

P.45 Inherent variability in the kinetics of autocatalytic protein self-assembly

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The self-assembly of protein molecules into amyloid fibrils is associated with many degenerative diseases [1], but also presents potential opportunities for the development of new materials [2]. Kinetic experiments present an important tool in unravelling the mechanisms of filamentous protein self-assembly, yet replicate experiments often show significant variability [3-5], which is not accounted for in deterministic models [2, 6, 7]. Here, we introduce a stochastic model for autocatalytic filamentous protein self-assembly that includes primary nucleation, irreversible filament elongation and autocatalysis via fragmentation (see Fig. 1). Our main result is a prediction for the full distribution of lag times arising from intrinsic molecular noise, which we compare with experimental results for the aggregation of bovine insulin (see Fig. 1). Our findings show that stochastic effects cannot be neglected in small volumes, which are of most interest as they are comparable to the volume of a human cell.

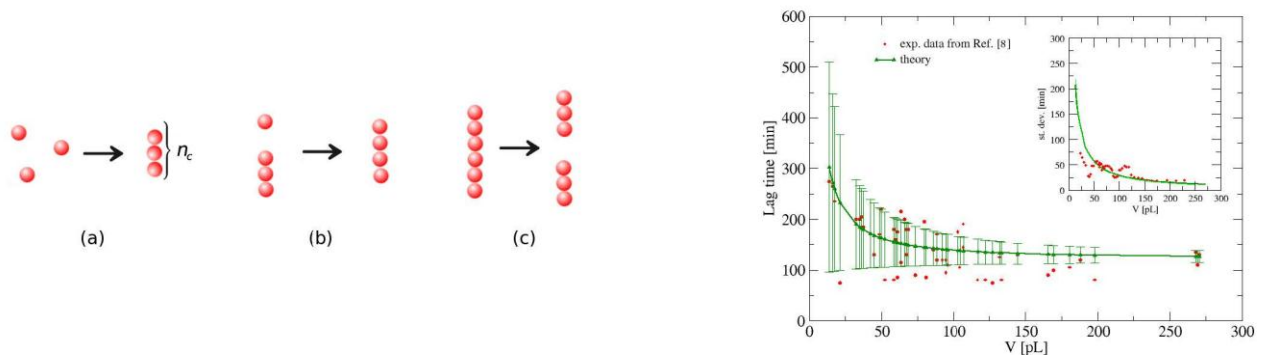


FIG. 1: Left: Schematic illustration of: (a) primary nucleation, (b) elongation via polymerization and (c) fragmentation. Critical nucleus size for primary nucleation is denoted by n_c . Right: Theoretical prediction for the mean lag time in small volume samples (with standard deviation as error bars), compared to the experimental data from Ref. [8]. Inset: Volume dependence of standard deviation as predicted from the stochastic model, compared to experimental results from Ref. [8].

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