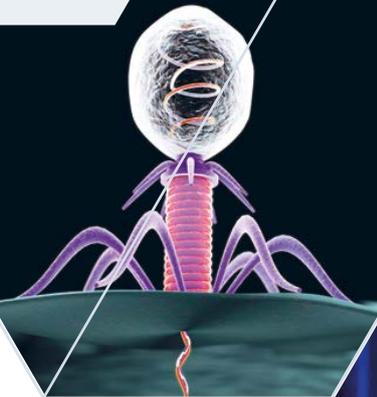


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A role
for phages in
personalised
medicine

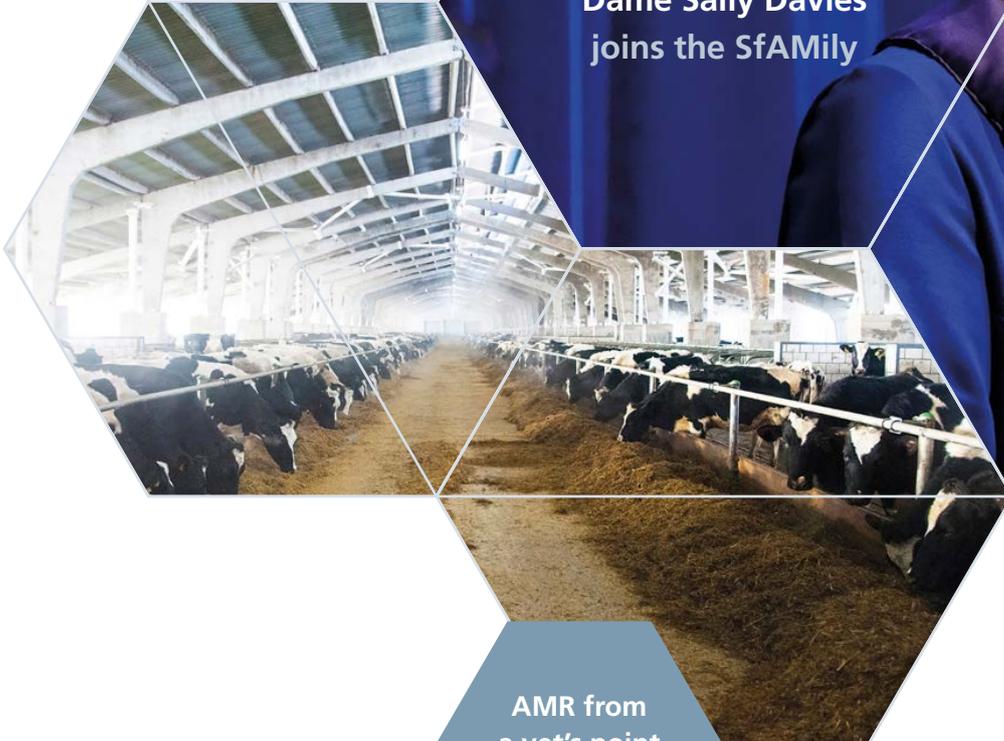


Professor
Dame Sally Davies
joins the SfAMily



Phage ecology:
a master
manipulator

AMR from
a vet's point
of view



microbiologist

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The enemy of my enemy is my friend



I really do get excited by phage, not just because they look like the Apollo Lunar Module, but because they are believed to be the most abundant life form on earth. Rough estimates suggest 10 million trillion trillion of them are floating about.

The potential of phage as antibacterial agents (I assume) was recognised almost immediately upon the discovery that these viruses were bacteriolytic entities. The clue is in the name. Bacteriophage from bacterio- ('bacteria') + -phage ('eater').

Although we have never been more aware of the urgent need for new antibacterials, the use of phage for this purpose has never appeared to be widely adopted. Is it economics? Efficacy? Specificity? For the 5 years I have worked for the Society for Applied Microbiology I have read countless articles stating that 'phage therapy is the next big thing and will solve the antimicrobial resistance (AMR) crisis'. But, I read very little about tried and tested treatments or any significant research breakthroughs showing phage as a viable alternative to our current antibiotics.

Maybe I was just not looking in the right places. So, for this issue, I have asked authors with expertise to look at the past, present and future of phage. I even did a little research myself. Certainly, the applications of phage are vast and currently being used in many more ways than I initially realised, and I hope that you readers learn a little something new too.

We are sad this month to be losing our Policy Manager, Dr Chris Brown, who leaves us to go and work in the Houses of Parliament. Chris has completely transformed SfAM's policy output and will be hugely missed. You can read his last article on page 56 and if you want to learn more about science policy you may even wish to attend the policy workshop he helped design on **25 November 2019** (see page 58). The workshop, held in partnership with the Microbiology Society, will highlight how the science of microbiology can inform and shape public policy and demonstrate how microbiologists can boost their impact through engaging with policymakers and the policymaking process. Delegates do not need any prior science policy experience and applications are particularly encouraged from scientists who are at the early stages of their career. Visit sfam.org.uk for more details.

Paul Sainsbury

Editor

We're going to have to change how we live to protect our environment but also to protect our health

Professor Dame Sally Davies

*Fellow of the
Society for Applied Microbiology*

SfAM Fellowship Reception
BMA House, London, UK
18 June 2019



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Professor Dame Sally Davies joins the SfAMily

In June 2019, I had the pleasure of presenting our third Fellowship Award to Professor Dame Sally Davies who has made an outstanding contribution to antimicrobial resistance (AMR) awareness.

She commissioned the AMR Review in 2014 and continues to ask the questions that we need, as a community, to answer. It was interesting to hear her discussions with the young scientists from the ECS Committee around tackling AMR in the future. The subjects of improved rapid diagnostics, better antibiotic stewardship, novel drugs and so on were all addressed. What was also evident in the conversations was the need for alternatives to these ideas such as vaccination and the potential use of phages.

Vaccination surely has to be one of mankind's great achievements? The use of vaccination has restricted the effects of many previously problematic diseases in both human and animal medicine. It has the potential to be a fantastic tool or adjunct to other treatments in the face of antibiotic resistance, further demonstrating its worth as an intervention tool in helping to control infectious disease. Despite the apparent benefits of vaccines and vaccination there is still a strong lobby that feels differently and is strongly averse to this approach. Many arguments are cited as to why vaccination, especially in the young, is not advised, including the overloading of the immune system as a result of the vaccination process. I cannot support this view at all. The amount of antigen encountered by a child as they grow toward vaccination age is undoubtedly vast

and does not overload the immune system. It is unlikely then that the act of vaccination would cause such an issue.

What is clear is the wider public health benefits of vaccination, which has led to many diseases being kept to a minimum for a number of years. Only recently have we seen an increase in some diseases where vaccine coverage has been lowered – perhaps as a result of the antivaccination messages that have become more prevalent in recent years. The importance of vaccination is clear and has not yet been fully exploited in a role to help challenge the spread of AMR globally. I think it is up to us as the scientific community to defend and indeed promote vaccination as an important control measure in limiting the spread of pathogens and improving herd or community immunity wherever possible and practicable. I certainly will continue to do so whenever and wherever the opportunity arises.

Similarly, we should also not shy away from other potentially viable options to control infectious disease, perhaps in the form of bacteriophages. These small viruses have potential to be exploited in many areas to treat infections with a minimal chance of resistance occurring. They may well be a true 'One Health' applicable treatment to counter the drug-resistant bacteria. They are possibly the medicine that keeps on giving! I mean this in the sense that not only can a single dose of therapeutic phage continue to target a particular bacterial host, it can do so without upsetting the other components of the microbiome too much.

Mark Fielder

President of the Society for Applied Microbiology

The importance of good governance



During 2018, the Society went through an extensive governance review, which was completed at the Annual General Meeting in July 2019. With the help of governance expertise from an independent consultant (Lucy Devine), our decision-making processes, committee meetings and governing documents were scrutinised and recommendations made to ensure we are operating as effectively, openly and transparently as possible.

The first phase of SfAM's governance review involved interviews with trustees and team members who were asked their opinion about the effectiveness of meetings, decision-making and the robustness of our committees and governing documents. In the case of the trustees, they were also asked to rate their own knowledge of their role(s) and responsibilities as a trustee, including their legal duties and liabilities.

Following this came various working group meetings involving a variety of stakeholders to assess some initial recommendations for change. The final recommendations were signed off by the Executive Committee in November 2018 and since then work has been ongoing in implementing these recommendations. One recommendation was that the Society move to reporting by exception at Executive Committee meetings. This means that the trustees are updated with developments at the Society in real time through access to a secure electronic cloud drive. This enables the agenda of the Executive Committee meeting to move away from providing updates to the trustees on progress in various areas of the Society's work, and instead to focus on strategic items for discussion, decision or celebration.

The second phase of this work was a thorough review of our Memorandum and Articles of Association. The conclusion of this review was that there was a need for a refresh of our governing documents. The language in the previous document was considered dated and there was a recognised omission of some clauses needed to bring our decision-making processes into the 21st century. For example, we lacked a clause regarding the potential for our Executive Committee meetings to include virtual attendance by trustees, either by telephone or through video conferencing. With such facilities being available in the majority of meeting spaces, this seemed like a logical step in future-proofing our governance.

I've provided a couple of examples to illustrate why the review of our governance arrangements was needed. There were many more and we now have a new and robust set of governing documents and rules (processes). I'd like to extend my thanks to all trustees and members who've been involved in the development of these new Articles of Association, which were confirmed at the Annual General Meeting in July 2019.

Lucy Harper

Chief Executive of the Society for Applied Microbiology



Getting to know the CMO

I was lucky enough to attend another presentation of SfAM's Fellowship Award in June this year. The worthy recipient was Professor Dame Sally Davies for raising awareness of antimicrobial resistance (AMR) and leading the UK government's response to health emergencies including Ebola and pandemic flu.

Although my work has never been allied with healthcare, I have wanted to meet the first female Chief Medical Officer (CMO) for a few years now. During her time as CMO, not only has she raised awareness of AMR, she has also looked at the potential of using genomics to target treatments, tackled obesity and lowered the male low-risk alcohol guideline to match the level for females, based on experimental evidence.

Throughout her tenure, Dame Sally has expressed her concerns of the disease burden and death rate from AMR and the declining supply of new antimicrobials. She was also key to instigating the widely lauded *Review on Antimicrobial Resistance (AMR)*, which was commissioned in July 2014 by the UK Prime Minister and led by another SfAM Fellow, Lord Jim O'Neill.

As with previous Fellowship Award events, Dame Sally was questioned by members of the Early Career Scientist (ECS) Committee. Although I was not on the interviewing panel this time, I was able to enjoy watching my fellow ECS members Phil, Caleb, Lucky and Rob as they interviewed Dame Sally. During this interview, two questions and answers stuck out in my mind. Phil asked Dame Sally

whether she had come across conflict with scientific evidence and political ideology. Unsurprisingly she said "yes" and that although her advice is evidence-based, the politician takes the decision, therefore leading to evidence-informed rather than evidence-based policy.

She explained that "evidence is a social construct so what you'll find is not just ministers but all sorts of people saying 'but my auntie – this happened' or 'they said this to me' or 'I read in a newspaper' and for them, that's evidence". I had never thought of this concept before, but since then I have realised how many facts I have taken at face value because I heard them from someone who seemed to be 'in the know' or read them in a magazine. Dame Sally has certainly encouraged me to be more critical of what I hear.

The next question to attract my attention was asked by Caleb. He asked Dame Sally if there were any policies where she struggled to practise what she preached. Dame Sally jogs twice a week, eats healthily and drinks within the CMO low-risk guidelines – but she did outline how living a healthy life in our environment is not easy when that very environment pushes us toward unhealthy choices. This stuck in my mind as Dame Sally is an incredibly

Alli Cartwright

ECS Communications Officer

intelligent women who has undoubtedly seen the effects of poor diet, lack of exercise and excessive alcohol consumption, and yet her response showed that she struggles to live a completely healthy life. This reminded me that we are all human and, given the daily exposure to tempting food or drink, we will struggle with making the right choices. It also made me feel a bit less guilty for breaking my diet and eating a chocolate in the airport en route to the interview.

After the interview Dame Sally took a few minutes to talk to me before running to the airport for a ministerial event in Amsterdam. This gave me the opportunity to ask her, 'If you could eradicate one microbe what would you choose and why?' She outlined how she could not answer this question without consulting the experts – the microbiologists. Dame Sally explained that she was a haematologist specialising in sickle cell disease before she became the CMO in 2011, giving a voice to the expert microbiologists about the problem of AMR. She was unsure whether it should be a bacterium, a virus or a fungus, and outlined how she was getting increasingly worried about fungi.

It was an honour to meet Dame Sally; many see her as an inspiration to female scientists as the first female CMO, but she is an inspiration to ALL scientists. I can't wait to see what legacy she leaves from her new role as Master of Trinity College, Cambridge.



Members of the ECS Committee interview SfAM Fellow Professor Dame Sally Davies.

FURTHER READING

O'Neill J. (2016) Tackling drug-resistant infections globally: final report and recommendations. Available from:

https://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf



ENVIRONMENTAL MICROBIOLOGY LECTURE 2019

15 October 2019 | TBC London, UK

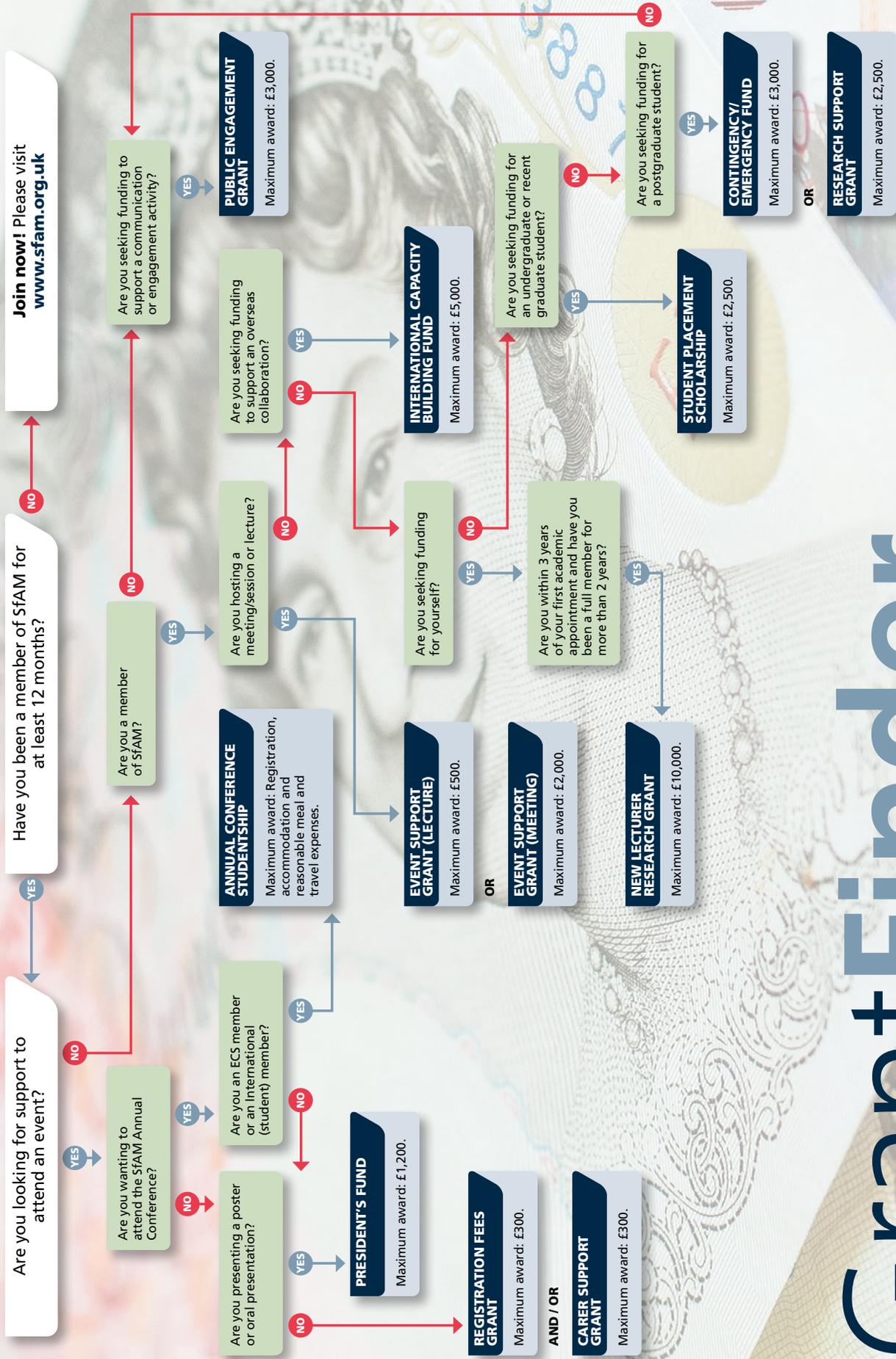
Juan Luis Ramos

The double life of *Pseudomonas putida*: ubiquitous soil bacteria and useful microbial chassis

Juan Luis Ramos is a Full Professor at the Spanish National Research Council (CSIC). From October 2013 to September 2017 he was the Director of the Biotechnology programme of Abengoa Research. He received the King Jaime I prize for his achievement in environmental research and the FEMS-Lowff award in 2013 for achievements in environmental microbiology. In 1978, he graduated from the University of Seville where he obtained his bachelor's degree. In 1981, he was awarded his PhD with a thesis on *The Bioconversion of Solar Energy into Chemical Energy*. He spent almost 2 years as a postdoctoral researcher at the Unit of Nitrogen Fixation in Brighton (UK), supported by an EMBO fellowship and over 2 years at the Department of Medical Biochemistry in Geneva (Switzerland), where he started working on the metabolism of aromatic hydrocarbons in *Pseudomonas*.



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Applications are invited from potential supervisors for PhD studentships.

The closing date for applications is 15 November 2019.

<https://sfam.org.uk/grants/basil-jarvis-phd-studentship-2020.html>

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Phage ecology: a master manipulator

Lucy Kelly

University of Warwick, UK

Over 100 years ago, Felix d'Herelle and Frederick Twort independently discovered bacteriophage. This great discovery led to the development of molecular biology, a field of science in which phage have featured heavily over the years. However, these viruses are much more than just molecular workhorses. Recent advances in technology and culturing methods have led to the belief that phage are the most abundant biological system worldwide. With an estimated population of over 10^{30} phage particles, we are only now finally beginning to uncover the important and multifarious roles these viruses play in ecosystems worldwide.

Under the sea

Marine phage, and their role in the upkeep of our oceans, is an area of phage research that has blossomed in recent years. It is easy to see why such viruses excite scientists, when just 1 ml of seawater contains (up to?) 10 million phages. Marine phage infect and multiply within ocean-dwelling and sedimental bacteria; up to a staggering 80% of bacteria living in ocean sediments are killed by these phage. Organic matter is released by the dead bacteria into the ocean environment, where it is reused and recycled by other organisms. The 'viral shunt', as this process is known, is believed to help fuel the carbon, nitrogen and phosphorus cycles in the oceans. Without the actions of marine phage, the richly nutritious environment of the ocean would suffer.

Down to earth

Another ecosystem where phage dominate is in the soil, but these viruses are less well-characterised than their marine counterparts, as they have proved more difficult to culture in the lab. Soil is an integral part of the environment for obvious reasons, providing numerous different ecological niches, supporting numerous

biogeochemical cycles and proving essential for the agricultural industry. Studies using the soil-based bacteria *Serratia* and *Pseudomonas* spp. revealed that around 5% of these soil-dwelling bacteria are infected with phage at any one time. Current estimates of phage abundance place the number at around one billion per gram. Similar to their role in the ocean biosphere, these phage help to free up organic matter within the earth. Again, these nutrients are recycled and used by other organisms, helping other microorganisms and plants to thrive in nutritionally limited environments.

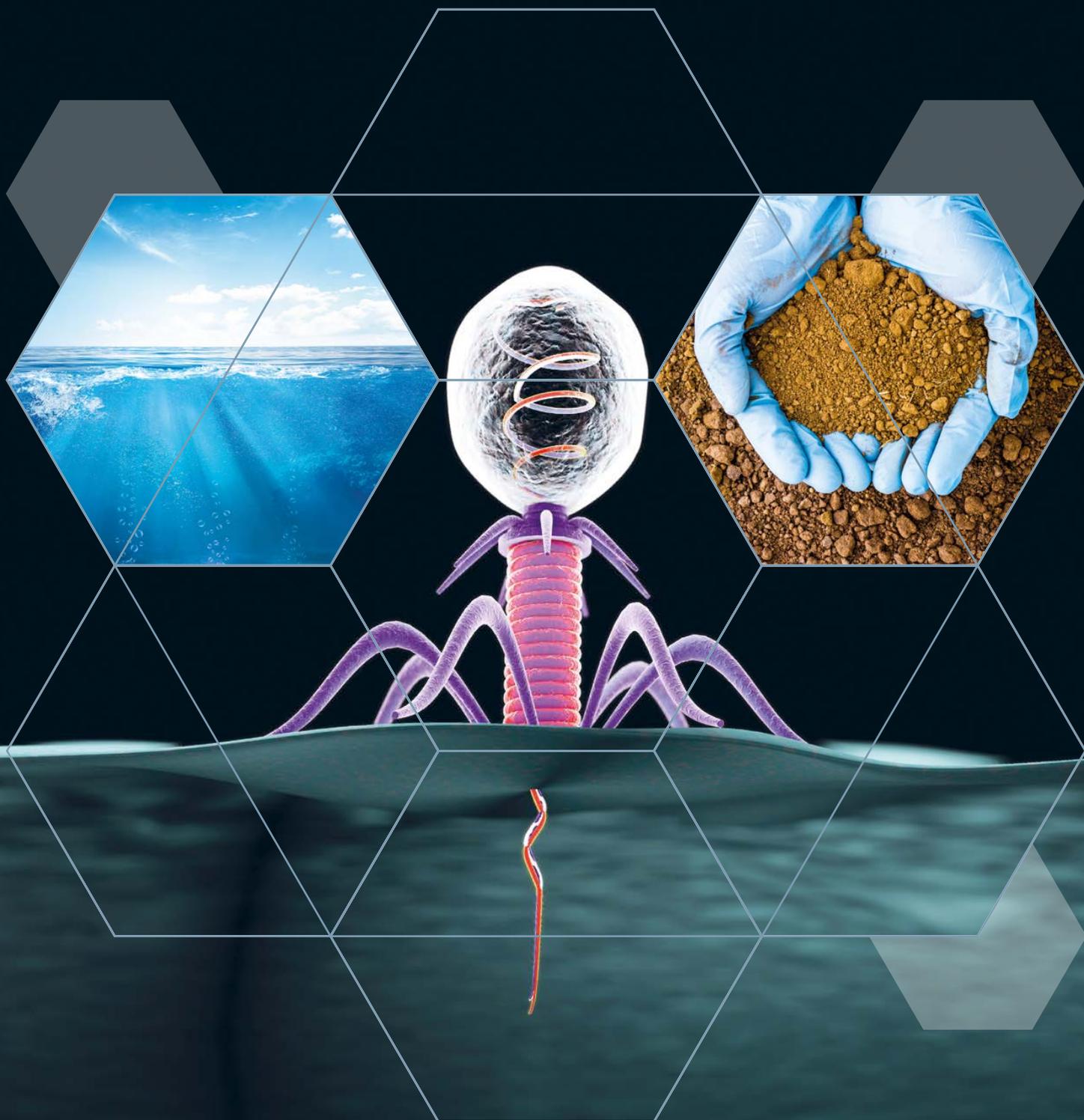
Molecular manipulators

Not only can phage shape the population of bacteria and influence nutrient availability, they also change the genetic make-up of their hosts. Phage can transfer parts of their DNA to host bacteria, with horizontal gene transfer (HGT) being the most widely spread form of genetic manipulation. Under optimal laboratory conditions, transduction occurs once in every 10^8 phage infections. When this figure is extrapolated upwards to account for the global marine population of bacteria, transduction occurs 20 million billion times per second in the oceans. In reality, this number is likely lower due to the harsher environmental conditions and, with it, a decreased transduction efficiency in the marine environment. Nevertheless, HGT is still a hugely important and prevalent process. HGT can influence the spread of antibiotic resistance genes, turning non-pathogenic environmental isolates into disease-causing ones. This is documented in many bacterial species including *Escherichia coli*, *Salmonella* spp. and *Vibrio cholerae*. In fact, the major virulence factor responsible for production of the cholera toxin in *V. cholerae* is encoded by a phage known as CTX ϕ . The CTX ϕ phage carries and donates the gene which converts non-pathogenic *V. cholerae* into the pathogenic strain with the potential to cause devastating disease.

Are bacteriophage the future?

Over one century since their discovery, phage have been recognised to be hugely important for both ecology and biotechnology. The future for phage looks promising, with ever new and more exciting research emerging surrounding their potential uses in the environment. They could become powerful biocontrol agents for diseases affecting much-needed crops. Plant diseases such as blight, bacterial wilt and potato tuber soft rot could be both prevented and treated by these phage, this being one area of agricultural research where phage will look to make a

massive impact. The use of phage as a biocontrol agent is an attractive idea, especially compared with chemical methods, as phage treatments can be tailor-made to specifically combat the disease. In addition to being used in human medicine to tackle diseases caused by antibiotic-resistant bacteria, phage could be used to further prevent the spread of antimicrobial resistance by replacing antibiotics as growth promoters given to animals in the agricultural industry.



Phage and bacteria: a war in a biofilm

Nicola Stanley-Wall

University of Dundee, UK

It is clear that bacteria and phage coexist in many diverse, complex environments. However, it perhaps is not always clear which party will win when an interaction occurs. To add to the complexity, recent work has shown that bacteria can tip the balance to survive in the presence of predatory phage when they form biofilms. It is the change in lifestyle that results in protection, not genetics.

Biofilms are structured communities of microorganisms that are attached to a surface and are encased in a self-produced extracellular matrix. The biofilm matrix is dynamic in nature and fulfils multiple functions for the sessile community. This includes nutrient sequestration and water adsorption, shielding the resident cells from environmental stress and competition, and acting as a signalling facilitator for cells both within and outside the biofilm. Research over the last 10–15 years has shown that there is great diversity in composition of the biofilm matrix across both polymicrobial and between single-species biofilms; however, commonly occurring constituent parts are emerging. These include polysaccharides, extracellular DNA, lipids and proteins, some of which are fibrous in nature. Growing evidence suggests that at least one fibre-forming protein, which provides structural integrity to the biofilm, can additionally provide protection to the resident bacteria from phage predation.

FURTHER READING



Erskine E, Morris RJ, Schor M, Earl C, Gillespie RMC, Bromley KM *et al.* Formation of functional, non-amyloidogenic fibres by recombinant *Bacillus subtilis* TasA. *Molecular Microbiology* 2018; 110(6), 897–913

Serra DO, Richter AM, Klauck G, Mika F, Hengge R. Microanatomy at cellular resolution and spatial order of physiological differentiation in a bacterial biofilm. *mBio* 2013; 4(2), e00103-00113

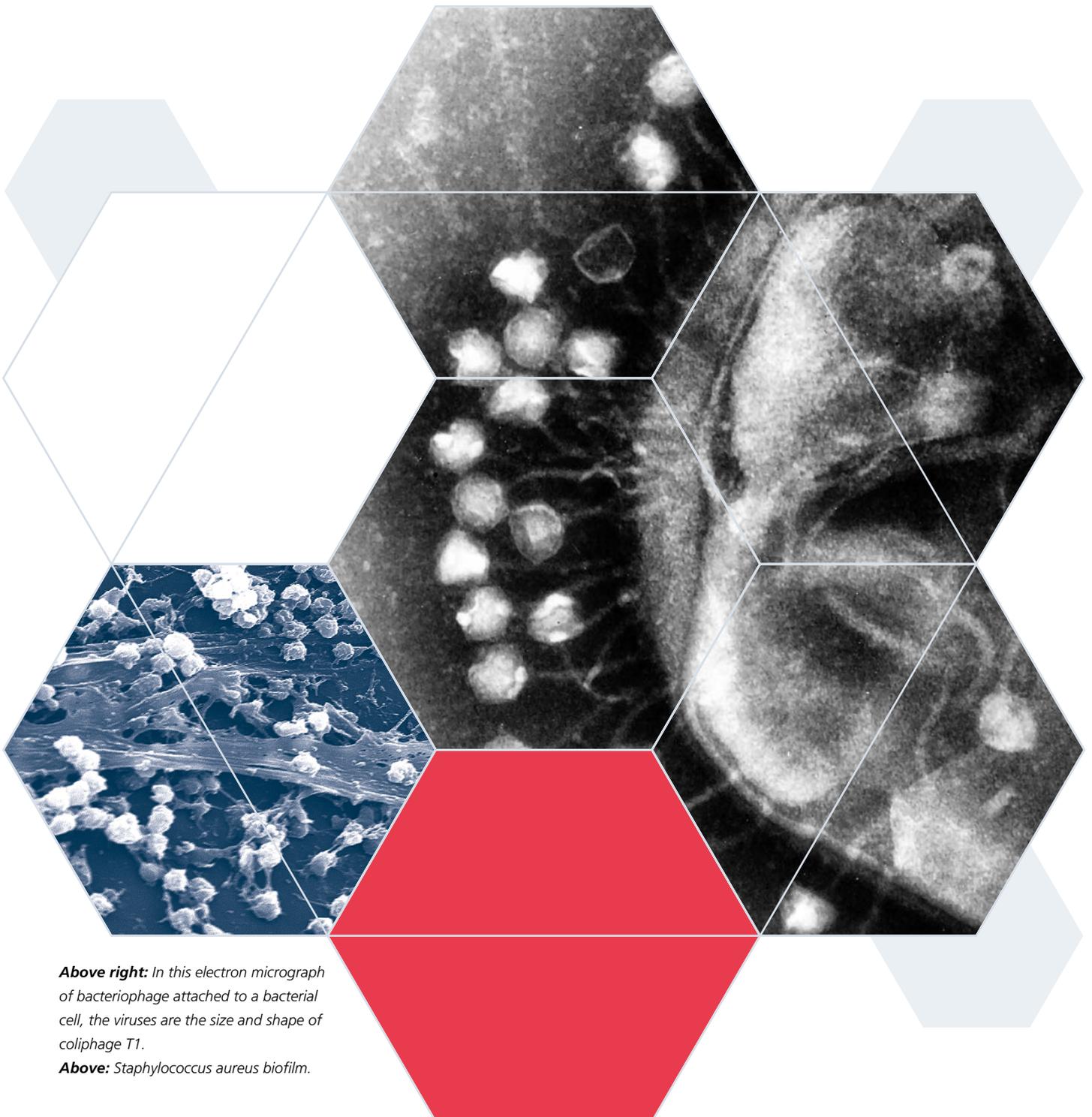
Vidakovic L, Singh PK, Hartmann R, Nadell CD, Drescher K. Dynamic biofilm architecture confers individual and collective mechanisms of viral protection. *Nature Microbiology* 2018; 3(1), 26–31

The biofilm matrix of the *Escherichia coli* biofilm has recently been shown to both sequester and hinder diffusion of a predatory lytic T7 phage. Using a series of bacterial strains, it was shown that the protection offered by the biofilm was dependent on 'curli', protein fibres found in the extracellular matrix. Curli fibres made by *E. coli* were first visualised by transmission electron microscopy and were quickly noted for their high level of insolubility and resistance to proteases. Curli production is dependent on the starvation response of the cells, which can occur in a multi-layered biofilm due to the stratification

Biofilms are structured communities of microorganisms that are attached to a surface

of cells with respect to a nutrient source. Microscopy analysis has shown that the starved *E. coli* cells become highly 'curliated'; in essence, the protein fibres form a network of 'cell-moulded baskets' throughout the intercellular space. It is this protein network that provides structure to the bacterial community, which is the element of the biofilm that is critical to protect the cells from lytic phage. The curli fibres work in two ways. First, they bring the cells in the biofilm together in a closely connected structure. This physically prevents the phage from entering the biofilm. However, curli can also bind phage, restricting phage mobility by sequestration. The consequence is that

the phage are prevented from reaching the cells within the interior of the community. The outcome of this intricate phage–bacterium interaction was revealed through the use of high-resolution microscopy of living biofilms. This allowed the T7 phage and bacterial community to be followed in both space and time. It will now be of interest to see if there are other ways by which the outcome of an interaction between phage and bacteria can be manipulated. The mechanisms known are likely to diversify as the study of bacteria–phage interactions, and the methods by which the analysis is conducted, continues to grow.



Above right: In this electron micrograph of bacteriophage attached to a bacterial cell, the viruses are the size and shape of coliphage T1.

Above: *Staphylococcus aureus* biofilm.

Applications of bacteriophage: advances and possibilities

Paul Sainsbury

Society for Applied Microbiology, UK

Recent advances in the field of phage research have pushed forward current phage technologies, going beyond bacterial control using whole phage, to areas including biocontrol utilising phage-derived enzybiotics, novel drug-delivery systems, bionanotechnology and diagnostics.

Antibacterials and biocontrol

In addition to phage being used to combat pathogenic bacteria in infected humans, phage are also useful tools within the food industry. Phages are already in use to eliminate pathogenic bacteria in foods, with Listex™ being founded in 2012 and used to target a number of important food pathogens such as *Listeria monocytogenes*, *Escherichia coli* and *Salmonella* spp. Alternatives to whole-phage bacterial control include engineered phages that deliver Clustered Regularly Interspaced Short Palindromic Repeats-associated protein-9 nuclease (CRISPR-Cas) nucleases into antibiotic-resistant cells and knock out antibiotic resistance genes, rendering resistant cells antibiotic sensitive.

Bacterial diagnostics

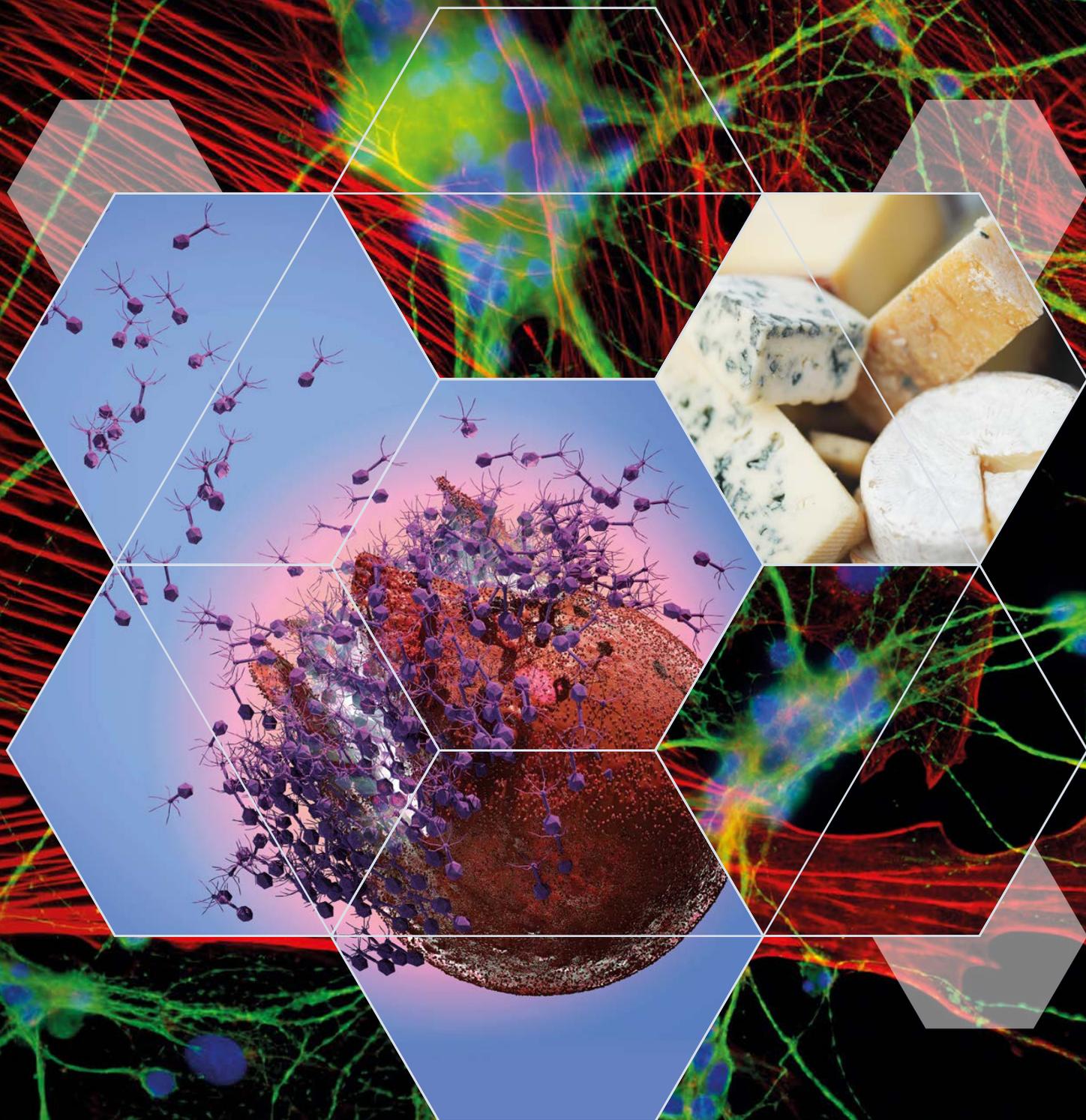
Phage virions and their encoded proteins can also be useful for the detection and specific identification of bacteria. The simplest of these is where a standard number of specific phages are incubated with a food material or some other test sample. If the bacterial target is present and viable, detectable phage numbers will increase through amplification on the pathogen. In addition to traditional plaque and culture-based assays, molecular phage-based methods have allowed rapid diagnostics to be developed. In the case of *Yersinia pestis*, Sergueev *et al.* have developed a quantitative real-time PCR technique to detect an increase in phage DNA if the bacterium is present.

Reporter phages can also detect the presence of bacteria without needing to produce progeny phages and lyse the host cell. In this case, phage genomes are modified to carry bioluminescence or fluorescence genes that the phage alone cannot express. Upon injection of the phage DNA into its host, active bioluminescent or fluorescent proteins are synthesised using host bacterial machinery, facilitating visual detection.

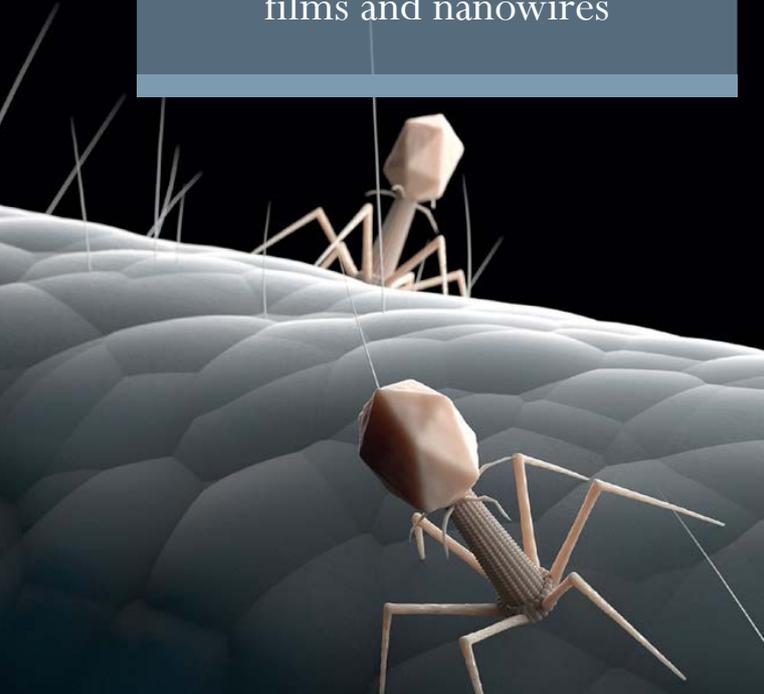
Phage receptor-binding proteins (RBPs) can also be used in bacterial detection and identification. A simple glass-slide agglutination test for *Campylobacter* was developed by fusing the receptor-binding domain of the RBP in a *Campylobacter* phage to green fluorescent protein. *Campylobacter jejuni* and *Campylobacter coli* could then be detected using fluorescence microscopy. Because of the wide diversity of phages, a plentiful source of host-specific proteins are available to create simple identification tests such as the agglutination assay mentioned above. Both RBPs and whole phage can be bound to a biosensor surface for bacterial detection, allowing high specificity. Whole phage are more difficult to attach to a surface, whereas RBPs can be recombinantly produced and have better stability than antibodies.

Phage endolysins can be used in an additional capacity of detection as endolysins can be used instead of the more traditional reagents for DNA extractions. Staphylococcal endolysin ClyH degrades the peptidoglycan of *Staphylococcus aureus* more rapidly than lysostaphin, decreasing sample preparation time for real-time PCR of DNA when endolysin is used. Another method of detection is phage display, whereby phages are genetically modified to carry a foreign peptide on their surface. Lee *et al.* created a phage detection system using phage display

Phages are already in use to eliminate pathogenic bacteria in foods



Genetically modified filamentous phages have even been utilised in the field of material synthesis to construct films and nanowires



where the phage displayed two different peptides: one with specificity to a target protein and the other with an affinity to gold nanoparticles. Through this method, they could detect as few as 25 femtomoles of their target antigen by measuring the UV absorbance of the phage. Phage display techniques have been incorporated into systems capable of real-time detection of bacteria and endospores, through the use of display peptides that are capable of binding to a magnetoelastic resonator.

Drug discovery and phage-based drug-delivery systems

Since the advent of phage display in 1985 by Nobel Prize Laureate George Smith, phages have been used to identify receptor–ligand interactions of numerous infectious diseases and cancers, leading to drug discovery and aiding vaccine design. Phage display allows modification of phages into nanocarrier vehicles for chemotherapy through attachment of a drug molecule to the surface of the phage. Phage displaying therapeutic peptides could cross the blood–brain barrier and have the potential to treat diseases such as Parkinson’s and Alzheimer’s. Cancer cells that express particular molecules can be targeted by phage with an affinity to these specific cell receptors, exploiting phage beyond drug-delivery systems to allow target

detection by phage display reporter molecules or detection of bound phage DNA using real-time PCR.

Empty phage capsids are being utilised as carriers containing molecules such as therapeutic compounds, RNA and peptides. Capsids and virus-like particles can be modified to present ligands on their surface to deliver RNA-guided endonucleases to specific cell types to be used for *in situ* genome editing. Using phages as nanocarriers for cancer treatment through delivering chemotherapeutic drugs allows the half-life of drugs to be extended and keeps the toxicity of the drug contained to the site of interest, reducing the damage caused to body tissues.

Biotechnology

Genetically modified filamentous phages have even been utilised in the field of material synthesis to construct films and nanowires for semiconductors, piezoelectric energy generation and used for their photo-response properties. These materials can be used for catalysts and batteries; the M13 phage was used to produce nanowires for scaffolding to guide cell growth for the formation of human tissue.

Phage-derived enzymes are being purposed for novel techniques in the biotechnology field: RNA polymerase and ribonuclease H have been used to develop *in vitro* genetic circuits with future potential applications to be used in nanodevices and to regulate processes within artificial cells. Recombinase enzymes are extending the memory capacity of these circuits to be used in construction.

Summary

This commentary provides a snapshot of the increasing diversity of phage research in recent years and shows that it is advancing rapidly and that new applications are being reported frequently. Since the discovery of phage a century ago, their research focus has diversified from applying these agents to simply treat bacterial infections to a broad range of useful functions including biocontrol, diagnostics, drug discovery and drug delivery, as well as several applications in nanomedicine.

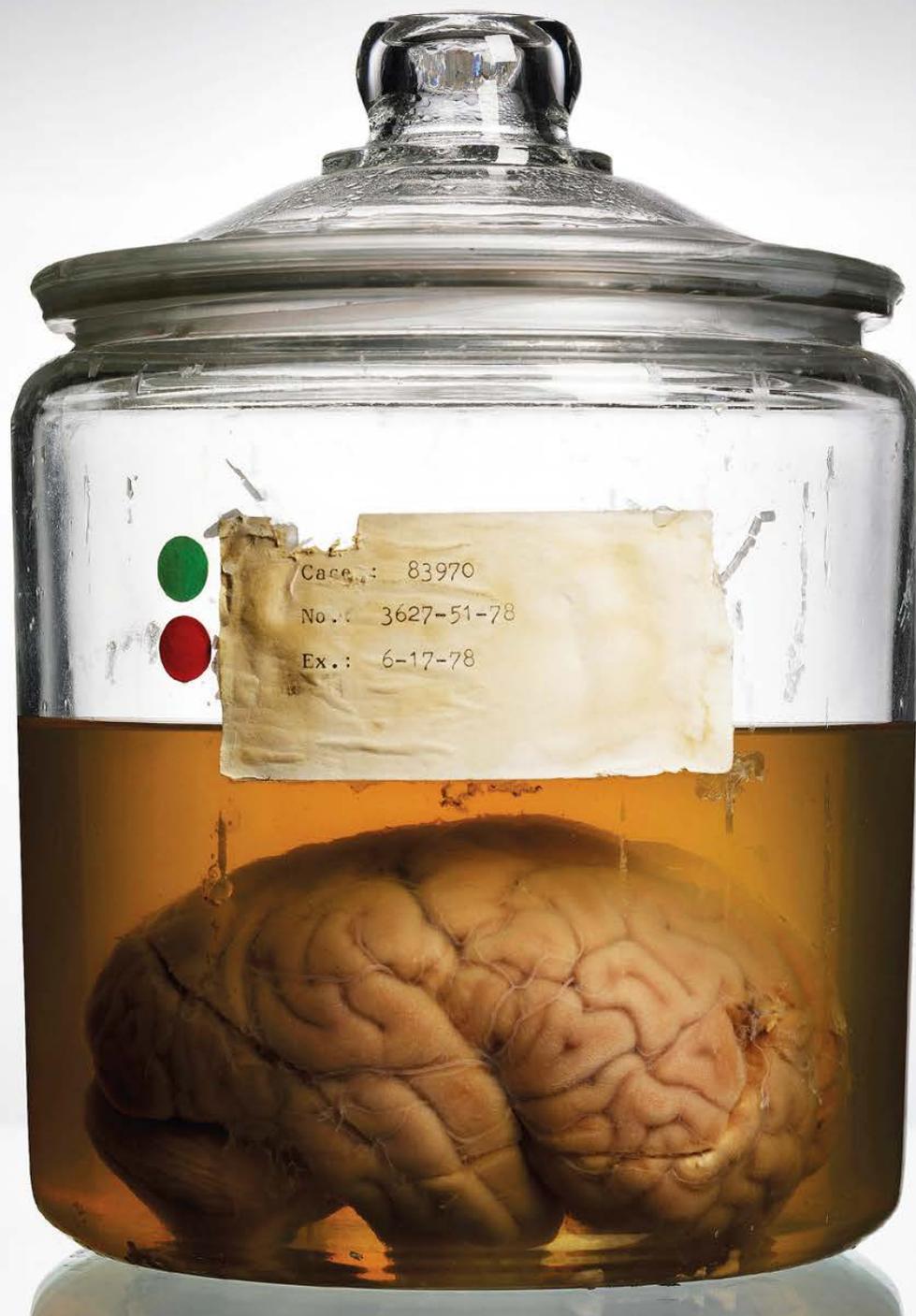
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Phage displaying therapeutic peptides could cross the blood–brain barrier and have the potential to treat diseases such as Parkinson’s and Alzheimer’s



Antimicrobial resistance from a vet's point of view

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Introduction

Does antimicrobial resistance (AMR) change my working life? While we have seen some shift in susceptibility patterns of the common pathogens identified as part of the UK's programme of surveillance, in farm animal practice AMR very rarely causes issues clinically. That said, the topic of responsible medicine use is a constant feature of clinical discussions with clients. Writing in 2010, Henderson highlighted some of the potential misconceptions of how antimicrobials are used in the veterinary sector, saying 'There is a school of thought, mostly in medical circles, that vets are guilty of antibiotic overuse in clinical situations where their capacity to modify the progress and treatment of the condition is limited, if not entirely absent'. I would like to take this opportunity to demonstrate how we are working with our clients more closely than ever to address the issue of AMR.

The drivers of change

The publication of the O'Neill Review, in May 2016, saw the first figures for overall antimicrobial usage being suggested: 'we see 50 mg/kg as a broadly reasonable target for high-income countries to aim for in the short term'. The report also set in motion the consideration of whether individual antimicrobial classes should be treated differently and whether targets should be broken down by animal type (e.g. poultry, cattle etc.). In response to the report DEFRA committed to an overall target of 50 mg/kg across the animal sectors by 2018 (a 20% reduction in 4 years); it also committed to evidence-based goals for each individual livestock species sector being agreed by 2017.

In 2017, at the same time it was announced that the overall usage figures for 2016 were below the 50 mg/kg target, the RUMA Target Task Force Report was published, laying

out more details on how an overall reduction can be achieved through specific activities in each agricultural sector (Table 1).

TABLE 1 SUMMARY OF KEY AREAS OF FOCUS FOR THE RUMA TARGET TASK FORCE REPORT

- Overall reduction in antimicrobial usage tailored to individual sectors.
- Reduction in use of high-priority critically important antimicrobials.
- Reduction in prophylactic use.
- Promotion of preventative medicine: husbandry, biosecurity and herd health planning.
- Data collection and benchmarking.
- Training and knowledge exchange for both vets and farmers.

Alongside the RUMA Target Task Force Report we have seen several other initiatives that have brought about changes in prescribing behaviour and on-farm usage. Within the UK farm sector, assurance schemes are widely adopted by producers to promote consumer confidence. The leading scheme is Red Tractor Assurance, which has a membership of over 40,000 beef, lamb and dairy producers across the UK. While these schemes are not compulsory, they are frequently required for farms to market their products; for instance, 98% of UK dairy farms are registered members of Red Tractor. On 1 June 2018, new standards came into force with a specific focus on the responsible use of antimicrobials. The key requirements were:

- All farms must collate their annual medicine usage and review with a vet.
- Vet review of collated medicines usage data includes discussion on the use of critically important antimicrobials.
- Third- and fourth-generation cephalosporins, fluoroquinolones and colistin are used only as a last resort under vet direction, guided by sensitivity or diagnostic testing.

We have also seen retailers and first purchasers bring in contractual requirements for farms supplying them; these started with antimicrobial usage reporting but have progressed to the banning of certain classes of antimicrobials. The focus initially was on the third- and fourth-generation cephalosporins and fluoroquinolones; however, we are now also seeing an increased focus on the macrolides.

Because of the changes in the assurance standards and retailer requirements we have seen increased client engagement with the topic of AMR and prudent use, and



requests for medicines reviews. The discussions resulting from medicines reviews have resulted in significant changes in the antimicrobial sales patterns, especially in relation to high-priority critically important antimicrobials. Over 2018, our usage of third- and fourth-generation cephalosporins and fluoroquinolones dropped by over 99.9%. Over the same period, we have seen an overall drop in antimicrobial usage across our business, so it has not simply been a case of swapping one product for another. This reduction in antimicrobial usage has been helped by changes in farm management practices, such as increased uptake of vaccination and disease eradication programmes, all facilitated by better engagement of farmers with their vets.

When we first started talking to clients about responsible use and antimicrobial usage reduction, the most frequent concerns we were presented with revolved around animal welfare. Producers were concerned that they would not be able to treat animals and welfare would suffer. Our approach to this has always been about 'as little as possible, as much as necessary', with the message to clients not simply being to cut usage but avoiding the need for treatments in the first place and when antimicrobials are required ensuring that the right product is being used in the right way.

Let us take a look at one specific disease example, bovine respiratory disease (BRD), which is one of six conditions highlighted by the RUMA Targets Task Force Report as being a main reason for antimicrobial usage in beef cattle. BRD is a multifactorial syndrome that can be caused by both viruses and bacteria. Often the role of bacteria is as a secondary invader following an initial viral infection so there has been interest in how we can prevent the disease progression from the initial viral stages. The challenge in this situation is therefore identifying disease early enough that an antimicrobial treatment is not required. The traditional method for on-farm disease detection is for farm staff to evaluate the health of their stock subjectively, based on behaviour and appearance; this unfortunately has limited sensitivity (62%) for detecting BRD due in part to cattle's natural tendency as prey animals to mask signs of disease and weakness. Detection is further hampered because the clinical signs being observed (e.g. depression, loss of appetite, respiratory character change and increased rectal temperature) are not specific for BRD. This can lead to cattle with BRD often being detected late in the disease process or not detected at all. This observation is supported by abattoir studies, which identified moderate to severe lung lesions in 35% of animals, of which 64% had no recorded treatments for BRD. The use of non-steroidal



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Williams P, Potter T, Cooper R. Associations between lung consolidation, bovine respiratory disease treatment and live-weight in UK veal cattle. World Buiatrics Congress, Dublin, July 2016, oral communication

anti-inflammatory drugs (NSAIDs) alone in early cases of respiratory disease, as identified by temperature monitors placed in the ears of calves, has showed some promise, with 25.7% of cases treated with an NSAID alone not requiring any further treatment. The other focus for the control of BRD is vaccination; figures published in 2018 show that there has already been an increased uptake of pneumonia vaccines, with the percentage of cattle under 1-year-old being vaccinated estimated at 29% in 2011, rising to 38% in 2017; however, it also highlights the large proportion of animals that are not receiving any pneumonia vaccines and the opportunity for further engagement.

Where next?

The European Commission's 5-year action plan for AMR, published in 2011, highlighted 12 actions to be undertaken to help reduce the impact of AMR. In these action points the need for development of new effective antimicrobials for human use was highlighted; however, for veterinary medicine the action point was 'analyse the need for new antibiotics in veterinary medicine'. We are therefore unlikely to see new molecules for veterinary use and it is essential that we take steps to preserve the efficacy of what we already have. Most clinicians have probably

resigned themselves to the fact that we are unlikely to see new compounds in the veterinary sphere, a point seemingly echoed by the animal pharmaceutical companies who are now positioning themselves as animal health providers rather than basing their business purely around drug development and sales. We now have the large companies increasingly investing in data collection and analysis, diagnostic and monitoring solutions, as well as seeing a shift towards the development of vaccines.

The responsible use of medicines and the reduction of antimicrobial usage remain the key agenda for farm animal practice but need to be viewed as part of a holistic approach to animal health and welfare. Many of the successes we have had so far have been through veterinary education and engagement with our clients, but further sustainable reductions are going to require increased uptake of things such as vaccination, selective breeding for disease resistance and disease eradication programmes, as well as looking at the way in which we manage animals. The agricultural sector is under pressure to meet the requirements of an increasing population, but this must be achieved through management systems that meet both society's demands for food production and their need to preserve the effectiveness of antimicrobials.



The traditional method for on-farm disease detection is for farm staff to evaluate the health of their stock subjectively

Arsenic: smartphone-friendly biosensor to tackle an insidious global threat

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Background

It was the largest mass poisoning of a population in history – bigger even than Chernobyl. This alarming assessment by the WHO in the 1990s marked a dark period in Bangladesh. The country faced a silent killer threatening the lives of millions. Nearly 30 years later they are still struggling with its devastating consequences.

The tragedy is that this was the unintended consequence of a project designed to bring safe drinking water to millions. In the 1970s, one of the biggest killers of children in Bangladesh was drinking stagnant water contaminated by microorganisms. To tackle this, an internationally funded effort installed tube wells across the country, tapping into underground water sources. The private sector soon stepped in to install millions more. By 1997, 80% of the population had direct access to 'safe' water that had travelled through rocks and sediments, filtering out the most harmful microorganisms.

But in the years that followed tube well installations, people began to display worrying symptoms. Skin lesions were the first sign of many potentially fatal health problems. The cause was arsenic, a natural but highly toxic component of the earth's crust. Arsenic has a long history as a poison, used by the ruling classes during the Middle Ages and Renaissance to murder rivals. Odourless and tasteless, it became known as the 'Poison of Kings and the King of Poisons'. Its insidious nature contributed to the crisis in Bangladesh. The lower levels typically found in contaminated water meant that it did not kill quickly – the first symptoms could take 10 years to appear.

It was the private installation of shallow and more affordable tube wells in many Bangladeshi households that raised the risk of arsenic contamination compared with deeper government and community wells. Half of the 10 million tube wells were found to be contaminated.



Microfluidic encapsulation-enabled microbial sensor array for monitoring arsenic contamination, showing different output patterns on various arsenic (As³⁺) levels. Left, middle, right panels: images acquired by a Nikon microscope, USB fluorescence microscope and cell phone camera.

While skin lesions led to social stigma, the most serious consequences of long-term arsenic exposure are cancers, diabetes, cardiovascular disease and impaired intellectual development in children.

Despite intensive efforts to reduce arsenic exposure, an estimated 39 million people in Bangladesh are still consuming contaminated water. In the worst affected areas around 20% of all deaths can be attributed to arsenic poisoning and it claims 43,000 lives every year. Whilst Bangladesh has endured the greatest burden, arsenic contamination at levels above WHO guidelines is a global issue, affecting at least 140 million people in 50 countries.

Researchers from the Centre for Synthetic and Systems Biology at the University of Edinburgh are finding new ways to tackle this threat. Our group has developed a user-friendly bacteria-based biosensor to detect unsafe arsenic levels. The portable device could prove a game changer for resource-limited countries, costing just 30 pence per test.

In Bangladesh, arsenic monitoring is challenging and expensive. Water samples need to be analysed in specialist laboratories by atomic absorption spectroscopy (AAS). There is typically only one laboratory for every five districts. Remote communities face long journeys to drop off their samples and the success of public awareness campaigns has led to backlogs as long as 2 months. Although portable test kits are available, they are expensive and produce toxic chemicals. Household filtering systems are a promising solution, but water must be regularly tested to ensure they work correctly.

Biosensors have long been championed as a potential solution to meet the urgent need for affordable, on-site testing. Many bacteria, such as *Escherichia coli*, grow easily in the presence of arsenic and have genetic machinery encoding metabolic processes that detect and pump out this toxin. By altering their genetic circuit to produce visual pigments in the presence of arsenic, bacteria could provide a simple and self-renewing form of detection.

However, the technology has struggled to make it out of the lab – biosensors are often difficult to use and rarely sensitive enough for real-world conditions. Attempts to



Cascaded amplifying circuits enable ultrasensitive cellular sensors for water contaminants.

FEATURES

improve biosensors have often focused on one feature over another leading to trade-offs.

To create a biosensor that tackled these market barriers we combined several approaches. To improve sensitivity we needed to adjust the biosensor's sensing module. In *E. coli* the presence of arsenic functions as an 'on switch'. It binds to the surface of particular protein receptors that repress the genetic circuit, disrupting their function. This activates the genetic circuit, producing an output – in our biosensor, green fluorescence protein (GFP). The threshold for this switch depends on the amount of 'binding'. By simply reducing the number of arsenic receptors we increased sensitivity 5000-fold, allowing detection of arsenic levels below WHO guidelines of 10 parts per billion (ppb).

Whilst improving sensitivity was important, we needed to ensure that enough fluorescent protein was produced to be visible to the human eye. To achieve this we introduced genetic parts that function as biological amplifiers. Similar to boosting the horsepower of a car's engine, these amplifiers act as turbo boosters converting the signal received by the bacteria's sensing module into a stronger output. We tested the performance of a number of these genetic amplifiers and then created a cascade, installing them one after another, to boost GFP production.

The downside of increasing sensitivity and output is that it increases background noise. For genetic machinery to work effectively it is never fully switched off. This means that small quantities of GFP are produced in the absence of arsenic and could result in a false-positive reading.

To tackle this trade-off we used two approaches. By altering the genetic circuit to include an extra binding site for the repressor proteins we created a 'roadblock' that reduced background GFP production. We also modified the fluorescent protein reporter, including a degradation tag that triggered it to be broken down by the bacteria. However, we didn't want GFP to be continuously degraded in the presence of arsenic so we added another protein,

which acts as 'biological scissors', cutting off the degradation tag as arsenic levels rise.

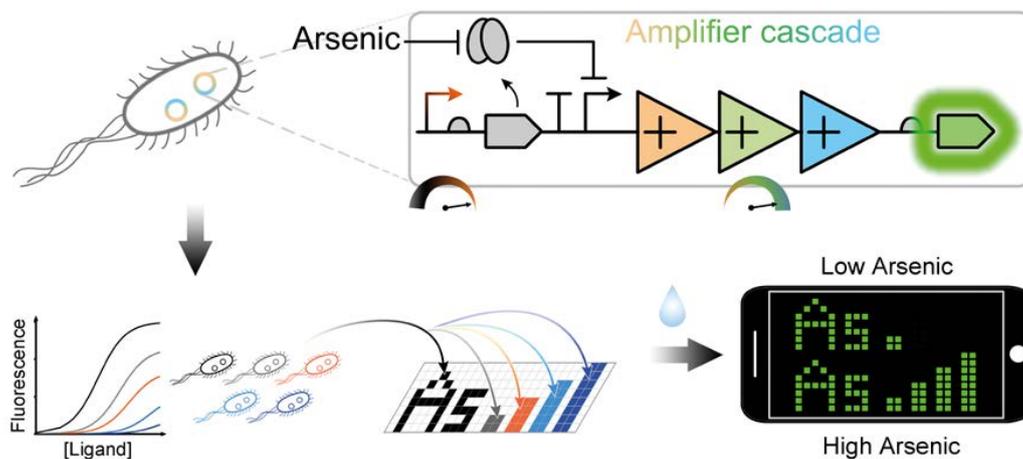
These advances provided precise mechanisms for controlling sensitivity, but we also needed to translate GFP production into an accurate measurement of arsenic levels. To do this we created bacteria with different levels of arsenic sensitivity and placed them inside a clear plastic device – seeding them in patterns, similar to volume bars, displaying the level of contamination. After allowing time for GFP to be produced, the device is attached to a smartphone, using the camera to illuminate the volume bars.

Working with local partners in Khulna University and monitoring offices allowed us to test the biosensor. We travelled to Bangladesh to collect well water samples from villages in some of the worst affected regions, with arsenic levels up to 20 times higher than WHO guidelines. The arsenic levels reported by the biosensor were consistent with lab-based standard tests, proving its accuracy.

However, there are still hurdles in the journey to market. Devices using genetically modified bacteria face an uncertain path through Europe's regulatory environment. We used microfluidic devices and hydrogel to trap bacteria and tackle safety concerns. But we are also exploring cell-free systems. If successful, the genetic circuits, floating in a cytoplasmic soup, could be freeze-dried onto paper with a hydrophobic barrier that prolongs its shelf life. When ready to use it is simply rehydrated with a water sample. We also aim to improve speed as the current biosensor requires 24 h of incubation. Increasing bacterial cell densities and exploring alternatives to GFP, such as enzymes that produce a faster, colorimetric output, could help to achieve this.

The real advantage of our approach is that it's not limited to arsenic. It opens the door to a new generation of ultrasensitive biosensors with many uses, including detecting other environmental toxins, disease diagnosis or even detecting landmines.

A microbial sensor array displaying an easy-to-read volume bar-like pattern for mobile phone-based field monitoring of arsenic contamination.



Despite intensive efforts to reduce arsenic exposure, an estimated 39 million people in Bangladesh are still consuming contaminated water





A role for genetically engineered phages in personalised medicine?

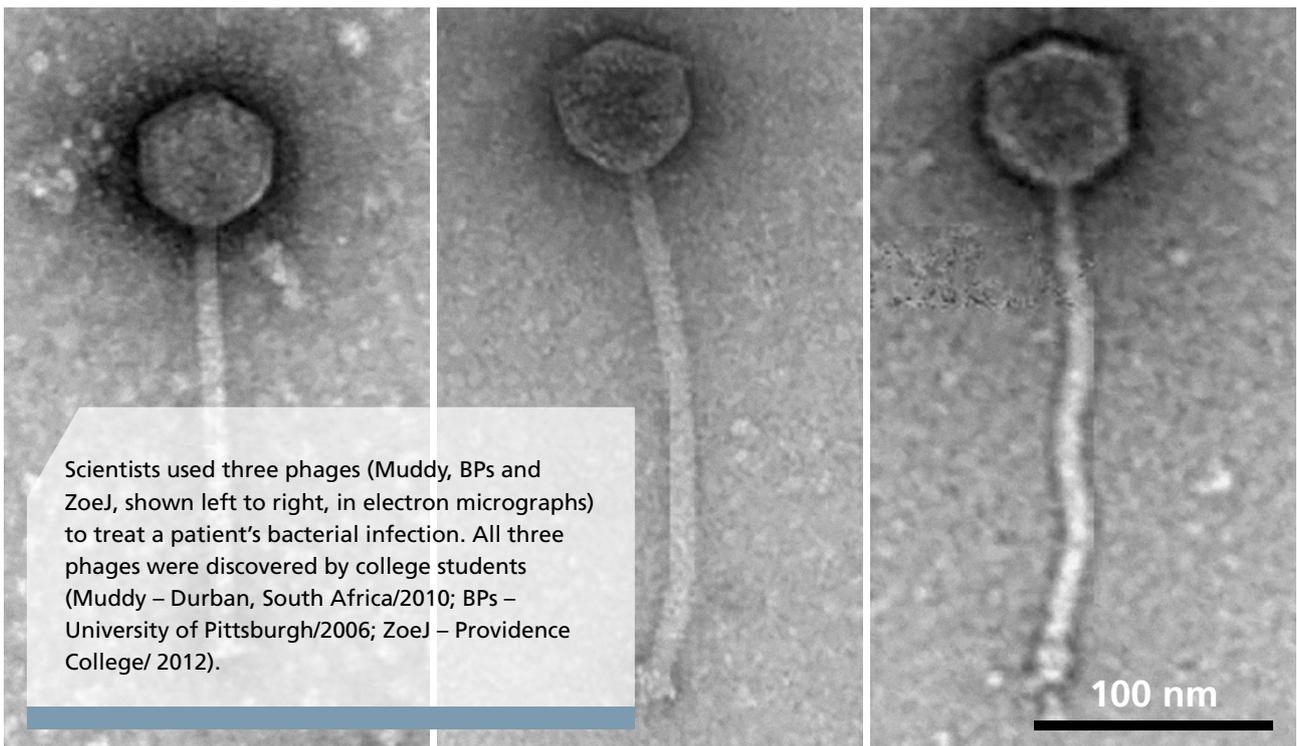
Sophie Foley

Edinburgh Napier University, UK

In May 2019, Great Ormond Street Hospital (GOSH) made headline news with a report of pioneering bacteriophage therapy in the treatment of a 15-year-old cystic fibrosis (CF) patient with a life-threatening *Mycobacterium abscessus* infection. The nontuberculous mycobacterium (NTM) *M. abscessus* is amongst the most serious emerging threats for CF patients and difficult to treat owing to both intrinsic and acquired multidrug resistance.

Key to the GOSH case was the availability of a bank of in excess of 10,000 phages isolated over the last decade or so by Professor Graham Hatfull and his team at the University of Pittsburgh, using *Mycobacterium smegmatis* as the

propagating host. This phage bank has expanded through the PHIRE and SEA-PHAGES programmes, discovery-based programmes for high school and undergraduate students. Screening of this collection identified three phages that are capable of infecting *M. abscessus* subsp. *massiliense* GD01, a rough-colony morphotype recovered from skin lesions on the GOSH patient: phages Muddy, BPs and ZoeJ (so-named by the students who isolated the phages in Durban, South Africa, 2010; University of Pittsburgh, 2006; and Providence College, 2012, respectively). All three phages were genetically distinct, based on whole-genome sequence analysis. This finding is significant since the use of



Scientists used three phages (Muddy, BPs and ZoeJ, shown left to right, in electron micrographs) to treat a patient's bacterial infection. All three phages were discovered by college students (Muddy – Durban, South Africa/2010; BPs – University of Pittsburgh/2006; ZoeJ – Providence College/ 2012).

a cocktail of phages is the preferred path for development of a therapeutic, in order to reduce the probability and timescale for the emergence of phage resistance.

While phage Muddy kills GD01 efficiently, limitations were observed for phages ZoeJ and BPs. Both are lysogenic (i.e. they each have the capacity to integrate their genomes into the host bacterium). This is considered to be an undesirable trait in any phage being developed for use as a therapeutic because of the propensity for gene transfer

and the ability of a phage to introduce new genes with undesirable properties, including enhanced virulence.

Hatfull and his team therefore set about to engineer ZoeJ and BPs, tailoring them for therapeutic application, using the Bacteriophage Recombineering of Electroporated DNA (BRED) technology previously developed by the Hatfull laboratory to generate mutations including unmarked deletions, point mutations, small insertions and gene replacements in lytically replicating mycobacteriophages.



A bank of in excess of 10,000 phages isolated over the last decade or so by Professor Graham Hatfull was made available to GOSH.



It is the first example of using genetically engineered phages in a therapeutic application

In this case, BRED was used to precisely remove the gene encoding the repressor protein, the key protein that governs the switch between the lytic (killing) and lysogenic (dormant) stages, thereby locking the phages in their host-killing mode. For phage BPs and its deletion mutant, an additional problem was observed: that of relatively poor infection of the GD01 test bacterial strain. To address this issue, spontaneous mutants were isolated with higher levels of infectivity for GD01 that harboured single point mutations in the portal gene. Within 6 months of treatment with the phage cocktail (10^9 plaque-forming units per dose of each phage) given twice per day, lung and liver function improved, and infected areas on the patient's skin resolved with only one new infection appearing. No side effects of phage treatment have been observed. The patient has been released from hospital while continuing to receive infusions.

The GOSH clinical case is significant for two reasons. First, it is a pioneering use of phages in humans for the treatment of mycobacterial infections; these are notoriously difficult to treat because of their ability to survive and persist in the host macrophage. Second, it is the first example of using *genetically engineered* phages in a therapeutic application. What is the regulatory position on this? Owing to the approach used for precise gene deletion, the engineered phages used in the cocktail were not considered to be genetically modified organisms (GMOs) by the UK Health and Safety Executive (HSE) on the basis that (a) they contained only native phage DNA sequences, and (b) no exogenous DNA sequences had been inserted. The phages were also considered to be unlikely to cause harm in humans, plants or animals. Accordingly, a case for phage treatment was made to the UK Medicines and Healthcare Regulatory Agency (MHRA) on the basis of the urgent clinical status of the patient on a palliative care

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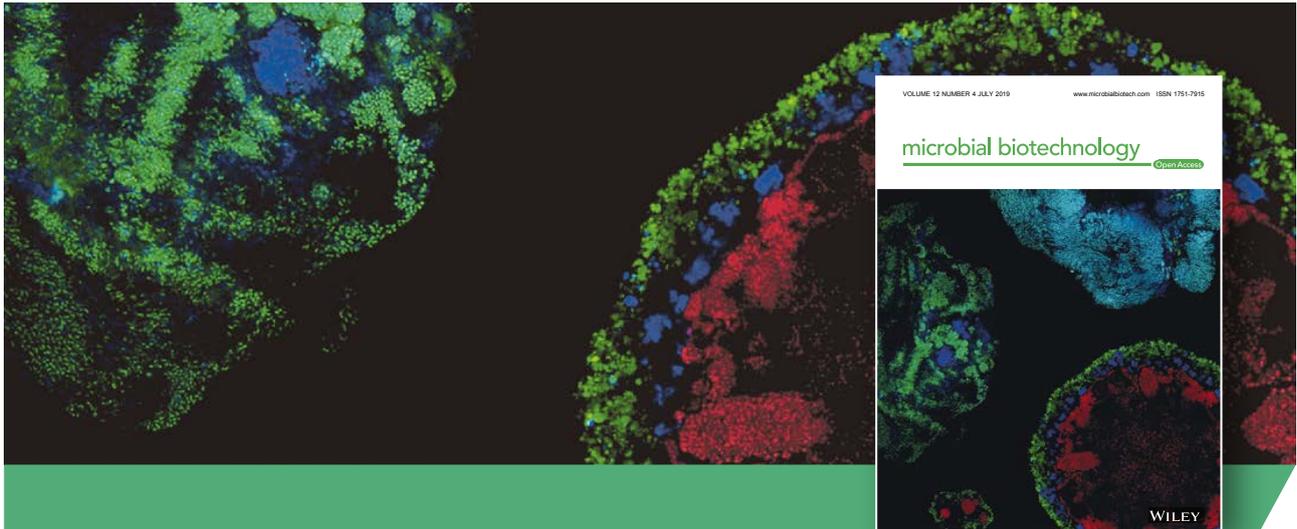
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<https://doi.org/10.1371/journal.pone.0003957>

pathway for which other treatments had failed, and the high mortality of other lung transplant patients with disseminated *M. abscessus* infections. Procedures were developed and approved to mitigate all risks associated with the import and administration of the phage cocktail, and the phage cocktail was therefore treated as an unlicensed product from a non-GMP research facility, under The Human Medicines Regulations 2012.

What does this mean for the future development of phage therapy? The scientists behind this treatment are quick to point out that, in the absence of a clinical trial, one cannot exclude the possibility that patient recovery could potentially have occurred in the absence of phage treatment. Identifying the appropriate phage for each patient is challenging and time-consuming. While this particular patient was successfully treated at GOSH, a second patient infected with a genetically distinct

M. abscessus strain died because of the failure to identify appropriate phages in time. Hence, the very feature that makes phage therapy attractive (specificity for a limited number of bacterial host strains), can also be a mitigating factor to a successful treatment outcome. Due attention also needs to be given to the possibility of developing phage resistance. While in the GOSH study a cocktail of phages was used from the outset as a strategy to delay or reduce the probability of emergence of phage-resistant GD01, the team is continually monitoring the patient who receives regular phage infusions. So far, resistance has not been observed in the patient but challenge tests undertaken in the laboratory have led to the isolation of GD01 mutants that are resistant to ZoeJ and BPs, while remaining sensitive to Muddy. So there is no room for complacency – Hatfull's team continue to search for new phages and they have already isolated a fourth phage that could be added to the cocktail.



Microbial Biotechnology

Dismantling the bacterial virulence program

Alford MA, Pletzer D, Hancock REW. Dismantling the bacterial virulence program. *Microbial Biotechnology* 2019; 12, 409–413.

Available from

<https://doi.org/10.1111/1751-7915.13388>

Two names come to mind when the dawn of the antibiotic era is mentioned: Paul Ehrlich and Alexander Fleming. We remember Ehrlich by his systematic screening approach that classical drug search strategies were founded on, and Fleming by his brilliant but adventitious discovery of penicillin in 1928. The drug discovery paradigm coined during their time worked well through to the 1960s but has been largely unsuccessful in the genomic and post-genomic eras, as evidenced by the fact that we are still battling to overcome Fleming's dire predictions regarding resistance.

As researchers continue to search for game-changing antibiotics, we call for a shift in research efforts toward characterising bacterial master regulators that are implicated in bacterial persistence and virulence. Targeting such regulators might lead to the development of broad-spectrum antimicrobial agents with a modest threat of resistance emergence. We exemplify the potential of these agents through novel synthetic peptides, based on natural host defence peptide templates, which inhibit the stringent stress response and synergise with antibiotics to reduce *in vivo* virulence and the biofilm and abscess growth mode of ESKAPE pathogens. We also discuss recently identified quorum sensing inhibitors as a means of dismantling the bacterial virulence program.

In combination with pioneering biotechnological approaches and re-emphasis on alternative approaches, improving our knowledge of bacterial master regulators can pave the way for discovery of efficient and affordable antimicrobial therapies.

Morgan Alford

University of British Columbia, Canada



On-site advanced biocleaning system for historical wall paintings using new agar-gauze bacteria gel

Ranalli G, Zanardini E, Rampazzi L, Corti C, Andreotti A, Colombini MP *et al.* On-site advanced biocleaning system for historical wall paintings using new agar-gauze bacteria. *Journal of Applied Microbiology* 2019; 126, 1–12.

Available from

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Microorganisms and works of art: barbarians or virtuosos? Harmful or useful? Old or new job opportunities? Here, we report the biocleaning of altered materials located in vertical and vaulted areas using agar-gauze biogel with short application times.

To apply a biocleaning technology to a different type of artistic material, such as wall paintings, specific analytical investigations must be performed to identify and distinguish organic compounds originally present in the paintings from those derived from restoration interventions. The materials undergo transformation through natural ageing processes, and these effects are no less important.

Cultural heritage artworks are obviously unique, so they are usually characterised by low homogeneity, and the various compounds to be identified are generally present in low concentrations. Once the unwanted organic matter has been identified on wall paintings and the difficulty in removing it by traditional methods has been verified, the use of biological systems may represent a valid, suitable alternative method.

The success of using new biogel systems activated with viable bacterial cells shows that biocleaning is also highly promising for wall paintings and for the removal of various alterations. This utility is attributable to the great versatility of bacteria and their wide range of enzymatic activities. Bacteria are known to produce not only constitutive but also inducible enzymes that can attack and degrade different types of molecules. The synthesis of inducible enzymes takes place only in the presence of a substrate, creating a regulatory effect. Thus, the use of microorganisms is more effective than the use of a single enzyme alone that attacks only specific bonds.

These findings are of great significance for future restoration activities and are crucial for determining the best preservation strategies in this field. It is a new application example of the virtuosity of the microbial world, of how they are useful in becoming potential job opportunities for young people.

Giancarlo Ranalli

University of Molise, Italy



An interview with

Lindsay Hall

Quadrum Institute, UK

Lindsay Hall

Clare Taylor

Edinburgh Napier University, UK

Each year we award the prestigious WH Pierce Prize to a young microbiologist who has made a substantial contribution to the science of applied microbiology. This year we were pleased to announce that the winner of the 2019 WH Pierce Prize is Dr Lindsay Hall, Research Leader of the School of Life Sciences, Quadram Institute.

SfAM General Secretary Clare Taylor was able to grab Lindsay and ask her a few questions.

Can you tell us about your current work?

My research involves exploring the first contact between microbes and their host during the early life developmental window, with the aim of understanding how these microbial communities, and specific keystone members like *Bifidobacterium*, help digest the food that we eat, programme our immune system and help fight pathogenic microbes. I am keen to understand the mechanisms by which these microbes provide these benefits, using cutting-edge experimental and computational tools, with the ultimate aim of developing new microbiome-based therapies to prevent and treat disease.

Who are your microbiology heroes?

Someone I read about a while back that really struck a chord was the Scottish virologist Dr June Almeida (yes I know I work on bacteria, but viruses are cool too). Despite having no 'formal' training, she was a pioneer of imaging viruses using immunostaining in electron microscopy. This just shows what you can do when you have passion and a vision, while being encouraged by those around you – showing what you can be, and what you can achieve.

I would also say Dr Gill Douce, who was my undergraduate supervisor at Glasgow, was a heroine – as she put up with me and really inspired me to be bold and curious, and to take a big step and move away for my PhD. This has been invaluable in my career as it taught me that I love being in new environments, learning new things and meeting new and interesting people. Gill was/is a fantastic teacher and scientist, and so supportive during my time in Glasgow and also throughout my career, so a big thanks and shout-out to Gill.

What are you most proud of?

Probably what I am most proud of, to date, is being awarded a Wellcome Trust Investigator Award at the end of 2013. At the time, I was the youngest person to have received one, which was crazy, but most importantly this was my first competitive grant so I was able to start my own group. Until that date I didn't have any resources (staff, students or a lab) – so it was all very exciting but also super daunting!

If you could be a microbe for a day, what would you be and why?

Bifidobacterium obviously! This is the main genus of bacteria we work on in the lab, and if I could be Biffy for a day this would help me figure out how it does all the amazing beneficial functions that help keep us (and particularly infants) healthy – and would also help with the grant writing!

Biffy Clyro's 'Questions and Answers' seems ridiculously appropriate for the Hall lab's scientific research focus!

What is the most exotic or interesting location your microbiology has taken you to?

This is a tough one, as meeting and collaborating with people around the world is one of the highlights of being a research scientist and group leader. I think for 'exotic' it would have to be India, as I had always wanted to go and I was lucky enough to be invited to give a talk at a microbiome conference in Pune at the end of last year, which was a fantastic and inspiring meeting. I also took some time for a wee trip to different parts of the region and it was such an amazing place; people, food, culture and history. I am also going to highlight an 'interesting' location – and this would have to be our local neonatal intensive care unit (NICU). We have been working with this excellent team, and others across the UK, for a few years now and the first time I went I was struck by the wonderful facilities and care these tiny fragile babies receive. It's been a great project, looking at how we can beneficially modulate their microbiota to promote health and reduce disease incidence in this at-risk population.

What key piece of advice would you give to early career microbiologists looking to establish themselves as independent researchers?

Only one piece? That's tough... So, I think what helped me establish was focusing on my 'niche'. What was I going to do as an independent PI? I was lucky enough to have a fairly diverse scientific background, but this also made deciding my initial 'path' a bit more tricky. In the end, I focused on what I really enjoyed (this is so important) and where I thought I could plug a gap; bringing in my previous background and skills. This also helped me decide on the group I eventually wanted to have in terms of expertise and enthusiasm.

What song would be a good theme tune for the Hall lab?

Biffy Clyro's 'Questions and Answers' seems ridiculously appropriate for the Hall lab's scientific research focus!

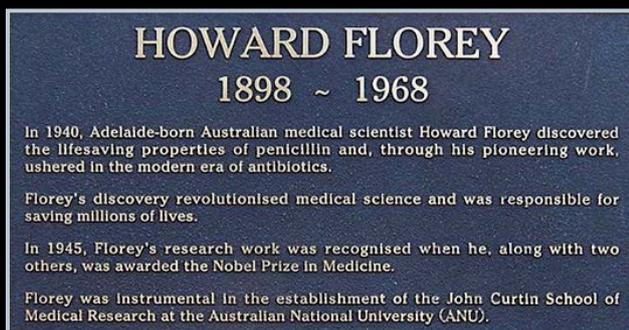
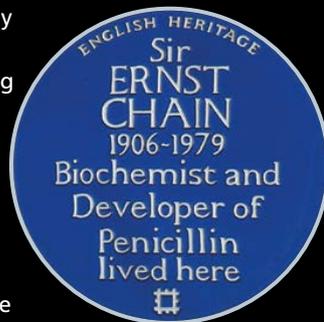
London's microbiota: blue plaque microbiology

Martin Adams

SfAM President 2011–2014

Marking sites associated with notable people or events is an estimable and widespread practice. London's Blue Plaque programme is said to be the oldest in the world – introduced in 1867 by the Royal Society of Arts and now run by English Heritage. Today there are more than 900 such plaques in London, revealing to the observant passer-by such gems as the fact that George Frederick Handel and Jimi Hendrix would have been next-door neighbours in Brook Street, but for the passage of 200 years.

Microbiologists are not overly represented by plaques, though Sir Alexander Fleming boasts two: one on his Chelsea home and the other on St Mary's Hospital, Paddington, where his laboratory is also preserved as a small museum. In fact the penicillin story as a whole is quite well covered. Ernst Chain has one on his Wimbledon home and the City of Oxford's Blue Plaque scheme has been admirable in honouring the crucial work done there. Two were unveiled in 2018, commemorating the first isolation and purification of penicillin at the Sir William Dunn School of the University of Oxford, and its first use at a former outpatient building



of the Radcliffe Infirmary. The latter supplements an earlier plaque in the main entrance hall of the hospital. Norman Heatley, often an unsung hero of the penicillin story, also has a plaque on his Oxford house, unveiled in 2010.

For Howard Florey though, the leader of the Oxford penicillin team, it doesn't stop there; he has plaques in his native Australia as well: one in South Australia (he was born in Adelaide) and another in Florey, a suburb of Canberra named in his honour.

Despite this plethora of plaques, it is probably still true to say that the role of Florey, Chain and Heatley in the development of penicillin is largely eclipsed in the public's perception by that of Fleming. His initial discovery at St Mary's in 1928, the result of chance contamination of a plate of staphylococci with spores of *Penicillium notatum*, is part of the popular history of science, as well as a fine example of Pasteur's dictum that 'chance favours the prepared mind'. The *Penicillium* spores that infected Fleming's plate most probably came from the mycology lab of CJ La Touche, a floor below Fleming's, where they were isolating and identifying moulds from the homes of asthmatics at the time. This view has not gone unchallenged, however. Across the road from Fleming's lab the landlord of the Fountains Abbey public house used to claim that his pub was the source of the spores, probably little realising the bad light this might shed on his stewardship of its beer and food. To settle this question at the bar of history, so to speak, I have visited the premises and can declare that it was most agreeable, with no swirling fug of spores or mycelial carpet underfoot.

Fleming worked in the Inoculation Department at St Mary's, run by Sir Almroth Wright. Wright was an advocate

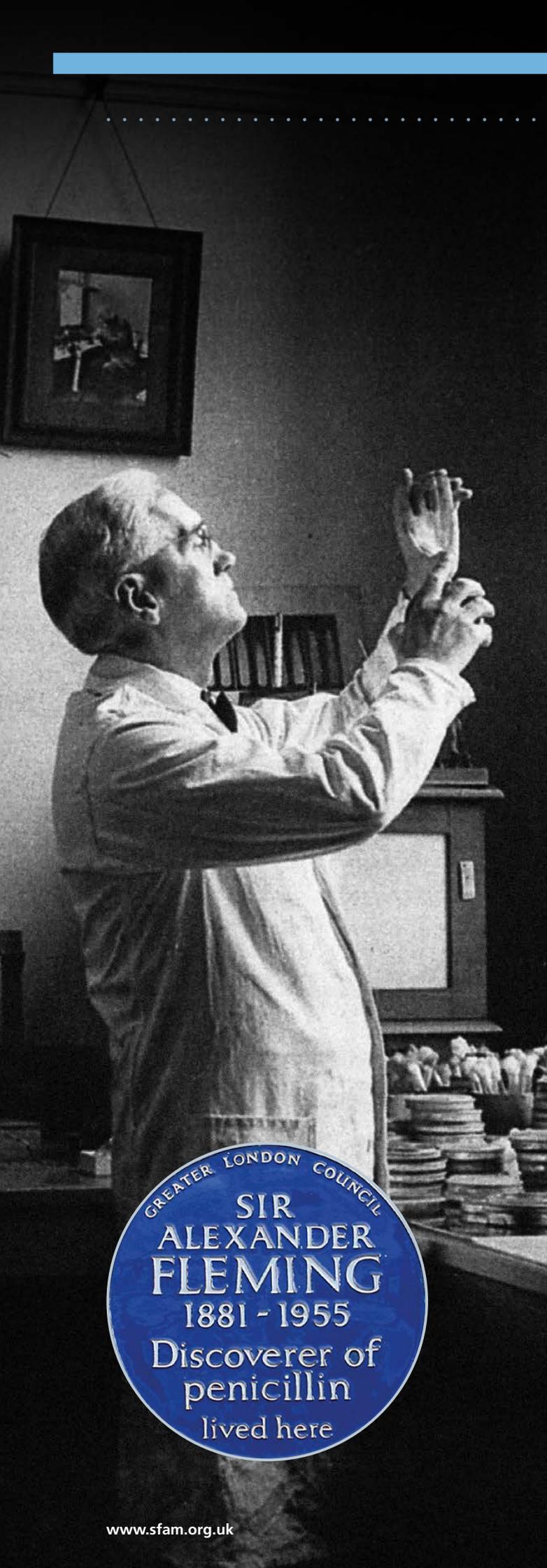


of harnessing the immune system to prevent and treat infectious disease through vaccination and immunotherapy. He was a towering and controversial personality in the medical world of his time. A prodigious intellect, he had studied medicine at Trinity College Dublin, while gaining a first in modern languages at the same time. He held strong views, fiercely expressed, once saying "I make it a principle never to write anything that won't give offence to somebody". He was vehemently misogynistic; opposing women's suffrage and professional advancement. He wrote a book on the subject: *The Unexpurgated Case Against Woman Suffrage* and a letter to *The Times* in March 1912, the reading of which today makes for toe-curling embarrassment at the ideas expressed. Somewhat surprisingly considering his views, he was a friend of the playwright George Bernard Shaw and is characterised as Sir Colenso Ridgeon in Shaw's play *A Doctor's Dilemma*. He also features prominently by name in Shaw's lengthy introduction to the play.

Modesty and diplomacy were not his strong suits and Wright accumulated enemies throughout his career. To some surprise, not being a military man, he became Professor of Pathology at the Army Medical School (RAMC) near Southampton, in 1892, ahead of Sir David Bruce who was an army officer at the time and had recently described brucellosis. Bruce has no blue plaque in London but his name does appear on the sculpted frieze that surrounds the London School of Hygiene and Tropical Medicine (LSHTM) in Keppel Street. Of course, he does also have a disease and bacterial genus named after him.

While at the RAMC, Wright developed a typhoid vaccine, based on heat-killed bacteria, but had difficulty in getting military cooperation to help prove its efficacy. He eventually accumulated what he considered convincing data from trials in India and during the Boer War, but a vitriolic dispute erupted when the eminent statistician Sir Karl Pearson (supported by Sir David Bruce) questioned the statistical validity of the results. (Pearson, incidentally, has a blue plaque on his home in Hampstead.) One consequence of this dispute was Wright's departure for St Mary's in 1902. His work was continued by his successor, Sir William Leishman (who has no blue plaque but is, like Bruce, on the LSHTM frieze and has a disease and a protozoan genus named after him). Eventually, the military authorities were persuaded and during World War I the RAMC's new premises on Millbank (next to Tate Britain and now the Chelsea College of Arts) and Wright's department at St Mary's were given over to the production of vaccines, resulting in the incidence of typhoid among troops declining from 27% during the Boer War to 0.6% in World War I.

Wright retired in 1946 to write books on philosophy. He has no blue plaque on his home in Pembroke Square but might derive some consolation from the fact that there is a ward named in his honour at St Mary's.



GREATER LONDON COUNCIL
**SIR
 ALEXANDER
 FLEMING**
 1881 - 1955
 Discoverer of
 penicillin
 lived here



Climbing greasy poles

My working life didn't start well. I spent several months as a junior technician in the media room at the Radcliffe Infirmary in Oxford and hated the continual mindless pouring of agar plates and the making of cotton wool plugs. I realised that microbiology would offer a more exciting challenge, if only I could get into the main laboratory.

It was in this environment where I first encountered the masculine hierarchy of science and I quickly learnt my 'place'. Technicians were very low down in the pecking order. For instance, I was asked (told?) to polish the director's desk. Another example was a debate among the medical elite about whether two of us could leave work early once a week during the academic year to catch the train to St Mary's Hospital, London, while we were studying for the 'Special' exam for fellowship of the institute now known as the Institute of Biomedical Science, IBMS. I resented so much during these first years that I kept needing to pass more exams and move posts to escape one lot of condescension, only to meet another.

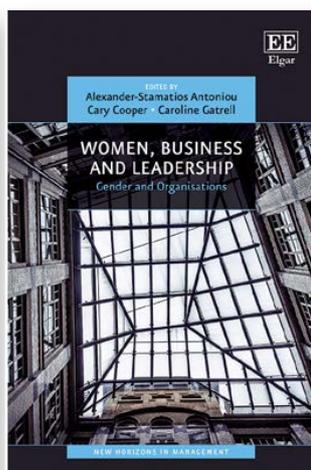
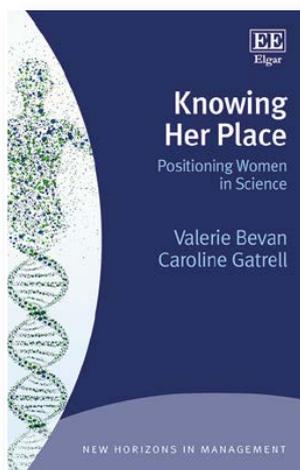
I passed the Special exam, becoming a fellow of the institute in 1971 and subsequently a senior technician. In 1973, I moved to the Royal Free Hospital, London, as a research assistant with the promise of working for a PhD. However, London University didn't recognise my institute exams as being the equivalent of a degree (they asked what this 'Special' microbiology exam was) but Brunel accepted me on their Applied Immunology course to study

for a master's degree. This was fascinating and I loved going to the bar at lunchtimes, where the professor and the 'real' immunologists debated the ethics and morality of science and immunology.

Climbing the greasy management pole, I moved to the Whittington Hospital, London, as a Chief Medical Laboratory Scientific Officer (MLSO; now Biomedical Scientist, BMS), then to Hope Hospital, Salford, as a Senior Chief MLSO and then back to Colindale in London when I joined the PHLS (now Public Health England, PHE) as Head of Technical Services in 1995. When the Health Protection Agency (HPA) was created, I became Director of the Department for Evaluations, Standards and Training and for nearly 20 years led the development of UK Standards for Microbiology Investigations (SMIs). I gained a second master's degree in Management and Learning at the University of York. At last I *really* rebelled against my place and developed a keen interest in feminism, critical management and diversity issues, moving on to Lancaster University to study (all study was part-time) for a PhD – both were amazing academic environments.

Valerie Bevan

*Honorary Teaching Fellow, Lancaster University Management School
Chair, British Society for Microbial Technology, UK*



FURTHER READING



Bevan V, Learmonth M. 'I wouldn't say it's sexism except that it's all these little subtle things': healthcare scientists accounts of gender in healthcare laboratories. *Social Studies of Science* 2013; 43(1), 136–158
<http://sss.sagepub.com/content/43/1/136>
 (Accessed 29 June 2019)

Bevan V, Gatrell C. *Knowing her Place: Positioning Women in Science*. (Cheltenham: Edward Elgar Publishing, 2017)

Bevan V. *Experiencing a Secret Career in Healthcare Science* in: Alexander-Stamatios A, Cooper C and Gatrell C (editors). *Women, Business and Leadership*. (Cheltenham: Edward Elgar Publishing, pp. 247–259)

House of Commons Science and Technology Committee (2014), *Women in scientific careers*, sixth report of session, pp. 2013–2014.
<https://publications.parliament.uk/pa/cm/201314/cmselect/cmsctech/701/701.pdf>
 (Accessed 29 June 2019)

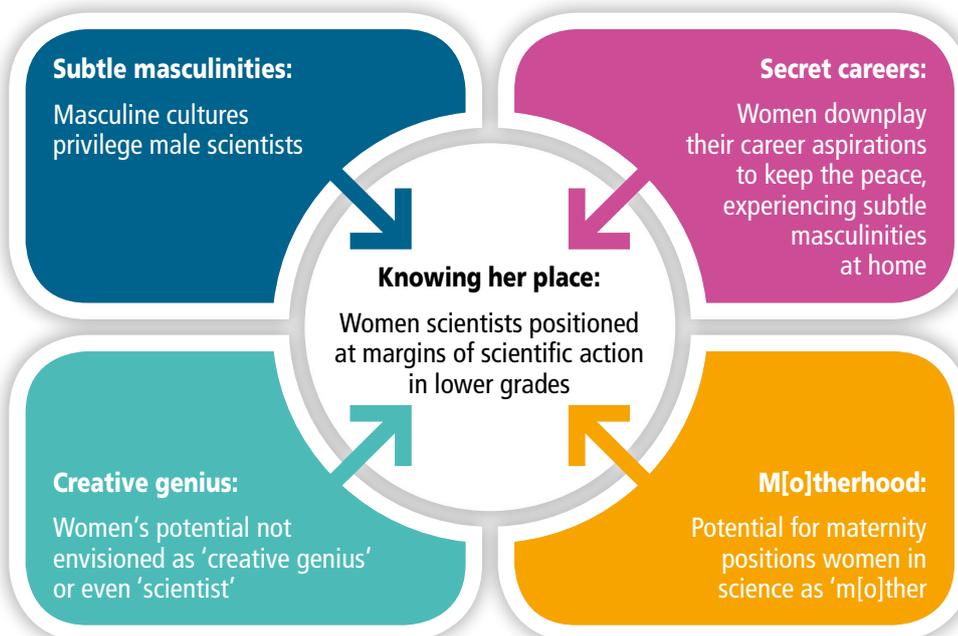
My perspective changed as I became an expert, not in science but in areas peripheral to science, where I began to confront the unfairness I saw around me in the HPA. I realised both science and management could be challenged and I felt a new freedom. I no longer 'knew my place' and prepared quantitative data (I needed to convince my scientist colleagues) showing that few women working in science made it to the top posts despite being in the numerical majority. Further qualitative research led to a PhD in Management Learning and Leadership. Publications followed including my book, *Knowing Her Place: Positioning Women in Science* (2017), followed by a book chapter in *Experiencing a Secret Career in Healthcare Science* (2019). The essence of why women scientists are often positioned at the margins in science stems from them experiencing its masculinised culture (see illustrated Framework).

I was a member of the IBMS Council from 2014 to 2015 and contributed to the Science Council Diversity Strategy Group for Diversity, Equality and Inclusion. I've written articles and spoken at conferences and universities on gender discrimination and sexism in laboratories and contributed to a parliamentary report on gender perceptions in STEM careers in 2014. I currently chair the British Society for

Microbial Technology (BSMT), am an Honorary Teaching Fellow at Lancaster University Management School and sit on the Advisory Board to the Critical Studies Research Group at Durham University. I 'retired' in 2012 and moved to Suffolk with my husband Byron, where we have a combined interest in classic cars. We have one son, Henry, who is a software developer in London. My new life has given me the opportunity to learn to draw and paint, take up the piano again and get involved in village life.

What advice can I give? Be professional, persevere and challenge unfairness.

Bevan and Gatrell Framework: *Knowing Her Place: positioning women in science.*



John Innes Centre: much more than compost

Jacob Hamilton

Kingston University, UK

The John Innes Centre (JIC) is probably most famous for John Innes compost, but a lot more goes on there. Situated on the Norwich Research Park, which contains the University of East Anglia (UEA), the JIC is known worldwide for the work it produces on plants and agriculture, including the plant microbiome and the infamous *Streptomyces* chemical factories, from which many modern drugs were developed. But how did the JIC become a world leader in its field (pun intended)?

A week before he died in 1904, philanthropist John Innes wrote a will stating that the bulk of his fortune should be used to establish a horticultural school. This led to the John Innes Horticultural Institution being founded in Merton Park, London, in 1910. Designed to be an advanced school for fruit breeding, it was headed by William Bateson, who had coined the word 'genetics' in 1905, and it was the UK's first research centre for plant breeding. Early work focused on just that, with genetic studies performed on *Pisum sativum* (the pea that Mendel used in his infamous experiments, still studied at the JIC today) and breeding new varieties of plants for agriculture. Released in the 1930s onwards, several of these fruits can be found in supermarkets today. Summer Sun cherries, for example, which are known to produce large crops and are resistant to the spring frosts common in the UK. Researchers at the institution also developed the aphid-resistant Malling-Merton rootstock, still used widely in apple orchards. When growing apples and pears, it is rare to grow the tree from seed in place; instead, a faster-growing rootstock is planted and cut once the trunk is thick enough to support the fruit tree, which is then grafted on top of it. This means the fruit tree jumps straight to the crop-producing stage of its life, instead of taking years before producing enough apples to be commercially useful.

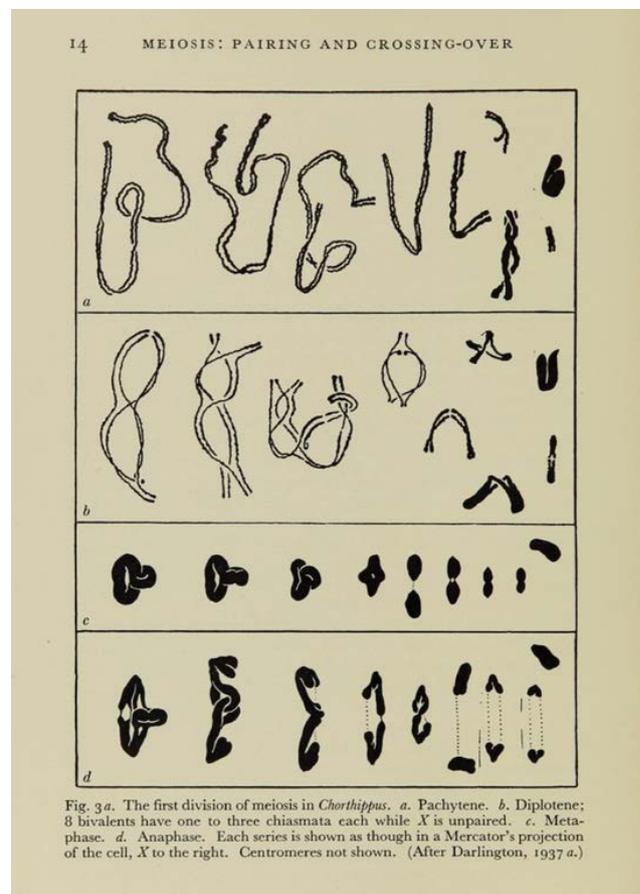


Fig. 3a. The first division of meiosis in *Chorthippus*. a. Pachytene. b. Diplotene; 8 bivalents have one to three chiasmata each while X is unpaired. c. Metaphase. d. Anaphase. Each series is shown as though in a Mercator's projection of the cell, X to the right. Centromeres not shown. (After Darlington, 1937 a.)

Images of mitosis and meiosis from Darlington's book *Evolution of Genetic Systems*.

It wasn't just plants studied at the JIC though. In 1937, J. Haldane, Head of Genetical Work at the institution and Julia Bell at University College London jointly published the first evidence of sex-linkage in humans, showing that haemophilia and colour blindness were genetic diseases, now used as examples of such diseases in high schools. Not long after, in 1939, the then John Innes Director, Cyril Darlington, published a book '*Evolution of Genetic*

Systems. This highly controversial piece introduced mitosis and meiosis to the world, discussing how chromosomes pair and recombine during meiosis and chromosomal crossing-over and how this related to heritability and genetics, explaining the genetic components of the diseases Haldane was working on at the time. Plenty of other genetics work was also ongoing at this time, including the beginnings of modern genetic modification of crops and plant-associated bacteria. One of the most important of these discoveries was the Holliday junction in the yeast *Saccharomyces cerevisiae* in 1964. Discovered by

Robin Holliday, the Holliday junction is the four-way joining of DNA during double-strand break repair. A critical intermediate in homologous recombination, the Holliday junction is critical both to life and to genetic modification techniques, where it is still the foundation of modern genetic recombination modelling.

Although microbiology had always featured in the institution's history, it was in 1968 that the JIC truly dived into microbiology by launching its *Streptomyces* genetics programme. The year before, the JIC had moved to its



Above: The John Innes Centre.

Above right: *Arabidopsis thaliana*, the thale cress, mouse-ear cress or arabidopsis, is a small flowering plant native to Eurasia and Africa.

current location on the Norwich Research Park, where the grandfather of modern *Streptomyces* research, David Hopwood, was a professor at UEA. Hopwood's group lay the groundwork for actinomycete research, mapping *Streptomyces coelicolor* and providing evidence for plasmid-determined mating, used today in some genetic modification tools for actinomycetes. This work established *S. coelicolor* as the model organism for the genus, as well as placing the JIC and UEA at the vanguard of *Streptomyces* research. Only a couple of years later, genetic modification of *Streptomyces* using protoplasts was performed by members of Hopwood's group, since widely used by pharmaceutical companies in the search for novel antimicrobials. Protoplast genetic modification uses cells, normally algae, which have had their cell wall removed to create the titular protoplast. This allows efficient transformation of plasmids from the protoplast into the target cell with high frequency. Given how difficult it is to

modify the genomes of actinomycetes, this was a major breakthrough and is still used today in strains that have proven difficult to modify with other techniques.

The ability to manipulate the genome of actinomycetes led to the first 'hybrid' antibiotics to be produced at the JIC in 1985. Francisco Malpartida isolated the gene cluster responsible for the production of three different antibiotics in various *Streptomyces* strains and transferred them to alternative strains that produced antibiotics from the same chemical class. This led to the novel antimicrobials being produced as the biochemical machinery for one antibiotic was applied to the other, leading to major changes to the compound. This technique was used by pharmaceutical companies until recently to iterate on existing antibiotics, at least until funding for antibiotic research was cut by the major companies.

Today, the JIC is still at the forefront of research into plants, plant pathogens and the plant microbiome. In 2000, a team headed by Anne Osbourn discovered that oat plants produce antimicrobials in their root systems in an attempt to manipulate the root microbiome. This work, along with the work of others, has led onto the idea of 'biocontrol' in farming, inoculating the soil around crops with beneficial fungi and bacteria to defend crops from pathogens and increase yields, akin to probiotics in humans. Earlier this year Anne's team worked jointly with the Chinese Academy of Sciences to show that even small changes in the chemicals produced by the model plant *Arabidopsis thaliana* caused major changes in the root microbiome (<https://science.sciencemag.org/content/364/6440/eaau6389>). Research is now ongoing into how we can manipulate the production of these chemicals to alter the bacteria associated with crops to increase yield or disease resistance.

Back in 2002, researchers at the JIC also produced the first full-genome sequence of *S. coelicolor* with help from the Sanger Centre, Cambridge. Understanding the whole



Streptomyces coelicolor.



Leafcutter ants (*Acromyrmex octospinosus*).

genomes of actinomycetes has led to 'genome mining' of strains today, using pleotropic and genetic techniques to activate dormant biosynthetic gene clusters. Researchers in Matt Hutchings' lab in UEA and Barrie Wilkinson's in the JIC jointly discovered the novel antimicrobial formicamycin from an ant-associated *Streptomyces* strain by using CRISPR/cas9 to remove sections of the genome responsible for producing previously known antimicrobials to prevent the possibility of rediscovery (<https://pubs.rsc.org/en/content/articlepdf/2014/SC/C6SC04265A?page=search>). These same groups also work on understanding how *Streptomyces* and chemicals produced by plants interact to unlock these dormant gene clusters, both for use in agriculture and to create new tools to fight antimicrobial resistance.

As science becomes ever more interdisciplinary, a large proportion of the work at the JIC focuses on bacteria, fungi and viruses, as human and plant pathogens and as sustainable replacements to agrichemicals. Genetic modification of plants to form new, better crops continues but so does research in understanding and combating the pathogens threatening food production. As climate change continues, reducing arable land and water availability, understanding how we can improve crop yields without



The petals from Arabidopsis thaliana.

using vast quantities of fertilisers and herbicides could help ensure we have enough food for everyone. Equally, the genetic tools discovered at the JIC, and used around the world today, are finding new antimicrobials to protect us from the other major threat to modern civilisation – antimicrobial resistance. By placing itself at the forefront of such critical issues, the JIC, UEA and the entire research park in Norwich is sure to be busy for a long time into the future.

The ability to manipulate the genome of actinomycetes led to the first 'hybrid' antibiotics to be produced at the JIC in 1985

1. Present:

Thirty-three members attended the AGM. This included:

President Professor Mark Fielder (MF)
General Secretary Dr Clare Taylor (CT)
Meeting Secretary Professor Ian Feavers (IF)
Trustee Dr Tim Aldsworth
Trustee Dr Elaine Cloutman-Green
Trustee Dr Mike Dempsey
Trustee Professor Stephen Forsythe
Trustee Mrs Claire Hill
Trustee Professor Sally Cutler

In attendance:

Dr Lucy Harper (*Chief Executive*)
Professor Brendan Gilmore (*see below*)
Dr Christopher Brown (*Policy and Public Affairs Manager*)
Luwam Mekonen (*Membership and Marketing Officer*)
Laura Lincoln (*Events Manager*)

Nineteen proxy votes had been received.

2. Apologies for absence

Professor Arthur Gilmour
Dr Linda Thomas.

3. Minutes of the 87th Annual General Meeting

The minutes of the 87th Annual General Meeting held in Brighton in 2018 were published in the September 2018 issue of *Microbiologist*. They were unanimously accepted by those present.

4. Matters arising from the previous minutes

There were no matters arising.

5. Report of the trustees of the Society 2018

The Chief Executive noted the success of the Society during the previous year, particularly with respect to the continued success of the Society journals. Dr Harper extended a special thank you to the Chief Editors and Editorial Boards.

Dr Harper summarised the three main areas of SfAM activities during 2018: Impact, Voice and Sustainability. Notable successes had included strong campaigns, wide-ranging inter-disciplinary collaboration and influential responses to government consultations. A particular success was the Congress itself: SfAM had forged a strong partnership with FEMS, and SfAM had a very strong presence at the Congress. SfAM had also strengthened its commitment to Equality, Diversity and Inclusion.

Dr Harper noted that membership to the Society through 2018 was strong, and thanked staff for their dedication and support. She also noted that she was delighted by the successful activities of the Early Career Scientists Committee, and thanked them for their energy and commitment.

Minutes of the 88th Annual General Meeting of the Society for Applied Microbiology

10 JULY 2019 | 17:45 | BOISDALE ROOM, THE SEC CENTRE, GLASGOW, UK

6. Adoption of the Annual Report and financial statements for 2018

Copies of the Annual Report and financial statements of the Society for 2018 had been distributed previously. Members noted receipt of the report and statements.

7. Election of new members (including honorary members), deaths and resignations

A list of the names of applicants for membership and a list of deaths has appeared in the *Microbiologist* throughout the previous year. The Society also holds a summary list of new members and resignations throughout the previous year.

8. Nomination and election of new Executive Committee members

1. Members voted unanimously to accept the Executive Committee's recommendation that Professor Brendan Gilmore be appointed Vice President of SfAM.
2. Members voted unanimously to accept the Executive Committee's recommendation that Mr Oern Greif be appointed Hon. Treasurer of SfAM.

3. Members voted unanimously to confirm the election of three other trustees, as indicated by the online ballot held before the AGM.

1. Dr Catherine Ludden.
2. Dr Marcela Hernández García.
3. Professor Stephen Forsythe (re-election).

Proxy votes were taken into account.

9. Special resolution to alter the Articles of Association

The President explained the background to this agenda item. Members unanimously agreed that the draft Articles of Association shown at the meeting, and for the purposes of identification, initialled by the Company Secretary, be adopted as the Articles of Association of the Charity in substitution for, and to the exclusion of, the existing Articles of Association, subject to and with effect from the approval of the Charity Commission of any changes which require its consent.

Proxy votes were taken into account.

10. Any other business

There was no other business.



The ripple effect from Magnificent Microbes 2010

Erin Hardee ¹ and Nicola Stanley-Wall ¹

¹ University of Dundee, UK

In 2010, the School of Life Sciences at the University of Dundee held its inaugural large-scale themed public engagement with research event. It was called 'Magnificent Microbes' and was run in collaboration with the Dundee Science Centre. The event had the aim of educating, inspiring and entertaining schoolchildren and family groups about microbes, the roles that they play in shaping our environment, and how they can be exploited in the food, health and green energy sectors of our economy. The pioneering event involved all of the academic groups in the Division of Environmental and Applied Microbiology and reached around 200 local schoolchildren. Additional outputs we wanted to achieve were to provide training and inspiration to PhD students, postdoctoral scientists and academic staff in the art of engaging with the public, so we arranged a series of bespoke training events prior to participation in the public engagement event.

Magnificent Microbes was funded in part by the Society for Applied Microbiology and provided a catalyst for a period of culture change in the School of Life Sciences. Magnificent Microbes proved such a success that it has been repeated biannually; 2020 will be the sixth instance of the event, which has grown and developed since its initial

inception. It also has since been successfully used as a template to develop our 'Incredible Immunology' programme (run by the division of Cell Signalling and Immunology) and provide inspiration for our annual 'Plant Power' event (run by the division of Plant Sciences). Funding for these events is now provided by the Wellcome Institutional Strategic Support Fund awarded to the University of Dundee, which has also allowed a strong programme of embedding support for public engagement across the school.

In 2013, Erin Hardee was appointed as the Schools Outreach Officer in order to grow partnerships with schools and other service providers. In 2016, Nicola Stanley-Wall was appointed academic lead for public engagement where she focused on coalescing the varied public engagement activities that were being undertaken. The School of Life Sciences now has an engagement programme that has strong links with local schools and colleges. Our ambition is to increase the quality and scope of our public engagement with research activities and to sustain training opportunities for researchers to enable greater participation in schools outreach by researchers at all levels. We prioritise increasing our interactions with schools in areas of severe social deprivation and promote widening of access to opportunities in science.

To do this we support in-depth engagement events that include:

- Teachers continuing professional development.
- Separate open days for schools and for the general public.
- Follow-up visits to schools.
- Provision of a potential longer-term research project across disciplines.
- A final celebration event where pupils present their own projects.



The Magnificent Microbes programme has also led to the creation of microbiology 'resource boxes', which contain a variety of hands-on activities and support materials for teachers and pupils to use in the classroom. We are currently testing these in schools and gathering teacher feedback to ensure they are as robust and useful as possible. We hope to expand this to other topics once we have finalised the contents of the microbiology box in response to feedback.

In short, the Magnificent Microbes project has had long-lasting and far-reaching effects much greater than we could have predicted when it was initially conceived. By providing a template for engaging with young people it has allowed other divisions to create their own programmes of engagement and this interest has allowed support for public engagement to become more embedded within the School of Life Sciences. Added to the resources that have been developed as a result of a decade-long ongoing programme and it is clear that Magnificent Microbes has had a huge impact on our public engagement practice, and will continue to do so for years to come.



Above top:
Erin Hardee and Nicola Stanley-Wall.



Sarah Alexander

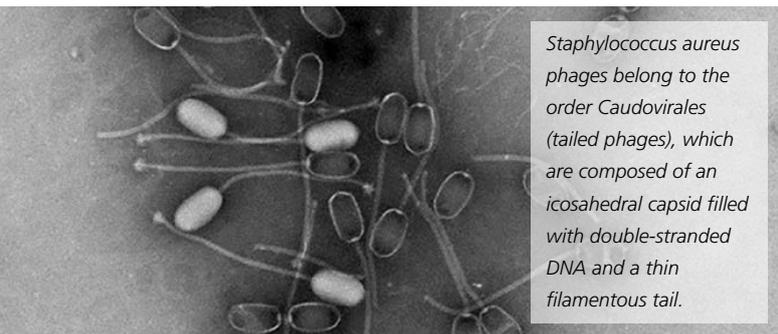
*The National Collection of Type Cultures (NCTC),
Public Health England (PHE), UK*

The importance of immortalising the bacteriophage

Bacteriophages, or phages, are viruses that infect bacteria and in recent years phages have been attracting increasing levels of attention from both scientists and the mainstream media alike due to their potential role in the treatment of bacterial infections (phage therapy). The first bacteriophages were described over 100 years ago concurrently by two scientists, Twort (1915) and d'Hérelle (1917). It was at this time that the name bacteriophage was formed, which literally means 'bacteria-eater'. Ever since, phages have played an instrumental role in our knowledge of molecular biology: T2 was the model organism used in the Hershey–Chase experiments that proved DNA was the key genetic material; and T4 was central in Crick's experiments that led to the discovery of the genetic code. The first organism to ever have its genome fully sequenced was the phage ϕ X174. Phages have also played a unique role in genetic engineering, where technology such as phage display has provided scientists with the first tools to produce novel proteins within the laboratory setting. Phages also proved to be valuable epidemiological tools, with phage typing schemes being described and applied to the outbreak investigation of many major pathogens including *Salmonella* and *Staphylococcus* species.

The significance of phages within the environment cannot be underestimated. It is well established that bacteriophages are ubiquitous in nature, where they have been isolated from almost every known ecological niche. Bacteriophages are also regarded as the most abundant life form on earth, with marine phages being known to play a key role in nutrient cycling (particularly of nitrogen and carbon) from the oceans. However, it is the therapeutic use of phages, when lytic phages are applied to treat bacterial infections, which is currently attracting the most attention. Phage therapy is not a new phenomenon; it was first described over 100 years ago, when its applications were used widely, particularly in Eastern Europe. The rise of antimicrobial resistance combined with several high-profile cases of successful phage therapy, when all other treatment options had been exhausted, has once again re-engaged interest in this approach.

As the application of phages for potential solutions to bacterial problems grows, having a repository from which scientists can both source and deposit bacteriophages is essential. The National Collection of Type Cultures (NCTC) is the world's oldest bacterial strain collection and has recently established a bacteriophage repository, which aims to provide a trustworthy source of authenticated phages. NCTC will also preserve all the deposited bacteriophages indefinitely and therefore ensures such precious biological materials are available for future scientific exploitation. The transient nature of both research groups and funding streams means that irreplaceable personal phage collections are frequently located in academic freezers and can become irretrievable in a short space of time. Indeed, nothing illustrates this message more clearly than the case of *Acinetobacter* bacteriophages. Since 1966, over 100 *Acinetobacter* bacteriophages have been described in the scientific literature; however, many are no longer accessible as they were not deposited within a culture collection and therefore the biological material has sadly been lost to science. The NCTC bacteriophage collection will be dynamic, representing a repository into which microbiologists can deposit phages, which in turn will support accessibility and reproducibility in science.



Staphylococcus aureus phages belong to the order *Caudovirales* (tailed phages), which are composed of an icosahedral capsid filled with double-stranded DNA and a thin filamentous tail.

FURTHER READING

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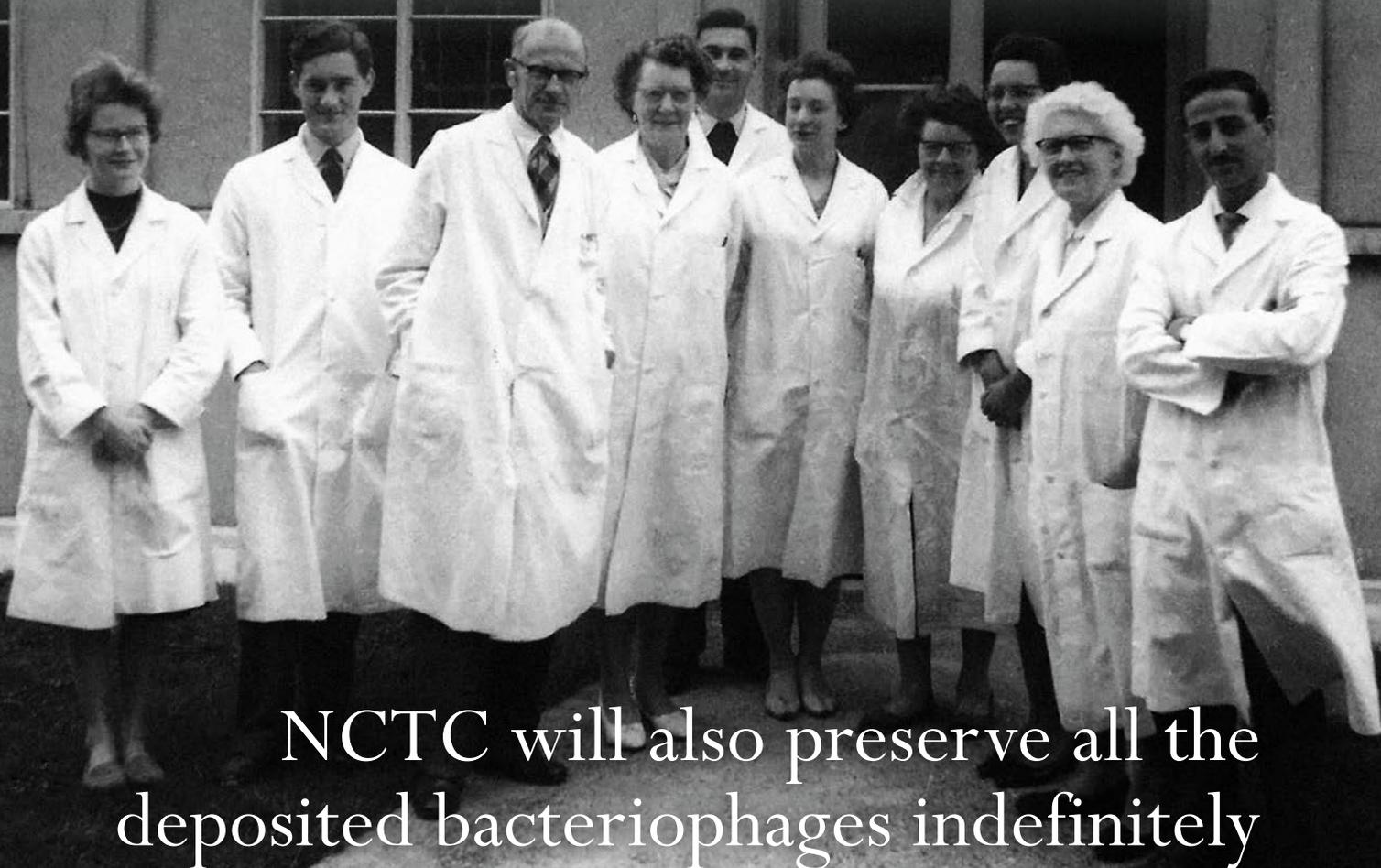
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<https://www.phe-culturecollections.org.uk/news/nctc-news/nctc-bacteriophage-collection-and-repository.aspx>



The 1962 National Collection of Type Cultures Team

Personnel from left to right: Unknown, K. Steele (Deputy Curator), Samuel Cowan (Curator 1949–1965), others unknown.



NCTC will also preserve all the deposited bacteriophages indefinitely

The latest news, views and microbiological developments

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GPS™, part of an H2020 project for the diagnosis of tuberculosis: ARREST-TB

The Spanish company **Genetic Analysis Strategies SL**, the owner of the GPS™ brand dedicated to developing genetic diagnostics methods, participates in an H2020 European project called **ARREST-TB** (*Accurate, Rapid, Robust and Economic diagnostic Technologies for tuberculosis*). The project brings together a consortium of academics from the University of Edinburgh, Heriot Watt University (Edinburgh) and the University of Padua, together with the SME companies **GPS™**, DestiNA Genómica and Optoi (Italy), in collaboration with the Central Institute of Tuberculosis Research (Moscow, Russia), the National Institute for Tuberculosis Research (Chennai, India) and ShanMukha Innovations Pvt. Ltd. The new technologies, based on molecular probes and optical devices for the diagnosis of *Mycobacterium tuberculosis* and its resistance to antibiotics, will be evaluated in countries with a high TB prevalence.

Tuberculosis is costing 1.3 million human lives annually (2016 WHO report), is the ninth leading cause of mortality in the world and participates in the global growth of resistance to multiple antibiotics that has been detected in many other pathogens. According to **Dr Antonio Martínez-Murcia**, Professor at the Miguel Hernández University (Alicante) and director of **GPS™**, 'as a result, drug resistance is considered to be the most acute and imminent threat to the population'.

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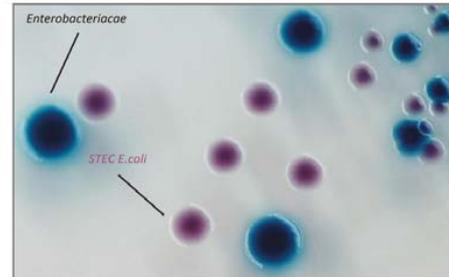
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A busy summer for the biosciences

The RSB has had, as always, a very busy summer, made even busier with our office move to our new home. Despite the location change, it has been business as usual with a jam-packed calendar of events and activities.

Summer is a particularly busy time for our outreach and engagement team as festivals and activities take advantage of the great weather. Outreach and engagement is essential for ensuring biology is as accessible as possible, bringing science to high streets, food festivals, street fayres and more.

This summer we spoke to thousands of people about marine plastics, plant science, anatomy and human health, in locations across the UK including Glasgow, Conwy, Abergavenny and the Isle of Wight.

Diversity and inclusion is a core theme for the RSB, as it is with many of our sister societies. This summer marks 50 years since the Stonewall riots which kick-started the LGBT+ movement, and it was fitting that we should be taking part in this year's Pride in London parade.

Forty individual members and RSB staff took to the street as part of the parade, and the event provided a valuable opportunity for LGBT+ members and LGBT+ allies to come together and celebrate how far liberation efforts have come, but also recognise how far left there is to go.

This year also marked the 31st year of our annual Parliamentary Links Day. A key event in the policy calendar, the day saw another packed-out Attlee Suite in Portcullis

House with researchers, policymakers, politicians and sector leaders all in attendance to discuss the future of science.

Dedicated supporters of STEM delivered insightful and passionate keynotes, including Rt Hon. John Bercow MP, Speaker of the House of Commons, Chi Onwurah MP, Shadow Minister for Industrial Strategy and Chris Skidmore MP, Minister of State for Universities, Science, Research and Innovation.

Members of the House of Commons Science and Technology Select Committee took part in panel discussions with STEM sector leaders, highlighting some of the triumphs of UK science research, alongside upcoming challenges, including Brexit.

All of those present were in agreement that science funding is vital for our growth, with Chris Skidmore stating that he believes government should pay for continued access to programmes such as Horizon post-Brexit if a deal can be struck. A good settlement for science in the upcoming Comprehensive Spending Review was his primary concern whatever the outcome of Brexit negotiations.

The day is only made possible through support from the organisations in RSB's Parliamentary Steering Group, which includes the Society for Applied Microbiology, eight other bioscience member organisations and five other science bodies such as the Royal Society of Chemistry and the Institute of Physics.

Mark Downs CSci FRSB

Chief Executive of the Royal Society of Biology

This summer we also took the opportunity to celebrate the outstanding achievements of teachers and pupils across this year's school competitions at our annual Education Awards Ceremony. The ceremony is an excellent way of championing both outstanding biology education, and the work of our volunteers who make the competitions a reality.

This year's Education Awards Ceremony saw more than 100 pupils travel from across the UK to celebrate their successes in the Biology Challenge or British Biology Olympiad competitions organised by our volunteer-led special interest group, UK Biology Competitions (UKBC).

We also announced this year's Teacher of the Year Gemma Singleton, the science lead at The Beacon School. Gemma has been teaching for 14 years, and received the award in recognition of her dedication to the profession, the creation of fantastic resources and innovative schemes of work.

Now in September, we are gearing up for Biology Week 2019, and also the beginnings of our anniversary year celebrations. We'll be launching our next programme with ITN Productions, celebrating all of this year's award winners at our Annual Awards Ceremony, and indeed biologists worldwide in our annual #iamabiologist social media campaign. Our Biology Week policy later returns to discuss insect decline, and we'll be back at the Royal Institution to discuss the impact of marine plastics.

Now firmly established at our new location, 1 Naoroji Street, just 15 minutes from King's Cross station, London. RSB members and associated membership organisations will be able to take advantage of the meeting rooms at discounted rates. We are especially looking forward to working with our sister societies in our new home and throughout our anniversary year.



Diversity and inclusion is a core theme for the RSB, as it is with many of our sister societies



A summer of parliamentary engagement

In June we joined with the Food Standards Agency (FSA) to participate in Evidence Week in UK Parliament. Our challenge was to help politicians gain an insight into how food safety decisions use evidence, what can go wrong when the evidence is misunderstood and how the public can get behind the headlines. In turn, we gained some insights into how to communicate more effectively with policy audiences.

In the corridors of power

The final week of June was a busy time for science advocates in the UK Houses of Parliament. In addition to the longstanding annual celebration that is Parliamentary Links Day (organised by the Royal Society of Biology), Evidence Week made a triumphant return following a successful first outing in 2018. This initiative, led by Sense about Science, aims to bring together MPs, peers, parliamentary services and people from different walks of life across the UK to talk about why evidence matters. A host of evidence-based organisations participated in this event, sharing insights into topics as diverse as drones, antimicrobial resistance, air quality and homelessness.

SfAM participated in this year's Evidence Week, partnering with the FSA to engage parliamentarians on food safety issues. Our challenge: to give 3-minute briefings to busy policymakers, during which we delivered insights including:

- How overstating the evidence early on during the 2011 European *Escherichia coli* outbreak led to unnecessary food waste, economic damage and political tensions.
- How the FSA adopted an evidence-based approach to reduce *Campylobacter* contamination in the poultry industry.
- The differences between types of evidence, hazard and risk, and absolute versus relative risk.

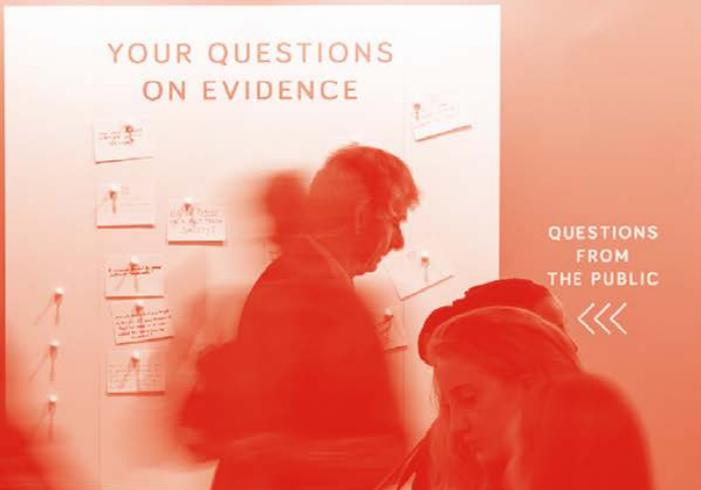
Throughout the day we engaged with a diverse audience, including parliamentarians across both major UK political parties, members of the public and government officials. We also enjoyed a visit from one of our Early Career Scientist members!

Getting the message across

Engaging with such a varied audience can be difficult, especially when trying to identify the messages that will have the most impact. As with many things, preparation is key. If you find yourself planning to engage with politicians and other policymakers, consider the following points during your planning:

Chris Brown

Policy & Public Affairs Manager of the Society for Applied Microbiology



- **Consider different angles:** some politicians will take interest in the economic costs associated with a particular issue, while some will respond more to the personal angle, such as the impacts on individuals and groups of people. Take the time to identify strong messages that appeal to different viewpoints.
- **Keep an eye on the news:** make sure your messages relate to current concerns and issues. In the political context, take a look at what policymakers have been saying recently about your topic of interest. Transcripts of political debates can be a good place to start.
- **Hold a conversation:** many politicians will not be interested in receiving a one-sided lecture. Take the time to ask what interests them and what particular questions they may have. You could be surprised by a politician's interests and it may just give you a reason to follow-up with them in the future.

A community effort

At the end of the day, engaging successfully with policymakers on science issues depends on the availability of clear, high-quality evidence. It is the main driving force behind the Society's external engagement, and is the common ground that brings together such vastly different organisations to make initiatives such as Evidence Week the success they are. It is the expertise of our members that enables the Society to continue making a voice for the wider microbiology community. We will continue to participate in events such as Parliamentary Links Day and Evidence Week to share the excellent achievements within our membership.



Left to right: SfAM Policy Manager Chris Brown, Neil Parish MP and FSA colleagues Julia Heckenast and Erin Oliver

*'At the FSA, science and evidence are at the heart of our decisions and advice. We were delighted to partner with SfAM and to be part of Evidence Week for the first time, talking to MPs and other parliamentarians about a range of food safety issues, from our evidence-based policy intervention to reduce food poisoning from *Campylobacter* to the future of plastic food packaging. Also on the forefront of MPs' minds were food safety issues hitting the headlines as we approach EU exit, which made for some interesting conversations.'*

Julia Heckenast

Chief Scientific Adviser's Team, FSA

Further information

EVIDENCE WEEK is an initiative organised by Sense about Science in partnership with the House of Commons Library, the Parliamentary Office of Science and Technology (POST), and the House of Commons Science and Technology Committee
<https://senseaboutscience.org/activities/evidence-week/>

FOOD STANDARDS AGENCY

<https://food.gov.uk>

Science Policy Workshop for microbiologists

25 NOVEMBER 2019 | THE WESLEY HOTEL & CONFERENCE VENUE | LONDON NW1 2EZ

This workshop, held in partnership with the Microbiology Society, will highlight how the science of microbiology can inform and shape public policy and demonstrate how microbiologists can boost their impact through engaging with policymakers and the policymaking process.



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Delegates do not need any prior science policy experience. This workshop is open to members of SfAM and the Microbiology Society and applications are particularly encouraged from scientists who are at the early stages of their career (PhD, postdoctoral researchers, new lecturers).

Throughout the workshop, delegates will have the opportunity to engage with science policy experts from UK Parliament and government and will participate in a group practical activity.



After this one-day workshop, you will understand:

- The differences between Parliament and government and how they make use of science.
- The different channels through which evidence informs policymaking.
- The role that SfAM and the Microbiology Society play in supporting the voice of microbiology and influencing policy stakeholders.
- How to communicate your research in a tailored way for policy audiences.

How to apply

There are 25 places available for members of the Society for Applied Microbiology to attend this workshop.

An administration fee will be charged upon registration for this workshop, which must be paid in full before arrival at the meeting. This administration fee is non-refundable.

EARLY BIRD ADMINISTRATION FEE: £10
Available until **Sunday 27 October 2019**

FULL ADMINISTRATION FEE: £15
Registration closes **Sunday 10 November 2019**

Attendance support

SfAM members attending this workshop will be eligible to apply for a grant to reimburse travel expenses up to £100. Support for members of the Microbiology Society may be found on their website.

Note: to be eligible for a grant you must be an SfAM member and have registered through our website:

www.sfam.org.uk

Venue

The Wesley Hotel & Conference Venue
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Directions and accessibility information may be found on the venue website at:

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Provisional agenda

- 09:30** | ARRIVAL AND REFRESHMENTS
- 10:00** | HOW DOES SCIENCE INFLUENCE PARLIAMENT AND GOVERNMENT, AND HOW CAN MICROBIOLOGISTS HAVE AN IMPACT?
- 11:30** | PANEL Q&A
- 12:00** | LUNCH
- 13:00** | AFTERNOON BREAKOUT ACTIVITY
- 14:30** | REFRESHMENTS
- 15:00** | RETURN TO BREAKOUT ACTIVITY
- 16:30** | DRINKS AND NETWORKING
- 18:00** | CLOSE

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