Unravelling the mechanisms of adaptation to high pressure in proteins

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The adaptation of proteins to high pressure is still an open debate, but understanding it could shed light on the origins of life [1], lead to a better understanding of protein dynamics, and deliver new tools to engineer pressure-resistant enzymes for biotechnological purposes. While the thermodynamic and dynamical properties of model proteins under pressure have been extensively studied [2], the evolutionary aspects of their adaptation are still unclear.
Disentangling the contributions of pressure adaptation from those of another adaptation, such as high or low temperature, is a difficult task. In fact, genomic studies could not determine a clear pattern among the order of Thermococcales.
Recent experiments by our group focused on whole cells of two closely related species (*Thermococcus barophilus*, Tba, and *Thermococcus kodakarensis*, Tko) that grow at the same optimal temperature (85°C) but differ only for the optimum pressure (400 bar for Tba, 1 bar for Tko), and they highlighted the differences in the dynamics of the two organisms' proteomes [3]. To take this investigation to the molecular level, we studied the *Phosphomannose Isomerase* and the *Ribosomal protein S24e* from the two organisms with Elastic and Quasi-elastic Incoherent Neutron Scattering, 2-D NMR Spectroscopy, X-ray crystallography and Molecular Dynamics Simulations. Our results evidence that the substitutions of amino acids enhancing pressure stability are those in the hydrophobic core, which eliminate cavities, and those on the surface, which modulate the interaction of the proteins with the surrounding water layer and give them the right flexibility to perform their function under high pressure (fig. 1). Therefore, the study of the dynamics of these proteins enabled us to gain detailed structural information, to describe their behaviour under extreme conditions and characterize their adaptation.

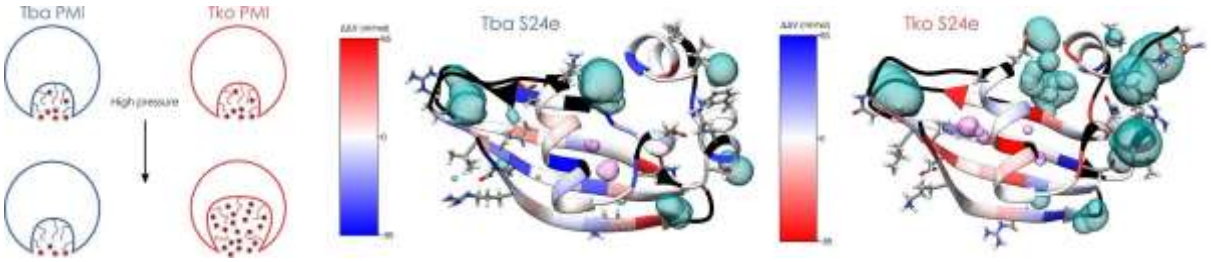

Figure 1: Left, a summary of the EINS and QENS results about the effects of high pressure on Tba PMI and Tko PMI. Center and right, residue-specific difference of denaturation volume (ΔΔV) between Tba S24e and Tko S24e as measured by 2-D NMR, represented as the colour of the ribbon. Internal cavities are represented in magenta, while solvent-accessible cavities are in cyan.

References

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