HIM Junior Trimester
Stochastic modelling in the life science: From evolution to medicine

Final report of the research group Micro2Macro

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Our group participated in the first month of the Junior Trimester Program at the Hausdorff Institute for Mathematics to carry on the research project concerning the **microscopic stochastic modelling of cell migration and the derivation of mesoscopic and macroscopic descriptions through classical tools of kinetic theory.** We both share the opinion that our stay at HIM was very pleasant and the working environment was very stimulating and fruitful for our research. We are therefore thankful to the HIM for giving us such a great opportunity.

Overview on topic and goal

The central focus of our project has concerned the study of the process of cell migration starting from microscopic stochastic models and deriving the corresponding mesoscopic and macroscopic descriptions. In fact, a microscopic stochastic formulation allows for a detailed description of the microscopic dynamics by which a single cell changes its velocity in response to random or directed stimuli. Then, using classical tools of kinetic theory, it is possible to move from the microscopic description to a velocity jump description at a mesoscopic level, from which we can recover macroscopic equations in the appropriate regime. Biologically, our specific focus has been on the analysis of the role that the fiber network has in influencing cell orientation, combining the contact guidance effects related to the fiber alignment with the scenario of a physical limit of migration. The latter refers to the situation in which a cell that would like to move in certain directions is hampered because of the presence of physical limits, for instance, due to the extracellular matrix (ECM) pore dimension or to crowded environments. Following the ideas we proposed in [1], we wanted to investigate the problem of how cells sort multiple directional cues, which can either support or impair their movements. Our main goal has been to improve the level of detail of the proposed approach by using a stochastic description of the microscopic dynamics.

Main advances

We developed a non-local model that describes the processes of contact guidance and steric hindrance depending on a single external cue. We consider the ECM that affects in a twofold way the polarization and speed of motion of the cells. Precisely, the underlying fiber structure and the fiber alignment influence the choice of the new cell direction, while the porosity of the ECM influences their speed. We start from a microscopic description of the stochastic processes underlying the cell re-orientation mechanism related to the change of cell speed v and direction $\hat{v}$. This mechanism may be described in terms of discrete in time stochastic processes for the random variables V_t and $\hat{V}_t$ which, during a time interval Δt, may change or not. Following, then, the classical kinetic theory approach presented in the literature of multi-agent systems, such velocity changes may be expressed by a collision-like model. From the microscopic description, we then formally derive the corresponding kinetic model that implements exactly the prescribed microscopic dynamics and, from it, it is possible to deduce the macroscopic limit in the appropriate regime. We use the derive to analyze several scenarios, investigating the minimal microscopic mechanisms that are necessary to reproduce cell dynamics by comparing the outcomes of our model with some experimental results related to breast cancer cell migration [3, 5, 4]. This allows us to validate the proposed modeling approach and to highlight its capability of predicting the qualitative cell behaviors in diverse heterogeneous microenvironments. The results of this study have been collected in the manuscript [2] submitted for publication.

Future goals

In the described model, we presented the derivation from microscopic processes of a specific expression of the transition probability T, which accounts for the velocity jump process. However, other formulations for this operator can be introduced. Our next goal would be to analyze how different descriptions of the microscopic phenomenon of cell reorientation allow us to recover different formulations for T. Precisely, using the approach introduced in [2], we aim at understanding which kind of cell behaviour it is possible to capture and under which hypothesis is possible to recover the formulation of the T proposed in [1]. Moreover, we would like to numerically observe the differences among the various derived formulations, applying our model to real biological settings. For instance, a possible application could concern the analysis of the process of cell invasion through the basal membrane.

Activities

Organisation of the summer school on "Stochastic modelling in the life sciences" (May 9-13, 2022).
We took part in the organization of this school together with the research group AC|DC. It was a great opportunity to get new insights into the role of stochasticity in several different biological phenomena as well as to learn new and powerful techniques allowing to mathematically treat such problems. The level of the courses was extremely good and the large

attendance and the good feedback received highlight the overall positive outcome of the school. In particular, among the invited speaker, we mainly took care of the lessons given by Prof. K. Painter, from Politecnico of Torino.

Organisation of the workshop "Interacting Particle Systems in Mathematical Biology" (July 25-28, 2022). We took part in the organization of this workshop together with the research group AC|DC. It was aimed at gathering researchers interested in interacting particle systems arising in mathematical biology. We proposed a wired range of sessions, in which stochastic analysis is used to describe biological phenomena ranging from coagulation-fragmentation models, ancestral processes in population genetics, inference, as well as models for cell migration and chemotaxis. We were mainly in charge of the session concerning "multiscale models for cell migration and chemotaxis & spatial modelling". The workshop was a great opportunity to enhance interactions with the prominent experts in the field and we profited from the talks and the discussions that emerged during it.

References

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