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Size distribution of amyloid fibrils. Mathematical models and experimental data.

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Abstract

More than twenty types of proteins can adopt misfolded conformations, which can co-aggregate into amyloid fibrils, and are related to pathologies such as Alzheimer’s disease. This article surveys mathematical models for aggregation chain reactions, and discuss the ability to use them to understand amyloid distributions. Numerous reactions have been proposed to play a role in their aggregation kinetics, though the relative importance of each reaction in vivo is unclear: these include activation steps, with nucleation compared to initiation, disaggregation steps, with depolymerization compared to fragmentation, and additional processes such as filament coalescence or secondary nucleation. We have statistically analysed the shape of the size distribution of prion fibrils, with the specific example of truncated data due to the experimental technique (electron microscopy). A model of polymerization and depolymerization succeeds in explaining this distribution. It is a very plausible scheme though, as evidenced in the review of other mathematical models, other types of reactions could also give rise to the same type of distributions.

Keywords: protein aggregation; PrP fiber; Becker-Döring system; statistical test; kernel density estimation.

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