

Physical Sciences: Chemistry

Biological Sciences: Biochemistry

Control of protein crystal nucleation around the metastable liquid-liquid phase boundary

Oleg Galkin,

Center for Microgravity and Materials Research, University of Alabama in Huntsville, Huntsville, AL 35899, USA

Peter G. Vekilov,

Department of Chemistry and Center for Microgravity and Materials Research, University of Alabama in Huntsville, Huntsville, AL 35899, USA

Abstract

The capability to enhance or suppress the nucleation of protein crystals opens opportunities in various fundamental and applied areas, including protein crystallography, production of protein crystalline pharmaceuticals, protein separation, and treatment of protein condensation diseases. Here we show that the rate of homogeneous nucleation of lysozyme crystals passes through a maximum in the vicinity of the liquid-liquid phase boundary hidden below the liquidus (solubility) line in the phase diagram of the protein solution. We found that glycerol and polyethylene glycol (PEG) (that do not specifically bind to proteins) shift this phase boundary and significantly suppress or enhance the crystal nucleation rates, although no simple correlation exists between the action of PEG on the phase diagram and the nucleation kinetics. The control mechanism does not require changes in the protein concentration, acidity and ionicity of the solution. The effects of the two additives on the phase diagram strongly depend on their concentration and this provides opportunities for further tuning of nucleation rates.