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Preface

The study of cell migration aims at explaining how biochemical, physical and mechanical events are related and organised in the cell in a given context of environmental conditions. The processes involved are non-linear by nature and that is why mathematical modelling and numerical simulations have an important role to play in the understanding and prediction of the results of such complex interactions. Control of cell migration remains one of the greatest challenges in cell biology due to the considerable implications at stake in fundamental physiological processes including embryogenesis or wound healing, but also in pathological processes related to cancer with tumour growth, tumour angiogenesis and metastatic invasion.

Although key elements have been identified, the description of the processes involved remains complex since they occur at many different time and space scales: from fast micro-second molecular interactions at the nanometer scale to slow cell movements at the minute and micrometer scales, ending with macroscopic systems of interacting cell populations at the day (or longer) and millimeter scales. A huge amount of models have been proposed over the last decades, being either discrete often related to events occurring at smaller scales, or continuous with coupled Partial Differential Equations for larger scales where densities rather than entities matter.

The study and understanding of cell migration starts by a minute observation of the cell behaviour. The identification of trends in cell behaviour requires the analysis of a huge quantity of data while limiting the impact imposed by the experimental constraints for observation. This special issue starts with the presentation of two methods for image analysis. Letort et al. present an automated cell tracking method allowing to quantitatively study a large amount of migrating cells observed with phase contrast microscopy, that is untagged/untransformed cells. The authors describe and analyze the regulation and spatio-temporal dynamics of melanocyte migration in vitro and its coupling to cell division and interaction with the extracellular matrix. In the second paper, Tyson et al. review recent approaches for cell segmentation and tracking used to quantify cell motility. The authors present a new and original method for cell boundary tracking based on the underlying concept of electrostatics.

In the second part of the issue, several theoretical models are considered from single cell motility to population dynamics modelling.

Controlling the cell micro-environment is one key to decipher the intimate functioning of the cell. The two papers by Franco et al. and Hawkins and Voituriez focus on the cellular scale by placing the cell in constrained environments in order to better understand its motile properties. In the first paper, a discrete adhesive pattern is proposed to the cell to investigate how the maturation processes of cell adhesions and actin fibres are coupled and can be regulated by the

distance between adhesive sites. On the other hand, Hawkins and Voituriez show that one cell is still able to migrate without forming any adhesions when placed in a confined environment such as micro-fabricated channels. The authors analyze the mechanism by which actin polymerization contributes in increasing the intracellular pressure and the resulting cell-wall friction, which leads to cell movement.

Collective cell migration is at the heart of morphogenetic processes and developmental biology. A proper description of this phenomenon requires considering cell-cell interaction mechanisms. Szabo and Czirok use a Cellular Potts Model to analyze sprout formation and elongation, one simple case of collective motility. The authors demonstrate that cell-cell contacts guide moving cells to form linear sprouts. This comes as an alternative to the commonly accepted explanation that leader cells pull the rest of the sprout forward. Then the contributions by Wrzosek and Marrocco et al. rise to the cell population level by means of continuous modelling. Wrzosek proposes an overview of chemotaxis models accounting for volume constraints in cell colonies. This allows to describe more realistically cells crowding effects. A mathematical analysis of the reviewed models is presented, where cell movement is described as nonlinear diffusion. Speci?c problems arising through degeneracy and singularity of the diffusion are then addressed. The contribution by Marrocco et al. is motivated by experimental observations of Bacillus subtilis swarming rapidly over a surface of synthetic medium, to create remarkable hyperbranched dendritic patterns. The authors review several parabolic PDE models reproducing such effects, accounting for the dynamics of motile and proliferative active cells, non-motile and non-proliferative passive cells as well as nutrient concentration. Numerical and experimental results are finally compared and discussed by the authors.

The importance and diversity of cell migration in cancer is highlighted in the two following contributions by McDougall et al. for tumour-induced angiogenesis, and Giverso et al. regarding transmigration in the metastatic invasion, respectively. The model of McDougall et al. considers endothelial cell and pericyte migration involved in the formation of a vascular network. This vasculature aims at supplying nutrients and oxygen required by the tumour to pursue its growth. The authors analyze implications of the coupling between vascular structure and perfusion upon strategies to disrupt pathological processes by means of chemotherapeutic, anti-angiogenic, and anti-vascular treatments. Giverso et al. derive a particular Cellular Potts Model to analyze transmigration, that is the ability of cells to interact with other cells and migrate through a tissue. More specifically, in vitro transmesothelial migration of ovarian cancer cells, isolated or aggregated in multicellular spheroids, is considered. The authors show through simulation that the overall process is regulated by the activity of matrix metalloproteinases. The interplay of the adhesive properties of the cells with the extracellular matrix and with other cells, either of the same or of different types, is also highlighted.

Finally, an insight in subcellular modelling is presented by Grise and Meyer-Hermann. An agent-based approach is proposed to describe the cell internal structure. The model thus provides a new potential to investigate the intracellular movement of molecules.

Cell migration is clearly a vast subject as illustrated by the diversity of the contributions we have selected for this special issue. For this reason, we do not pretend to provide a complete overview. We hope however that the interested reader will enjoy the issue.

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