Selection, folding, stability, and aggregation of proteins in a water-protein coarse grain model

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Proteins are molecules made of a sequence of amino acids that fold into the native structures. Such a structure is usually stable within a certain range of temperatures and pressures, beyond which a protein denaturate. Such a phenomenon is well known at higher temperatures, where the thermal fluctuations disrupt the native conformation. However, similar phenomena are observed by decreasing the temperature or by increasing the pressure, respectively known as cold- and pressure-denaturation. Moreover, in order to guarantee the correct biological functions, proteins have evolved to have a low enough propensity to aggregate within a range of protein expression required for their biological activity, but with no margin to respond to external factors increasing/decreasing their expression/solubility.

Indeed, protein aggregation is mostly unavoidable when proteins are expressed at concentrations higher than the natural ones. Water and the hydrophobic effect play a major role in these phenomena, affecting the hydrophilic/hydrophobic composition of stable sequences, driving the folding of the proteins and contributing to their stability.

Here, using a coarse-grain model on lattice [1, 2, 3, 4, 5], which includes the protein effects on the water properties in the hydration shell and accounts explicitly for the thermodynamic properties of water, we investigate the folding [2, 3], the stability [4] and the aggregation [5] of proteins.

[1] V. Bianco, S. Iskrov, and G. Franzese, Understanding the role of hydrogen bonds in water dynamics and protein stability, J. Biol. Phys. **38**, 27-48 (2012).

[2] V. Bianco and G. Franzese, Contribution of water to pressure and cold denaturation of proteins, Phys. Rev. Lett. **115**, 108101 (2015).

[3] V. Bianco, N. Pagès-Gelabert, I. Coluzza, and G. Franzese, How the stability of a folded protein depends on interfacial water properties and residue-residue interactions, J. Mol. Liq. **245**, 129-139 (2017).

[4] V. Bianco, G. Franzese, C. Dellago, and I. Coluzza, The role of water in the selection of stable proteins in extreme thermodynamic conditions, Phys. Rev. X **7**, 021047 (2017).

[5] V. Bianco and I. Coluzza, Pathways on protein aggregation, (in preparation).