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Introduction

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A note on how to develop interdisciplinary collaborations between experimentalists and theoreticians

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1. The programme

This special issue is inspired by and based on the six-month research programme held at the Isaac Newton Institute (INI) for Mathematical Sciences, Cambridge, UK between 13 July and 18 December 2015 entitled 'Coupling geometric partial differential equations with physics for cell morphology, motility and pattern formation'. The research programme was the first of its kind to bring together at the INI world-leading theoreticians, experimentalists, biomedical practitioners and statisticians. This diverse and large group came together to share paired goals: understanding 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 conversely, 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 three dimensions, necessitate new mathematical and computational theories to help guide, suggest, refine and sharpen further experimental hypotheses. The research programme laid down premises for topical research that mandated coupling molecular, cellular, tissue and fluid dynamics in a multi-scale interdisciplinary environment thereby enabling the generation of new scientific knowledge across several disciplines.

The six-month research programme included three workshops and an Open for Business event at the INI, a satellite meeting at the University of Sussex, and a unique hands-on experimental workshop in Germany on cell migration and advanced microscopy, hosted jointly by RWTH Aachen University and *Forschungszentrum Jülich*. Hence, with the goal of breaking barriers between these disciplines, the programme was tailored in a way that best harnessed expertise and knowledge between experimental and theoretical sciences.

2. The challenge of thinking big

On the first day of one of the workshops, participants engaged in a radical exercise to stimulate and initiate communications between participants. The workshop participants were told:

> We tend to spend time at workshops listening to colleagues explain answers. Each of us has our own pet equation, or gene, or organism that we are completely focused on, and we spend our careers trying to know everything about that one little thing. But as scientists what we are really doing, even though we may not realise it, is trying to answer much bigger complex questions. So what are the big challenging questions in cell morphology, motility and pattern for the next five to ten years?

The INI has a long tradition of making good use of its chalkboards. Participants pondered on ideas alone or in groups (see figure 1). Participants spent the next 30 minutes filling several chalkboards with big questions. Participants added to questions others had posed, and each question posed raised more questions, limited only by the time and chalkboard space available. The questions remained visible—and provocative—for the remainder of the week.

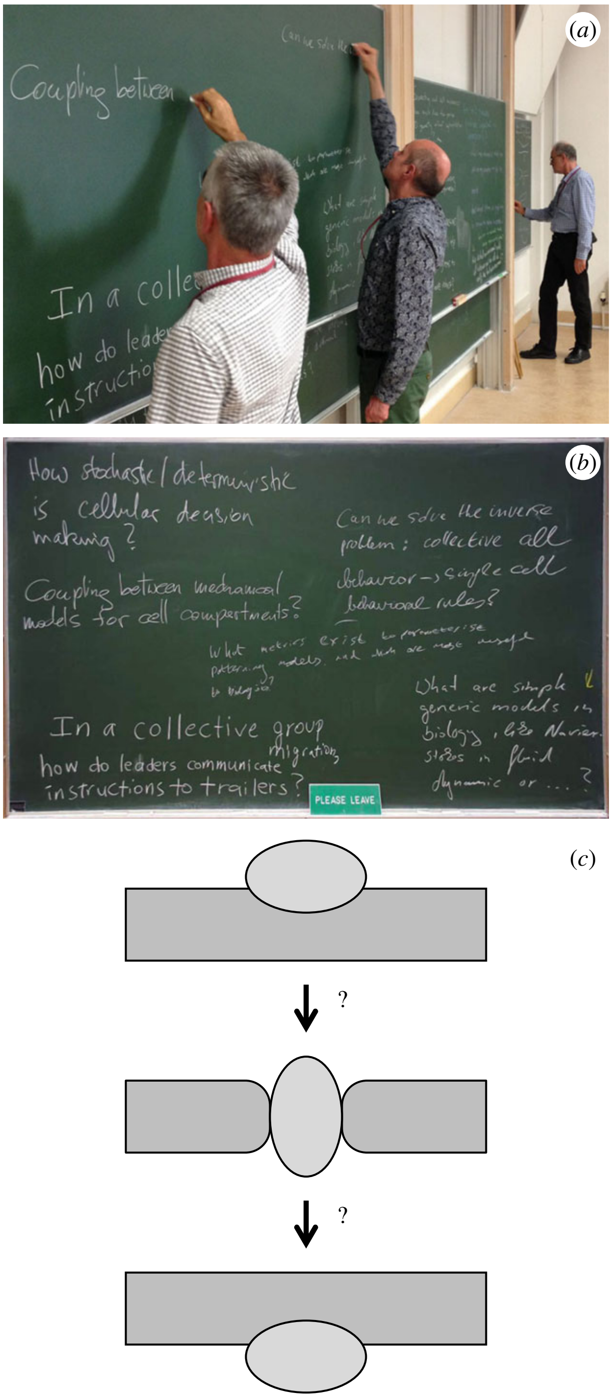

Figure 1. When prompted to share the big scientific questions that they are curious about, workshop participants quickly generated enough ideas to fill six boards (*a*) and (*b*). Some questions were nonverbal (*c*). (Online version in colour.)

We share below some of the verbal and non-verbal questions (slightly edited) that were scribbled on the chalkboards (see figure for greenboard pictures):

— How do we find the decisive molecular players?
— How do cells migrate in the extracellular matrix (e.g. fluid, tissue, etc.)?
— What are the main contributors to cytoskeletal organization?
— How do mechanical and chemical signals interact to generate the various patterns of different tissues?
— How does geometry constrain forms of life?
— Cells $\rightleftarrows$ tissue?
— Is it timely to start developing multi-scale modelling from molecules, cells, tissues, organs, to populations?
— How does the extracellular matrix affect cell shape and coordinate cell behaviour?
— How do cells determine the position of their cleavage plane? And can they form branching structures in this way?
— How do organs and tissues know when to stop growing?
— How stochastic and/or deterministic is cellular decision making?
— Coupling between mechanical models for cell compartments?
— What are we missing in our models?
— How can we validate models using experimental data?
— Can we solve the inverse problem: from collective to single-cell behavioural rules?
— In a collective group migration, how do leaders communicate instructions to trailers?
— What are some simple generic models in biology, like Navier–Stokes in fluid dynamics or if there is no Navier–Stokes in biology, what is there?
— How do cells recognize force and how is that signal processed?
— How do different interactions (including mechanics) help biological systems to become more robust?
— How do cells and/or tissues maintain sound structure despite growth and deformation?
— Geometry and cell mechanics: how much does the precise three-dimensional geometry affect cytoskeleton dynamics?
— Are self-generated gradients important in chemotaxis?
— How does local microenvironment regulate cell behaviour and how can cells modify this local microenvironment?
— What kind of geometrical objects or configurations would modellers like to simulate?
— Can we integrate filaments with hypersurfaces as descriptions of cells?
— What metrics exist to parametrize patterning models and which are the most useful to biologists?
— Mathematical analysis has been employed to show the existence of travelling pulse based on the interaction of activator and inhibitor. Would someone provide if such real phenomena happened in physiology or cell biology?
— What biological systems are people using to answer the questions I am interested in?
— Can we prove the convergence of surface finite-element methods for geometric partial differential equations?

Clearly, some of these questions are tightly focused within a discipline (e.g. 'Can we prove the convergence of surface finite-element methods for geometric partial differential equations?'), but the vast majority are truly big questions (e.g. 'How do cells and/or tissues maintain sound structure despite growth and deformation?'). These big questions—if we succeed in answering them—will have a correspondingly big impact on our understanding of the world. But the higher the level of the big question, the more likely it is to require an interdisciplinary approach. For example, 'How does geometry constrain forms of life?' is an important and irreducibly interdisciplinary question. It is impossible to answer outside of biology *and* mathematics, and it is impossible to address without high-quality interdisciplinary interaction.

3. The challenge of interdisciplinarity

Interdisciplinary research differs from multidisciplinary and transdisciplinary research in that it requires the contributions of expertise from various disciplines to provide holistic or systemic outcomes in an integrated framework. In

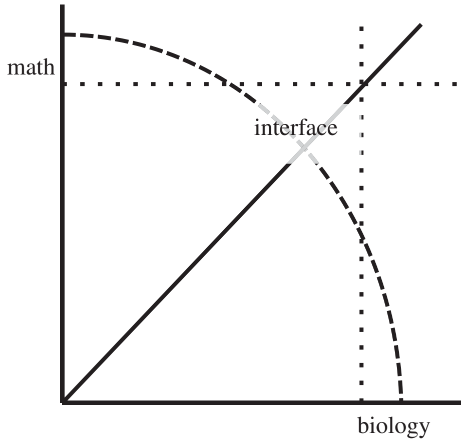

Figure 2. Interdisciplinary work can sometimes be held to an inappropriate standard, e.g. by disciplinary review committees. A discipline may have a particular standard, e.g. of merit, or novelty, or elegance (dotted lines). High-level interdisciplinary work may integrate well-established methods from individual disciplines, failing to pass disciplinary standards for novelty (dotted lines), yet be at a very high level (dashed line) when measured as interdisciplinary. Thus, it is important to judge interdisciplinary work by interdisciplinary standards.

multidisciplinary research, each discipline works in an independent self-contained manner with little cross-linking with other disciplines. By contrast, interdisciplinary research requires the integration and blending of single disciplinary knowledge and methods to bear fruit on a common goal, or scientific problem of significant importance, that cannot be otherwise addressed by single disciplines. Interdisciplinary research requires resources in time, imagination and funding, and yet it may also involve higher risks and consequences of failure (figure 2). To this end, the INI provided the critical resources of space, time and funding, while the programme participants provided the imagination and willpower to engage vigorously in research activities to investigate complex scientific problems in blending seemingly diverse expertise across disciplines.

By harnessing appropriate expertise and knowledge exchange across several disciplines, interdisciplinary research allows theoreticians and experimentalists to address problem complexity, derive general governing principles, and to answer problems central to society, health and well-being. During the six-month research programme, it became apparent that personality and attitudes of the collaborators are as important to the success of interdisciplinary research as is discipline expertise and specialization. Researchers who want to forge careers at the interface between theoretical and experimental sciences must be flexible, adaptable and creative. They must be curiosity-driven and willing to learn from other disciplines. This could for example be in the form of hands-on experiments through attachments to experimental laboratories (see figure 3). Furthermore, it is essential for the interdisciplinary researchers to be open-minded, good at communicating and breaking language barriers, and they should possess high levels of tolerance for ambiguity and strong listening skills.

4. The challenge of preserving one's disciplinary identity

To undertake interdisciplinary research, it is not necessary to train experimentalists to become theoreticians or vice versa. However, it is imperative to find commonality between disciplines without losing the strengths that come from individual disciplines.

Figure 3. Theoreticians in RWTH Aachen University's Molecular and Cellular Anatomy and Forschungszentrum Jülich's Institute of Complex Systems Biomechanics (ICS-7) laboratories. (Online version in colour.)

There exists a positive feedback between theory and experimentation. For example, mathematicians can contribute to advances in experimental sciences by identifying universality classes and general abstract rules; they could help biologists to sharpen their hypothetical questions and to make predictions testable in laboratories (to help biologists ask the right questions); they can generate tools for suggesting areas of parameter space to be explored experimentally and they can help develop, test and validate predictive virtual models that go beyond the limitations of experimental manipulations.

Conversely, advances in computing power, imaging and microscopy drive the emergence of new mathematics. For example, the need for more complex models, new fit-for-purpose numerical methods, more quantitative models, new theories, tools and techniques for large data analyses, new multi-scale and stochastic models, new or better tools to rigorously validate and test model selection versus data, new analysis of robustness of models with respect to parameter spaces and models; new tools to carry out detailed sensitivity analysis (local versus global) and new methods to study structural stability of the models under perturbations as well as developing new inverse problems in biology that allow for analysis of the correct behaviour of the biological model and help biologists to identify credible parameter regions of confidence where experimentalists are not able to measure such parameters.

5. The challenge of right sizing

In summary, we advocate for changes in higher education policy where new interfacial subjects are introduced to train a new generation of students and researchers who are competent at basic biology, and yet are experts in mathematics and physics and vice versa. This allows scientists to continue to specialize in their main fields of study without losing or re-inventing their identity at later stages of their career. Such training should not only consist of classroom teaching but should also be supplemented by regular attachments to laboratories (experimental or theoretical) in order to expose early career researchers or students to hands-on theoretical, computational or experimental manipulations.

This special issue presents a collection of timely papers at the fertile and broad interface between geometry, partial differential equations, pattern formation, shape evolution, and cell and tissue motion. In many of these papers, experts in theory and experimentation teamed up to work on a problem of significant importance during the programme thereby exemplifying the fruits of interdisciplinary research (articles that form this special issue; [1–11]).

On behalf of the INI, the programme organizers (Rudolf E. Leube, Anotida Madzvamuse, Rudolf Merkel and Hans Othmer), workshop organizers (Till Bretschneider, Alan Champneys, Bernd Hoffmann, Dagmer Iber, John King, Sharon R. Lubkin, John Mackenzie, Christian Schmeiser, Christina Surulescu and Reinhard Windoffer) and satellite organizers (Max Jensen, Charalambos Makridakis, Mattias Rogers, Vanessa Styles and Chandrasekhar Venkataraman), we hope you enjoy this special issue of the *Royal Society Interface Focus on Coupling geometric partial differential equations with physics for cell morphology, motility and pattern formation*.

Data accessibility. There is no data associated with this article.

Competing interests. We declare that we have no competing interests.

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