Size distribution of amyloid brils. Mathematical models and experimental data.
Stephanie Prigent, Hadjer Wafaa Haffaf, H. T. Banks, M. Hoffmann, Human Rezaei, Marie Doumic

To cite this version:

HAL Id: hal-00958785
https://hal.sorbonne-universite.fr/hal-00958785v2
Submitted on 7 Jul 2014

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L’archive ouverte pluridisciplinaire HAL, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d’enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.
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 discusses 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.

1Inria, Institut National de Recherche en Informatique et Automatique, Rocquencourt, France, and Pierre et Marie Curie University, Paris-Diderot University, CNRS UMR 7598, Paris, France.
2Corresponding authors. Email: S.prigent@hotmail.com, marie.doumic@inria.fr.
3Center for Research in Scientific Computation (CRSC), North Carolina State University, Raleigh, N.C., USA
4CEREMADE (Centre de REcherche en MAthmatique de la DEcision), CNRS-UMR 7534 and CREST, University Paris-Dauphine, Paris, France
5Institut National de Recherche Agronomique, Jouy-en-Josas, France