Cold denaturation

Most proteins can be thought like beady chains which form compact well-ordered coils whose surface protects the greasy-like interior from the contact with water molecules. We are studying what are the forces which keep the coil compact. We have found that if their surface has even a tiny strain between individual beads, proteins become susceptible to water molecules at low temperature and lose their ordered coiled structure. Everybody knows that proteins can be degraded by heat. A common experience is cooking an egg: after a few minutes of heating an egg above room temperature the egg white turns from a translucent jelly to a solid white substance. The change is brought upon by heat-induced degradation. Scientists call it also unfolding, because the process is similar to unravelling a ball of yarn. Proteins have a surprising property that makes them unlike many other natural objects: they can be degraded also by cooling them below room temperature. This phenomenon, called cold denaturation, has been known for several decades but is difficult to observe because degradation occurs at temperatures so low that water, the solvent of most proteins, freezes before the temperature of cold denaturation is reached.

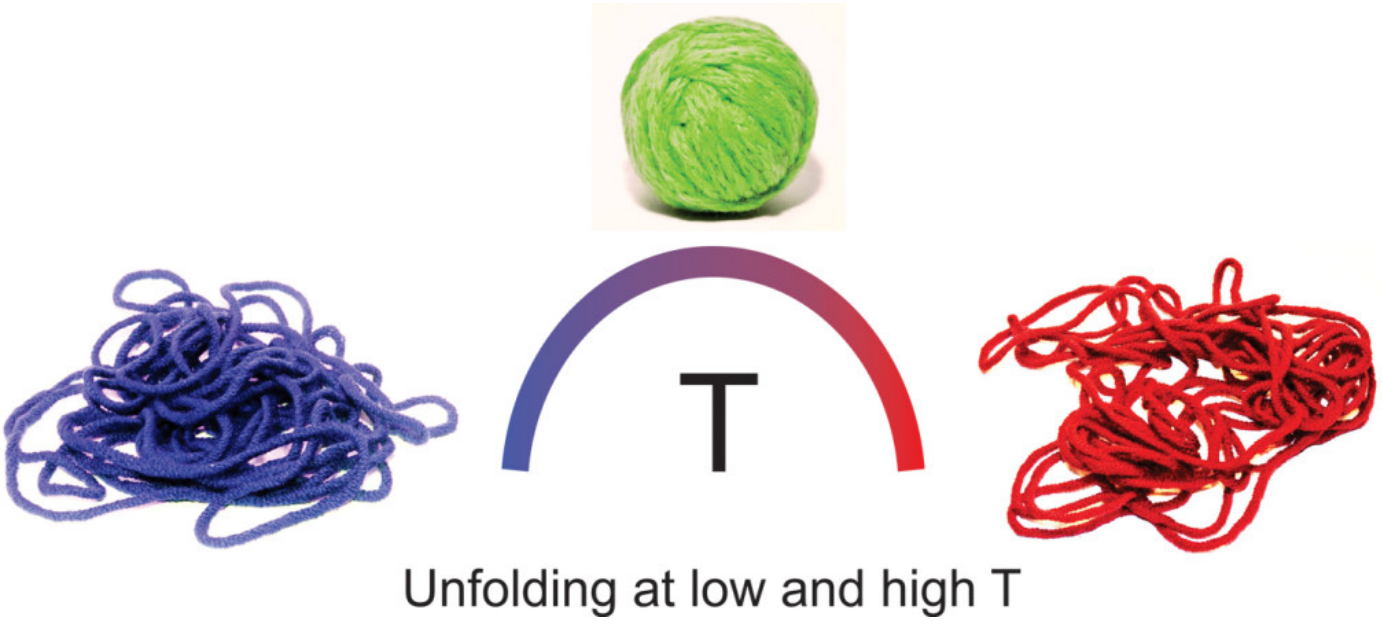

image description

We have discovered in Yeast a protein, called Yeast frataxin that can be unfolded at temperatures above the water freezing point and can thus be studied to understand the molecular causes of cold denaturation. In the present paper we have tested the hypothesis that the main cause of cold denaturation is the entrance of water molecules inside the protein (that is inside the ball of yarn). We identified a cluster of negative charges on the surface of the protein that can facilitate the entrance of water by opening a small “wound” through which water molecules can penetrate. By

neutralizing any of these charges we were able to suppress the phenomenon of cold denaturation. This finding can help protein scientists to better understand the parameters that affect protein stability, eventually helping to prevent diseases originating from protein unfolding, such as Alzheimer Disease.

Publication

Cold Denaturation Unveiled: Molecular Mechanism of the Asymmetric Unfolding of Yeast Frataxin.
Sanfelice D, Morandi E, Pastore A, Niccolai N, Temussi PA
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