Coupling geometric PDEs with physics for cell morphology, motility and pattern formation

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Report from the programme organisers

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The six months research programme on coupling geometric partial differential equations with physics for cell morphology, motility and pattern formation was the first of its kind to bring together at the INI for Mathematical Sciences world-leading theoreticians, experimentalists, bio-medical practitioners and statisticians with the goal of understanding, on one hand, how current mathematical techniques, including mathematical modelling and numerical and statistical analysis, can be used to formulate and analyse topical problems in cell motility and pattern formation and how diverse experimental results can be translated into predictive mathematical and computational models across several spatio-temporal scales. Recent advances in cell motility and pattern formation including high resolution imaging techniques in 3-dimensions necessitate new mathematical and computational theories to help guide, suggest, refine and sharpen further experimental hypotheses. The programme laid out premises for topical research that seeks to couple molecular, cellular, tissue and fluid dynamics in a multiscale interdisciplinary environment thereby enabling the generation of new scientific knowledge across several disciplines.

The programme was structured in such a way that best harnessed expertise and knowledge between experimental and theoretical sciences with the goal of breaking barriers between these disciplines. In the UK the programme hosted 3 workshops and an Open for Business event at the INI and a satellite meeting at the University of Sussex. In Germany, a lab workshop in cell migration was hosted jointly by RWTH Aachen University and *Forschungszentrum Jülich*. In between these workshops, two weekly seminars were held throughout the 6-months programme, ensuring continuous dissemination of knowledge as well as offering avenues for informal discussions and collaborations between programme participants.

An enormous challenge of running the program, but at the same time, the basis of one of its major successes, was the wide spectrum of disciplines represented by the participants. The programme changed some of the attitudes of participants who were sceptical about the role of mathematics, that it is not simply a way to describe what is observed experimentally in a highly specialised code but that it is can offer experimentalists new rigorous analytical and computational premises not only to verify what is experimentally observed but that mathematics can offer virtual models that can allow for new experimental insights without carrying out real experiments. Furthermore, by bringing expertise across several disciplines, the programme demonstrated that it is necessary to communicate effectively between these disciplines but not necessary to learn the tools of each other’s trade discipline in order to communicate. By selecting an unsolved and fundamental problem in cell biology and pattern formation, the program succeeded in connecting mathematical and life sciences through mutual introduction and initiation of joint projects. At the end of the program, the perception of the progress made, the challenges encountered and the perspectives developed still differ significantly, but there is a new understanding of the difficulties on each side, and the exposure to these difficulties was especially important for young scientists to understand as they forge new careers.

World-class experts and diverse speakers from theoretical and experimental sciences all succumbed to the unique pedagogical atmosphere at the INI that fostered a highly interactive environment (see blackboard pictures). The seminar talks ranged from introductory to highly specialised lectures offering expertise and training across different levels of prior knowledge. Continuous interruptions of the talks through questions slowed presentation speed down to such a degree that it matched the processing capacity of even the least well-versed and opened the forum to provocative thoughts by others. A spontaneous heated discussion took place during the second workshop dinner on "*How to develop interdisciplinary collaboration between experimentalists and theoreticians without losing one's identity*?" at the globally renowned debating Cambridge Union Society (see an Essay to appear in the Proceedings of the Royal Society Interface Focus).

One of the pioneering stories of the programme was that we were able to lure a busload full of participants from the INI to laboratories at RWTH Aachen University and the Forschungszentrum Jülich in Germany. The one weeklong workshop focused on introduction to laboratory techniques used to analyse cell motility. The challenge to have theoreticians using pipettes (see background images) and actually performing crucial experimental steps themselves while providing insights into the state-of-the art methodology was met at surprising ease with several immediate collaborations emanating among the participants. The lab activities were beamed live to the INI seminar rooms and also live online. The participants' feedback is that the lab experience was extraordinary, unique and extremely valuable.

Once the dust has settled, what remains for all who participated in the programme is an increased appreciation of the different disciplines and a basic understanding of the tool boxes in the various fields of expertise; a sufficient pre-requisite to formulate and pursue innovative research activities. Still, the gap is immense between pure mathematics and pure experimentation. An essential "stepping stone" between both are biophysicists and applied mathematicians who seem to be at ease to communicate with both worlds. Another realisation is the need for more interdisciplinary education that crosses the boundaries between mathematics and biology.

The manifold meetings helped to define concrete short-term goals and to formulate long-term goals to be reached within the framework that was laid out. Long lists of suggestions were communicated at the end of workshop 1 on the blackboard. In addition, a similarly long list was provided in response to the question posed by Prof A. Champneys in workshop 4 as to what one could do if awarded £100,000 from the Welcome Trust Seed Award.

Outcomes and achievements of lasting impact

- The development of new mathematics (e.g. keratin spatiotemporal organization, geometric PDEs for coupled bulk-surface dynamics for single and collective cell migration, coupling super-diffusion and keratin network organisation, coupled fluid-structure, fluid-fluid, tissue-fluid interaction models, new models on parameter identification, multiscale modelling of cancer invasion, tissue remodelling, etc.).
- The development of new numerical methods and algorithms for cell motility using geometric PDEs (see the INI Satellite meeting in Sussex and the workshop on Geometric PDEs: Surface and Bulk Processes, Oberwolfach, Germany).
- The realisation that experimental data sets should be standardised, quantitative and freely available for effective interdisciplinary interaction.
- A special issue reflecting some of the outcomes and achievements of the programme will be published by the Royal Society, Interface Focus journal.
- Beaming of live virtual lectures from Australia (Prof Kerry Landman) and experimental manipulations from Germany

- Several network and research grants (Horizon2020 MSC-ITNs, EPSRCs, Leverhulme Trust, London Mathematical Society, National Science Foundation, Royal Society, etc.).
- Several research follow-up meetings (Oberwolfach, Banff, Durham, etc.).
- Creating an environment for junior and early-career researchers to take their careers forward into new interdisciplinary frontiers.