Modelling protein aggregation: results and open questions

Marie Doumic
Inria, Paris, France
marie.doumic@inria.fr

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Mathematical modelling of protein polymerisation is a challenging topic, with wide applications, from actin filaments in myocytes (muscle tissues) to the so-called amyloid diseases (e.g. Alzheimer's, Parkinson's or Creuzfeldt-Jakob's diseases). In this talk, we will give an overview of recent results for both deterministic and stochastic approaches, envisaged as giving complementary insights on the still largely mysterious intrinsic mechanisms of polymerisation. We focus on nucleation-polymerisation-fragmentation processes taken in an homogeneous spatial environment, so that the equations are structured by the aggregates size, without a space variable.

Two main kind of problems are envisaged.

The first kind of problems is the study of the qualitative behaviour of the aggregates: for example their long-time asymptotics, or yet how oscillatory behaviours can emerge. We call them "direct problems"; they can consist in the study of finite or infinite differential systems, partial differential equations analysis, or stochastic processes. They are then qualitatively compared with experimental data, in order to get qualitative understandings of the dominant reactions. We shall give an overview of recent results and focus on the long-time asymptotics, to investigate under which assumptions a steady behaviour can emerge.

A second kind of problems consists in the quantitative comparison between model and data: reaction rates estimation, initial state estimation, model selection, nonparametric estimation of functional parameters. We call them "inverse problems". We have developed either a systematic data assimilation approach, able to be adapted to a very wide variety of models, in parallel with specific ad hoc methods, in particular for the estimation of fragmentation rate and kernel in the framework of growth-fragmentation equations.

References

[1] J. Calvo, M. Doumic, B. Perthame,*Long-time asymptotics for polymerization models*, Communications in Mathematical Physics, accepted, 2018.

[2] M. Doumic, M. Escobedo, M. Tournus, *Estimating the division rate and kernel in the fragmentation equation*, Annal. Non Lin. IHP Series C, accepted, 2018.

[3] M. Doumic, K. Fellner, M. Mézache, H. Rezaei, *An oscillatory kinetic model for the Prion aggregation process*, in progress.

[4] M. B. David, M. Tournus, R. Marchante, T. Purton, D P. Smith, M. F. Tuite, M. Doumic, W-F. Xue, *The division of amyloid fibrils*, in progress.

[5] M. Doumic, S. Eugène, P. Robert, *Asymptotics of Stochastic Protein Assembly Models*, SIAM Appl. Math. **76 (6)**, 2016.

[6] S. Eugène, W.F. Xue, P. Robert, M. Doumic, *Insights into the variability of nucleated amyloid polymerization by a minimalistic model of stochastic protein assembly*, Journal of Chemical Physics **144 (17)**, 2016.

[7] A. Armiento, P. Moireau, Davy Martin, M. Doumic, H. Rezaei, *The mechanism of monomer transfer between two structurally distinct PrP oligomers*, PLoS One **12 (7)**, 2017.

[8] A. Armiento, M. Doumic, P. Moireau, H. Rezaei, *Estimation from Moments Measurements for Amyloid Depolymerisation*, J. Theor. Biol., 2016.

[9] H. T. Banks, M. Doumic, C. Kruse , *A numerical scheme for the early steps of nucleation-aggregation Models*, Journal of Mathematical Biology, **74 (1-2)**, 259–287, 2017.