Abstract Submitted
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Concentrated dispersions of equilibrium protein nanoclusters that reversibly dissociate into active monomers[1] THOMAS M. TRUSKETT, KEITH JOHNSTON, JENNIFER MAYNARD, AMEYA BORWANKAR, MARIA MILLER, BRIAN WILSON, AILEEN DININ, TARIK KHAN, KEVIN KACZOROWSKI, The University of Texas at Austin — Stabilizing concentrated protein solutions is of wide interest in drug delivery. However, a major challenge is how to reliably formulate concentrated, low viscosity (i.e., syringeable) solutions of biologically active proteins. Unfortunately, proteins typically undergo irreversible aggregation at intermediate concentrations of 100-200 mg/ml. In this talk, I describe how they can effectively avoid these intermediate concentrations by reversibly assembling into nanoclusters. Nanocluster assembly is achieved by balancing short-ranged, cosolute-induced attractions with weak, longer-ranger electrostatic repulsions near the isoelectric point. Theory predicts that native proteins are stabilized by a self-crowding mechanism within the concentrated environment of the nanoclusters, while weak cluster-cluster interactions can result in colloidally-stable dispersions with moderate viscosities. I present experimental results where this strategy is used to create concentrated antibody dispersions (up to 260 mg/ml) comprising nanoclusters of proteins [monoclonal antibody 1B7, polyclonal sheep Immunoglobin G and bovine serum albumin], which upon dilution in vitro or administration in vivo, are conformationally stable and retain activity.

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