Isaac Newton Institute for Mathematical Sciences

Case study

Crossing the boundaries of subject and specialism

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

Stephen Hawking, who was a constant friend to the Institute, said: "*When we research across boundaries of subject and specialism, and delve deep into the mysteries of mathematical theory, we expand our understanding and illuminate the unknown. The Newton Institute exists to make this happen, and I have greatly valued my involvement with it*". Crossing the boundaries of subject and specialism is true of so many of the Institute's programmes: it was true for the 1994 programme Geometry and gravity (GGR) where Stephen Hawking and Sir Roger Penrose memorably debated "The Nature of Space and Time" over a series of six lectures; and it was equally true for the 2015 programme on Coupling geometric PDEs with physics for cell morphology, motility and pattern formation (CGP).

Exploiting recent advances in state-of-the-art experimental designs and techniques, genetic manipulation methods, cutting-edge imaging techniques and analysis tools, the CGP programme brought together theoreticians and experimentalists to address unsolved and fundamental problems in experimental sciences where mathematical sciences was the driver for innovative quantitative predictive methods.

Cell motility, morphogenesis, and pattern formation are all essential features of normal cell, tissue and organ development, and play a deleterious role in cancer progression. They involve biochemical and biomechanical processes that couple together spatial scales that span the intracellular level, the level of cell surface dynamics involved in cell-cell and cell-tissue interaction, and the scale of cell population behaviour required for organ formation and functioning. Enormous progress has been made on the experimental side of these problems in the last decades, and with that progress has come the realisation that fully understanding the complex interplay between the different factors that control cell shape changes and movement requires collective interdisciplinary expertise in a variety of fields in fundamental research and experimental sciences including (but not limited to): cell biology, plant biology, developmental biology, biophysics, image analysis, mathematical modelling, numerical analysis and scientific computing.

To promote and facilitate interaction between the wide variety of stakeholders involved, the CGP programme brought together world-leading theoreticians, experimentalists, biomedical practitioners and statisticians with the goal of understanding, on one hand, how current mathematical techniques can be used to formulate and

Figure 1: Appressorium formation in Magnaporthe oryzae.

analyse topical problems in cell motility and pattern formation and, on the other hand, how diverse experimental results can be translated into predictive mathematical and computational models across several spatio-temporal scales. The many applications of the mathematical models explored by programme participants included: embryogenesis, tumour growth and invasion, wound healing, tissue bioengineering, and biofilms. A highlight research output of the CGP programme was the recently published Nature paper on “A sensor kinase controls turgor-driven plant infection by the rice blast fungus” [1] which involves the use of geometric bulk-surface partial differential equations to predict the point at which the appressorium penetrates a leaf cutile during the rice blast disease plant infection [2] (see figures 1 and 2).

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Bridging the fields of expertise was a formidable task and the programme was structured in such a way to ensure that it broke down barriers between experimentalists and theoreticians. A key part of this, and a first for the institute, was a satellite workshop held in the laboratories at RWTH Aachen University and Forschungszentrum Julich, Germany: since the experimentalists could not bring their labs to the Institute, the Organisers decided instead to take the Institute to the labs! The insights gained by the theoreticians, armed with pipettes rather than their usual virtual models, cannot be overstated. The success of the CGP programme is reflected in the fact that it created a wider awareness of a broad class of scientific problems in need of mathematical modelling and analysis in the applied and computational mathematics community, and has led to the inclusion of programme participants in the U.S. National Institutes of Health (NIH) Physical Sciences in Oncology Programme (**physics.cancer.gov**). The CGP programme and its consequent research collaborations have also induced a number of graduate students in mathematics to pursue research in this area. The lessons learned during this programme, including the development of new numerical methods and algorithms, were captured in the Royal Society’s Interface Focus journal in the article “A note on how to develop interdisciplinary collaborations between experimentalists and theoreticians” [3] co-authored by programme organiser Anotida Madzvamuse (Sussex) and long-term participant Sharon Lubkin (North Carolina State University).

CGP programme organisers: *Rudolf Leube (RWTH Aachen), Anotida Madzvamuse (Sussex), Rudolf Merkel (Forschungszentrum Jülich) and Hans Othmer (Minnesota).*

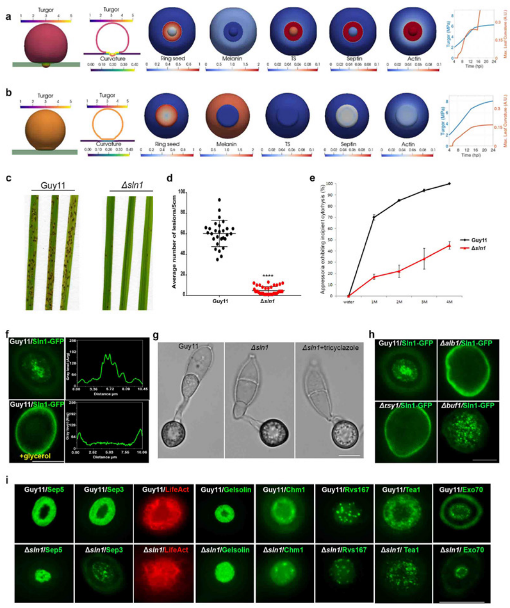

Figure 2: Identification of the Sln1 turgor-sensing kinase in M. oryzae.

References

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__2.__ Wilson, R.A. and Talbot, N.J. (2009). Under pressure: investigating the biology of plant infection by Magnaporthe oryzae. Nature Reviews Microbiology. 7. 185-195.

__3.__ Madzvamuse, A. and Lubkin, S.R. (2016). A note on how to develop interdisciplinary collaborations between experimentalists and theoreticians Interface Focus 6 http://doi.org/10.1098/rsfs.2016.0069

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