

CEMRACS PROJECT PROPOSAL

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Title: Mathematical modelling of cell aggregation and segregation

Description:

The organisation of biological tissues during development is accompanied by the formation of sharp borders between distinct cell populations. During the morphogenesis of numerous tissues/organs, cells of the same type regroup into regions, despite the potential for extensive intermingling due to cell intercalation and the intrinsic motility of some cell types. Usually, borders are initially imprecise, and then become sharpened to form a flat interface. One key mechanism by which border formation is achieved is through the segregation of the cell populations from each other, and concomitant restriction of intermingling across the interface. The maintenance of this cell segregation is key in adult tissue homeostasis, and its disruption can lead tumor cells to spread and form metastasis. Therefore, it is of tremendous importance to understand the underlying mechanisms of cell segregation. It is now widely accepted that cell segregation is due to three main mechanisms, namely adhesion, de-adhesion and repulsion.

Several models have been proposed for cell segregation. Usually, agent-based models are preferred due to their simplicity and flexibility. However their mathematical analysis remains limited due to a lack of theoretical framework. Macroscopic (continuous) models have the advantage to offer a mathematical framework to link the solutions to the model parameters. The goal of this project is to theoretically and numerically analyse models to study the role of each phenomena (adhesion, de-adhesion and/or repulsion) in the formation of cell aggregates. According to the students background and motivation, the following possible routes can be considered :

- Develop numerical methods to study a macroscopic model obtained by formal coarse-graining of a two-species microscopic model for cells interacting via a dynamical network of links [1] (cell-cell repulsion). The numerical analysis will either focus on comparing the micro- and macro- formulations, either aim at confronting the model to experimental data that will be provided.
- Investigate possible ways to enrich an existing continuous model of Keller-Segel type (chemotaxis) that has been introduced in [2] and show cell aggregation, by for instance adding cell-cell adhesion interactions. A numerical analysis and comparison with experimental data will be considered

[1] J. Barré, P. Degond, A. Khuong, D. Peurichard, E. Zatorska, A two-species macroscopic model for cell segregation and border sharpening by Eph receptor ephrin-mediated repulsion, in preparation

[2] L. Almeida, F. Bubba, B. Perthame, C. Pouchol, Energy and discretization of the Fokker-Planck and Keller-Segel equations, in preparation