

Title

Protein Dimer Stability in Concentrated Solutions of Sugar Polymers

Abstract:

Synthetic polymer solutions at concentrations of hundreds of grams per liter are used to stabilize proteins and mimic the crowded intracellular environment.¹ Several theories have been developed to explain the stabilizing effect of crowding, but almost all assume only contributions from hard (steric) contacts, ignoring soft (enthalpic) chemical interactions. We quantified the effects of the synthetic sugar-polymers, dextran and Ficoll™, as well as their monomers (sucrose and glucose, respectively), on two homodimer variants of the B1 binding domain of streptococcal protein G.^{2,3} One dimer forms *via* domain swapping, while the other involves simple side-by-side dimerization. The dimers are fluorine labeled to facilitate detection using ¹⁹F nuclear magnetic resonance spectroscopy. We measured the amounts of dimer and monomer as a function of temperature, cosolute size and cosolute concentration, allowing quantification of the stability (i.e., free energy), enthalpy, and entropy of dissociation. The cosolutes increase dimer stability and affect the enthalpy. We analyze the data using a recently developed, more inclusive protein crowding model.⁴

References

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