

# Microbiology TODAY

45:2 May 2018



## Microbial Tools

Building bacterial bridges  
Microbiology and the disposal of radioactive waste  
Influenza pseudotype research and development  
Using microbes for precision insect pest control  
Viruses: life-saving drugs?

5

## REASONS

## TO PUBLISH WITH US

**WE ARE A LEADING PUBLISHER IN THE  
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1

2

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# Editorial

**Welcome to the May edition of *Microbiology Today* – in this issue, we are celebrating the enormously varied world of microbial tools. Although when considering microbes we are so often focused on their harmful potential and the control of their influence, it is worth stopping to consider the other side of the story, and the many and wide-ranging ways in which their influence positively enhances our lives. From construction materials through to pest control, our authors reveal the fascinating ways in which microbes are used.**



Whole Picture

Starting off with a look into the use of bacteria in the construction industry, a team from the University of Bath – Timothy Hoffman, Bianca Reeksting, Richard Cooper, Kevin Paine and Susanne Gebhard – take us through the possibilities of using bacteria to create self-healing concrete. They outline the current problems of decay and damage in building materials, and highlight the way in which microbial metabolism can be harnessed to address these issues, demonstrating how this technology could have real potential to improve construction in the future.

Next up, with a specialised set of microbial tools, are Simon Gregory and Megan Barnett discussing how microbes can impact on the geological disposal of radioactive waste. They deliver an insight into how different microbes can alter the way in which radioactive waste is contained and degraded, either helping or hindering the containment process. Natural populations of microbes found deep beneath the earth have the potential to reduce the barrier abilities of material designed to keep waste in, while other microbes within the population reduce the solubility and mobility of radioactive molecules, helping to contain waste until it is less harmful.

Taking us on a walk through influenza pseudotype research and development, Nigel Temperton explains how the creation of viral pseudotypes can remove some of the obstacles traditionally encountered when working on novel therapeutics for emerging and potentially highly dangerous viruses. Not only has the design and construction of retroviral pseudotype viruses provided stable and safe mimics of pathogenic viruses, and allowed testing of vaccines, screening of monoclonal antibodies and resistance studies. It has also enabled these tests to be carried out in biosafety level 1 laboratories rather than BSL-3 or 4 laboratories, vastly increasing the global accessibility of the tests.

Moving on to another distinctive set of microbial tools, Paul Dyson and Miranda Whitten focus on the use of bacterial-mediated RNA interference of specific pests as a sustainable strategy for protecting crops, livestock and human health. The use of symbiont-mediated RNA interference has the potential to minimise the impact of pest control on beneficial insects such as pollinators, and also has implications for the control of insect-vector human pathogens.

Bringing us a piece on viruses as lifesaving drugs are Jonathan Welsh, Helen Young, Ruth Stephen and Sam

Laurel Stephen. The production of recombinant viral vectors that potentially could be used in gene therapy is complex, and the initial work can often be carried out in academia. For these viral vectors to make it through to a viable end product, there is the issue of scale to be addressed. Our authors explain how the Centre for Process Innovation can assist academics, industry and government in the development of large-scale processes to good manufacturing practice standards, hoping to make gene therapy more affordable and accessible to everyone.

When researching and developing within the world of microbial tools, thinking about how you can protect your intellectual property could be particularly pertinent. For our Comment piece, Alice Smart gives us some clarity about the uses of patenting, providing us with a list of dos and don'ts, as well as an idea of why you might want to patent. Alice gives a valuable guide through a process often neglected by those focused on research, often at the expense of protecting their inventions.

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## Rowena Jenkins

Editor

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# Contents

## Microbiology TODAY

### Articles

60

#### **Building bacterial bridges**

Timothy Hoffmann, Bianca Reeksting,  
Richard Cooper, Kevin Paine & Susanne Gebhard

Self-healing concrete technology.

64

#### **The unexpected influence of microbiology on the disposal of radioactive waste**

Simon Gregory & Megan Barnett

Micro-organisms aiding disposal.

68

#### **Influenza pseudotype research and development**

Nigel Temperton

Viral pseudotypes to target antibody response.

72

#### **Using microbes for precision insect pest control**

Miranda Whitten & Paul Dyson

Insect-microbe bio-insecticide strategies.

76

#### **Viruses: life-saving drugs?**

Jonathan Welsh, Helen Young, Ruth Stephen,  
Sam Laurel Stephen

Viral vectors and gene therapy.



45:2 May 2018

## Features

- 59 Science Media Centre (SMC)**  
Join the expert database.
- 84 Policy – Engaging in Science Policy**  
How to inform and influence policy.
- 86 International Committee on Systematics of Prokaryotes (ICSP)**  
Find out about the work of the ICSP.
- 87 iGEM: Get & Give (&Share)**  
An overview of the International Genetically Engineered Machine Competition.
- 88 Schoolzone – The Super Cells**  
Emma Henly from Sheffield Hallam University tells us about The Super Cells.
- 90 Journals update**  
Emerging Zoonoses and Antimicrobial Resistance (AMR) event, and call for papers on AMR.
- 92 Outreach – e-Bug**  
Catherine Hayes from Public Health England on the e-Bug educational programme.
- 94 ECM Forum update**  
Latest on the ECM Forum Summer Conference taking place in June.
- 95 Membership Q&A**  
Introducing member Ed Cunningham-Oakes.
- 97 Comment – To patent or not to patent?**  
**Alice Smart**  
When and when not to apply for a patent.

## Regulars

- 51 Editorial**
- 54 Council 2018**
- 55 From the President**
- 56 From the Chief Executive**
- 57 News**
- 80 Annual Conference**
- 82 Focused Meetings**
- 96 Reviews**

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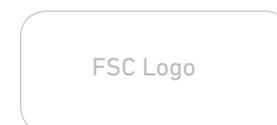
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Pre-filled syringes and vials containing the 2014/2015 seasonal influenza vaccine. Dr P. Marazzi/ Science Photo Library

# Council 2018

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# From the President

**With the Birmingham Annual Conference behind us, I can look back over the three Microbiology Society meetings of my Presidency and see the evolution of a brand and mechanism for delivery of scientific meetings that I believe will serve us well in the future.**



The strategy of having one major meeting organised by our Divisions, backed up by an expanding number of Focused Meetings that are predominantly conceived of by our members (sometimes teaming up with sister societies) seems to me to be an excellent and equitable way of “connecting and empowering communities worldwide”. The rationale has been to provide strategic vision and leadership while remaining responsive to new insights coming from our members, and a welcoming attitude for collaborations with other microbiology-focused organisations. Our Focused Meetings continue to grow in popularity and number (see, for example, the meetings taking place between June and October: [microbiologysociety.org/focusedmeetings](http://microbiologysociety.org/focusedmeetings)), and we have a new member of staff, Paul Taylor, Conferences and Events Manager, at the Society to enable this portfolio to be further expanded. Our overall formula seems to me to be working well in exploring the length and breadth of the microbiological landscape, while remaining nimble in identifying and supporting rapidly emerging themes brought to our attention by anyone with a vision or new idea. We have made every effort to gather frank and detailed feedback along the way, during and after all the meetings we run, and we

are always happy to receive ideas or criticisms at any time to enable us to sharpen our act.

Another success that has evolved during my term of office has been the Early Career Microbiologists' (ECM) Forum. On that note, can I highlight for your attention the ECM Forum Summer Conference on 14–15 June? The fulsome participation of our younger members in every one of our Committees has brought new insight and input to our core business, and there has been a healthy growth in our membership in the ECM sector, which has to be seen as a reflection of a better engagement of younger members with the Society. Understanding the needs of our community of research scientists and taking advantage of their vision and energy will remain a major commitment for the Microbiology Society. Having made inroads in addressing ECM careers, we are now extending the demographic analysis to use our Professional Development Team to focus on the needs of mid-career microbiologists. A new working group is seeking input and developing a new research project to examine how we might facilitate the careers of scientists who are established, but may not yet have achieved a stable and sustained presence in the field. The objective is to be able to provide different types of support to individuals at all stages of their careers

with bespoke resources, advice and mentorship.

A final word about our publishing activities. The Microbiology Society is a not-for-profit publisher. All the income generated by publishing in one of our journals is re-invested back into the Society's charitable aims and professional development opportunities. Our six journals pay for you and your students to attend meetings, and for the literally hundreds of small grants and scholarships that we award. We are also constantly refining how we publish to make sure that you, as a contributor, are well served, and your work is respectfully and efficiently peer reviewed. We are alert to new publishing opportunities – for example, our journal's antimicrobial resistance collection is currently being compiled, and we will be announcing new publishing opportunities for you in the coming months. Keep in mind, therefore, that when you pay an APC to one of our journals, that money is in fact eventually recycling right back to you. Therefore, when you publish within our portfolio of journals, you can have your cake and eat it too!

**Neil Gow**

President

[president@microbiologysociety.org](mailto:president@microbiologysociety.org)

# From the Chief Executive

**The Microbiology Society's Annual Conference in Birmingham last month was yet again a wonderful festival of microbiology, networking and friendship. Members of the Society were able to share the successes of your research, discuss the challenges you face, and identify new and exciting opportunities. The vibrancy of the event shows just how strong our community is, and how valuable the Society is as a vehicle for connecting and empowering communities of microbiologists.**



As always, the Prize Lectures were inspiring. Jill Banfield's expertise in environmental microbiology proves how studying very small things can answer questions about very large-scale processes, while Geoff Smith and Sharon Peacock, in different ways, demonstrate the intensely practical use to which microbiology research can be put in terms of human health. Sarah Coulthurst showed expertly how to tell a clear and compelling story about microbes, and Tansy Hammarton's work illustrates how to take those stories to a wider audience. These motivating lectures are only possible because members take the time to nominate exceptional microbiologists for the Prizes, so please look out for the call to nominate for next year's Lectures – the deadline is in early June.

Annual Conference is a highlight of my year because I get to interact with lots of members, to listen to your talks, to discuss your posters and to chat about what is important to you. This helps me to make sure that the Society's staff are supporting your careers. Equally important are those occasions when I meet you individually or in smaller groups, and I try to get out and about to visit members as much as possible. I greatly valued two recent visits.

It was an enormous pleasure to visit Belfast at the invitation of Lindsay Broadbent, who won the Howard Dalton Young Microbiologist of the Year competition in 2016. The early career research community there is vibrant and productive, and it was inspiring to talk to a number of postdocs and students, including Joana Sa Pessoa Santos and colleagues, who are organising a Young Microbiologists' Symposium in August. The Society is delighted to support the event through the Society-Supported Conference scheme, and I look forward to hearing about the constructive interactions between junior Principal Investigators, postdocs and PhD students.

I also had a great time when I went to Birmingham for the JAM talks, which are organised by a committee that includes two of the Society's Champions, Alice Lanne and Anja Đokić. There are far more early career researchers from around the UK and Ireland who want to take part than there are available slots, and the committee had a challenging job choosing who to invite. On the day I visited, it happened that one of the talks was by Helen Brown, who is chair of the Microbiology Society's Early Career Microbiologists' Forum. The science was great, the questions and discussions were illuminating, and everyone enjoyed

themselves. I was particularly struck by Helen's observation that the project she described had come about from a casual conversation at the Society's Annual Conference last year, when she happened to fall into conversation with Professor Sheila Patrick, the Chair-Elect of our Prokaryotic Division – a straightforward example of the unpredictable benefits of the networking opportunities the Society provides.

Throughout the year, the Society aims to provide members with chances to come together and talk about science, and also to engage in activities that support your careers. As well as scientific events, the Society's Council, Committees, and Divisions provide fantastic opportunities to ensure that your priorities get the attention they deserve. If you are interested but not sure what is involved, we now have a shadowing scheme that allows you to have a taster before making a commitment. Feel free to contact me if you want to know more, and bear in mind that I'm always delighted to visit your lab or attend your own events to learn more about what the Society can do for your communities.

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## **Peter Cotgreave**

Chief Executive

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# News

## Society informs Parliament on Industrial Strategy and Brexit

The Microbiology Society recently informed two parliamentary inquiries about microbiology and our members' views on Brexit and the Industrial Strategy.

Professor Paul Kellam, Chair-Elect of the Society's Policy Committee, gave evidence for the Society about the Life Sciences Industrial Strategy. He spoke about the broad importance of microbiology for biomedical science and other areas of bioscience research and innovation, and the needs to deliver the Strategy.

The Society also submitted evidence and participated in a summit for the House of Commons Science and Technology Committee's Brexit Science and Innovation Inquiry, informing the Committee of MPs about our members' views and concerns relating to mitigating risks and exploiting opportunities for UK science and innovation in the short-term and post-Brexit. Professor Kellam again represented the Society at the summit. We also appreciate the number of members who contributed to a call for comments from our President, Professor Neil Gow, and participated in a roundtable to inform the Society's response.

Further information about the inquiries, and the Society's responses and engagement with Brexit, can be found on our website: [microbiologysociety.org/consultationresponses](http://microbiologysociety.org/consultationresponses)

## Annual Conference 2018

Year on year, the Annual Conference is a bigger and bigger success. With over 900 abstracts, two Hot Topic Lectures and three dedicated professional development sessions, the Annual Conference 2018 in Birmingham was an incredible event. Thank you to all those involved in organising the Conference, as well as our fantastic exhibitors and sponsors. Watch our video from the Annual Conference on our YouTube channel (<https://microb.io/2Hz53W0>) and read more on page 80.



All photos: Ian Atherton



### New cross-disciplinary pop-up journal: X-AMR

Recognising the fact that antimicrobial resistance (AMR) is important across multiple disciplines, the Society is launching a new pop-up journal on the timely topic. Published papers that are added to this collection will be hosted on a microsite on the journals' platform. Find out more about how to submit on [www.microbiologyresearch.org](http://www.microbiologyresearch.org).

## Grant deadlines

Date	Grant
1 June 2018	Travel Grants – to support members attending a conference or training course anywhere in the world.
11 June 2018	Society-Supported Conference Grants – to support members organising a microbiology conference, to help towards invited speakers' costs.
19 July 2018	Society Conference Grants – to support members presenting at our Focused Meetings: 9th International Symposium on Testate Amoebae (ISTA9); the Molecular Biology and Pathogenesis of Avian Viruses.

Check the website for details about applying for grants ([microbiologysociety.org/grants](http://microbiologysociety.org/grants)).

## Upcoming Society events

Annual Conference 2018 may be over, but the Society has plenty of events coming up for the rest of 2018. There are six Focused Meetings taking place across the UK and Ireland, and our Early Career Microbiologists' Forum's inaugural Summer Conference is being held in June at the University of Birmingham.

Planning for Annual Conference 2019 is also already well underway – save the date: Annual Conference 2019 takes place from Monday 8 April to Thursday 11 April in Belfast. Read more about our upcoming events on page 80.

## 2019 Focused Meeting proposals

The deadline date for proposals for Focused Meetings in 2019 is 11 June 2018. If you have a topic you would like to organise an event for, don't forget to submit your idea by this date for consideration by the Society's Scientific Conferences Committee. Read more on page 82.

## Full events listing

If you are organising or hosting a microbiological meeting, of any size and anywhere in the world, the Society can help spread the word. Complete the online form ([microbiologysociety.org/submitevent](http://microbiologysociety.org/submitevent)), and we will add your event to our full events listing.

## Voting for Council, Committees and Divisions roles

The Society elections for Council, Committee and Division members will be opening later this month. Find out more about the roles up for election on our website: [microbiologysociety.org/nominations](http://microbiologysociety.org/nominations).

All eligible members will receive emails containing information on how to vote from Electoral Reform Services shortly before voting opens.

## Deaths

We are sad to announce the passing of **Professor Vivian Moses**, who joined the Society in 1994. You can read an overview of his career from a previous article in *Microbiology Today*: [microb.io/2EMyBM1](http://microb.io/2EMyBM1).

Please contact [mtoday@microbiologysociety.org](mailto:mtoday@microbiologysociety.org) if you wish to notify the Society of the death of a member whose details can be included in this section.

## Contributions and feedback

The Society welcomes contributions and feedback from members. Please contact [mtoday@microbiologysociety.org](mailto:mtoday@microbiologysociety.org) with your ideas.

Get the latest updates, follow the Microbiology Society on:



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# Joining the Science Media Centre expert database

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**The Science Media Centre (SMC) would not be able to function if it were not for the 3,000+ scientists, engineers and other experts who have agreed to be on our database. Our broader aim is to ensure that news journalists have access to good evidence-based science, and great media-friendly experts, when science hits the headlines.**

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**W**e do this in several ways: through being a first port of call for journalists looking for a scientist to interview, proactively promoting reaction from the scientific community when a big science story is in the news, or by running briefings for specialist correspondents on hot topics in science. By being an SMC expert you are helping us to help the news media cover science in the best way possible.

## What does being a Science Media Centre expert mean?

We would like to be able to contact you when your area of expertise becomes topical in the media. This could be for a request for an interview with a newspaper or broadcaster, a comment for one of our 'round-ups' of scientists' comments, or to speak on the panel of a press briefing. As the SMC deals primarily with topical science stories in the news, there may be long periods of time when we do not get press enquiries in your specialist area and you don't hear from us – but that doesn't mean you have dropped off our list. It's also important to stress that because we are responding to breaking news stories, we could call you at any time of day, including outside normal office hours. However, such occasions are rare, and we would always take no for an answer if you are unable to respond.

Whenever we approach you, we will ask you to declare any relevant interests; declarations will be made available to journalists for transparency.

## How you can help us

The SMC has had tremendous success in getting the views of scientists represented in the national media. To get these results we provide a quick response to journalists' enquiries, and although we know that you are very busy, we would really encourage you to make room in your schedule to put your scientific expertise over to the press. We also rely on up-to-date contact details, so we would be very grateful if you could inform us of any changes of telephone/mobile number or address. Home phone numbers are also useful to have on the database, although we would only use these in an emergency. The SMC aims to provide journalists with cutting edge information on the hot issues in science; to do this it would be great if you could let us know if your area of science is likely to hit the headlines or if you are working on something that is likely to attract media interest, and we are always happy to receive suggestions for press briefings in these areas.

## Science in the headlines

The nature of the SMC means that, in addition to media enquiries from

national science correspondents, we routinely deal with science when it becomes front-page news. We feel science in the headlines gives the perfect opportunity for scientists to communicate their views to the public when interest is at its highest. Most of the time a story will only be big for a day, giving only a small window of time for us to react. At these times we would really like it if priority could be given to media work as this is when responding will undoubtedly have the biggest impact.

## Confidentiality

It is important to stress that personal details on the database are confidential and are only available to SMC staff. As part of this work we may liaise with the press office in your organisation and in doing so may tell them we are working with you; if this is a problem, please let us know. We will never give your number out to the press directly, unless you have specified that this is okay - we will always contact you first to check you are available and we will always take no for an answer. All data held by the SMC are maintained in accordance with the Data Protection Act 1998, and the SMC is registered as a Data Controller under the Act. If you are employed by an institution subject to Freedom of Information requests, which includes all publicly funded academic institutions, funding bodies and government agencies, all correspondence with the SMC can be requested under the Freedom of Information Act 2000.



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# Building bacterial bridges

Timothy Hoffmann, Bianca Reeksting, Richard Cooper, Kevin Paine & Susanne Gebhard

**Microbes live all around us: in the soil we grow our food in, in the air we breathe, in the water we drink and even inside our bodies. These microbes are often thought of in a negative light, for example, as a causative agent of sickness and food spoilage. However, the reality is that microbes are essential for life and play key roles in the ecology of natural environments, as well as in many biotechnological applications.**

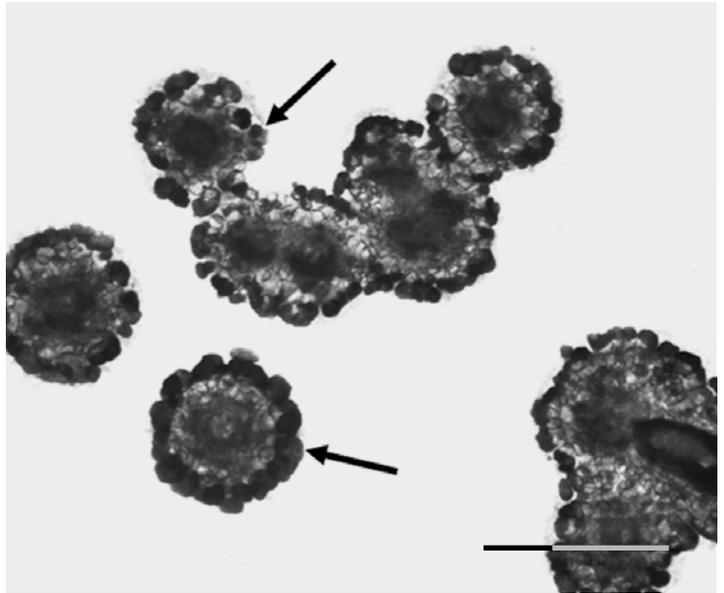
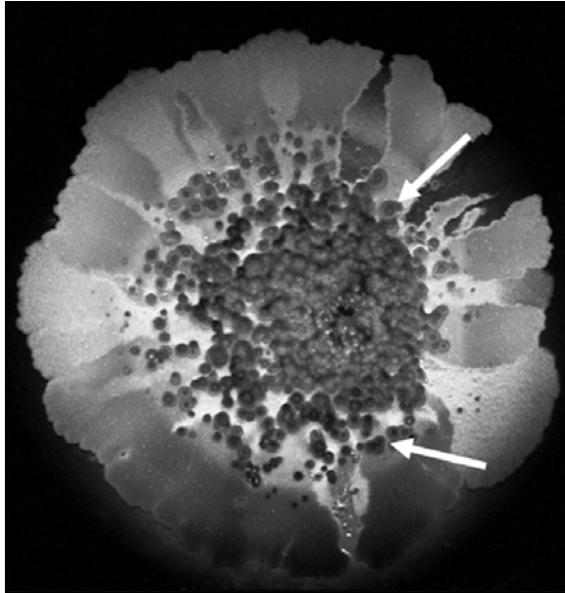
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Indeed, it is becoming the norm to exploit bacteria in industrial processes for their ability to act as 'cell factories' that can produce important speciality products such as detergents, plastics, fuels and essential oils. Apart from the production of important compounds, they are also useful in the breakdown of environmental contaminants such as pesticides, petroleum additives and plasticisers. The successful use of bacteria on the industrial scale has prompted expansion into more diverse areas. A recent addition to the résumé of these tiny organisms is the utilisation of biomineralising bacteria in self-healing construction materials.

## **Constructive bacteria**

Often, the first things that come to mind when we think about microbes in the built environment are damage, decay, discolouration and staining to building materials and their surfaces. What we don't consider is their ability to act as

'bioengineers'. This is despite the fact that microbes are often involved in important natural processes such as sediment formation in marine and freshwater environments, as well as stalactite and stalagmite formation in caves. In geotechnical applications, bacteria are now being used as part of the engineering 'toolbox' for the consolidation and stabilisation of soils to counteract erosion, enhance bearing capacity, and enable excavation and tunnelling. This is due to the intrinsic ability of a wide range of bacteria to promote the precipitation of mineral carbonate, such as calcium carbonate, as a by-product of their metabolism. Several core metabolic processes in the bacteria lead to an increase in the pH and concentration of carbonate in the surrounding microenvironment. This in turn causes supersaturation and thus precipitation of the carbonates as minerals, for example as calcite. The precipitates decrease the pore space in the soil and act as a glue



Calcite crystals on bacterial colonies. Bar, 1 mm. B. Reeksting

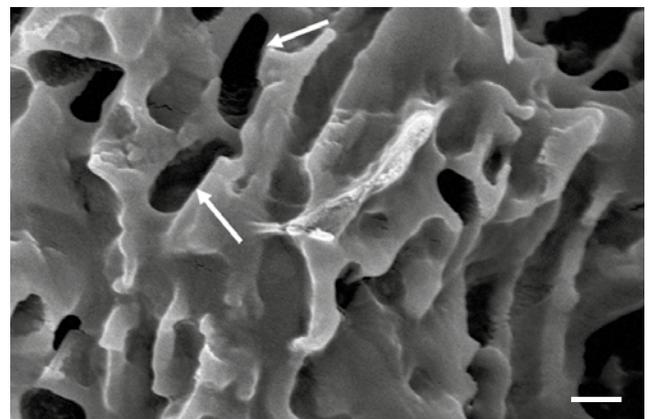
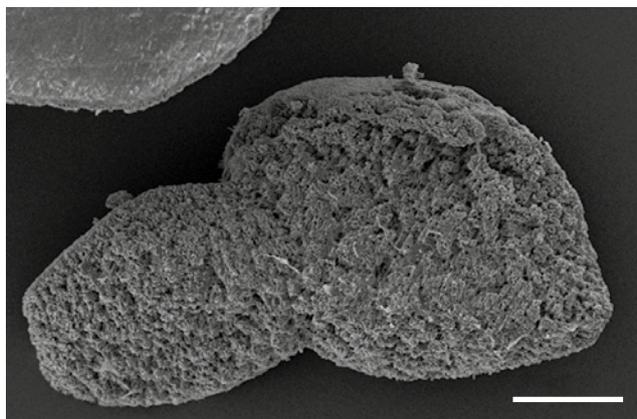
that binds together soil particles, leading to densification. In addition to changing the pH, the presence of bacterial cells can directly aid the precipitation of carbonate minerals. This is because bacterial cell surfaces are usually negatively charged, which attracts positively charged calcium ions and can act as a nucleation site for formation

of calcite crystals. The successful use of microbes as soil improvement tools has led researchers to explore whether these bioengineers could also be useful in the construction industry.

### ***Bacillus* buildings**

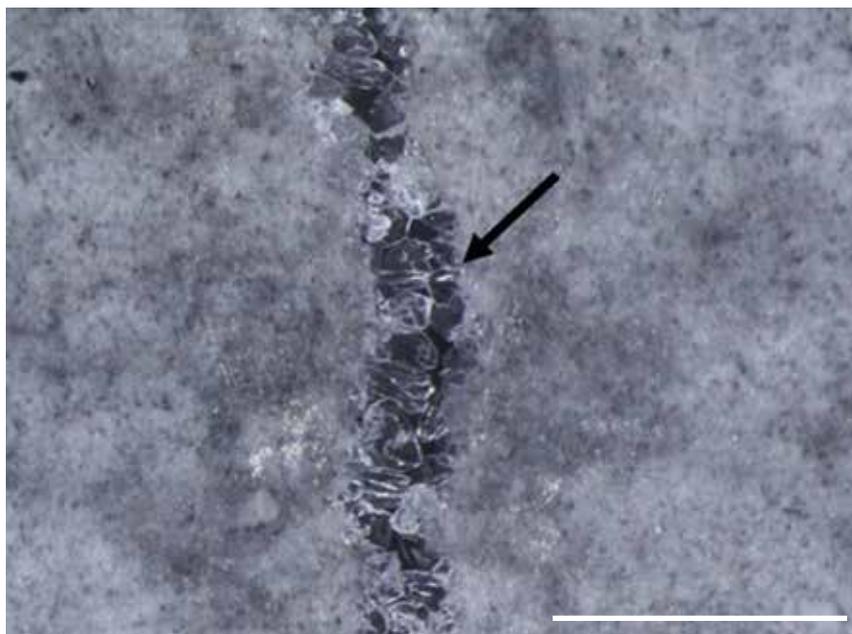
The application of bacterial biomineralisation is an attractive idea in

prolonging the lifetime of cement-based materials, e.g. concrete, and structures such as buildings, bridges and tunnels. Over time, weathering and tensile stresses contribute to the progressive decay of concrete due to the formation of micro-cracks. These micro-cracks allow ingress of water, along with harmful ions such as chlorides that



Calcite crystal (left; bar 50  $\mu\text{m}$ ) and imprints of bacteria in calcite (right; bar 1  $\mu\text{m}$ ). B. Reeksting

may trigger corrosion of the internal steel reinforcement and sulfates that can attack the internal structure of the concrete itself. The enormity of this problem is evidenced by the large cost of repair and maintenance in the UK construction industry, which is estimated as nearly £50 billion per year. Aside from cost, concrete production contributes up to 7% of global anthropogenic carbon dioxide emissions, emphasising the need for lower-maintenance and longer-lifespan products. The possibility of self-healing concrete that can automatically seal up any micro-cracks is therefore highly appealing. Not only would this reduce repair costs, but it would also negate the need for many new structures. How then do we use these bacterial engineers to improve concrete? Concrete poses a harsh alkaline environment (pH 9–12), so bacteria are needed that can survive and grow under such conditions. Members of the genus *Bacillus* and the related *Sporosarcina* are ubiquitous in nature, and are relatively robust in their resistance to harsh chemical and physical environments. They also have the added advantage that they can form spores to facilitate long-term survival. The concept of self-healing materials such as concrete is to include these bacteria during the mixing phase so that they are present within the final structure, but cannot immediately grow because of absence of nutrients. Once a crack develops in the concrete, the bacteria gain access to water and nutrients via this crack and start growing. Their metabolism increases the local pH and the bacterial cell surfaces act as initiation sites for crystal growth. This triggers precipitation of calcite minerals and subsequent sealing of the crack. Calcium carbonate provides the ideal environmentally friendly filler for



Calcite crystal formation within cracked concrete. Bar 500  $\mu\text{m}$ . University of Bath

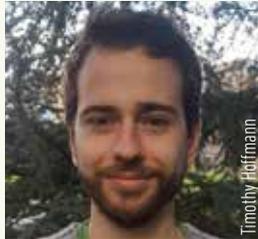
concrete, because it naturally forms within concrete during maturation and is therefore highly compatible with cementitious materials. Initial explorations have already shown that inclusion of bacteria can indeed improve the quality of cementitious construction materials.

### Building the future

The usefulness of microbial biomineralisation in construction materials has been established in principle in the laboratory and in several field trials. However, several challenges still have to be overcome. For example, methods for optimising the survival of the bacteria within concrete are currently being developed. A promising approach is encapsulation, where the bacteria are protected within porous solids such as perlite or polymer-based microcapsules. These capsules are directly incorporated into the concrete mix, and will only release the bacteria when a micro-crack forms and breaks the capsule. Another line of research is looking at the potential of bacteria to perform many cycles of healing. This will entail bacteria germinating from

their spores upon formation of the initial crack, inducing precipitation of calcite, and subsequently returning to spore form to await the formation of further cracks. A final challenge will be to upscale this process from the lab scale to being suitable for commercial use. Self-healing concrete technology would be ideal in the construction of difficult-to-access structures such as tunnels, bridges and underground drainage pipes, which are exposed to constant tensile and weathering stresses, and are difficult and costly to repair and maintain. Although room for improvement remains, current research into such self-healing biomaterials is intense and promising. Ultimately, this approach will allow us to build bacterial bridges towards a brighter, more sustainable future.

The authors are members of the EPSRC-funded Resilient Materials for Life (RM4L) project (Twitter: **@Materials4Life**), where they work with colleagues from the Universities of Cardiff, Cambridge and Bradford to develop self-diagnosing, self-healing construction materials.



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**Timothy Hoffmann** is a PhD student at the University of Bath in the Department of Biology and Biochemistry. His research focuses on areas of synthetic biology and metabolic engineering of micro-organisms for application towards self-healing concrete technologies. Timothy has been a member of the Microbiology Society since 2017.



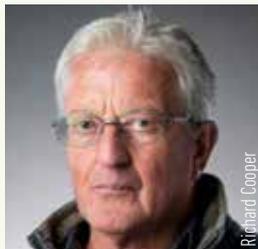
Bianca Reeksting

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**Bianca Reeksting** is a Research Associate in the Department of Biology and Biochemistry at the University of Bath. Her research focuses on the selection and characterisation of bacteria for industrial application, such as for the incorporation into concrete for self-healing. She has been a member of the Microbiology Society since 2017.



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**Richard Cooper** is a Reader in Plant–Micro-organism Interactions at the University of Bath. His research investigates the mechanisms by which microbes can cause disease and how this knowledge can be applied to disease control. He is also interested in how micro-organisms can be applied in other contexts, such as self-healing building materials.



Kevin Paine

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**Kevin Paine** is a Reader in Civil Engineering and Deputy Director of the BRE Centre for Innovative Construction Materials at the University of Bath. He carries out research in the area of smart and innovative concrete technology, and in particular the development of self-healing, self-sensing and self-diagnosing concretes.



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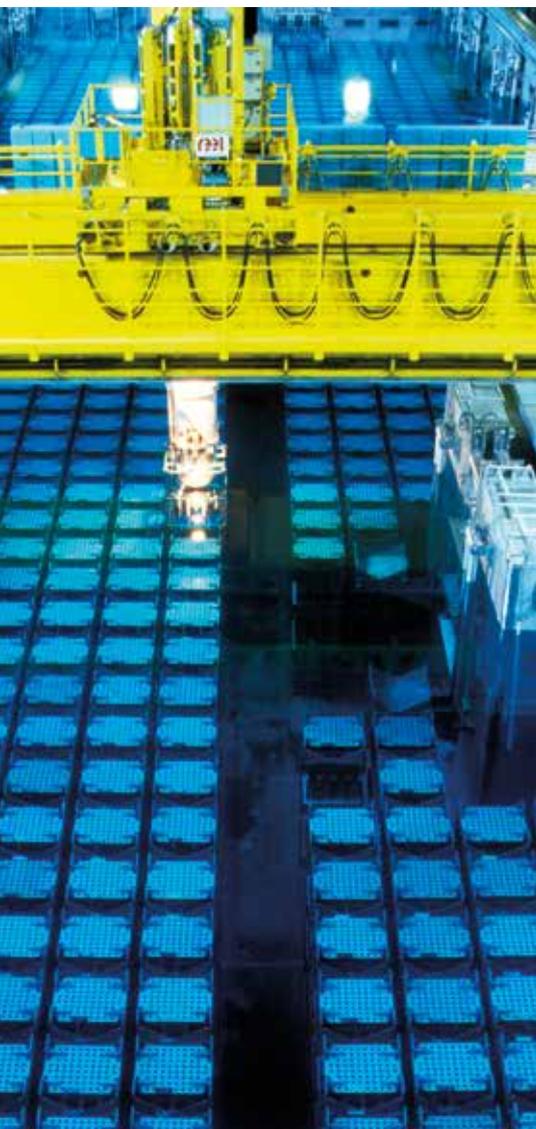
**Susanne Gebhard** is a Senior Lecturer in Medical Microbiology at the University of Bath. Her research interests focus on how bacteria respond to hostile conditions in their environments, such as antibiotics, but also how particularly stress-tolerant bacteria can be applied in an industrial setting. She is a member of the Microbiology Society, having joined in 2014.

### What is the best career decision you have ever made?

**Susanne:** Not giving up on pursuing an academic career.

### What parts of your job do you find most challenging?

**Susanne:** Managing my time between all the different duties as a lecturer (teaching, research and admin) to do a good job with all of them, while still trying to be a good colleague and supportive supervisor.



Nuclear fuel and containers at a reprocessing centre in France. Patrick Landmann/Science Photo Library



# The unexpected influence of microbiology on the disposal of radioactive waste

Simon Gregory & Megan Barnett

**The safe disposal of radioactive waste in repositories constructed deep underground might not sound like a topic that requires much input from microbiologists, but a surprising amount of work has been carried out around the world on how micro-organisms might be beneficial or harmful for the safe containment of such waste.**

The UK has a legacy of radioactive waste from activities such as power generation, medical applications, defence and research. This material is currently securely stored at sites around the UK. The UK Government, and those of many other countries, have identified that the best and safest approach to long-term management of this waste, in particular, higher-activity waste, is through 'geological disposal': placing the waste in carefully engineered chambers deep underground. This repository will be constructed between 200 m and 1,000 m below the surface, in a geological setting that has been carefully selected for its ability to contain the waste for hundreds of thousands of years, and will isolate waste until harmful radionuclides have decayed sufficiently. The repository itself will be highly engineered and contain multiple barriers (the last of which is the mass of rock between it and the surface), designed to limit any release of radionuclides. The UK Government published a White Paper in 2014 setting out how it will implement geological disposal and is currently undertaking a national exercise collating information about the different types of rocks that occur to depths of about 1,000 m beneath England, Wales and Northern Ireland.

### **Microbes in deep subsurface environments**

So, what is the relevance of microbiology to the disposal of radioactive waste? The conventional view used to be that the subsurface was inhospitable to life below a depth of more than a few metres, but as microbiologists have searched deeper, they have continued to find signs of life. Micro-organisms are now known to persist to several

**The complex processes that will occur following the closure of a radioactive waste repository, the long timescales involved and its inaccessible nature make research challenging. However, close collaboration between scientists and organisations tasked with managing and disposing of radioactive waste have, over many years, significantly advanced our understanding.**

km below the surface – for example, bacteria have been found living 3,200 m below the surface in the Witwatersrand Basin, South Africa. However, it is generally true that as you go deeper, microbial number and activity declines. At the proposed depth of a repository, microbial activity will typically be low. This decline relates to a number of factors, including the consumption of oxygen and easily available organic carbon sources near the surface, and the availability of physical space in rocks. Work at underground research laboratories in rock types under consideration for hosting a repository often reveals a sparse but diverse microbial community. Certain clay formations, identified as suitable rock types, present a particularly challenging environment for micro-organisms: the pore space is much smaller than the size of a typical bacterial cell, water is not freely available, and any organic carbon tends to be either inaccessible, or unavailable to micro-organisms, or both. Researchers from other European countries, working on their own disposal plans, have identified viable, though largely dormant, communities of micro-organisms in clay formations that could be suitable for a disposal facility, for example, the Boom Clay at Moll in Belgium or the Opalinus Clay at Mont Terri in Switzerland. Research

in other suitable rock types, such as at the Äspö Hard Rock Laboratory in Sweden, has identified a metabolically active microbial community in water flowing in fractures in the rock. Microbial metabolism in these subsurface environments is often driven by hydrogen-consuming autotrophs. These in turn can provide the organic matter to support other micro-organisms such as fermenters and heterotrophic sulfate-reducing bacteria.

### **Potential impacts of micro-organisms around a repository**

Based on this research, we can expect that the rock surrounding any proposed repository is likely to be able to maintain micro-organisms. The excavation of a repository will dramatically change the environment, temporarily introducing an oxygenated atmosphere and a variety of nutrients associated with contamination and waste that any construction operation brings. This is likely to alter the microbial community in diversity, activity and biomass. Once a repository has been filled, it will be sealed, trapping any micro-organisms that have been introduced, along with materials used in construction that could act as nutrient sources for micro-organisms. Extensive lists of these materials have been drawn up describing potential substrates that micro-organisms could utilise, including

rubber from tyres, diesel, hydraulic oils, fibres from clothing and organic material from explosives. Following closure, any micro-organisms will have to endure a number of stresses including high radiation, high temperatures and exposure to hyperalkaline conditions, but again research points to the remarkable ability of microbes to survive these stresses. The challenges are to

understand what microbial activity might be supported in this extreme and inaccessible environment, to understand how this may change over the lifetime of the repository, and to understand what the potential positive or negative impacts might be. This often requires complex, high pressure experiments (see figure).

Metal waste containers are selected to resist corrosion; however, over the

long periods of a repository lifetime, they, and waste metals, may corrode, producing hydrogen. This hydrogen is then available for certain groups of micro-organisms to use. Sulfate-reducing bacteria are a particular concern in this respect as they consume hydrogen and produce hydrogen sulfide that can accelerate the corrosion process. However, there are also potential benefits from such a microbial ecosystem. Post-closure, microbial metabolism will produce carbon dioxide and in an anoxic environment, methanogens could combine hydrogen and carbon dioxide to form methane, reducing the overall volume of gas and gas pressure generated within the repository, thus reducing risk.

In many proposed repository designs, swelling clays will be used as part of the multi-barrier system. Blocks or pellets of this clay packed into the disposal facility will become saturated by groundwater, causing the clay to swell to fill the voids in the repository, creating a further barrier to the escape of radionuclides. This clay itself contains micro-organisms, especially spore-forming, sulfate-reducing bacteria, which survive the industrial processing of the blocks and pellets. Microbial reduction of iron within clay minerals has been demonstrated and alters the structure of clays, reducing their swelling capacity and potentially reducing the ability of the clay to act as an effective barrier.

Micro-organisms could be beneficial in other ways. For example, the ability of a wide range of micro-organisms to reduce uranium is known from lab and field studies. The reduction of soluble U (VI) to insoluble U (IV) retards uranium transport and has been suggested as a method of bioremediation in contaminated soils. Micro-organisms could perform the same



Apparatus used to conduct experiments used to study the impact of micro-organisms in swelling clays on swelling capacity and steel corrosion. Two high pressure pumps (A) control the flow of groundwater through a clay sample held in a bespoke flow cell (B). The flow cell has continuous monitoring to record changes in flow and in the force exerted by the swelling clay (C). Megan Barnett, BGS

reactions around a repository, retarding the movement of radionuclides. Uranium is also mobile when it forms soluble complexes with some organic molecules that will occur as breakdown products of intermediate-level waste. Microbes have been identified that consume these molecules, further reducing the mobility of complexed uranium. This is another example of microbial activity that could be beneficial around a repository.

The complex processes that will occur following the closure of a radioactive waste repository, the long timescales involved and its inaccessible nature make research challenging. However, close collaboration between scientists and organisations tasked with managing and disposing of radioactive waste have, over many years, significantly advanced our understanding. For the UK, this means that there is a strong science base to draw on when considering our own repository. As far as microbes are concerned, the key processes are now understood, though research will be required to understand site- and repository-specific factors that may influence microbial activity.

### Suggested reading

For general background on the UK plans for geological disposal of radioactive waste: <https://www.gov.uk/government/news/geological-disposal-understanding-our-work>

Review of work relating to microbiology at the Mont Terri Rock Laboratory (Switzerland) Leupin, O. X., Bernier-Latmani, R., Bagnoud, A., Moors, H., Leys, N., Wouters, K. & Stroes-Gascoyne, S. (2017). Fifteen years of microbiological investigation in Opalinus Clay at the Mont Terri rock laboratory (Switzerland). *Swiss Journal of Geosciences* **110**, 343–354.

Recent paper on the microbiology at the Äspö Hard Rock Laboratory (Sweden):

Hubalek, V., Wu, X., Eiler, A., Buck, M., Heim, C., Dopson, M., Bertilsson, S. & Ionescu, D. (2016). Connectivity to the surface determines diversity patterns in subsurface aquifers of the Fennoscandian shield. *The ISME Journal* **10**, 2447–2458.

Recent paper on how consumption of organic molecules could retard radionuclide transport:

Bassil, N. M., Bryan, N. & Lloyd, J. R. (2015). Microbial degradation of isosaccharinic acid at high pH. *The ISME Journal* **9**, 310–320.



### Simon Gregory

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Simon Gregory has taken a circuitous route through neuroscience, human population genetics and aquaculture to get to where he is now. He leads the geomicrobiology research at the British Geological Survey. His current research interest include microbial aspects of radioactive waste disposal, carbon capture and storage, biomining and shale gas extraction.



### Megan Barnett

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Megan Barnett discovered her interest in microbiology while studying fossil biofilms for her geology degree dissertation. She went on to gain a PhD from Cranfield University, looking at adapting instrumentation for microbial detection and identification in the field. Megan has worked at the BGS since 2015 on deep and surface microbiology.

### What do you find most enjoyable about your job?

**Simon:** I enjoy the fact that I work with a lot of experts in other disciplines (mineralogists, petrologists, geochemists, rock mechanics, etc.) who bring a different point of view to the table. It truly is a multidisciplinary task to understand geomicrobiological processes, and I am constantly learning new things from them.

### How do you see this field changing in the future?

**Simon:** Only a very foolish person would be prepared to offer predictions in any area of science, but what I would like to see is continued effort to develop robust ecology theories that can be applied to microbiology. Doing this will allow us to understand the mechanisms of how microbes interact with the environment and to better predict what the impact of those interactions will be in a vast range of natural and engineered environments and at a range of scales, from site-specific locations such as a geological disposal facility to global biogeochemical processes.

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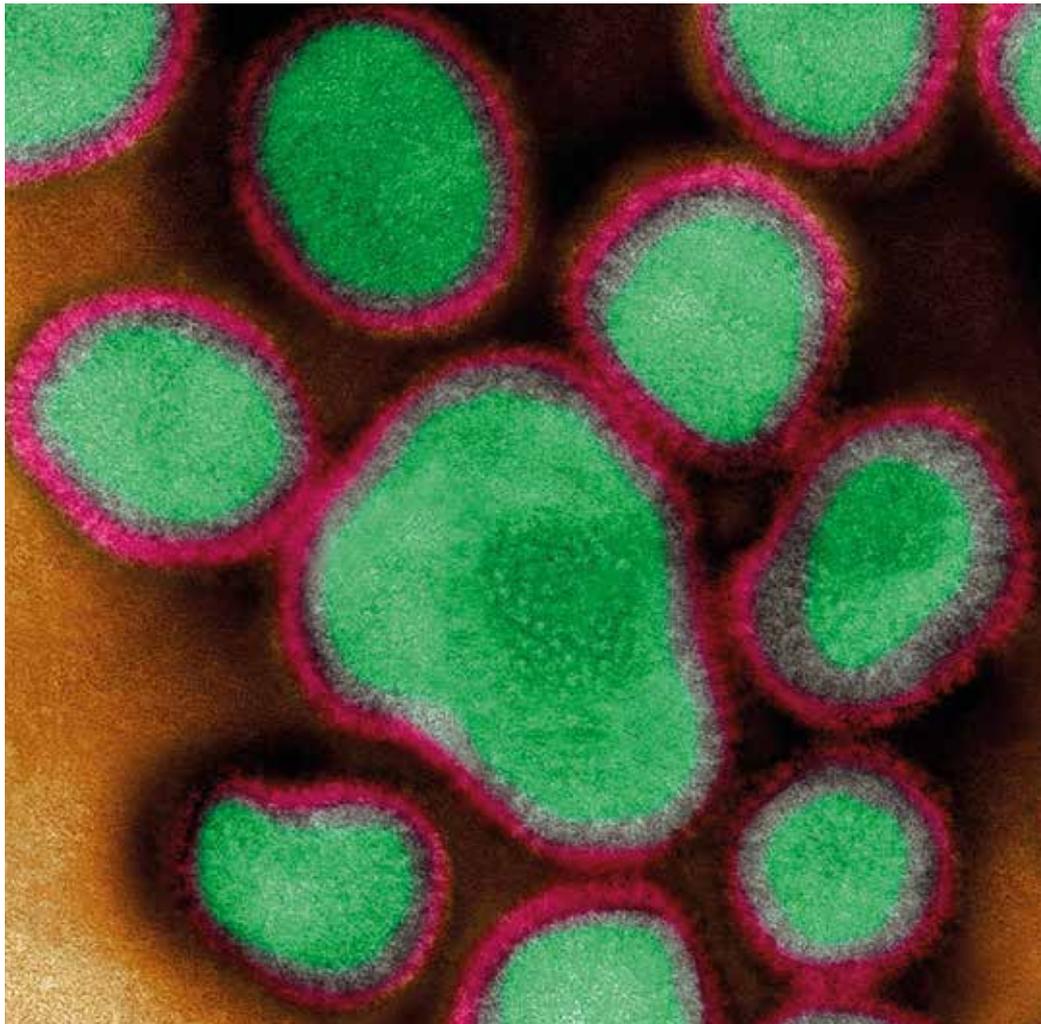
# Influenza pseudotype research and development

Nigel Temperton

**Undertaking research and development (R&D) on novel therapeutics and vaccines for emerging viral pathogens is fraught with numerous obstacles, one of which is the requirement for high-containment laboratory facilities.**

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Coloured transmission electron micrograph of swine influenza (H1N1) virus particles (virions) determined to be the cause of the April 2009 outbreak (originated in Mexico City, Mexico). Dennis Kunkel Microscopy/Science Photo Library



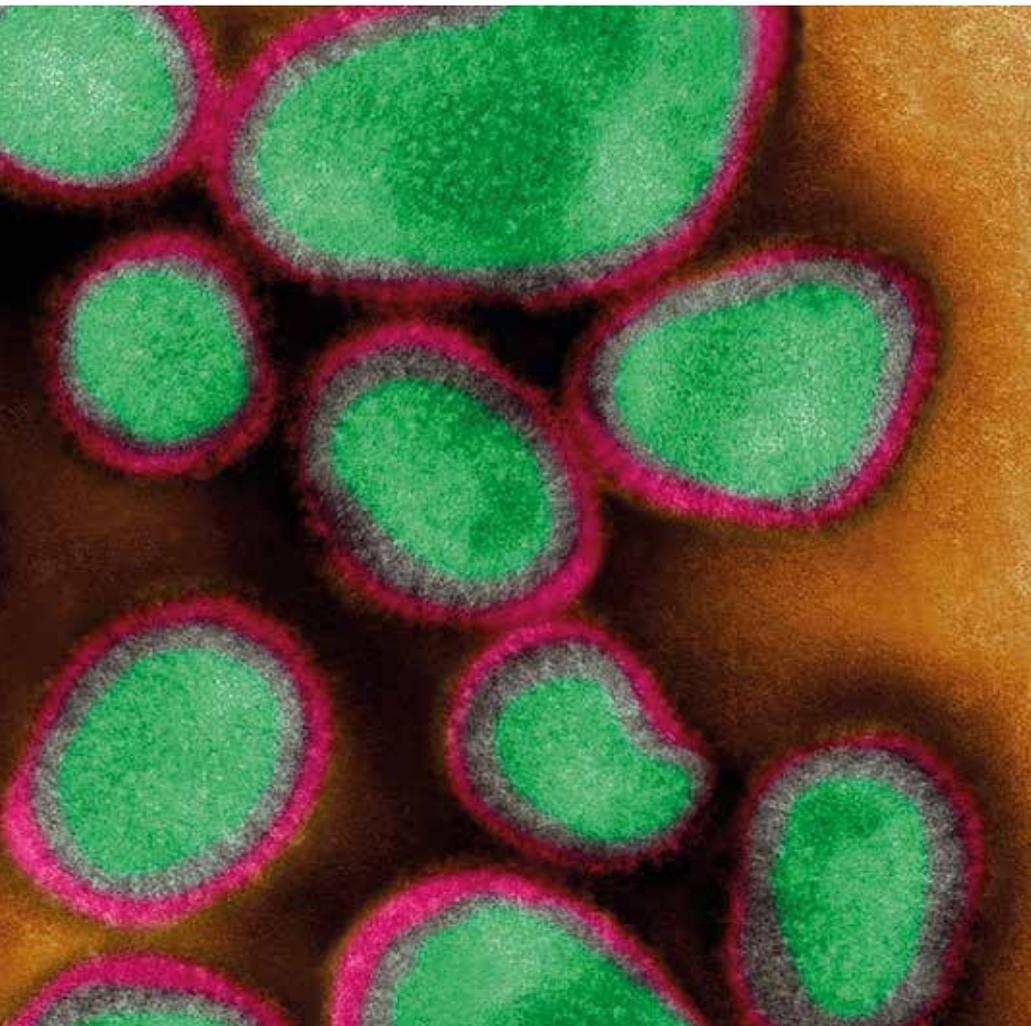
We and others have pioneered the design, construction and deployment of retroviral pseudotype viruses (PV) that are now having significant impact on preclinical research undertaken by pharma, and by public and animal health institutes worldwide. These pseudotypes are biosafe, replication-defective retroviruses and lentiviruses that have been repurposed from gene therapy applications. They have heterologous (foreign) viral glycoproteins on their

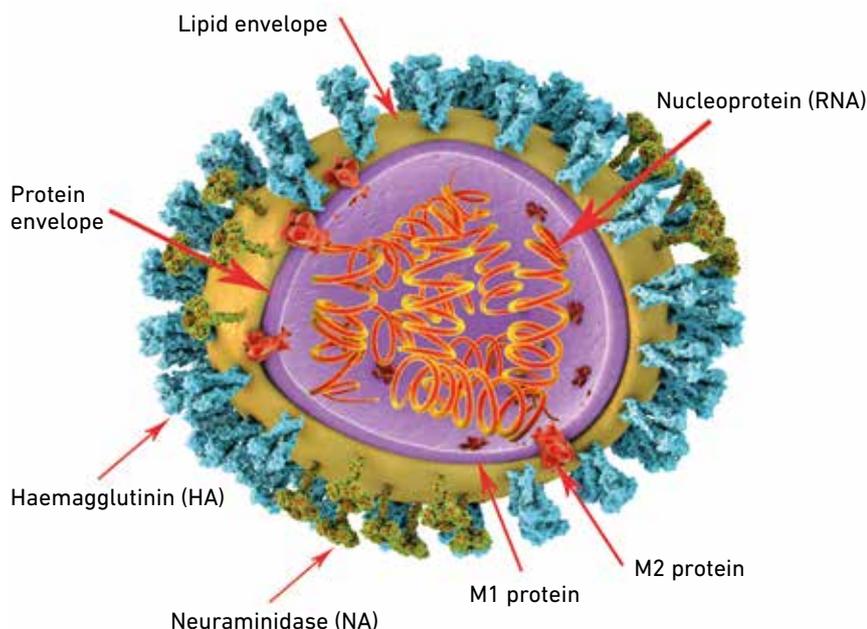
surface that originate from the viral pathogen. They thus mimic the wild-type virus with respect to cell entry, but can be handled by end users in biosafety level (BSL)-1 instead of BSL-3/4 laboratories. They have been described elegantly by Robin Weiss FRS (a former President of the Microbiology Society) as 'sheep in wolves' clothing'. These incorporate a quantifiable reporter, usually firefly luciferase or GFP (which is integrated into the target cell genome), enabling sensitive and

high-throughput cell entry-based assays to be performed. The pseudotype-based assays are simple to upgrade, as only the nucleotide sequence of the surface glycoprotein(s) is required. These sequences are readily obtained from NCBI and GISAID. This makes them particularly ideal for emerging RNA viruses, e.g. avian influenza, rabies, SARS/MERS coronaviruses, Ebola. These pseudotype viruses are very stable over a range of temperatures and can be freeze-dried for efficient deployment to end users. It is hoped that this will facilitate the roll-out of such assays to low- and middle-income countries (LMIC). The virus neutralisation assays performed using pseudotype viruses are both serum and antigen sparing, and enable the study of functional responses, which correlate strongly with those measured using cognate wild-type virus assays. This results in significant cost saving for the end user, given the exorbitant infrastructure and staff costs of undertaking serological assays with high-containment viruses of human and animal importance.

### Viral Pseudotype Unit

Expertise at the University of Kent in pseudotype technology led to the creation, in 2011, of the Viral Pseudotype Unit (VPU). The VPU acts as an interface between academia, industry, and animal and public health laboratories, with the purpose of translating basic virus research into *in vitro* cell culture pseudotype-based assays that can be readily employed for the characterisation of vaccines, antivirals and therapeutic antibodies. This has led to the use of pseudotype assays in the following broad R&D areas: immunogenicity testing of current and preclinical viral vaccines including new





3D illustration of influenza virus particle structure. The virus consists of a ribonucleic acid (RNA, orange coils) core, surrounded by a nucleocapsid (purple) and a lipid envelope (yellow). Spanning the capsid and envelope are M2 proteins (red) that act as proton pumps. In the envelope are two types of protein spike, haemagglutinin (H, blue) and neuraminidase (N, green), which determine the strain of virus. Kateryna Kon/Science Photo Library

'universal' vaccine prototypes; screening of monoclonal antibodies to isolate those that broadly neutralise across multiple subtypes/species of the same virus; characterisation of antibody standards for serological assays; study of virus restriction factors (entry); and drug screening/resistance studies.

### Functional serological assays to measure antibody responses against the haemagglutinin (HA) globular head, HA stalk and neuraminidase (NA)

Influenza pseudotypes have been used to undertake serological assays for big pharma and biotech clients, and will hopefully contribute one day towards the licensure of influenza vaccines, at least as an adjunct assay. In a joint study with Novartis Vaccines, we showed that pseudotypes could be used to quantify neutralising antibody responses elicited by a pre-pandemic H5N1 vaccine and that these correlated significantly with those measured by haemagglutination inhibition (HI), single radial haemolysis (SRH) and

microneutralisation. Pseudotype neutralisation assays for influenza have been shown to be exquisitely sensitive for the measurement of responses to the HA stalk, which is one of the primary targets of many big pharma 'universal vaccine' approaches. The responses directed against the stalk can be separated from those against the head by making use of a hybrid HA pseudotype. One such virus that we have created has an HA stalk derived from the 2009 pandemic H1N1 strain, and an HA globular head derived from an H11 strain which is found in wild birds. Humans have negligible serological reactivity to H11, so if a neutralisation assay is undertaken with this hybrid HA

pseudotype, one can readily measure the response against the HA stalk only. The traditional HI assay (for which a correlate of immunity exists) used by the regulators only measures responses against the globular HA head and thus is not fit for purpose for the licensing of many new 'universal vaccines'. HA stalk serological assays, such as those based on pseudotypes or ELISA, will no doubt gain prominence as many of these new vaccines move down the clinical pipeline.

Recently, a pseudotype-based enzyme-linked lectin assay (PV-ELLA) has been developed, which allows the quantification of antibody responses against NA. This assay innovatively uses NA-only pseudotypes as a source of NA. The availability of this PV-ELLA to the R&D community is instrumental as it means that ELLA assays can be performed without requiring access to reverse genetic (RG) viruses, which often have IP attached. Also, there are moves towards standardising the amount of NA in recombinant vaccines, making PV-ELLA assays increasingly important.

Pseudotypes are also gaining acceptance as a method for the identification of antibody standards that can be used to harmonise serological outputs across multiple different assays. This was recently undertaken for the Ebola virus by the NIBSC.

**The availability of pseudotype viruses to industry has resulted in significant time/cost savings and increases in assay sensitivity and ultimately productivity, and has been moved forward into other pipelines for rabies, Ebola and MERS.**

## Characterisation of therapeutic mAbs

The influenza HA pseudotype neutralisation assays and know-how have been used in pivotal collaborations with pharma companies that isolate monoclonal antibodies derived from individuals whose immune systems have successfully responded to influenza infection. One of these monoclonals, FI6 developed by Humabs in Switzerland, targets the fusion peptide on the HA stalk and is thus able to protect against all subtypes of influenza and therefore critical for informing universal vaccine design. Pseudotype viruses were instrumental in the characterisation of this broadly neutralising antibody. The availability of pseudotype viruses to industry has resulted in significant time/cost savings and increases in assay sensitivity and ultimately productivity, and has been moved forward into other pipelines for rabies, Ebola and MERS.

## New viruses, new reservoirs

Not all influenza A subtypes have their reservoir in wild birds. Two new influenza subtypes, H17 and H18, have been discovered in bats, and the potential for spillover into humans or intermediate hosts is unknown at the present time. However, using our pseudotype technology, we have been able to construct an H17N10 pseudotype and shown that this virus (unlike H1–H16) does not use sialic acid as its receptor. Research is ongoing in our and other laboratories to identify this receptor. We additionally showed that H17N10 can be efficiently neutralised by the mAb FI6, and also by serum from individuals who have a high antibody response against the H1 stalk (as measured using the hybrid HA pseudotype assay).

In conclusion, I would say that the

future is bright for using pseudotypes in virology R&D. As surrogates of the wild type, they offer significant safety advantages, and their readily adaptable and upgradable nature allows them to be used to study multiple targets of the antibody response.

## Further reading

**Biuso, F. & others (2017).** The study of antibody responses to influenza neuraminidase using a lentiviral pseudotype based ELLA. *bioRxiv* (preprint).

doi:10.1101/218800

**Carnell, G. W. & others (2015).** Pseudotype-

based neutralization assays for influenza: a systematic analysis. *Front Immunol* **6**, 161.

doi:10.3389/fimmu.2015.00161

**Ferrara F. & others. (2015).** The application of pseudotypes to influenza pandemic preparedness. *Future Virol* **10**, 731–749.

doi:10.2217/fvl.15.36

**Temperton, N. J. & others (2015).** Retroviral Pseudotypes – From Scientific Tools to Clinical Utility. In *eLS*, John Wiley & Sons, Ltd (Ed.).

doi:10.1002/9780470015902.a0021549.pub2

**Temperton, N. (2016).** The Viral Pseudotype Unit: viral pseudotype R&D, dissemination and education. *Future Virol* **11**, 113–116.

doi:10.2217/fvl.15.109



## Nigel Temperton

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**Nigel Temperton's** research interests lie primarily in emerging/re-emerging and transboundary viruses (SARS/MERS coronavirus, pandemic/inter-pandemic influenza, and Ebola), and the methods for their control – in particular, control by vaccination-induced antibody responses. He has established novel virus antibody neutralisation assays for these high-containment viruses by exploiting retroviral and lentiviral vector technologies.

Nigel has been a member of the Microbiology Society since 2003. The Society has contributed significantly towards the impact and reach of his group's pseudotype work by giving platforms for PhD students to present their work to a wide spectrum of microbiologists.

## How did you enter this field?

I entered this field during my time as a Wellcome Trust-funded postdoc studying endogenous retroviruses in Robin Weiss' group at UCL. After a lunchtime seminar given by a Hong Kong academic visitor who had himself been infected by the SARS coronavirus, Robin said to me "Nigel, what you need to do is develop a SARS pseudotype so we can do some serology". The rest is history. I have dedicated my career to exploiting these pseudotypes ever since.

## What is the most rewarding part of your job?

The most rewarding part of my job is first and foremost the nurturing and training of the next generation of 'pseudotypers'. I also enjoy promoting pseudotype technologies by any means available, including over social media @ViralPseudotype.

# Using microbes for precision insect pest control

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Miranda Whitten & Paul Dyson

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**It is time to reduce the environmental footprint of insect pest control. Bacteria are the ideal tools for developing 'smart' precision bio-insecticides and preventing disease transmission by insects.**



Fig. 1. Pollinators are under threat from climate change, pollution and habitat loss. Miranda Whitten

Despite the current US President's denials, there is incontrovertible evidence that human activity has negatively impacted our environment. Changes in the abundance, diversity and distribution of invertebrates (and insects in particular) are being brought about by climate change, intensive agriculture, pollution and habitat loss. The windscreen 'splatometer' test – a crude gauge of the flying insect populations on our roads – suggests that insects are declining precipitously. As the great majority of insects are beneficial in some way (such as pollinators, Fig. 1) and integral to ecosystems, we should all be concerned. Other species have proven more adaptable, but these include the 'undesirables': species such as the western flower thrips (WFT), an agricultural pest that has surged outwards from the USA into every cultivated continent of the world in just six decades. *Aedes aegypti*, a mosquito vector of arboviruses such as Zika, has also spread across continents in the same period (Fig. 2).

### Testing times for pesticides

Our attempts to increase yields of crops and control insect vectors of disease through the use of conventional chemical pesticides have undoubtedly been met with fantastic short-term successes. However, evolution never stands still and the use of each new insecticide eventually selects for resistance in the target insect population. Moreover, many of these chemicals indiscriminately kill non-target species including beneficial pollinators and aquatic larvae in surface waters polluted with insecticide-contaminated run-off. Many regulatory agencies have exercised prudence by imposing reductions or bans on certain pesticides (e.g. neonicotinoids, now

notorious), rather than gambling on the expedient evolution of resistance in non-target species. But how will farmers fill this pesticide vacuum, if – as it must – agricultural output is to continue to increase? One increasingly mainstream alternative is integrated pest management (IPM) schemes that rely on biological control agents such as predatory insects, nematodes, insect-pathogenic fungi and the bacterium *Bacillus thuringiensis*. These may have a smaller environmental footprint, but may be less easy to apply in an effective manner by inexperienced farmers, with consequences for productivity.

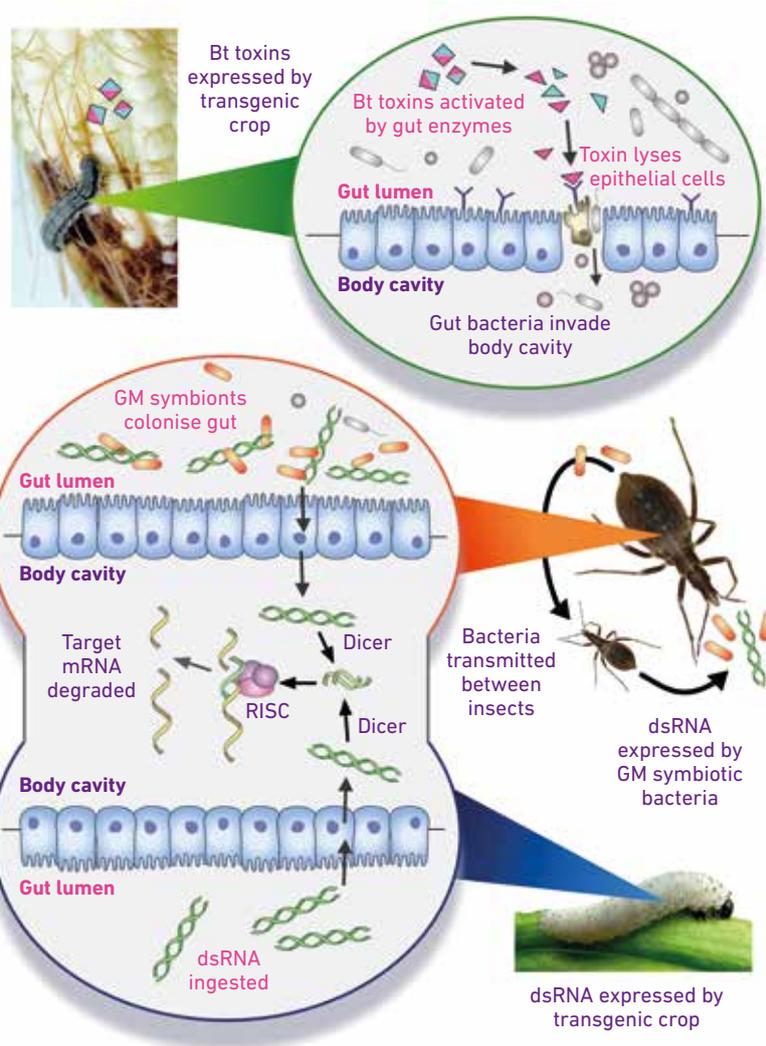
### Release of modified insects as a population control measure

Smart measures to control pest insect populations should have little or no impact on the other flora and fauna. For example, an understanding for how bacterial symbionts can impact the biology of their insect hosts has led to a control strategy that limits the transmission of dengue virus. This intervention is urgently needed as dengue fever outbreaks now affect

almost 2.5 billion people globally. Strains of the endosymbiont *Wolbachia* isolated from fruit flies are used to infect *A. aegypti* mosquitoes. The bacteria modify the breeding success of these mosquitoes so that the infected insects, once released into the environment, become dominant in the population. Moreover, the bacteria effectively reduce the mosquito's viral load and this diminishes their ability to transmit the virus (at least for now – another mosquito species, *A. albopictus* that naturally harbours *Wolbachia*, is very effective at virus transmission). This highly targeted intervention to control insect-vectored disease is believed to have little or no impact on other animals or plants. It requires the breeding and release of huge numbers of modified insects, an expense that can be justified because of the protection afforded to humans. Although screwworms – which are livestock parasites – have been controlled for decades via the mass release of radiation-sterilised male insects, the costs associated with equivalent targeted insect releases cannot be justified for protecting arable



Fig. 2. The mosquito *Aedes aegypti* during a blood meal. James Gathany – <http://phil.cdc.gov/phil/home.asp> ID#: 8932 US Department of Health and Human Services (Public Domain)



**Fig. 3.** Major bio-insecticide strategies using genetic modification approaches. Top: Insects ingest Bt toxins from engineered crops. Middle: Symbiont-mediated RNAi delivers target gene knockdown for insect pest control, or to interfere with disease transmission. Bottom: RNAi via dsRNA-expressing transgenic crops. Top left, Jack Dykinga [www.ars.usda.gov/is/graphics/photos/aug11/k2627-14.htm](http://www.ars.usda.gov/is/graphics/photos/aug11/k2627-14.htm); middle and bottom, Miranda Whitten

crops, fruit and forestry because of their relatively low value and high acreage. Alternative 'smart' measures are needed to support the productivity of non-animal based agricultural systems.

### Bt crops producing a *Bacillus thuringiensis* endotoxin

The soil bacterium *Bacillus thuringiensis* (Bt) produces endotoxins during sporulation that have specific toxicity to several insect species. The inactive crystal protein is enzymatically converted to an active toxin inside an insect's gut. Bt spore and crystal preparations have been used for a century to control crop and disease pests, and in the last two decades, Bt toxin genes have been expressed in transgenic crops (Fig. 3). Notable successes are Bt cotton varieties that resist pests like bollworms, and Bt corn, which controls the European corn borer, corn rootworm and corn earworm. Taken as a percentage of total farmed acreage, transgenic Bt varieties represented more than three quarters of all US corn and cotton crops by 2013. Farmers report substantial improvements in productivity concomitant with reduced insecticide usage, and a Chinese study indicates that these conditions allow populations of beneficial insects (such as ladybirds and lacewings) to recover, while suppressing aphids and other pests. However, the rapid and extensive adoption of these GM crops, if not cautiously managed, can drive (and already has driven) the evolution of Bt toxin resistance in target species.

### Bacteria-mediated RNA interference to control insect pests

While it is generally accepted that Bt crops have little effect on non-target insects, another genetically modified (GM) crop variety has been developed that offers potentially still greater insecticidal

precision. Maize has been engineered to produce double-stranded (ds) RNA that, once ingested by a pest insect, can induce RNA interference of an essential insect gene. By this mechanism, the western corn rootworm is killed by the very crop upon which it feeds (Fig. 3). The specific sequence of the dsRNA is such that it should target the pest gene and not orthologs (genes of same or similar function) in non-pest species. Indeed, safety tests show that the dsRNA has no adverse effects on a battery of non-target organisms. It is also encouraging that there are no reports of insects evolving resistance to these plant-based RNAi-based biocides.

Transgenic Bt and dsRNA crops work best against insects that feed exclusively on one crop species. But many pests are polyphagous – they can feed on a variety of plants. In this situation, plant-

based biocides are unlikely to offer much protection to other crops in the vicinity, and it is hardly feasible to engineer every species of vulnerable crop with a pest-specific biocide.

One polyphagous insect of global importance is the diminutive but highly destructive WFT, which not only feeds on an enormous range of plants, but also transmits tospoviruses – plant pathogens with a broad host range. An approach to deliver sustainable biocidal RNA interference to this insect involves engineering a symbiotic bacterium related to *Pantoea* to continuously produce dsRNA from within its niche in the insect's gut (Fig. 3). The dsRNA targets an essential WFT gene, with lethal consequences. The technology, symbiont-mediated RNAi (SMR), is in the early stages of development, but offers two-tier specificity – combining the

specificity of symbionts for their host with the sequence-specificity of RNAi. Because symbiotic insect bacteria have co-evolved with their hosts and typically exhibit genome reductions that render them ill-equipped to survive elsewhere, GM versions of these symbionts are likely to have little or no impact on other species.

SMR can be utilised in other ways, such as reducing the fertility of blood-sucking insects called kissing bugs, which transmit Chagas disease. Their symbiotic rhodococci are transmitted among a colony of the insects due to their charming behaviour of probing each other's excreta (coprophagy). The bacteria can also remain dormant in the excreta for long periods, so this application of SMR could provide a useful, targeted approach to limit Chagas disease in rural populations of South and Central America. SMR could be used in IPM to increase a pest's susceptibility to biological control agents such as entomopathogenic fungi, and there are also prospects for using SMR to target insect-vectored pathogens *in insecta*.

Many of these smart methods of insect control depend on microbes, and the more we understand about insect-microbe interactions, the more we can exploit them to develop targeted interventions with reduced environmental footprints.

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### Miranda Whitten

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<https://www.youtube.com/watch?v=NYiEMUT0zBU>

Miranda Whitten's background is in insect physiology and host-pathogen interactions, and the use of bacterial symbionts for reverse genetic approaches to pest control and disease transmission. She is also a member of the Guild of Natural Science Illustrators. This is Miranda's third year of Microbiology Society membership.



### Paul Dyson

Professor of Molecular Microbiology, Institute of Life Science, Swansea University Medical School, Singleton Park, Swansea SA2 8PP

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After a PhD at the University of Glasgow, and three postdoc positions spanning six years, Paul Dyson established his own group at Swansea University, focusing primarily on antibiotic-producing *Streptomyces*. More recently, his research has embraced the use of bacteria to deliver gene silencing in insects and solid tumours. He has been a member of the Microbiology Society for 35 years.

### How did you enter this field of work?

**Paul:** With experience of genetic manipulation of *Streptomyces*, Miranda asked me if we could genetically manipulate another actinobacterium: *Rhodococcus rhodnii*, a symbiont of 'kissing bugs'. This was the beginning of a fruitful collaboration to develop symbiont-mediated RNAi for insects.

### What parts of your job do you find most challenging?

**Paul:** The most challenging aspects of the job are managing the expectations of members of my research group and maintaining funding streams to keep them in post.

# Viruses: life-saving drugs?

Jonathan Welsh, Helen Young, Ruth Stephen & Sam Laurel Stephen

**Imagine a future in which someone suffering from a debilitating disease such as diabetes, instead of taking daily insulin injections, need to take only one injection in their entire life? No more panic attacks when the insulin syringe goes missing, and they can have a life just as the non-diabetics enjoy. Welcome to the world of gene therapy, dubbed the 'medicine of the future'.**

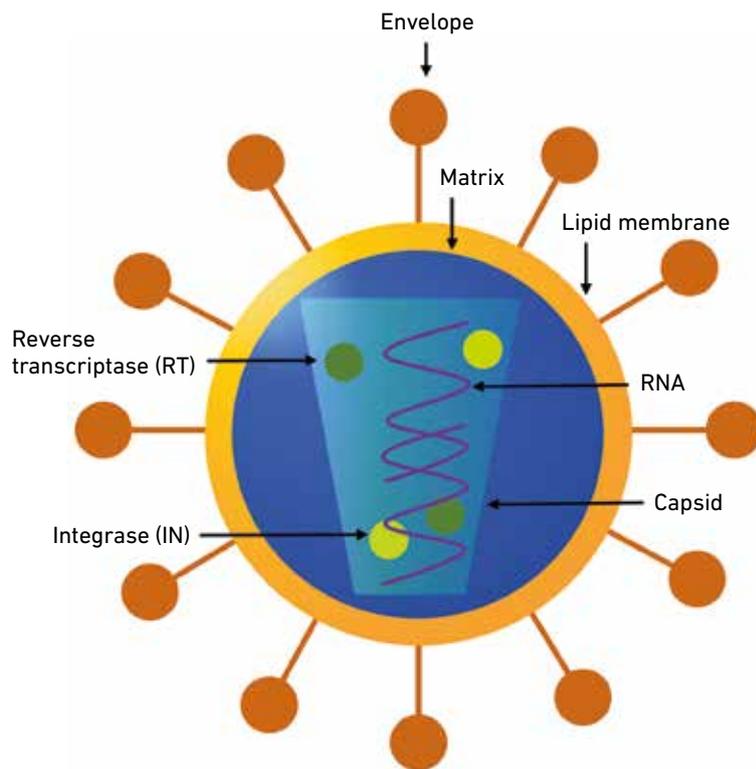


Viral vectors can be made in small scale, in cell culture plates, to optimise conditions. © CPI 2018

A century has passed since Garrod, in his seminal work on alkaptonuria, discovered that genetic disorders can result in diseases. Now, we know that a significant number of health problems have genetic causes. One approach is to treat fire with fire (genetic diseases with genetic medicine). This is 'gene therapy', and to transfer the gene therapy medicine from the laboratory bench to the hospital bed, we need vehicles (vectors).

Preparing vectors can be compared to preparing fish for consumption. The fish is gutted ('bad' genes are removed), stuffed (therapeutic genes are put in), baked (the vector is produced) and consumed (administered to the patient).

Viruses are ideal vectors since they have specialised mechanisms to bypass the host immune system, whereas, broadly speaking, non-viral systems are hampered by a lack of ability to target the relevant tissues. Viruses are microscopic (visible only by electron microscopy) infectious organisms with an obligatory parasitic phase in their life cycle. They may or may not have an outer covering made of proteins or lipids (envelope), but they all do have a protein shell (capsid) that protects the genome (the complete genetic material of an organism) and some essential



**Fig. 1.** A schematic of a representative virus. Retroviruses, depicted here, have an RNA genome, which, along with essential proteins RT and IN, is protected by a protein shell (capsid). Retrovirus is an enveloped virus with a lipid membrane and envelope proteins. © CPI 2018

proteins (Fig. 1). The viral genome is the epitome of space-saving and genome organisation. Though viruses have dogged our footsteps since the dawn of civilisation (as hieroglyphics of an Egyptian priest from around 1500 BC maimed by polio show), and viral diseases such as smallpox and influenza have changed the course of history – for example, more people were killed by the Spanish flu than World War I – we can harness and exploit their built-in abilities by using them as vaccines or as gene therapy vectors.

The idea of gene therapy has been mooted since the 1970s, but it was after the tragic case of the ‘bubble boy’, David Vetter (1971–1984), that the idea really took off. David suffered from a genetic mutation resulting in a severe combined immunodeficiency (SCID). In the early 1990s, researchers used a retrovirus to achieve a lifetime correction of a similar genetic mutation in two human volunteers. Since then, viral gene

therapy research and production has greatly accelerated.

### How are viral vectors produced?

An analysis and understanding of the life cycle of the viruses is essential. This includes picking only those genetic elements absolutely essential for the growth and packaging of the nucleic acid genome into the protein capsid.

**Table 1.** A table detailing the three major viral vectors used for gene therapy (© CPI 2018)

Vectors based on	Genome, cloning capacity	Pros	Cons
Retroviruses Lentiviruses	RNA 8 kb	Long term expression	Low titre, genotoxicity
Adeno-associated viruses	DS-SS DNA 4kb	Very high titre, targets more tissue types	Small size, questions about genotoxicity
Adenoviruses	DS DNA 8–36 kb	Very high titre, large transgene capacity	Immune response

This new genome is provided in the form of a DNA plasmid. The viral vector still needs the proteins produced by the ‘non-essential’ genes. So we put it in a totally different DNA plasmid (in *trans*), and because this plasmid does not have the part of genetic material essential for it to be packaged in the plasmid capsid, it is not packaged. All these plasmids are transfected into producer cells, and the viral system hijacks the cell mechanism and harnesses it towards the production of the viral proteins. The recombinant viruses assemble in the producer cells. They are then purified, concentrated, characterised and are ready for administering to the patient.

There are now different gene therapies, viral vector systems each with particular advantages and disadvantages (Table 1). The problems with immune response and genotoxicity which plagued the initial clinical trials have been largely solved by the increase in our knowledge of basic virology, and we now know a lot more about viral vectors and how to make them safer and more effective than we did 20 years ago.

In academia, where usually only small amounts of recombinant viruses are needed for experiments, the



Large-scale production for commercial purposes can be carried out in 250 l bioreactors. © CPI 2018

amounts of cells needed to produce the vectors are smaller. Small-scale (< 1.0 l) static systems (Petri dish, T-cell culture flasks or multiwall plates) are generally used to culture cells. The vectors are generally purified using gradient ultracentrifugation, a technique from the 1950s. Vectors are usually not produced under good manufacturing practice (GMP) conditions, since the overhead costs for maintaining GMP facilities are very high.

However, in industry, a robust and consistent production process with control over variables that can't be realised in plates and scalability is the key. Production is carried out at a large scale (from one litre up to thousands of litres); therefore, ultracentrifugation, despite being an excellent method to purify vectors, is not scalable as it has low throughput. Therefore, translating an excellent research idea from academia to industry may not be simple, since it will need process development. This could be a scenario where the Centre for Process Innovation (CPI) can help.

CPI is a not-for-profit technology and innovation centre based in the North East of England that helps bridge the gap between academia and industry (the 'valley of death' of scientific innovation). Through our knowledge, expertise and state-of-the-art-facilities, CPI enables groups to develop, prove, prototype and scale-up the next generation of products and processes.

Viral vectors are routinely produced at CPI, starting with the basics of

virology and optimisation of the plasmid transfection and using either chemical or physical GMP-approved methods to produce the viral vectors in our biosafety level 2-approved laboratories. The vector-producing cells are cultivated in closed systems – the bioreactors, which primarily provide containment and suitable conditions for cell growth and product formation.

Fully automated micro bioreactor systems can be used to model the ideal growth conditions to produce viral vectors in larger bioreactors. Traditionally, this includes parameters such as temperature, pH and dissolved oxygen. Dynamic cell culture bioreactors are, however, most commonly used for larger-scale cultivation. To maintain culture homogeneity, these bioreactors are mixed by internal impellers (stirred-tank), rocking motion (cell bag) or pneumatically driven (airlift). Scalable filtration and chromatography methods are used to purify the vectors to the quality that is expected from ultracentrifuge-purified counterparts. Once the vectors are purified, optimised cryoprotectants are added to preserve the viability of the vectors. Vectors can then be titred, and the ratio of infectious units to non-infectious particles is calculated. If the ratio is too high, there is a risk of a dangerous immune response, which has often been the cause of unsuccessful gene therapy trials in the past. The genotoxicity of the vectors can be ascertained, and CPI has GMP simulation suites where we can mimic

the production of the vectors under GMP conditions before commercial partners with licensed GMP facilities can take over the production.

After decades of blood, sweat and toil, gene therapy is now poised to make a breakthrough in human health. Viral gene therapy treatment is now available in clinics with approval in the EU in 2012 of Glybera, an adeno-associated virus (AAV) vector targeting acute pancreatitis. Since then, Strimvelis, a retroviral vector used in treatment of SCID; Kymriah™, where immune cells, transduced by a lentiviral vector, can fight cancer; and Luxturna, an AAV vector used to treat blindness, are available. To date, around 2,600 gene therapy clinical trials have taken place, so more gene therapy medicine might be available soon. Currently, there is huge investment in the field, and the global gene therapy market, which is expected to grow at a compound annual growth rate of 40.8% from 2017 to 2022, is predicted to be worth over US\$10 billion by 2025. The high manufacturing costs associated with the existing gene therapy medicines might put them beyond the reach of most of the public, so more process development is needed to make this medicine more affordable. CPI has a strong desire to support academics, government agencies and industries in driving this technology forward.

### Further reading

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### Jonathan Welsh

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**Jonathan Welsh** completed his MSc and PhD in Biochemical Engineering at the University of Birmingham. He gained industrial experience working for a contract manufacturing organisation (CMO) on the development and optimisation of cell lines for production of therapeutic proteins. He joined the Centre for Process Innovation in 2014 to oversee the upstream bioprocessing capabilities.

### Helen Young

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**Helen Young** holds a BSc in Genetics from the University of Liverpool and a PhD in Molecular Cancer Studies from the University of Manchester. After her PhD, Helen worked as a postdoctoral researcher at the University of Manchester studying the inflammatory microenvironment in melanoma progression and its role in tolerance to current therapies. Helen is a Bid/ Proposal Development Manager at the Centre of Process Innovation. She is involved in supporting the development of collaborative research and development applications for public sector funding and focuses on driving innovation in the biologics sector, working with academic institutions, small and medium-sized enterprises (SMEs) and industry.

### Ruth Stephen

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**Ruth Stephen** completed her PhD in Molecular Genetics from the University of Reading and her MBA from Sidney Sussex College, Cambridge. She carried out postdoctoral research in cancer biology and molecular pharmacology at Georgetown University, Cancer Research UK and the University of Cambridge, before moving into industry. Currently, she works for Affirm Medical Communications.



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**Sam Stephen** completed his BSc from University College, Trivandrum, and MSc from Pembroke College, Oxford, before finishing his PhD on molecular virology at the University of Cologne on genotoxicity of adenoviral vectors. Dr Stephen's postdoctoral research at University College London involved lentiviral vector genotoxicity and generation of clinical-grade cell lines for viral vector production. At the University of Leeds, he worked on the use of viral gene transfer to elucidate mechanisms in cardiovascular diseases and cancer, as well as the use of various virus-like particles for use as vaccines. He joined the Centre for Process Innovation in 2016 to oversee vector and vaccine research using recombinant viruses.

### Can you describe what you would do/what skills you would need in a typical day or week in your job?

**Sam:** I am the senior scientist in charge of the viral vectors team. I use virology, molecular and cell biology, biophysics, biochemistry, management skills and planning skills routinely.

### What is your favourite part of your job?

**Sam:** There is innovative research at CPI, and the management is very supportive of this. I had worked in academia and had seen many excellent projects bite the dust for lack of process optimisation and patent development. At CPI, I see projects moving forward from the basic research to the benefit of humanity and feel a sense of satisfaction in seeing the tangible impact of the research. That is the favourite part of the job.

# Annual Conference 2018 #Microbio18

## 10–13 April, ICC, Birmingham, UK

This April we welcomed over 1,600 of you to the ICC in Birmingham to once again enjoy some amazing science and unlimited socialising opportunities over the course of four days.

Delegates attended our Conference from all over the globe to hear breakthrough research, take part in debates, and to network and build new connections. Our 2018 Conference programme included:

- 28 scientific sessions
- talks from over 130 invited speakers
- over 200 offered talks
- over 450 posters
- three sessions dedicated to developing essential skills:
  - Funders Round Table

- Exploring data tools and resources at EMBL-EBI
- Engaging in science policy
- two Hot Topics:
  - **Kevin O'Connor** Plastic Waste is a global challenge. Are plastics the answer?
  - **Derek Smith** and **Richard Pebody** Déjà Flu: Can science help the NHS cope with the annual burden of respiratory infections?
- and awarded three poster prizes:
  - Microbiology Society journals 'most promising science'
  - Early Career Microbiologists' Forum Poster Prize
  - People's choice poster prize

To see for yourself what we got up to at Conference, why not check out our YouTube video (<https://microb.io/2Hz53W0>).



All photos: Ian Atherton

Keep up-to-date with events, follow the Society on Twitter: **@MicrobioSoc**



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# Annual Conference 2019

## 8–11 April 2019, Belfast Waterfront

Preparation is underway for Annual Conference 2019, and the programme is coming along nicely – as always, considerations have been made to complement and cover the breadth of microbiology research developments. Session topics have now been confirmed, and key speakers are being identified to ensure that, again, our Conference provides delegates access to hot topics and leading researchers. Keep an eye on social media and our website for abstract opening dates and updates on our programme throughout the year.

Sign up to our newsletter to ensure you are receiving regular updates about Conference and other Society news, and visit [microbiologysociety.org/events](http://microbiologysociety.org/events) for further information.

## Applications now welcome – Society-Supported Conference Grants!

The Microbiology Society is pleased to announce that 10 meetings have been already awarded funding this year. The supported conferences include national and international events that are expected to attract about 2,000 delegates.

Event Name	Date	Location
XVth Archaeal UK Workshop at Lancaster University	11–12 January 2018	Lancaster, UK
23rd Glasgow Virology Workshop (GVW)	10 February 2018	Glasgow, UK
ECFG14 – The 14th European Conference on Fungal Genetics	25–28 February 2018	Haifa, Israel
Microbial Stress: From Systems to Molecules and Back	23–25 April 2018	Cork, Ireland
16th UK Hepacivirus and Flavivirus meeting	18–20 May 2018	Cumbria, UK
Biofilms 8	27–29 May 2018	Aarhus, Denmark
22nd Meeting of the International Society of Evolutionary Protistology	28 May – 1 June 2018	Paphos, Cyprus
Young Microbiologists Symposium 2018	27–28 August 2018	Belfast, UK
MedVetPATHOGENS 2018 – 5th Prato Conference on Animal Bacterial Pathogenesis	8–11 October 2018	Prato, Italy
25th International Symposium on Hepatitis C Virus and Related Viruses	8–11 October 2018	Dublin, Ireland

Applications are now invited for a second round of submissions, and the next closing date is 11 June 2018. Further information and application guidelines can be found here: [microbiologysociety.org/ssconferencegrants](http://microbiologysociety.org/ssconferencegrants)

# Focused Meetings 2018

## Registration now open

You can now register and submit your abstract for our 2018 Focused Meetings, which will be taking place all around the UK and Ireland between June and October. Places at these meetings are limited so we advise you secure your place as soon as possible, and please make a note of key dates for each meeting to avoid missing out on submitting your research. Society Conference Grants are available to members attending Focused Meetings. To find out more, including deadlines, visit [microbiologysociety.org/focusedmeetings](http://microbiologysociety.org/focusedmeetings).



### Microbes and Mucosal Surfaces

21–22 June 2018

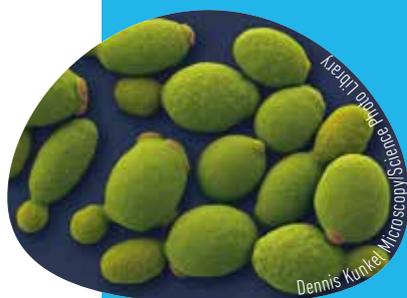
University College Dublin, Ireland

#### Key topics:

- Infection and immunity
- Microbe–host interaction
- Microbe–host cross talk and signalling
- Therapeutics and vaccine development for mucosal infections

**Early bird rate ends:** 14 June 2018

#MMS18



### British Yeast Group: Embracing Variation

27–29 June 2018

Stamford Court, University of Leicester, UK

#### Key topics:

- Biotechnology and non-conventional yeasts
- Complex traits
- Fundamental processes
- Ecology and evolution
- Yeast as human disease models

**Early bird rate ends:** 7 June 2018

#BYGEV18



### Emerging Zoonoses and AMR: A Global Threat

2 July 2018

School of Veterinary Medicine, University of Surrey, UK

#### Key topics:

- Emerging technologies for detecting and tracking pathogens and AMR
- New and emerging viral, bacterial and parasitic infections of animals and humans
- Novel and emerging antimicrobial resistance in animals and humans
- Understanding global reservoirs of zoonotic diseases

**Early bird rate ends:** 27 May 2018

#EZAMR18

Keep up-to-date with events, follow the Society on Twitter: @MicrobioSoc

## Molecular Biology and Pathogenesis of Avian Viruses

3–4 September 2018, St Catherine's College, University of Oxford, UK

#AVIAN18

### Key topics:

- Emerging and variant viruses
- Host antiviral responses and virus immunomodulation
- Molecular biology and genetics of avian virus replication
- New and improved approaches to the control of avian viruses
- Pathogenesis of avian viruses
  - Tropism and host range restriction

**Abstract submission deadline:** 24 June 2018

**Early bird rate ends:** 5 August 2018



## 9th International Symposium on Testate Amoebae (ISTA9): Recent Advances and Future Research Priorities

10–14 September 2018, Riddel Hall, Belfast, UK

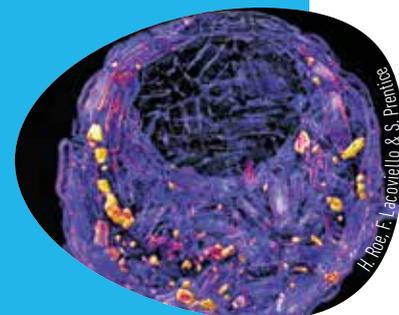
#ISTA9

### Key topics:

- Ecology and bioindication
- Functional traits, morphometrics and novel analytical approaches
- Palaeoecology and palaeoclimatology
  - Phylogeny and biogeography
- Role of testate amoebae in microbial foodwebs and nutrient cycling
- Taxonomic advances

**Abstract submission deadline:** 24 June 2018

**Early bird rate ends:** 12 August 2018



## Microbiomes Underpinning Agriculture

1–2 October 2018, Rochestown Park Hotel, Cork, Ireland

#MUAFM18

### Key topics:

- Animal microbiomes underpinning agriculture
  - Methods for exploring microbiomes in agriculture
- Plant microbiomes underpinning agriculture
  - Soil microbiomes underpinning agriculture

**Abstract submission deadline:** 24 June 2018

**Early bird rate ends:** 21 September 2018



## Call for Focused Meetings proposals 2019!

All of our Focused Meetings are the result of successful proposals submitted to our Scientific Conferences Committee by our members. These meetings are delivered in partnership with those members, and the Society is able to support all of the logistical and practical arrangements, leaving the scientific organisers to focus on the content of the meetings.

We are now in a position to welcome proposals for 2019 and beyond, and encourage submissions from our members and wider microbiology community for consideration during the next Committee meeting. The form and terms & conditions can be found on the Society website: [microbiologysociety.org/conferences](http://microbiologysociety.org/conferences). The deadline for proposals is **11 June**, and these can be submitted to [conferences@microbiologysociety.org](mailto:conferences@microbiologysociety.org). Please ensure you approach the relevant Division before submitting to enable them to present your proposal at the Scientific Conferences Committee in July.

## Engaging in Science Policy

Following the 'Engaging in Science Policy' session at Annual Conference 2018, our speakers share some top tips for members who want to get involved in informing and influencing policy concerning microbiology.



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### What is Parliament and how can it use my research?

Sarah Bunn, Senior Scientific Advisor at the Parliamentary Office of Science and Technology (POST)



“A common misconception is that Parliament and Government are the same, when they are in fact separate institutions with distinct functions. The Government runs the country, develops and implements policy, and is formed by the party holding the most seats after a general election. Parliament comprises MPs and Peers from all

political parties. Its main functions are to check and challenge the Government's work, to make and change laws, to approve budgets and tax, and to act as a forum for topical debate.

“Few politicians have scientific or research backgrounds, but they are faced with making policy decisions with widespread societal implications, for example, tackling antimicrobial resistance. Politicians need to be well briefed on many topics, and to be able to communicate their ideas about them in and outside Parliament.

“Scientists can play their part by ensuring that accurate information about their work is effectively communicated so

that politicians can make informed decisions when faced with a call for action from a constituent, pressed for action by a lobby group, or before voting in Parliament.

“You can engage with Parliament directly or through the Microbiology Society, including contributing evidence to a Select Committee inquiry and writing to your MP or meeting them face-to-face. Scientists also contribute to POST's work briefing parliamentarians.”

#### Top tips for communicating with policy-makers:

- **Be objective** – let the research speak for itself.
- **Keep it simple** – avoid jargon and don't assume too much knowledge.
- **Think about the wider context** – how does your research fit into the bigger picture?
- **Be brief** – can you summarise your research into five simple points?
- **Be clear about the action or recommendations you are proposing** – what are you asking the politician to do?

## How can you help influence government science policy?

James Tooze, Policy Officer, Campaign for Science and Engineering (CaSE)



“Key to engaging with policy is being clear in communicating your priorities and concerns to a non-scientific audience. Your ability to talk about the ways your research impacts the wider world, and what is needed to enable you to effectively conduct and translate research, is important in informing

government policies for research and innovation.

“Membership organisations such as the Microbiology Society can enable you to help inform and influence Government and Parliament. At CaSE, we represent the views of the science sector in meetings with Ministers, MPs

and Peers, and government officials. We represent issues affecting scientists in areas such as Brexit, funding and immigration; positions that are informed through consultation with our membership. This includes the Microbiology Society who represent the views of you as a member and your microbiology community.

“Importantly, we don't expect you to be a policy expert! Your knowledge of what helps and hinders the research you do and how it can benefit society are the fuel for our organisations to effectively communicate and represent the views of scientists to policy-makers. Your personal contributions will ultimately help add weight to our ability to influence science policy.”

## How can I engage in policy through the Society?

Paul Richards, Policy Manager, Microbiology Society



“The changing research environment and global challenges mean it is more important than ever to champion the value of microbiology,

ensure it is supported, and inform policy with microbiologists' expertise. Our Policy Team are here to support you in communicating and connecting with policy-makers, and to enhance the influence of your research.

“Responding to calls to inform our responses to government consultations and parliamentary inquiries is a key way you can support us in representing microbiologists' views to policy-makers. Recently, we communicated your concerns and recommendations for Brexit and science at a summit, and in writing to the House

of Commons Science and Technology Committee.

“Our Microbiome Policy Project illustrates how we also proactively publish resources and organise meetings to champion microbiology and connect members with a range of science policy stakeholders. Workshops brought together representatives from research, regulation, industry, government and funders. A report and briefings then communicated recommendations about the key research, innovation and societal opportunities and challenges for this emerging area of microbiology to policy audiences.

“We want to get more members engaged in our policy work. Our impact depends on your input. Make sure we know about your interest in policy and your areas of expertise via the Mi Society online area. Contact the Policy Team to tell us about your interest, or if there is

an issue or opportunity you think we should know about. And if you want to help guide our policy work, why not consider nominating yourself for our Policy Committee?”

### Further information:

Campaign for Science and Engineering

[www.sciencecampaign.org.uk](http://www.sciencecampaign.org.uk)

Parliamentary Office of Science and Technology

[www.parliament.uk/post](http://www.parliament.uk/post)

Policy at the Microbiology Society  
[microbiologysociety.org/policy](http://microbiologysociety.org/policy)

### Roya Ziaie

Policy Officer, Microbiology Society

### Paul Richards

Policy Manager, Microbiology Society  
[policy@microbiologysociety.org](mailto:policy@microbiologysociety.org)

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# “The beginning of wisdom is to call things by their proper name”

(proverb, deriv. Confucius)

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**In July last year, it was my pleasure to travel to Valencia as the Microbiology Society delegate to the plenary meeting of the International Committee on Systematics of Prokaryotes (ICSP) – at which I was honoured to be elected Chair of the ICSP Executive Board. Here, I provide an introduction to the work of the ICSP and some challenges we face.**

---

**M**icrobial systematics is entering into an exciting period: culture-independent sampling methods have already provided breath-taking insights into the enormous diversity of the microbial world (with much less than 1% of microbes yet studied in culture) and now genome-based methods are expected to drive the discipline forward. It is the goal of the ICSP (and its ‘Judicial Commission’) to help microbiologists work within a functional and effective taxonomic framework as we attempt to deal with this greatly expanded view of the microbial world.

These impressive developments illustrate that systematics remains a vital microbiological discipline, despite a common misconception that taxonomy is bedevilled by *rules*. In fact, there are no rules dictating how taxonomy should be done! The only rules relate to nomenclature of micro-organisms, as I shall explain below.

As Confucius recognised, names are important. They provide the basis by which scientists can communicate with each other without confusion. This means that the correct proposal and formulation of names is important too. Consequently, a principal role of the ICSP is to ensure that appropriate steps are followed when prokaryotic micro-organisms are named, as specified in the International Code of Nomenclature of Prokaryotes (‘the Code’), so that prokaryotes have only one name and each name refers to only a single prokaryote. Much work in this area appears in the *International Journal of Systematic and Evolutionary Microbiology* (IJSEM), which is published by the Microbiology Society on behalf of the ICSP.

The Code is a complex but elegant document that provides *Principles, Rules and Recommendations* for nomenclature. My favourite is Principle 4: “Nothing in this Code may be construed to restrict the freedom of taxonomic thought or action.” It is this Principle that ensures that there are no rules as to how taxonomy must be done. Many of the Rules relate to forming

binomial names in Latin, but there are also stipulations regarding priority of names, the designation of type strains and their deposit in culture collections. However, it is also important to emphasise that the Code is a living document – the Judicial Commission considers formal proposals for revisions to the Code, and ICSP oversees the production of new editions. Indeed, a new edition is currently in press at IJSEM, and significant new revisions have already been proposed, such as the possibility of allowing sequence data to be used as type material. If adopted, this revision will have major implications for microbiologists’ ability to formally name taxa which are recognised in culture-independent studies, such as single-cell genomic analyses.

There are definite challenges ahead for the ICSP. Maintaining and adapting the Code such that it is fit for purpose as we strive to classify >10<sup>6</sup> bacterial species is one. Helping microbiologists respond to the Nagoya Protocol is another (there is useful information on our website). Probably, the most significant is attracting able and enthusiastic early career scientists into the field to ensure it remains a vigorous and stimulating discipline. I look forward to Chairing the ICSP as we engage with these challenges!

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## Further reading

ICSP website [www.the-icsp.org](http://www.the-icsp.org)

Parker, C.T., Tindall, B.J. & Garrity, G.M. (2018). International Code of Nomenclature of Prokaryotes. *International Journal of Systematic and Evolutionary Microbiology*, in press. doi:10.1099/ijsem.0.000778

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## Iain C. Sutcliffe

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# iGEM: Get & Give (&Share)

**International Genetically Engineered Machine Competition, or iGEM, is a synthetic biology event which first began at the Massachusetts Institute of Technology as a lab course in 2003. In 2017, iGEM became an international science competition involving nearly 6,000 people, including over 300 teams from 42 countries. Each team may consist of several graduates, undergraduates, or high school students. With help from university or institute advisors, the team works together to come up with their own proposals, design experiments, compose a wiki page to explain their methods, and finally present their work to compete with other teams.**

One important philosophy spread by iGEM, in hopes of supporting the field of synthetic biology, is to 'Get & Give (&Share)'. This feature is especially embodied by the 'BioBrick' project. A BioBrick is analogous to a LEGO brick, but in an engineered gene sequence format. It is standardised for "interchangeable parts developed with a view to build biological systems in living cells." In other words, anyone with basic biological knowledge should be able to turn their biological circuit design into reality by assembling BioBricks together like LEGO. Since all iGEM teams are required to standardise their synthetic genes into BioBrick format, the BioBrick library is growing larger with every year. Additionally, any iGEM participant or iGEM lab subscriber has access to these standardised BioBricks.

Like all previous years, teams from iGEM 2017 shared a wide range of ideas and designs filled with creativity and enthusiasm. Topics covered different fields, from basic biochemistry studies to projects with specific social backgrounds including public health, natural resource discovery, and renewable energy. Cutting-edge tools like CRISPR/Cas systems also found their way into iGEM.

TU Delft was the winner of the grand prize in 2017. They designed and tested a 'BioDetector' which helps dairy farmers to quickly determine if the milk is contaminated with antibiotic-resistant bacteria. They used a CRISPR/Cas system, Cas13a, which targets RNA derived from the bacterial antibiotic-resistant genes in the milk samples. To visualise the Cas13a-RNA complex without additional instrumentation, a positively charged polymer is also added to the sample. If there is no target RNA present, Cas13a will remain unbound, causing the negatively charged RNA to precipitate with the positively charged polymer, causing turbidity. If target RNA is present, Cas13a will bind to it and lead to the degradation of other negatively charged RNA, preventing turbidity in presence of the polymer additive. The team demonstrated the feasibility of their 'BioDetector' in a local milk farm, showing the spirit of iGEM, to let science 'give' back to society.

In addition to the real-world applications of iGEM projects, the advancement of fundamental biology is also pursued by iGEM teams. One team, Bielefeld-CeBiTec, challenged the problem of unnatural amino acid incorporation in *Escherichia coli* through a suite of *in silico* prediction and *in vitro* selection cycles. This project brought in collaboration and consultations from multiple universities and individuals. The collaborative nature of iGEM projects not only testifies for the 'Get & Give (&Share)' philosophy held by iGEM, but also advances the future of synthetic biology research in academia.

## **Linna An**

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# Schoolzone

## The Super Cells: how bacteria and your immune system work together to keep you healthy

**The immune system protects us from pathogens and works together with our commensals to keep us healthy. To understand immunology is to understand infectious disease and how vaccines work. There has been a steady decline in childhood vaccinations in recent years, so I wanted to create a new resource to educate children about how pathogens infect us and how our commensals work with our immune system to keep us healthy, to help encourage young children (and their parents!) to keep up-to-date with their vaccines!**

I always imagined the immune system as a team of superheroes that come together when the body is in danger, and each type of cell has its own superpower. I thought that commissioning an animation (rather than displaying the information in a book) would be more effective at communicating science in a fun and engaging way. The animation can be played while the children complete activities and answer questions. I also hope that this will encourage more children (especially girls) to learn about science and study it beyond school.

When I found out that I had been awarded the grant money I contacted Cosmic Monocle animation studios in Sheffield. I have been really impressed by the quality of work that they have produced in such a short space of time. The animation



really looks like a retro-style superhero cartoon! We hope to make the resources (animation and question booklet) publicly available so it can be used for lesson plans.

It's been such fun working on this project - if you want to see the finished result you can access it via this link:

[www.vimeo.com/cosmicmonocle/supercells](http://www.vimeo.com/cosmicmonocle/supercells).

### Emma Henly

Sheffield Hallam University

[hwbeh4@exchange.shu.ac.uk](mailto:hwbeh4@exchange.shu.ac.uk)

View *The Super Cells* on YouTube: <https://www.youtube.com/watch?v=C1TiN-BaXCo>. The Super Cells resources are also available on the Microbiology Society website: [microbiologysociety.org/thesupercells](http://microbiologysociety.org/thesupercells).



All images: [www.cosmicmonocle.com](http://www.cosmicmonocle.com)

# Annual Conference 2019

8–11 APRIL, BELFAST WATERFRONT, UK

**Registration and  
abstract submission  
open August 2018**

**Abstract submission deadline:**

10 December 2018

**Grants deadline:**

31 January 2019

**Registration closes:**

11 March 2019



@MicrobioSoc  
#Microbio19



Discover more at: [microbiologysociety.org/annualconference](http://microbiologysociety.org/annualconference)

Email: [conferences@microbiologysociety.org](mailto:conferences@microbiologysociety.org)

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Join over 1,400 delegates for three and a half days of presentations, posters and networking.

# Journals update

## Emerging Zoonoses and AMR: A Global Threat 2 July 2018

*Journal of Medical Microbiology's* Section Editor for One Health, Roberto La Raggione at the University of Surrey, is hosting this Focused Meeting. The event will take place at the School of Veterinary Medicine, University of Surrey, UK.

Key topics to be covered include:

- Novel and emerging antimicrobial resistance in animals and humans
- Emerging technologies for detecting and tracking pathogens and AMR
- New and emerging viral, bacterial and parasitic infections of animals and humans
- Understanding global reservoirs of zoonotic diseases

Abstracts, oral communications and posters are welcome at this meeting. For more information please see our guidelines on the event page ([microbiologysociety.org/EZAMR18](http://microbiologysociety.org/EZAMR18)).

*Journal of Medical Microbiology* will be sponsoring the 'Most Promising Science Prize' at the Focused Meeting. The prize will be awarded to a poster or oral communication that presents particularly compelling or novel research in the journal's subject field, and will be presented by Roberto La Raggione.

The winner will receive a cash prize, certificate and a year's membership to the Microbiology Society. All submissions are automatically entered.

*Journal of Medical Microbiology* provides comprehensive coverage of medical, dental and veterinary microbiology and infectious diseases, including bacteriology, virology, mycology and parasitology. Papers are published in the following areas: Pathogenicity and Virulence/Host Response; Clinical Microbiology; Microbial Epidemiology; Microbial Ecology and Health; One Health; and Prevention and Therapy.

For more information, visit [microbiologyresearch.org](http://microbiologyresearch.org).

## Journal links

### *Microbiology*

[mic.microbiologyresearch.org](http://mic.microbiologyresearch.org)

### *Journal of General Virology*

[jgv.microbiologyresearch.org](http://jgv.microbiologyresearch.org)

### *Journal of Medical Microbiology*

[jmm.microbiologyresearch.org](http://jmm.microbiologyresearch.org)

### *Journal of Medical Microbiology Case Reports*

[jmmcr.microbiologyresearch.org](http://jmmcr.microbiologyresearch.org)

### *Microbial Genomics*

[mgen.microbiologyresearch.org](http://mgen.microbiologyresearch.org)

### *International Journal of Systematic and Evolutionary Microbiology*

[ijs.microbiologyresearch.org](http://ijs.microbiologyresearch.org)

## Call for cross-disciplinary papers on antimicrobial resistance

The Microbiology Society and Guest Editors Jodi Lindsay, Edward Feil, Mark Holmes, Helen Lambert and Gwen Knight invite submissions to a special cross-disciplinary pop-up journal on antimicrobial resistance (AMR) *X-AMR*. This coincides with the Society's upcoming Focused Meeting on ([microbiologysociety.org/EZAMR18](http://microbiologysociety.org/EZAMR18)). We recognise that AMR is a cross-disciplinary subject and seek contributions from researchers across all disciplines, including life scientists, chemists, material scientists, social scientists, clinicians, veterinarians and engineers, among others.

Topics include:

- Resistance to antimicrobials, antifungals or antivirals
- Diagnostics and therapeutics (novel, combination and alternative)
- Epidemiology and infection control
- Mathematical modelling
- Stewardship and surveillance
- Pharmacokinetic behaviour and pharmacodynamics
- Environment and ecology of resistance
- Societal, cultural or economic determinants
- Veterinary, One Health and agricultural dimensions
- Policy and regulatory perspectives
- Genomic and microbiological studies

This list is indicative and not restrictive. We welcome reviews, mini-reviews, original research, methods articles and commentaries that are cross-disciplinary.

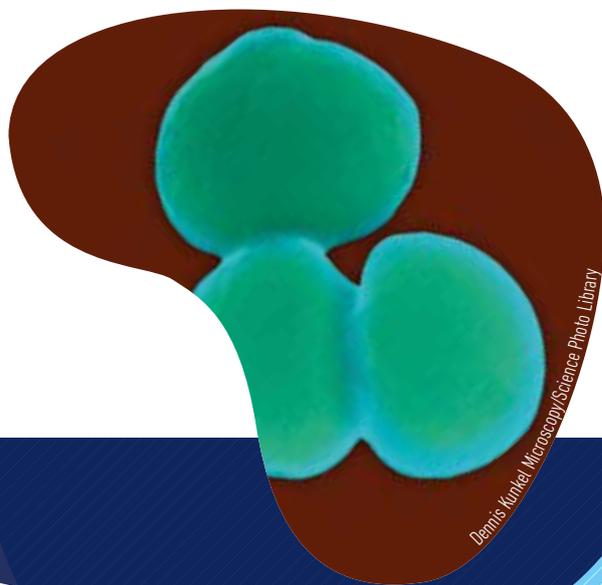
Papers submitted to *X-AMR* will be peer reviewed and

published in the Society's portfolio of journals. All articles for *X-AMR* will then also be published in a microsite that will host the entire collection on AMR.

Authors are encouraged to submit articles to any of the four Society journals: *Microbiology*, *Journal of General Virology*, *Microbial Genomics*, or *Journal of Medical Microbiology*. Guidelines for authors on how to submit and peer review process are available on [microbiologyresearch.org/X-AMR](http://microbiologyresearch.org/X-AMR). When submitting to a Society journal, please mention **'Submission to X-AMR'**.

For any queries, contact [x-amr@microbiologysociety.org](mailto:x-amr@microbiologysociety.org).

The Microbiology Society is one of the few societies who self-publish, and all surpluses from the journals goes back to the Society to support its charitable activities.



# Outreach



## Schools and outreach: How peer education can educate young people about hygiene, infection and antibiotic resistance

**e-Bug is an educational programme for schools and the community operated by Public Health England. The author, Catherine Hayes, is the e-Bug project assistant and has worked on this project since 2015.**

Antimicrobial resistance (AMR) is no longer a far-off threat of the future, but a healthcare crisis affecting us today. Across the globe, organisations are taking a multidisciplinary approach to tackling AMR, involving continued research into new antimicrobials, improved diagnostics and education of the public. Educational initiatives that promote prudent antimicrobial behaviours and correct perceptions around antimicrobials are critical in our fight against AMR.

Most importantly, it is our next generation that will have to keep up this fight and who will be our future antibiotic users and prescribers. Therefore, educating children at a young age to instil good hygienic behaviours to reduce the spread of infection, as well as an understanding of prudent antibiotic use, will provide them with the best chance of beating AMR.

### Educating young people about AMR

Educating youths on concepts such as AMR and microbiology is very

challenging and requires innovative teaching practices and methodologies. e-Bug has utilised peer education as a



Students acting as peer educators during the e-Bug Science show. Public Health England

new method to educate young people about AMR. Peer education involves students adopting the role of teacher and educating their peers on key topics.

This initiative has been used in schools, community groups, universities and even workplaces. Peer education has been used extensively for sexual health and HIV education in low-income countries, where it has been shown to significantly improve behaviour outcomes (Medley *et al.*, 2009) and there has been similar success for sexual health education in high schools (Caron *et al.*, 2004). Peer education has been used previously to educate children about prudent antibiotic use and led to an improvement in awareness around the uses of antibiotics (Cebotarenco & Bush, 2008).

### The e-Bug peer education model

e-Bug has added to the bank of evidence to support peer education as a successful tool to educate about microbiology and AMR. e-Bug have a multi-topic science show for secondary school students involving five interactive stands on microbes, hand hygiene, respiratory hygiene, food hygiene and antibiotics. As the flow chart depicts, the peer education model involves students receiving training on a stand by public health researchers and then delivering their knowledge to other students from the school and/or local primary school.

The evaluation of the science show confirms that peer education provides unique benefits to students and is an effective AMR and microbiology education tool (Young *et al.*, 2017). Children acting as peer educators were able to retain knowledge of the topic better than regular teaching, while benefiting from a whole range of



#### e-Bug Peer education model.

skills and behaviour changes including science communication, confidence and team working. Students being taught by their peers also benefited from greater knowledge gain.

e-Bug has also developed peer education for A-level students aged 15–18, which involves young adults delivering an antibiotic-themed lesson to their peers. This includes interactive demonstrations of how antibiotic resistance occurs, correcting common misconceptions and promoting antibiotic stewardship in young people. This model is currently being investigated and evaluated in collaboration with Cardiff and Manchester Universities.

To summarise, peer education is an effective method to educate young people on microbiology and AMR, and provides a unique opportunity to

mould and enthuse the scientists of tomorrow.

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*e-Bug is an educational resource operated by Public Health England for young people aged 4–18 years old, and will be celebrating its 10th birthday in 2019!*

Access the wide range of resources hosted by e-Bug, available in 23 different languages, at: [www.e-bug.eu](http://www.e-bug.eu)

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### References

- Caron, F., Godin, G., Otis, J. & Lambert, L. D. (2004). Evaluation of a theoretically based AIDS/STD peer education program on postponing sexual intercourse and on condom use among adolescents attending high school. *Health Education Research* **19**, 185–197.
- Cebotarenco, N. & Bush, P. J. (2008). Reducing antibiotics for colds and flu: a student-taught program. *Health Education Research* **23**, 146–157.
- Medley, A., Kennedy, C., O'Reilly, K. & Sweat, M. (2009). Effectiveness of peer education interventions for HIV prevention in developing countries: a systematic review and meta-analysis. *AIDS Education and Prevention* **21**, 181–206.
- Young, V. L., Cole, A., Lecky, D. M., Fettes, D., Pritchard, B., Verlander, N. Q., Eley, C. V. & McNulty, C. A. M. (2017). A mixed-method evaluation of peer-education workshops for school-aged children to teach about antibiotics, microbes and hygiene. *Journal of Antimicrobial Chemotherapy* **72**, 2119–2126.

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### Catherine Hayes

e-Bug Project Assistant at Public Health England

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# Early Career Microbiologists' Forum Update: May 2018

This update from the Early Career Microbiologists' Forum is possibly our most exciting so far! When we first got together as the inaugural ECM Forum Executive Committee, we knew that we wanted to do more to reach out to undergraduates who were considering microbiology as a potential career path. We also wanted to give PhD students and early postdocs the opportunity to develop skills and techniques that they might otherwise be missing. Many ideas and discussions (and a lot of hard work from Conferences Representative Amy Richards and her team of Division Representatives) later and we have arrived at the ECM Forum Summer Conference!

The Summer Conference, hosted by the ECM Forum Executive Committee, will run 14–15 June in Birmingham and gives delegates the chance to listen to invited speakers talking about broad areas of microbiology, from vaccines to gene editing and everything in between. We are delighted that the keynote

speaker will be Dr Adam Roberts from the Liverpool School of Tropical Medicine. He will be describing his life in microbiology in what I am certain will be a hugely interesting talk. There will also be a poster session and a BBQ (included in the ticket price) to provide plenty of opportunities to meet people and make new contacts. The professional development workshop promises to give inspiring advice on microbiology careers both in and outside of academia.

I caught up with Amy to get her views on why the Summer Conference is so important. She said that after being elected as the Conferences Rep, she quickly realised that those in the very early stages of their career may be overwhelmed by attending the Annual Conference and so designed the Summer Conference to combat this.

*“We have developed an event focused on the needs of undergraduates, Masters students, and first-year PhD students, providing*

*an introductory experience to scientific conferences in a reassuring, collegiate and peer-led environment. We have received abstract submissions from undergraduates, Masters students and PhD students for both offered oral and poster presentation slots, and postdoc ECM Forum members have been invited to give all of the scientific talks. Tailored career advice will also be available in two professional development sessions, making this a must-attend meeting to really enhance your career as a Forum member.”*

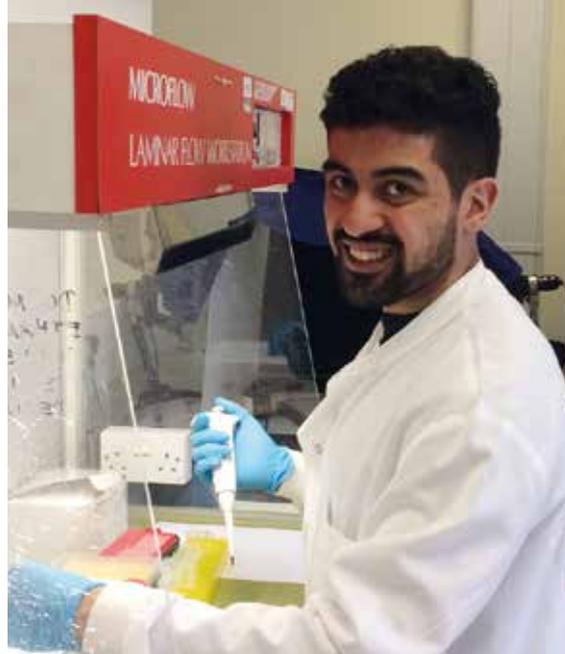
So what are you waiting for? We are really looking forward to hosting you in June, so be sure to register as soon as possible! [microbiologysociety.org/ecmsummerconference](http://microbiologysociety.org/ecmsummerconference)

## Rebecca Hall

ECM Forum Communications Representative

# Membership Q&A

This is a regular column to introduce our members. In this issue, we're pleased to introduce **Ed Cunningham-Oakes**.



Ed Cunningham-Oakes

## Where are you currently based?

Cardiff University, under Professor Eshwar Mahenthiralingam in a BBSRC CASE-Studentship sponsored by Unilever.

## What is your area of specialism?

Cultivation-independent microbiology.

## And more specifically?

Using whole genome sequence to understand the basis for bacterial resistance, and to anticipate adaptation in response to preservatives, which is important for industry to develop novel product preservation strategies.

## Tell us about your education to date.

I underwent primary and secondary education in Stoke-on-Trent in Staffordshire. I then graduated from King's College London with a BSc in Pharmacology with Extra Mural Year degree.

## Where did your interest in microbiology come from?

Whilst I was studying Pharmacology, I undertook a one-year placement at St George's, University of London. During this time, I was researching the synergistic efficacy of aminoglycoside

antibiotics and nordihydroguaiaretic acid against resistant and sensitive strains of *Staphylococcus aureus*, and was fortunate enough to publish. This experience spurred my interest in microbiology and development of antimicrobial resistance, leading me to my current project.

## What are the professional challenges that present themselves, and how do you try to overcome them?

Working alongside industry is a fast-paced, busy, but enjoyable change from the pure academic research that I have been used to in the past. It requires a different type of organisation and the strictest confirmation to time-constraints. Additionally, it teaches to you to always bring your a-game with regards to work, data sharing, confidentiality and interacting with collaborators. It has been a real eye opener!

## What is the best part about 'doing science'?

The discovery, and knowing that you are contributing to the wider knowledge of the field (every little helps, right?)

## Who is your role model?

Frank Zane aka 'The Chemist' – he won the bodybuilding competition

Mr Olympia three times, was one of three people to ever beat Arnie (Arnold Schwarzenegger), had a masters in experimental psychology, and taught mathematics and chemistry for 13 years to boot! Truly a talented, well-rounded individual.

## What do you do to relax?

Blog writing, playing video games and weightlifting.

## What one record and luxury item would you take to a desert island?

*The Black Parade* album by My Chemical Romance (a major part of my formative years), and a mobile phone to call for help.

## Tell us one thing that your work colleagues won't know about you.

I can actually be quiet (sometimes).

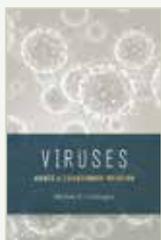
## If you weren't a scientist, what would you be?

Potentially an editor or writer. My opinion changes daily though!

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If you would like to be featured in this section or know someone who may, contact Paul Easton, Head of Membership Services, at [p.easton@microbiologysociety.org](mailto:p.easton@microbiologysociety.org).

# Reviews



## Viruses: Agents of Evolutionary Invention

Written by M.G. Cordingley  
Harvard University Press (2017)  
£39.95 ISBN 978-0674972087

To many, viruses are merely agents of disease. However, over the years we have exploited them as reagents and tools for scientific investigation, as vaccines to protect against disease, and more recently, even for the treatment of human disease. Challenges such as viral outbreaks and epidemics, or antiviral drug resistance, demonstrate that viruses can change their characteristics, but the cells that viruses are dependent upon can change as well because of the infection. *Viruses: Agents of Evolutionary Invention* lays out the effects that viruses have on their hosts, whether single-celled like bacteria, or multicellular like plants and animals. The book covers how the changes that viruses have brought about over millions of years of evolution have contributed to the development of key processes like photosynthesis and the evolution of mammals.

Changes caused by viruses allow their hosts' cells to behave differently under different environmental conditions, decreasing the survival potential of some and increasing the survival potential of others within a population. These environmental conditions act as selective pressures, thus driving the evolution of the viruses' hosts and leading to the 'invention' of new forms of life, as suggested in the book title.

This book is a virology course in itself, describing the features that are important for replication, transmission and virulence in the context of the effects that viruses have upon their hosts. However, since *Viruses* describes the long-term effects on the evolution of species, as well as the short-term effects on individual hosts, the book will be of interest to not only virologists, but also those interested in evolution and biology in general. Despite being a wealth of information about viruses and their effects, it is a narrative, not a textbook. It is very well written, but it would benefit from a cheaper, more accessible paperback version.

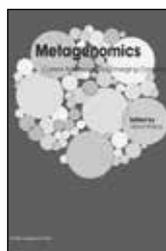
### Christopher Ring

Middlesex University

For more reviews, please visit the online issue of *Microbiology Today* at [microbiologysociety.org/microbiologytoday](http://microbiologysociety.org/microbiologytoday)



## Life Sciences Books



**Metagenomics:**  
Current Advances and Emerging Concepts  
**Edited by:** D Marco  
vi + 146 pages, May 2017

*"presents those new to the field with important aspects of metagenomics"* (*Eur. J. Soil Sci.*)

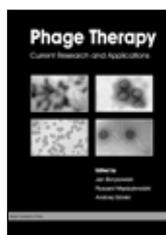
See: [www.caister.com/metagenomics2017](http://www.caister.com/metagenomics2017)



**Microbial Biodegradation:**  
From Omics to Function and Application  
**Edited by:** J Długoński  
x + 238 pages, September 2016

*"a valuable companion to both early and established researchers"* (*Micro. Today*)

See: [www.caister.com/biodegradation](http://www.caister.com/biodegradation)

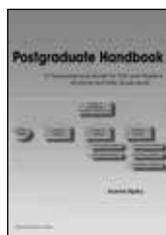


**Phage Therapy:**  
Current Research and Applications  
**Edited by:** J Borysowski, R Międzybrodzki, A Górski  
xvi + 378 pages, April 2014

*"timely and comprehensive"* (*Clinical Infectious Diseases*)

See: [www.caister.com/phagetherapy](http://www.caister.com/phagetherapy)

### New!



**Postgraduate Handbook:**  
A Comprehensive Guide for PhD and Master's Students and their Supervisors  
**Edited by:** A Nyika  
vi + 114 pages, February 2018

*Easy-to-read handbook for postgraduate students and their supervisors. Explains complex research concepts and methodologies in simple terms.*

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# Comment

## To patent or not to patent?

Alice Smart



Claudio Ventrella/iStock

### When to apply for a patent... and when not to

There's a common misconception that, to be granted a patent, you have to invent something ground-breaking, but this is not true. A useful question to ask is: have you discovered something which is beneficial enough for someone to want to copy it? This could be a simple product improvement, but nonetheless it may be patentable. A patent is granted for inventions which

are useful, and new and inventive over everything else that has gone before. A patent is a 'negative right' in that it doesn't enable you to start making or using an invention, but it does allow you to stop others from doing so. Therefore you should also consider if you will infringe someone else's patent before exploiting your invention. The Espacenet website (<https://worldwide.espacenet.com>) run by the European Patent Office (EPO) is a fantastic starting point to search

**An application for a patent is a deal between the inventor(s) and the country in which it is filed. In exchange for full disclosure, the inventors can protect their invention for up to 20 years. In theory, by revealing their invention publicly, others can benefit by using it as a springboard for further developments. Without a patent, inventors are almost powerless to stop someone else exploiting their invention.**

for similar, previously filed patent applications which might have an impact on the assessment of novelty and inventiveness.

Once a patent is granted, renewal fees have to be paid to keep it in force, and to enforce your patent against infringers, you need the money to fund a potential court action. Therefore, you need to decide if you think you can make enough money from your invention to fund these or if your invention is

attractive enough for businesses to invest in and/or license it.

### How to apply for a patent

You can apply for a patent yourself, and the UKIPO has many resources to help you do this (<https://www.gov.uk/apply-for-a-patent>).

However, this does involve risks that the patent may not be sufficiently robust and could be exploited by competitors. Patent attorneys train for many years to be able to draft good applications which not only maximise protection for inventions, but also minimise the risk of others circumventing the patent. They can also guide your application through to grant of the patent and help you file applications abroad. This comes at a cost, however, and for preparing and filing a UK application, a patent attorney will typically charge between £4,000 and £6,000.

An application comprising a description of and the claims covering the new invention must be submitted. The description is similar to a scientific publication in that the background, methods and results are described. The claims are statements which set out the boundaries of the protection you want. It is possible to make applications in individual countries, collectively in Europe or to make an international application.

### Dos and Don'ts

#### Do:

- Keep the invention confidential before filing an application.
- Research – not just Google, use Espacenet and, if you can afford it, request a professional patentability search.
- Get advice.
- File as early as possible – the earlier

you file, the fewer prior publications can be cited against your application and the earlier protection can begin.

- Check your freedom-to-operate so you won't infringe someone else's patent rights.

#### Don't:

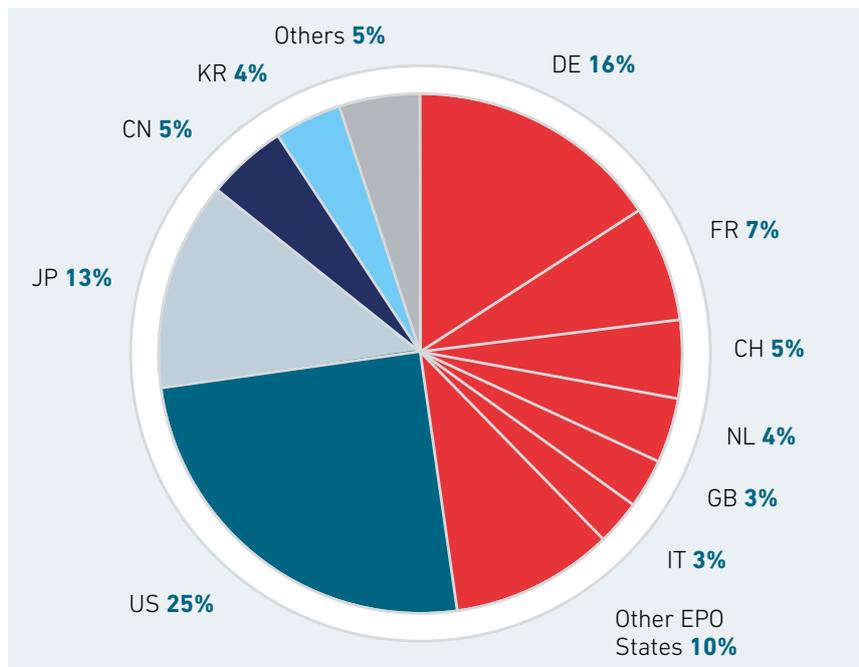
- Publicly disclose the invention.
- Talk to anyone about your invention pre-filing – if you absolutely have to, get a signed NDA first.

- Think that copyright will protect your invention.

### Biotechnological inventions

In Europe and the UK, there are many rules on what can and can't be patented in relation to biotechnological inventions. Pre-existing phenomena and creations of nature are non-patentable, but non-naturally occurring organisms constructed using biotechnology are patentable. For example, human cloning,

Origin of patent applications at the EPO in 2016. Source: EPO website



Number of patent applications filed at the EPO and USPTO in 2015 per originating country.

Source: EPO website

Country of origin	No. of European patent applications	No. of US patent applications
UK	5,051	6,417
France	10,760	6,565
Germany	24,807	16,549
US	42,597	140,969
China	5,728	8,116
Japan	21,421	52,409

modification of the human genome and commercial uses of human embryos are not patentable. However, human genes, stem cells, and micro-organisms themselves, such as bacteria, yeast, fungi, algae, protozoa and human, animal and plant cells can all be patented. Patents can also be obtained for products produced by micro-organisms, such as antibiotics or enzymes, and processes involving micro-organisms. Micro-organisms freely occurring in nature are not patentable as such, but they could be if isolated from their environment or produced by a technical process.

There are also unique considerations when filing biotech patent applications such as making a deposit of a micro-organism and filing sequence listings for nucleotides and amino acids.

### Depositing micro-organisms

A patent relating to a micro-organism must provide enough information to put the invention into practice. If this is not possible in writing then a deposit of any disclosed micro-organisms should be made. Samples of micro-organisms can be deposited under the Budapest Treaty with an International Depository Authority (IDA).

### Patent filings

In the UK, academics are often under pressure to publish their work in high-profile journals rather than file patent applications. Therefore, UK institutions may be losing out on potential revenue from patented inventions. In contrast, industrial research groups focus on building a strong patent portfolio rather than a publishing record. A publication can provide status and more grant funding, but it does not give you the legal right to

stop someone gaining financially from your research.

Biotechnological patent applications represented about 4% of patent applications filed at the EPO in 2015, but this is a growing area. The top applicants in the biotech field in 2016 at the EPO included many universities and public research institutions, including the Institut national de la sante et de la recherche medicale (111 applications), Harvard College (37 applications) and the Technical University of Denmark (30 applications) (Source EPO website, Annual Report 2016). Disappointingly, despite their global reputations, no UK universities appeared among the top applicants.

As shown opposite, only 3% of total patent applications filed at the EPO in 2016 were from the UK.

As shown in the table opposite, the UK also lags behind in terms of

US patent application filings. The table shows the number of patent applications per originating country filed at the USPTO and EPO in 2015.

### Conclusion and the future

Even in a world where developments are seemingly occurring at a faster and faster rate, the importance of patent protection in attracting potential investors is still vital, and no other system exists which can provide fair protection for inventors whilst fuelling innovation by providing public disclosure of inventions.

The UK currently seems to lag behind the US, China and Germany in terms of filing patents, and it appears that UK universities are not maximising potential income opportunities through patenting their inventions. Awareness of patents needs to be raised so that opportunities to patent inventions and to generate income from them are not missed.



#### Alice Smart

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**Alice Smart** has a BSc in Genetics and Biochemistry from Aberystwyth University, and a PhD in Pharmaceutics from UCL. Alice has also worked for Wyeth Research and Astra Zeneca. Since 2014, Alice has worked at Appleyard Lees, specialising in the filing and prosecution of biotechnological patent applications.

#### What is the most rewarding part of your job?

Helping inventors obtain the protection they deserve for their inventions. I find it particularly satisfying when I can find strong arguments to overcome objections raised by patent offices.

#### How do you see this field changing in the future?

I believe patent applications for biotechnology-based inventions will continue to rise. Inventors will continue to push the boundaries in this field and challenge the law, and those who interpret it, on what can and should be patented.



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