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Session Title: Platform AI: Protein Assemblies and Aggregates

Presentation Number: 1509-Plat

Abstract Title: A Mathematical Model of Amyloid Fibrillation: The Case for Insulin

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Topic: 1K Protein Assemblies & Aggregates

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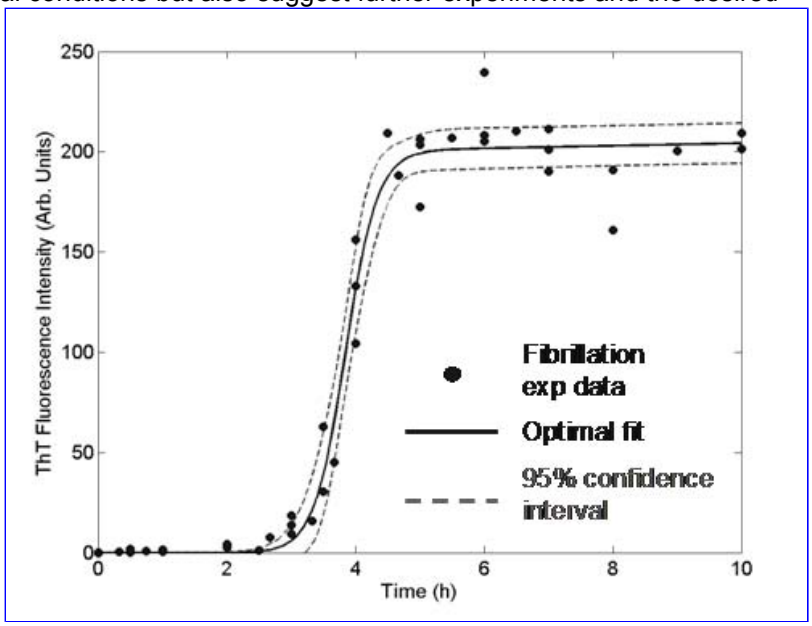
Amyloid fibrillation is the progress of native soluble proteins converting to amyloid fibrils rich in β-sheet and is associated with various physiological disorders. Insulin fibrillation was chosen as our case study because of its importance in understanding injection-localized amyloidosis and in preventing fibril formation during large scale recombinant insulin manufacturing. This paper describes the development of a new mathematical model of insulin fibrillation that incorporates the physics and chemistry of nucleation, coagulation and growth dynamics. The basic kinetic model consists of three steps -- natural insulin dissociation, nucleation, and fibril elongation. Predictions of the kinetic model were compared against Thioflavin T (ThT) measurements. A non-linear least squares algorithm was used to estimate the kinetic rate constants and the associated statistics of the parameter values. The model was applied to study several critical factors that affect fibrillation kinetics including: initial concentration, seeding, and agitation. The simulation results not only reproduced the observed fibril formation dynamics over a wide range of experimental conditions but also suggest further experiments and the desired properties of potential fibrillation inhibitors.



Simulated and measured response of insulin fibrillation

Commercial Relationship: **C. Lee**, None; **A. Nayak**, None; **G. Belfort**, None; **G.J. McRae**, None.