An Interview with Reidun Twarock FIMA

Professor Twarock (University of York) has led a sizeable team of researchers since 2007, with funding from a Leverhulme Trust Research Leadership Award, followed by large grants from EPSRC, BBSRC and the Wellcome Trust. Her team of typically three PDRAs, spans expertise in Mathematics, Biophysics and Bioinformatics, working on interdisciplinary projects in which Mathematics plays a key role and acts as driver of discovery in virology.

She was awarded the 2018 IMA Gold Medal earlier this year and was the IMA Lighthill lecturer in 2018.

You have recently won the IMA Gold Medal for your work in Mathematical Virology. Can you tell us a bit more about your research?

My research focuses on the development of group, graph, and tiling theoretic approaches to address open problems in virology. Through applications of these techniques either in isolation, or via novel combinations with other theoretical and experimental disciplines, I have contributed to paradigm shifts in our understanding of how viruses form, evolve and infect their hosts.

Viruses package their genetic material into protein containers, called capsids, that deliver their genetic cargo into a host cell, akin to Trojan horses. In the majority of viruses capsids are organised with icosahedral symmetry. Understanding the mathematical principles governing their structures and formation therefore requires solutions to interesting mathematical problems.

In particular, I introduced viral tiling theory to explain the structures of cancer-causing viruses. I have since developed an overarching theory of virus architecture that contains the polyhedral models of the seminal Caspar–Klug theory as a special case and also explains its outliers. I have also created group theoretical techniques in order to describe virus structure at different radial levels. Using insights from that work, I developed an approach based on Hamiltonian paths to interrogate the structures of the packaged viral genomes inside their capsids. This has been instrumental in the discovery of genome-encoded virus assembly instructions – a *virus assembly code* embedded into the genetic code – in collaboration with experimentalist Peter Stockley from the University of Leeds, and we are now jointly named as inventors on patents for the exploitation of this discovery in anti-viral therapy.

My mathematical results have thus acted as drivers of discovery in virology, and enabled the development of novel strategies to combat viruses. In particular, my work on viral geometry has enabled novel applications in nanotechnology, for example in the context of malaria vaccines, and has provided a basis for the design of virus like particles for drug delivery and vaccination purposes.

It is a really exciting time to work in this area! The research described above has created a platform for the research programme that I am currently pursuing under the auspices of my EPSRC Established Career Fellowship and a joint Wellcome Trust Investigator Award with Peter Stockley.

What do you think is your most exciting or important discovery so far?

My work on virus structure has provided solutions for long-standing structural puzzles, and has enabled profound insights into viral life cycles that could only be achieved through the lens of viral geometry. A very exciting result is the discovery of the *virus assembly code* that has overturned the existing paradigm in virus assembly and has opened up novel avenues for anti-viral intervention.

Image credit: Dr Giuliana Indelicato

How did you become interested in mathematical biology/virology?

My research career started in Mathematical Physics, focussing on applications of algebra and group theory in quantisation methods and aperiodic structures. At a major Mathematical Physics conference in Paris in 2002, I attended a talk about icosahedral viruses by biophysicist Robijn Bruinsma from UCLA. As icosahedral symmetry is non-crystallographic, I realised that the mathematical techniques I was working on at that time could be further developed for applications in virology. However, I was too much involved with other projects to immediately act on this observation. Working with mathematician Walter Mazorchuk at Uppsala University in the following summer, I had the opportunity to visit virologist Lars Liljas at the Biomedicum. He drew my attention to the structural puzzle of the cancer-causing viruses that I then tackled over the coming months with my background in non-crystallographic symmetries and aperiodic tilings. This was the beginning of Mathematical Virology.

Explain what you do on an average day at work.

There is no average day – luckily! Since last summer I have been an EPSRC Established Career Fellow, which means that I currently don't have any teaching commitments. But that doesn't make my day any less busy. Running a large interdisciplinary team with several PDRAs and PhD students together with my colleagues Eric Dykeman and Rich Bingham in York, working closely with the experimental team of Peter Stockley in Leeds, whilst also pursuing research projects with many other colleagues across different countries and disciplines, guarantees that every day is eventful and fun. I love being hands on in my projects, and I pursue many different interconnected projects that work towards a larger overarching goal. Depending on the stage a project is at, this can involve anything from mathematical work on paper, computational work, the writing up of results for publication, or the planning of new projects. Communication with project partners is important, and there is at least one call or Skype session with collaborators every day.

The mentoring of junior colleagues and research staff is also very important to me, and I am taking an active part in their career planning, including preparations for conference presentations, and applications for follow-up positions, fellowships or other funding. Some days involve the refereeing of research papers and grant applications, editorial work, and sometimes also work on outreach activities with artists. For example, we are working with computer artist William Latham and his team at Goldsmiths, who have a strong track record in showcasing their work at events such as the Viennale and at Open Days at the Crick, to create virtual models of virus structure based on our research. This work was also showcased at the Royal Society after my Gold Medal lecture.

… There are so many exciting open problems where mathematics can make a real difference in our understanding of biology …

What do you like most about your job?

The joy of solving mathematical puzzles, and creating mathematical concepts and approaches that can act as drivers of discovery in biology. I take great pleasure in translating difficult biological questions into mathematics in order to solve them through the lens of viral geometry. In this process, both the mathematical and the biological questions are equally important to me. From a mathematical point of view, I particularly enjoy developing techniques that are of interest beyond the application area they have been designed for. For example, it is nice for me to see that my models of virus architecture also account for nested carbon cage structures called carbon onions, and apply to different types of protein containers in nanotechnology.

I really enjoy working in a highly interdisciplinary environment in close collaboration with other theoreticians, such as computational biophysicists, and experimentalists, and to jointly tackle biological questions that none of the disciplines could solve in isolation. This enables me to develop predictive – rather than descriptive – models, that deliver insights with profound impact in virology.

… I take great pleasure in translating difficult biological questions into mathematics in order to solve them through the lens of viral geometry …

What stimulated your interest in maths, and when?

I have had a fascination for shapes and numbers from a very early age. Apparently – though I have no memory of this as I was only 3 years old at that time – I had a secret arrangement with children attending a nearby school to do all their maths homework, until I was found out … and told off! Generally, pursuing mathematics and solving puzzles makes me profoundly happy, so that I gravitate towards it naturally … I just cannot imagine a life without mathematics!

What influenced your career choice?

As long as I can remember I wanted to be a mathematician, apart from a short spell contemplating a career as a ballet dancer. However, when I announced among friends and family that I was going to study mathematics at university I was warned that this would mean I would eventually be without a job. But I just loved mathematics way too much to care – luckily!

Which skills do you consider to be essential for your job?

Mathematical creativity, analytical and lateral thinking, a joy of puzzles, and perseverance in the face of difficult problems are all equally important in my view. I often come across people thinking that creativity is more important in the humanities and arts than in science and mathematics. This could not be further from the truth! There is a fantastic recent book on the topic by Tom McLeish FRS [1] that explains this beautifully from a physicist's perspective.

In addition, the ability to communicate across discipline boundaries, curiosity, and intuition for biological concepts, are vital for interdisciplinary work in Mathematical Biology. As a leader of a large team, I also consider interpersonal skills and empathy for the people working with me as absolutely essential. It is such a privilege to work with smart young mathematicians and scientists, and I take great joy in nurturing their careers.

Do you have any advice for other individuals who are considering working as mathematical biologists?

Do come and join the party – it's a wonderful career! There are so many exciting open problems where mathematics can make a real difference in our understanding of biology, and where biological questions can spur the invention of new mathematical concepts and approaches. Whichever field within biology you choose to address with your mathematical skills, be sure to work in close collaboration with experimentalists, and get a clear understanding of the fundamental open questions that biologists care about, so that you can make profound contributions in both mathematics and biology.

Do you think that mathematical biology will continue to grow in the future?

Absolutely. We are only beginning to see the enormous contributions mathematics will make in biology in future. Subjects like physics and chemistry are traditionally intertwined with mathematics, and this relationship has triggered important developments in mathematics over the last centuries. The same will be true for mathematics and biology, as is visible in the number of new journals and conferences dedicated to different aspects of mathematical biology. We have also already seen the emergence of novel sub-disciplines in mathematical biology, such as the nascent area of molecular mathematical biology of which mathematical virology is an integral part, and this trend is likely to continue. We are also going to see more blurring of disciplinary boundaries, with mathematics developed synergistically with other theoretical and experimental disciplines in order to tackle fundamental open problems in science.

It is so exciting to be part of these developments at this pivotal time!

References

1 McLeish, T. (2019) *The Poetry and Music of Science: Comparing Creativity in Science and Art*, Oxford University Press.