

**Normal-to-Amyloid-protein transition, and reversible pre-fibril fold/unfold process, in lysozyme and lactalbumin.**

Nolene Byrne and C. Austen Angell  
Dept. of Chemistry and Biochemistry,  
Arizona State University, Tempe AZ 85287.

Starting from the observation that proteins enjoy an increase in stability against hydrolytic decay and aggregation when dissolved in “ionic liquid” media of appropriate proton activity, we have explored the consequences of deliberate excursions away from the stable zone. We find, for both lysozyme and lactalbumin, surprising thermal events on the acid side of the stable zone. Under conditions in which these proteins are partially or fully denatured at ambient temperature they suddenly, during heating, reorganize with release of an energy that is larger, by a factor of three, than the normal folding energy. The product of this exothermic process, which exhibits longer term stages, proves to be an amyloid entity *that remains in solution*. This new species is found to be in a metastable state in which it can be unfolded and refolded multiple times before finally, on a time scale that depends on the temperature, it fibrillizes to give insoluble materials that are very similar in electron microscope appearance to those produced in previous studies of prion protein fibrillization. In the early stages, globular entities connect and the connections then thicken to give uniform dimension fibrils throughout. The features that are in common with fibrils produced from lysozyme in previous work, using alcohol or other fibrilizing agents, will be discussed - as will be the reverse process, fibril dissolution.