Pressure-based mapping of protein conformational landscapes

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Proteins are dynamic molecules. They undergo conformational transitions on multiple timescales, populating low lying excited states, partially folded states and the unfolded ensemble. These high energy conformers can play important roles in protein function, post-translational modification, turnover and aggregation. Given their implication in protein function and homeostasis, it is of interest to characterize the structural and energetic properties of these states. We have used a combination of high pressure and many biophysical techniques, including multi-dimensional NMR, small angle x-ray scattering (SAXS), FTIR, fluorescence, pressure perturbation calorimetry (PPC) and structure based simulations, to map protein folding landscapes. It is likely that the structures and relative stabilities of these states have been subject to evolutionary pressure. Over 80% of the Earth's microbial biomass lives at high pressures. To begin to understand the molecular basis for life in extreme environments, we have also probed the effects of pressure on protein interactions in living bacteria using advanced fluorescence microscopy methods.