SOUTENANCE de THESE
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« Thermophilic proteins: stability and function »

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BIBLIOTHEQUE

Temperature is one of the major factors governing life as demonstrated by the fine tuning of stability and activity of the molecular machinery, proteins in particular. The structural stability and activity of proteins have been often presented as equivalent. However, the thermophilic proteins are stable at ambient condition, but lack activity, the latter recovered only when the temperature increases to match that of the optimal growth condition for the hosting organism. In discussing the protein stability and activity, mechanical rigidity is often used as a relevant parameter, offering a simple and appealing explanation of both the extreme thermodynamic stability and the lack of activity at low temperature. The reality, however, illustrates the complexity of the rigidity/flexibility trade off in ensuring stability and activity through intricate thermodynamic and molecu-lar mechanisms. Here we investigate the problem by studying three study cases. These are used to relate the thermal effects on mechanical properties and the stability and activity of the proteins. For instance, we have probed the thermal activation of functional modes in EF G-domain and Lactate/Malate Dehydrogenase mesophilic and thermophilic homologues and verified a “universal” scaling of atomistic fluctuation of the Lysozyme approaching the melting in different environmental conditions. Our conclusions largely rest on an in silico approach, where Molecular Dynamics and enhanced sampling techniques are utilized, and are often complemented with Neutron Scattering Experiments.