Pressure? What a strange idea! Why would I do that?





Protein folding and conformational landscapes





The molar volume of proteins

$$\Delta V_{F-U} = \Delta V_{vF-U} + n_s (V_{sb} - V_{sp})$$

Solvent excluded voids in the folded state

Depends on packing efficiency

Non-uniformly distributed

n, solvent molecules move from the bulk to interact with U

Any changes in solvent density between the bulk and the protein would lead to a change in volume



Electrostriction of charges provides a negative contribution to the value of ΔV (un)folding

But only for buried charged or ionisable groups, of which there are few



Average difference = - 24 +/- 6 ml/mol



ΔV (un)folding correlates strongly internal cavities

T4 lysozyme

variants



Ando et al. Biochemistrv 2008









High Pressure NMR on a repeat protein reveals deviation from 2-state unfolding





Folding landscape from structure-based simulations constrained by the NMR data



Configurations are clustered and rebuilt to an all atom model



Explore how mutations affect conformational landscapes



P-jump kinetics to probe effects of mutations on folding rates and routes





Roche et al, JACS 2013



Pressure disrupts domain and subunit interactions



Silva, Foguel & Royer TiBS, 2001



Pressure perturbs RNA structures too

RNA folding intermediates





Lipid phases are strongly dependent on pressure



So et al 1993, Phys. Rev. Lett

Pressure perturbs protein LLPS transitions in unexpected ways



Cinar, ...Chan, Winter Chemistry: A Eur. J., 2019



Pressure disrupts the ParA/B condenstates of E. coli in vivo

A ParB-HU at 0.1 MPa



B ParB-HU at 100 MPa



C ParB-HU back 0.1 MPa



>80% of the microbial biomass on Earth lives at high pressure



What are the sequence determinants of biomolecular function in the deep biosphere?

Extreme Biophysics Research Coordination Network: Exploring the molecular limits of life





SAXS