Conformational stability of globular proteins: a simple model

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The polypeptide chain of a globular protein can access a huge number of different conformations, a fundamental distinguishing property of which is their solvent-excluded volume [1]. The latter can be “measured” by the water accessible surface area, WASA, that represents the layer around the polypeptide chain where the center of water molecules cannot physically enter. There is a large WASA decrease associated with the folding of a globular protein and it leads to a large increase in the translational entropy of water molecules due to the increase in the accessible configurational space. The magnitude of this entropy gain depends upon temperature. Classic scaled particle theory calculations over the temperature range where liquid water exists at 1 atm indicate that the entropy gain of water molecules upon folding has a parabola-like temperature dependence [1]. There are two temperatures where the destabilizing contribution of the polypeptide chain conformational entropy exactly matches the stabilizing contribution of the water translational entropy, leading to cold and hot denaturation [1]. The same theoretical framework clarifies that: (a) the denaturing action of urea and GdmCl is due to their direct energetic interactions with the polypeptide chain [2]; (b) the effect of sodium salts on the coil-to-globule collapse transition of poly(N-isopropylacrylamide), a homopolymer considered to be a model of globular proteins, is mainly due to their ability to increase the density of the solution, increasing the magnitude of the solvent-excluded volume effect [3].

References