

# MAFELAP 2019 abstracts for the mini-symposium Analysis and simulations of coupled-bulk-surface PDES with applications to Biology

**Organisers: Anotida Madzvamuse and Fred Vermolen**

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# FINITE ELEMENT SIMULATIONS AND TRACTION FORCE MICROSCOPY INVERSE PROBLEMS

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Traction force microscopy measures the deformation of the substrate when a cell migrates. The inverse problem—the recovery of the force applied by the cell—can be solved directly for a linear elastic substrate, but presents more difficulties in complex media.

We present a Bayesian approach to solve the inverse problem in traction force motility by means of a finite element approximation of the forward problem and a parallel Markov Chain Monte Carlo method. We use a linear elasticity model as a benchmark for the method, but our approach is readily applicable to more complex substrates, such as anisotropic media and three-dimensional cell migration.

In order to validate the results, we use an experimental dataset that includes not only the substrate deformation but also the focal adhesions. We solve the inverse problem using only the substrate deformation information, and we verify the result by comparing the recovered force with the location of the focal adhesions.

As an example of the application of this results, we use a simple coupled-bulk-surface model to predict the direction of migration of the cell when the force is known.

# A COUPLED BULK-SURFACE MODEL FOR CELL POLARISATION

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Cell polarisation is the result of intricate networks of biochemical reactions. Recent work on balancing biological complexity with mathematical tractability resulted in the proposal and formulation of a famous minimal model for cell polarisation by [2], known as the wave pinning model. In this talk, we present a three-dimensional generalisation of this mathematical framework through the maturing theory of coupled bulk-surface semilinear partial differential equations in which protein compartmentalisation becomes natural [1]. We show how a local perturbation over the surface can trigger propagating reactions, eventually stopped in a stable profile by the interplay with the bulk component. We present the bulk-surface finite element method which is used to generate numerical simulations over simple and complex geometries, showing pattern formation due to propagation and pinning dynamics. From the mathematical point of view, of the interesting features of the model regards its long time behavior. This will be shown with some explicative and novel simulations over different three-dimensional geometries. The generality of our mathematical and computational framework allows to study more complex biochemical reactions and biomechanical properties associated with cell polarisation in multi-dimensions.

## References

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# VIRTUAL ELEMENT METHOD FOR ELLIPTIC AND PARABOLIC BULK-SURFACE PDES IN TWO DIMENSIONS

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We present a novel method for the numerical approximation of elliptic and parabolic bulk-surface PDEs in two dimensions. To the best of the authors’ knowledge, the proposed method is the first application of the Virtual Element Method [1] to bulk-surface PDEs. The method is based on the discretisation of the bulk into polygonal elements with arbitrarily many edges, rather than just triangles. The bulk-surface finite element method on triangular meshes [2] is a special case of the proposed method. The advantage is twofold. First, we show that the ability of the new method of handling general polygons can be exploited to reduce the computational complexity of matrix assembly. Second, we introduce an optimised matrix implementation that can be also exploited in the pre-existing special case of bulk-surface finite elements on triangular meshes [2]. Numerical examples illustrate our findings and experimentally show the optimal convergence rate in space and time.

## References

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# A MOVING GRID FINITE ELEMENT METHOD APPLIED TO A MECHANOBIOCHEMICAL MODEL FOR 3D CELL MIGRATION

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I will present the development, analysis and numerical simulations of a biophysical model for 3D cell deformation and movement, which couples biochemical reactions and biomechanical forces.

The mechanobiochemical model considers the actin filament network as a viscoelastic and contractile gel. The mechanical properties are modelled by a force balancing equation for the displacements, the pressure and contraction forces are driven by actin and myosin dynamics, and these are in turn modelled by a system of reaction-diffusion equations on a moving cell domain.

The biophysical model consists of highly non-linear partial differential equations whose analytical solutions are intractable. To obtain approximate solutions to the model system, we employ the moving grid finite element method. The numerical results are supported by linear stability theoretical results during the early stages of cell migration. Numerical simulations show both simple and complex cell deformations in 3-dimensions that include cell expansion, cell protrusion and cell contraction.

The computational framework sets a strong foundation that allows the study of more complex and experimentally driven reaction-kinetics involving actin, myosin and other molecular species that play an important role in cell movement and deformation.

# VARIOUS MATHEMATICAL APPROACHES TO MECHANICAL SIMULATIONS IN WOUND HEALING PROCESSES

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Deep tissue injuries often result in contractions of skin due to mechanical pulling forces exerted by skin cells in the dermal layer. If contractions are morbid, then they are referred to as contractures. Contractures cause disabilities to the patients, by, for instance, loss of mobility of a joint. By the use of modelling, we aim at understanding the mechanisms behind the formation of a contracture and we aim at predicting which wound is likely to develop a contracture and which treatments can be employed to minimize the likelihood of a contracture. We used the immerse boundary approach based on a superposition of Dirac Delta functions to describe the forces exerted by individual skin cells. The use of this superposition of Delta functions results in a numerical solution that is not in  $H^1$ . Therefore we investigate alternative finite element methodologies, such as the mixed finite element method, next to standard Galerkin finite element techniques. Next to the mixed finite element method, we also analysed an approach based on Green's fundamental functions and an approach based on formulating the surface forces at the cell by means of a force boundary condition. The simulations and results will eventually contribute to modelling the contractions of the wound.

# ISOGEOMETRIC ANALYSIS OF A REACTION-DIFFUSION MODEL FOR HUMAN BRAIN DEVELOPMENT

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Neural development has become a topic of growing interest in the past decades. On the one hand healthy adult individuals exhibit qualitatively similar neural structures, on the other hand neural development exhibits a substantial degree of randomness, which is largely confirmed by the observation that even monozygotic twins exhibit significant anatomical differences. Among other factors, this neural ‘fingerprint’ manifests itself mainly through the patterns formed in the neural folding and buckling process occurring naturally after the twentieth week of fetal development.

This suggests that environmental factors can have a profound influence on the course of neural development, which in turn suggests that the underlying biological process, mathematically, exhibits a high degree of sensitivity toward perturbations in the initial condition. On the other hand, a proficient model for human brain development should be capable of producing qualitatively similar outcomes for similar setups and explain neural pathologies like lissencephaly and polymicrogyria by quantitatively different starting conditions. The derivation of proficient models for human brain development is greatly hindered by the unethicalness of experimentation on human fetuses.

We propose a numerical scheme based on Isogeometric Analysis (IgA) for the development of the geometry of a brain. The development is modelled by the use of the Gray-Scott equations for pattern formation in combination with an equation for the displacement of the brain surface. The method forms an alternative to the classical finite-element method. Our method is based on a partitioning of a sphere into six patches, which are mapped onto the six faces of a cube. Major advantages of the new formalism are the use of a smooth reconstruction of the surface based on the third-order basis functions used for the computation of the concentrations. These features give a smooth representation of the brain surface. Though the third order basis functions outperform lower order basis functions in terms of accuracy, a drawback remains its higher cost of assembly. This drawback is compensated by the need of a lower resolution in case of higher order basis functions.

## PHASE-FIELD SIMULATIONS OF LUNG BRANCHING MORPHOGENESIS

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A Turing Pattern-based framework can predict the experimentally determined growth field and thus locations of the emerging branches in lung morphogenesis. We developed a phase-field model to describe the lung geometry and model the non-linear interaction of the involved proteins in the bulk and on the surface of the growing lung. This way we can circumvent meshing problems due to the complex deformations during morphogenesis. In this talk, we show the modelling aspect as well as simulation results and compare to biological data.