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Metastable Amyloid Phases and their Conversion to Mature Fibrils MARTIN MUSCHOL, TATIANA MITI, MENTOR MULAJ, Dept. of Physics, University of South Florida, Tampa FL 33620, JEREMY SCHMIT, Dept. of Physics, Kansas State University, Manhattan, KS 66506 — Self-assembly of proteins into amyloid fibrils plays a key role in both functional biological responses and pathogenic disorders which include Alzheimers disease and type II diabetes. Amyloid fibril assembly frequently generates compact oligomeric and curvilinear polymeric intermediates which are implicated to be toxic to cells. Yet, the relation between these early-stage oligomeric aggregates and late-stage rigid fibrils, which are the hallmark structure of amyloid plaques, has remained unclear. Our measurements indicate that lysozyme amyloid oligomers and their curvilinear fibrils only form after crossing a salt and protein concentration dependent threshold. These oligomeric aggregates are structurally distinct from rigid fibrils and are metastable against nucleation and growth of rigid fibrils. Our experimental transition boundaries match well with colloidal model predictions accounting for salt-modulated charge repulsion. We also report our preliminary findings on the mechanism by which these metastable oligomeric phases are converted into stable amyloid fibrils.

Martin Muschol
Dept. of Physics, University of South Florida, Tampa FL 33620

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