Analysis of spatial patterns formed during Prion dissemination in cerebellar tissue.

Katarzyna Adamczyk* Florence Hubert† Angélique Igel‡ Mathieu Mezache*

Motivation : Prion diseases occur when normal proteins, found on the surface of cells, change conformation and start aggregating in the brain, causing brain damage. This abnormal accumulation of protein in the brain can cause memory impairment, personality changes, difficulties with movement , etc. The relationship between protein aggregation processes and the degradation of the central nervous system is still poorly understood and is likely to involve a multitude of factors.

Recent in vitro experiments on Prion dissemination in neuronal organoids show patterns corresponding to specific spatial distributions of prion fibrils. The mechanisms behind the patterns are likely to involve multi-scale processes: at the molecular level, the kinetics of Prion assemblies are driven by polymerization/depolymerization processes involving different subassemblies [1]. At the cellular level, the interactions between neurons and Prion assemblies drive the growth in density and the diffusion of Prion fibrils [2]. At the macroscopic level, the accumulation of fibrils affects the functional neuronal connectome and the connectome in turn affects the replication and dissemination of Prion fibrils.

Expected work : The main objective of this project is to build and study a mathematical model that formalizes the Prion replication/tissue spreading processes into a reaction-diffusion system. A second objective is to quantitatively characterize observed spatial patterns and extract summary statistics from them [3]. Once the model has been built and the experimental data have been carefully analysed, calibration of the model with experimental data will enable the modelling to be validated and in silico hypotheses to be explored. The numerical study of the model will then help to identify key features in order to understand the pattern formation.

Working environment : The work will take place in laboratory MaIAGE and laboratory VIM (Virology and Molecular Immunology) of Inrae institute in Jouy-en-Josas. The project will be supervised by Katarzyna Adamczyk, Florence Hubert and Mathieu Mezache. Regular contacts with the consortium partners (Angélique Igel and other members of the VIM unit) are planned. Within MaIAGE, the candidate will have access to the Migale bioinformatics platform, with a computer cluster. The internship can start on February or March 2026 and lasts 6 months. The salary is 4.35 euros per hour.

Keywords : Mathematical modelling, Spatial point processes, Reaction-diffusion equation, Prion diseases
Desired Profile : The candidate must be enrolled in an M2 program (or equivalent) in Applied Mathematics. A strong interest in mathematical modelling and partial differential equations is advised, as well as basic knowledge of statistics (parameters estimation, hypothesis testing, etc). Programming skills in Python, R or another scientific computing language are also essential.
Contacts : Katarzyna Adamczyk, Florence Hubert, Mathieu Mezache
e-mail : katarzyna.Adamczyk@inrae.fr, florence.hubert@univ-amu.fr, mathieu.mezache@inrae.fr

References

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*Université Paris-Saclay, INRAE, MaIAGE, Jouy-en-Josas, France
†Aix Marseille Univ, CNRS, Centrale Marseille, I2M, Marseille, France
‡Université Paris-Saclay, INRAE, VIM, Jouy-en-Josas, France