VRG17-014 - Kinetic Theory Applied to the Study of Fertility, Cancer and Development

Abstract

Kinetic theory provides powerful tools to study how macroscopic phenomena (observable dynamics) emerge from the underlying microscopic dynamics. Coarse-graining, i.e., the rigorous mathematical derivation of macroscopic equations from microscopic ones is the central theme of kinetic theory. This process involves the analysis of partial differential equations, probability, asymptotic analysis, and aims at the development of efficient numerical methods for the macroscopic equations, as simulations of the microscopic dynamics become inefficient when the number of particles is large. Kinetic theory has first focused on problems arising from Mathematical Physics but in recent years it has found multiple applications in biology, where linking micro-macro dynamics is of paramount importance. The rigorous coarse-graining guarantees that the macroscopic models are consistent with the underlying microscopic ones, which mainstream phenomenological approaches hardly do. However, the application of kinetic theory to biological systems poses new modeling challenges and requires the development of new coarse-graining tools in both its analytical and numerical aspects. The kinetic theory framework will be applied to different biological scenarios explained next. Artificial insemination (AI) plays a major role in our society, firstly because many couples resort to it when fertility problems arise, and secondly, it has a huge financial impact through the breeding industry (which will increase with UN's prediction of population reaching 10 billions by 2050). A key aspect of AI is determining the quality of sperm. Fertility assessment based on mass sperm motility (corresponding to wave motion) is done manually at centres of AI by trained experts. A more objective automatized process would be highly desirable, for which a better understanding of mass motility is required. However, it is not yet known how mass motility emerges from the individual spermatozoon's motility. To explore this, we will consider a phenomenological approach where rather than dealing with hydrodynamic interactions (interactions between spermatozoa mediated by the fluid), we build Vicsek-type models for collective motion (which arises as a consequence of these interactions) and couple them to Stokes-like modelling for the background fluid. These coupled dynamics will be reworked in different directions to investigate the influence of sperm concentration, head morphology, head coordination and the seminal fluid in mass motility. Once these models are assessed with experimental data, we will apply them to investigate interactions between sperm and the female tract, which could spur improvements in Computer-Aided Sperm Analysis software in the automation of scoring sperm samples. Triggered by recently developed algorithms for sphere packing, we will build particle models for cell dynamics in three different scenarios. The evolution of these systems is based on given minimization rules (for an energy functional) subject to non-overlapping constraints for the cells. These models will be coarse-grained to investigate emergent phenomena at the tissue level from the underlying cell mechanics. Particularly, we will use this set up to investigate mechanical factors leading to metastasis using the neural crest as a biological model. We will also model the development of epithelial tissue in the imaginal disc of the Drosophila looking for mechanical rules at the cellular level to explain large-scale phenomena like the shape, size and growth termination of the tissue. Finally, new cancer therapies are being investigated based on affecting the tumour's microenvironment, consisting of a network of collagen fibers. We will build a two species model representing the cancerous cells and the collagen fibers. After coarse-graining, we will quantify the relation between the rigidity of the collagen micro-network with the large-scale growth and shape of pancreatic mouse tumours. Project core team (at the Fak. Mathematik): PI: S. Merino-Aceituno "Tandem Partner": C. Schmeiser Partners: P. Markowich, N. Mauser The project also includes biology/medicine teams in Vienna led by: Michael Sixt (IST Austria) Alexander Dohnal (Children's Cancer Research Institute) Carl-Philip Heisenberg (IST Austria). The 2 Postdocs and 2 PhD students funded by the project will work on the development of mathematical models, their analysis and simulations in

direct contact with experimentalists.

Scientific disciplines:
Biomathematics (60%) | Reproductive medicine (20%) | Cancer research (20%)

Keywords:
hydrodynamic limits; kinetic theory; collective motion; cancer; cell migration; sperm; metastasis; epithelial tissue

---

VRG leader:	Sara Merino Aceituno
Institution:	University of Vienna
Proponent:	Christian Schmeiser
Institution:	University of Vienna

Status: Ongoing (01.10.2018 - 30.09.2028)
GrantID: 10.47379/VRG17014

Further links to the persons involved and to the project can be found under
https://www.gmbh.wwtf.at/funding/programmes/vrg/VRG17-014/