

Simulation of the Kinetics and Inverse Problem for the Protein Polymerization in Amyloid Diseases (Prion, Alzheimer's)

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Principal Investigators

Institution

Contact information of lead PI

Country

European Commission

Title of project or programme

Simulation of the Kinetics and Inverse Problem for the Protein Polymerization in Amyloid Diseases (Prion, Alzheimer's)

Source of funding information

European Commission FP7-Seventh Framework Programme

Total sum awarded (Euro)

€ 1,203,569

Start date of award

01/12/2012

Total duration of award in years

5.0

The project/programme is most relevant to:

Alzheimer's disease & other dementias|Prion disease

Keywords

Research Abstract

Amyloid diseases are of increasing concern in our aging society. These diseases all involve the aggregation of misfolded proteins, called amyloid, which are specific for each disease (PrP for Prion, Aβ for Alzheimer's). When misfolded these proteins propagate the abnormal configuration and aggregate to others, forming very long polymers also called fibrils. Elucidating the intrinsic mechanisms of these chain reactions is a major challenge of molecular biology: do polymers break or coalesce? Do specific sizes polymerize faster? What is the size of the so-called nucleus, i.e., the minimum stable size for polymers? On which part of the reactions

should a treatment focus to arrest the disease ? Up to now, only very partial and partially justified answers have been provided. This is mainly due to the extremely high complexity of the considered processes, which may possibly involve an infinite number of species and reactions (and thus, an infinite system of equations).

The great challenge of this project is to design new mathematical methods in order to model fibril reactions, analyse experimental data, help the biologists to discover the key mechanisms of polymerization in these diseases, predict the effects of new therapies.

Our approach is based on a new mathematical model which consists in the nonlinear coupling of a size-structured Partial Differential Equation (PDE) of fragmentation-coalescence type, with a small number of Ordinary Differential Equations.

On the one hand, we shall solve new and broad mathematical issues, in the fields of PDE analysis, numerical analysis and statistics. These problems are mathematically challenging and have a wide field of applications. On the other hand we want to test their efficacy on real data, thanks to an already well-established collaboration with a team of biophysicists. With such a continuing comparison with experiments, we aim at constantly aligning our mathematical problems to biological concerns.

Lay Summary

Further information available at:

Types:

Investments > €500k

Member States:

European Commission

Diseases:

Alzheimer's disease & other dementias, Prion disease

Years:

2016

Database Categories:

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