

School of Mathematics Newsletter

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Resistance is futile: using maths to fight bacteria

by Paul Roberts

As the development of new classes of antibiotics slows, bacterial resistance to existing drugs is becoming an increasing problem, with many fearing the advent of a post-antibiotic era. To counter this threat, we are developing a two-pronged attack: using a novel treatment strategy, guided by mathematical modelling.

Antibiotics act directly upon bacteria, either killing them or inhibiting their growth. Within any population of bacteria some will be susceptible to a chosen antibiotic, whilst others may exhibit varying degrees of resistance. Therefore, antibiotics exert a 'selective pressure' upon bacteria, favouring the resistant strains, such that they become dominant in the population. If bacteria become resistant to a particular type of antibiotic, then an alternative variety may be used. In many cases this will clear an infection, in others the bacteria become resistant to this second treatment. At this point the bacteria are said to be multidrug resistant, and are often referred to as 'superbugs'.

The danger is that bacterial infections may develop resistance to all available antibiotics, rendering them untreatable. As we begin to lose this arms race, it is imperative that we open up the battle on

other fronts, developing alternative treatments and using them as effectively as possible.

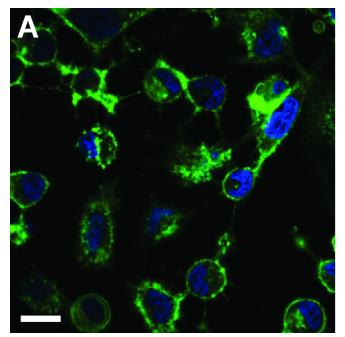
We are building mathematical models to optimise the treatment of bacterial infections, using a new therapy developed by our collaborators in the Krachler Lab, here at UoB. In order for bacteria to gain a foothold in a host, they must bind to the host cells. This both protects them from mechanical clearance and assault by immune cells, and allows them to deploy an arsenal of so called 'virulence mechanisms', which reprogram the host cells to facilitate infection. Krachler has developed a new molecule, called MAM7, which binds to host cells, preventing the invading bacteria from doing likewise. In theory, this treatment should exert no selective pressure upon the bacteria, since any adaptation would merely result in them binding less effectively to host cells. Bacteria may then be cleared from the body by a combination of mechanical forces, the immune system and antibiotics.

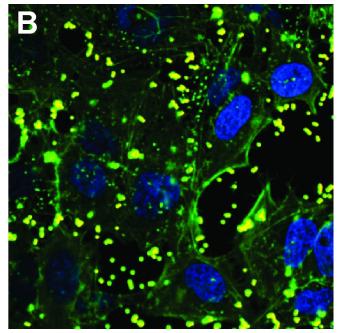
Mathematical models may be used to determine the optimum treatment regimen, ensuring that bacteria are cleared as quickly as possible, whilst minimising the risk that resistance develops.

Mathematics enables us to extend the reach of experimental and clinical studies in at least three ways. Firstly, it allows us to understand and predict the behaviour of inherently 'nonlinear' biological systems. These nonlinearities are caused by feedback within the system. For example, a nonlinear system could be represented as follows: $A \rightarrow B \rightarrow$ $C \to A$, where the letters represent components in the system and the arrows represent effects exerted by one component upon another. In this case A feeds back on itself via B and C. Secondly, it enables us to manipulate the system in ways that may not be possible experimentally. In this way we may evaluate the relative importance and effect of each component. For example, we could vary the rate of exchange of genes coding for antibiotic resistance between bacteria, to test the effect this has upon the size of the bacterial population over time. Lastly, it enables us to consider a wider range of scenarios and hypotheses than would be experimentally feasible, due to time, space or financial limitations.

Thus, theoretical modelling complements exper-

imental studies, forming an experiment/modelling cycle: models are used to test biological hypotheses, and may then be used to make predictions which can be tested experimentally. It is hoped that this study will help us to keep a step ahead in the fight against bacterial infections. A fight that it is critical we win.





Treatment of epithelial cells using MAM7. The green staining shows the skeletons of the cells and the blue staining shows the DNA-containing nuclei. A) untreated cells. B) cells treated with beads coated in MAM7 (beads are seen as yellow blobs). Figure reproduced, with permission, from Krachler et al. (2012).

Maths Outreach

by KAT GROVER

Thank you to all staff that have helped with the school's outreach work so far this academic year. Below are some highlights of the year so far along with details of upcoming events.

One of our key public engagement and outreach activities is our successful Birmingham Popular Mathematics Lecture series which runs monthly in the autumn and spring terms. The 2015/16 series kicked off with the annual LMS popular lecture held in the Bramall building's Elgar concert hall with guest speakers Professor Martin Hairer (University of Warwick) and Professor Ben Green (University of Oxford). Our series continued with talks held in the Watson building on a Wednesday Evening; this year the speakers are Dr. Alessandro Mottura (Met-

allurgy and Materials), Dr. Andrew Treglown, Dr Thomas Woolley (University of Oxford), Dr Richard Pinch (Cheltenham), Dr. Jennifer Rogers (University of Oxford) and Dr. David Leppinen. So far we have had an average of 80 attendees at each of our lectures, made up of a mix of the interested public and local school pupils. Please see the webpage www.birmingham.ac.uk/bpml for details of upcoming lectures. If members of staff would like to give a talk in the next series or have a suggestion for a guest speaker please let me know.

Staff from the department have been involved in a wide variety of outreach events, trips to schools, and campus visits aimed at 10-18 year olds. Thanks go to Rosemary Dyson, Chris Good, Simon Goodwin, Sara Jabbari, Guillem Perarnau, Martyn Quigley and Dave Smith who have been involved in these visits and masterclasses. Our widest reach has come from the Training Partnership talks given by Sara, Chris

and Rosemary each to hundreds of pupils at various locations across the country. If I have missed your name it is because your visit isn't in the outreach database, please do let me know so I can correct this oversight.

There are plenty of big events to come this year to promote Mathematics to under 18s. The Maths Big Quiz on the 11th of March is our biggest purely Maths focused campus event with 400 year 10 pupils registered. We will also be repeating our Maths Taster Day on the 29th June for around 100 year 12 students thinking of studying Maths at university; this was run successfully for the first time last year. To see our full list of activities visit the website www.birmingham.ac.uk/schools/mathematics/outreach. Thank you to all those who have agreed to help with these upcoming events.

Outreach and public engagement often overlap, so if you are interested in interacting with older audiences I'm happy to support you in this and I am on the Public Engagement with Research Committee for the University. Last term the committee ran a very useful workshop day and I am happy to share any of these presentations including an interesting look at public engagement and REF impact. To keep up to date with Public Engagement training and events across the University please visit http://thinkpe.wordpress.com. Finally, I'm always looking for more help with outreach events and am very happy to talk about your outreach and public engagement ideas, just send me an email or see me in Room 218 in the Watson Building.

The workshop "Adaptive algorithms for computational PDEs"

by Alex Bespalov and Daniel Loghin

In the early days of 2016, the School of Mathematics at the University of Birmingham hosted the two-day workshop "Adaptive algorithms for computational PDEs". The workshop brought together established and early career researchers as well as PhD students working on mathematical foundations, design and implementation of adaptive algorithms for numerical solution of PDE problems. Eleven invited talks were given by international experts from the UK, Ireland, France, Austria, Netherlands, and Germany. Furthermore, three contributed talks were given by early career researchers.

The speakers covered a wide range of topics. Rob Stevenson (Amsterdam) opened the proceedings by presenting new results in adaptive wavelet methods. Paul Houston (Nottingham) then gave an illuminating talk on using adaptive discontinuous Galerkin methods for PDE problems on complicated domains (e.g., domains with microstructures). Dirk Praetorius (TU Vienna), despite his travel disrupted by a delayed flight, was very enthusiastic to tell the audience about an axiomatic approach to proving convergence properties of adaptive algorithms. New contributions to a posteriori error analysis and adaptivity on anisotropic meshes were presented by Natalia Kopteva (Limerick) and Gabriel Barrenechea (Strathclyde). Andreas Dedner (Warwick) discussed a posteriori error estimation for conservation laws. The first day of the meeting was wrapped up by two contributed presentations: Uwe Köcher (Hamburg) discussed software engineering aspects of adaptive solvers and Carlo Marcati (Paris VI) gave a talk on h-p adaptivity for electronic structure calculations.

On the second day, the first session featured two talks with a common theme: Martin Vohralík (INRIA Paris-Rocquencourt) discussed the use of local stopping criteria in the design of fully adaptive solvers, whereas Mario Arioli (Wuppertal) addressed the design of stopping criteria for linear algebra solvers. Then, after the coffee break, the talk by David Silvester (Manchester) focused on the development of adaptive algorithms for PDE problems with random data, followed by the contributed talk by Philip Browne (Reading) discussing the design of adaptive meshes for meteorological applications. During the final session, Emmanuil Georgoulis (Leicester) discussed the use of adaptive procedures for blow-up detection in solutions to non-linear evolution PDEs and Omar Lakkis (Sussex) presented novel results in a posteriori error analysis of time-stepping schemes for the wave equation.

The presentation slides of all talks at the workshop are available at http://web.mat.bham.ac.uk/A.Bespalov/adapt16_workshop/speakers.html.

The talks stimulated lively discussions that were not bound to the lecture room and flowed seamlessly into the social areas of Bramall Music Building, Staff House and later on the first day of the meeting into the elegantly decorated interiors of the Indian-cuisine restaurant. All participants found the workshop to be very stimulating and inspiring. PhD students, in particular, benefited from ample oppor-

tunities to discuss their research with established colleagues in informal settings and to interact with their peers from other institutions.

The workshop was organised by Alex Bespalov

and Daniel Loghin (the members of the Numerical Analysis group). The meeting was supported by the London Mathematical Society and the School of Mathematics at the University of Birmingham.



Adaptive algorithms for computational PDEs workshop photo.

News in brief

- Many congratulations to Professor Daniela Kühn on being awarded an EPSRC Established Career Fellowship for the project "Combinatorics, Probability and Algorithms". The grant will support Daniela's work for 5 years and will also support two Research Fellows.
- A workshop on the "Mathematics of Dispersion in the Environment", jointly organised by Gavin Esler (UCL), Alexandra Tzella (UoB) and Jacques Vanneste (Edinburgh), will take place on April 4-5 2016 here, in the School of Mathematics. Supported by the EPSRC network "Maths Foresees", the workshop's aim is to gather researchers working across a number of applications and methodologies related to the transport of (reacting) scalars in complex fluid flows and/or domains, stochastic models of turbulent transport and probabilistic predictions and sampling. Each of these themes has an immediate practical interest, associated with the prediction and management of risks of air, water or soil pollution. For more details

see: http://web.mat.bham.ac.uk/A.Tzella/workshop.html.

- The annual School of Mathematics trip to Coniston takes place 11-13 March. All students and staff are welcome to join the trip to the University's outward bound centre, with walking and enjoying the beautiful Lake District scenery top of the agenda! The cost of the trip is £60 per person. Please speak to Sally Schofield (Room 229) for more details.
- Professor Sergey Shpectorov was one of eight plenary speakers at the 8th Iranian Group Theory Conference held at the University of Tabriz 3–5 February. His talk was entitled 'Axial Algebras and Groups of 3-Transpositions'.
- The next Mathematics Colloquium will be held on February 24th at 4pm in Watson Lecture Room A. The speaker is Corinna Ulcigrai (University of Bristol). On March 9th the colloquium talk will be given by Beatrice Pelloni (University of Reading). All staff and students are welcome to attend!