton model of protein folding", Phys.

Rev. Lett. 97, 068106 (2006).

[3] A. Imparato, A. Pelizzola and M. Zamparo, "Ising-Like Model for Protein Mechanical Unfolding", Phys.

Rev. Lett. 98, 148102 (2007).

[4] A. Imparato and A. Pelizzola, "Mechanical Unfolding and Refolding Pathways of Ubiquitin", Phys. Rev.

Lett. 100, 158104 (2008).

[5] A. Imparato, A. Pelizzola and M. Zamparo, "Equilibrium Properties and Force-Driven Unfolding

Pathways of RNA Molecules", Phys. Rev. Lett. 103, 188102 (2009).

[6] M. Caraglio, A. Imparato and A. Pelizzola, "Pathways of mechanical unfolding of FnIII10: Low force intermediates", J. Chem. Phys. 133, 065101 (2010).

[7] M. Faccin, P. Bruscolini and A. Pelizzola, "Analysis of the equilibrium and kinetics of the ankyrin repeat protein myotrophin", J. Chem. Phys. 134, 075102 (2011).

Scientific responsible (name, surname, role)

Alessandro Pelizzola, Associate Professor, Theoretical Physics

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Number of vacancies for XXVIII cycle (begin January 2013)

1 (one)

Specific requirements (experiences, skills)

M. Sc. degree in theoretical physics

Website of the research group (if any)

http://staff.polito.it/alessandro.pelizzola/