**ABSTRACT:** Although the critical causative proteins for more than 20 amyloid diseases have been identified, the process and mechanism by which these proteins induce disease are unknown. What is known is that these proteins are converted to cross-β-sheet rich fibril structures called amyloid fibrils. For over 100 years, the presence of these fibrils in brain tissue has been associated with disease (i.e. Alzheimer’s). As a result, there is a great need to study the thermodynamic, kinetic and toxic properties of the oligomer-fiber transition. We chose human insulin as a model amyloid protein for this *in vitro* study because it is an amyloid protein, it forms fibrils in ~3 h at pH 1.6 and 65 C, exhibits the usual sigmoidal fibril growth curve, and has been widely used by others. We are interested mainly in both the kinetics and the structural conversion process of native insulin to fibrils and the dissolution of preformed fibrils in order to isolate, purify and identify the toxic species. Hence, we probe the so-called nucleation process for converting a native folded protein to a β-sheet rich amyloid fibril and the reverse process. Using a rigorous mechanistic reaction model that incorporates the physical chemistry of nucleation and fibril growth dynamics, we show that the rate constants for nucleation are ~10 million times smaller than those for fibril growth (Lee et al. 2007). During lag phase and prior to the formation of fibrils, we provide, using small angle neutron scattering, consistent evidence of the composition of the insulin nucleus that comprised three dimers or six monomers (Nayak et al. 2009) and it was likely asymmetric polytetrahedron rather than symmetric octahedron (Meng et al. 2010). Cooling during the lag phase prior to the onset of fibril formation indicated that the oligomers changed linearly with time and that fibril growth was slowed at the expense of producing more nuclei (Sorci et al. 2009). Recently, we have isolated toxic and non-toxic oligomers from fibril dissolution experiments (Heldt et al. 2011). Also, using the final fibril length distribution, we back-calculate for the first time the initial nuclei concentration to be in the range of 20-200 pM (Sorci et al. 2010). This very low concentration of monomers, dimers and trimers could explain the difficulty in isolating, detecting and blocking oligomers or nuclei toxicity and the long onset time for amyloid diseases (Pease et al. 2010).