Moving boundary problems for multicellular dynamics

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Biomathematical background

PDE-based models are well-suited for describing the dynamics of structured populations in a compact way. Moving or free-boundary problems arise naturally from multicellular morphogenetic processes, where cell proliferation and mechanical forces interplay to shape developing, renewing or growing tissues. The moving boundary can be interpreted as the external boundary of a compact cell aggregate with its surrounding cells/medium, like free-boundary problems in avascular tumor growth (*e.g.* [11]), or as the interface between several phases in multi-phasic or multi-species problem involving for instance cellular structures embedded in fluid dynamics as encountered in biofilms (*e.g.* [3]), or multiphase models of tumor growth [1]. The equations underlying these biomathematical models typically share common features with the porous medium equation [7], and are formulated as nonlinear advection-reaction PDEs, where the velocity speed of each phase is derived either from simple standard physical laws (e.g. Darcy's law), possibly treating cell populations as an incompressible fluid, or from more elaborate, dedicated behavior laws derived from the balance of mechanical forces (*e.g.* [10]).
In our team, we more specifically encounter such issues in the context of developmental biology (development of ovarian follicles [5, 6] or of cerebral cortex [8]).
In collaboration with Erwan Hingant (LAMFA, Université de Picardie) and Magali Ribot (IDP, Université d'Orléans), we have been designing and analyzing a porous-medium like equation to study the growth of terminally developing ovarian follicles. Ovarian follicles consist of a germ cell, the oocyte (the future female gamete) and populations of somatic cells. Follicle growth first involves an increase in the oocyte diameter coupled with cell proliferation, building a multi-layered spheroid centered on the oocyte. Then, a critical transition occurs to the antral stage, when a fluid-filled cavity (the antrum) is formed within the mass of somatic cells, resulting in symmetry breaking and oocyte eccentricity.

Working plan

The model represents the growth of an antral-like structure in a simplified geometry with spheric symmetry (two nested spheres), to capture the double moving boundary problem associated with antral follicle growth, i.e. the inflation of the cavity (inner moving boundary), which eventually occupies most of the follicle volume, and the increase in the follicle diameter (outer moving boundary, delimited by the cell wall). The unknown represents the spatial density of cells in between the boundaries. The depth of the cell wall varies according to the balance between antrum growth and cell proliferation. Hence, the cell density function has a time-varying support; the cell wall can either expand or shrink, and might also be subject to oscillations as observed in the embryo blastocyst [9].
We have formulated the model in a simplified 1D geometry, proved the wellposedness, and checked that the model behavior captures the most salient features of antral growth. The postdoc work will first consist in extending the theoretical results to the 3D formulation. In parallel, the postdoc

fellowship will develop appropriate numerical schemes, ensuring both mass conservation and accurate location of the boundaries, implement numerical simulations and roughly calibrate the model parameters to operate in a realistic regimen, thanks to datasets monitoring the size of growing follicles. The final step will consist in adapting the model formulation to a more realistic geometry, for instance using the coordinates introduced in [4].

Formation and kills

Ph.D in Applied Mathematics, with expert knowledge in the theoretical and numerical analysis of PDEs.
Motivation for biological applications and work in an interdisciplinary context.

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