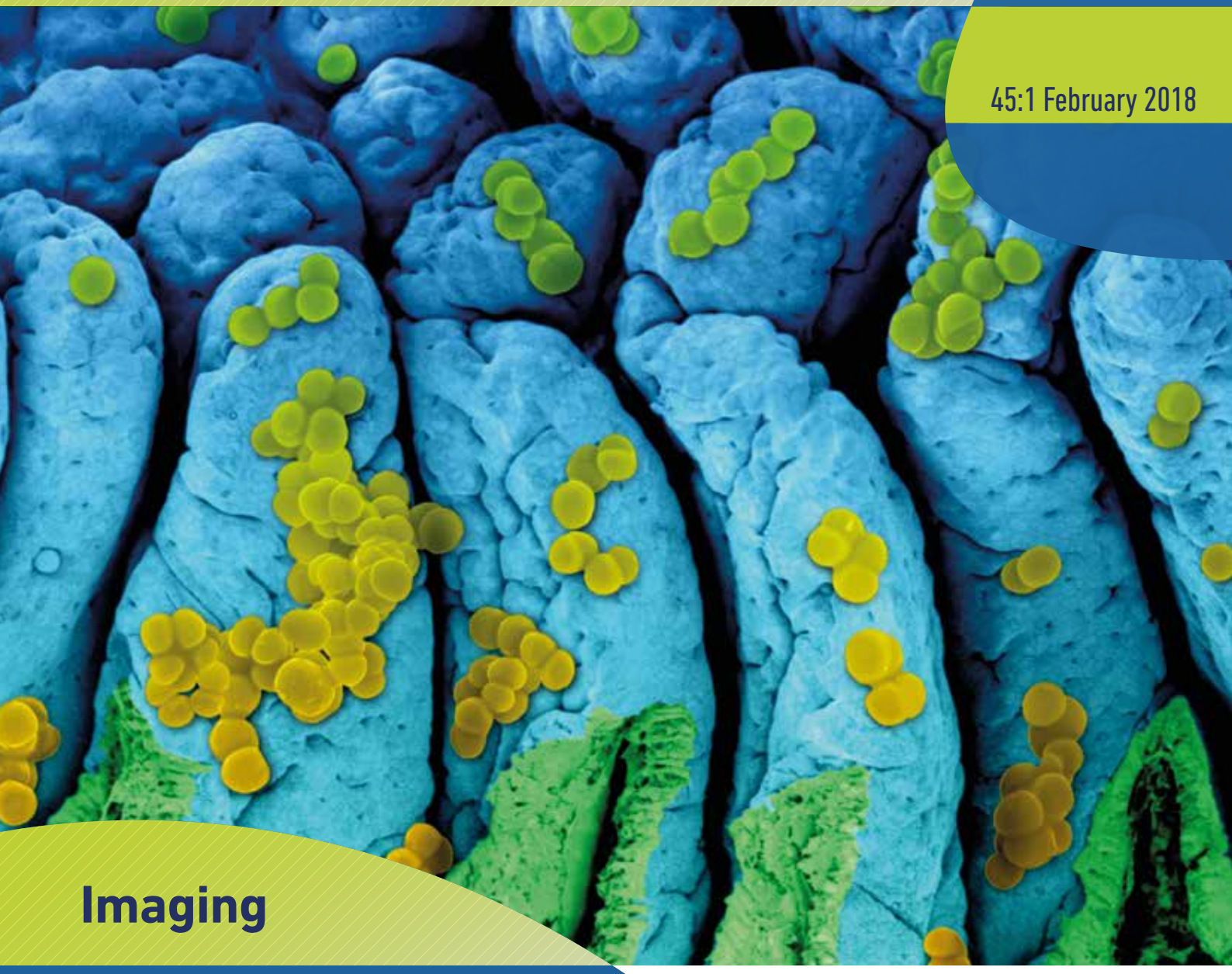
Microbiology TODAY

45:1 February 2018



Imaging

How do you image an exotic virus?
Keep PALM and STORM on
FISH: making microbes glow to see how they organise
Can the Mesolens help the microbiologist?
Imaging aggregates: a look inside the cell

MICROBIOLOGY SOCIETY

CHLORAMPHENICOL

CAPSULES

- Widely distributed throughout the body, including CSF[1]
- Oral levels comparable to i.v. levels[2-5]
- Rarely implicated with *C.difficile*[6-8]

Effective against serious infections including:

- *H. influenzae*[1,2,9]
- Typhoid[1,2,9]
- MRSA[10]
- VRSA[11]
- Neisseria[1,2,9]
- Legionella[1,2]
- Rickettsia[1,2,9]
- *C.difficile*[6-8,12]
- *E. coli*[1,13]

Abbreviated Prescribing Information
Chloramphenicol Capsules BP 250mg
Presentation: Hard Gelatin Capsules.
Indications: Typhoid fever and life-threatening infections, particularly those caused by *Haemophilus Influenzae*, where other antibiotics will not suffice.
Posology: For oral administration.
Adults and elderly: 50 mg/kg body weight daily in 4 divided doses. For severe infections (meningitis, septicaemia), this dose may be doubled initially, but must be reduced as soon as clinically possible.
Children: Not recommended.
Contra-indications: Known hypersensitivity or toxic reaction to chloramphenicol or to any of the excipients. Should not be used for the prophylaxis or treatment of minor infections; during active immunisation; in porphyria patients; in patients taking drugs liable to depress bone marrow function; during pregnancy, labour or by breast-feeding mothers.
Special warnings and precautions for use: Use only if other treatments are ineffective. Use should be carefully monitored. Reduce dose and monitor plasma levels in hepatic or renal impairment; in the elderly; and in patients concurrently treated with interacting drugs.
Interactions: Chloramphenicol prolongs the elimination, increasing the blood levels of drugs including warfarin, phenytoin, sulphonylureas, tolbutamide. Doses of anticonvulsants and anticoagulants may need to be adjusted if given concurrently. Complex effects (increased/decreased plasma levels) requiring monitoring of chloramphenicol plasma levels have been reported with co-administration of penicillins and rifampicin. Paracetamol prolongs chloramphenicol half-life and concurrent administration should be avoided. Chloramphenicol may increase the plasma levels of calcineurin inhibitors e.g. ciclosporin and tacrolimus. Barbiturates such as phenobarbitone increase the metabolism of chloramphenicol, resulting in reduced plasma chloramphenicol concentrations. In addition, there may be a decrease in the metabolism of phenobarbitone with concomitant chloramphenicol use. There is a small risk that chloramphenicol may reduce the contraceptive effect of oestrogens. Chloramphenicol reduces the response to hydroxocobalamin. Chloramphenicol is contra-indicated in patients taking drugs liable to suppress bone marrow function e.g. carbamazepine, sulphonamides, phenylbutazone, penicillamine, cytotoxic agents, some antipsychotics including clozapine and particularly depot antipsychotics, procainamide, nucleoside reverse transcriptase inhibitors, propylthiouracil.
Pregnancy and Lactation: The use of chloramphenicol is contra-indicated as the drug crosses the placenta and is excreted in breast milk.
Effects on ability to drive and use machines: No significant effect on driving ability.
Undesirable Effects: Reversible dose related bone marrow depression, irreversible aplastic anaemia, increased bleeding time, hypersensitivity reactions including allergic skin reactions, optic neuritis leading to blindness, ototoxicity, acidotic cardiovascular collapse, nausea, vomiting, glossitis, stomatitis, diarrhoea, enterocolitis, Gray Baby Syndrome particularly in the newborn, which consists of abdominal distension, pallid cyanosis, vomiting, progressing to vasomotor collapse, irregular respiration and death within a few hours of the onset of symptoms.
Overdose: Stop chloramphenicol immediately if signs of adverse events develop. Treatment is mainly supportive. If an allergy develops, oral antihistamines may be used. In severe overdosage e.g. Gray Baby Syndrome, reduce plasma levels of chloramphenicol rapidly. Resin haemoperfusion (XAD-4) has been reported to substantially increase chloramphenicol clearance.
Pack size and Price: 60 capsules £377.00
Legal Category: POM.
Market Authorisation Number: PL17736/0075.
Market Authorisation Holder: Chemidex Pharma Limited, 7 Egham Business Village, Crabtree Road, Egham, Surrey TW20 8RB, UK.
Date of preparation: January 2016.
See Chloramphenicol Capsules Summary of Product Characteristics for full prescribing information.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Essential Generics on 01784 477167.

References:
1. Martindale: The Complete Drug Reference. Chloramphenicol. [Online]. Available at: https://www.medicinescomplete.com/mc/martindale/current/ms-49-p.htm?q=chloramphenicol&t=search&ss=text&tot=833&p=1#_hit. [Lat accessed: November 2017]. **2.** Feder. HM Jr. "Chloramphenicol: what we have learned in the last decade". *South Med J.* 1986; 79(9): 1129-34. **3.** Kramer WG *et al.* "Comparative bioavailability of intravenous and oral chloramphenicol in adults". *J Clin Pharmacol.* 1984; 24(4): 181-6. **4.** Kauffman RE *et al.* "Relative bioavailability of intravenous chloramphenicol succinate and oral chloramphenicol palmitate in infants and children". *J Pediatr.* 1981; 99(6): 963-7. **5.** Ambrose PJ "Clinical pharmacokinetics of chloramphenicol and chloramphenicol succinate". *Clin Pharmacokinet.* 1984; 9(3): 222-38. **6.** NICE. "Clostridium difficile infection: risk with broad-spectrum antibiotics". March 2015. Available at: https://www.nice.org.uk/advice/esmpb1/chapter/full-evidence-summary-medicines-and-prescribing-briefing#evidence-review-2. [Last accessed: December 2017]. **7.** Slimings C, Riley TV "Antibiotics and hospital-acquired Clostridium difficile infection: update of systematic review and meta-analysis". *J Antimicrob Chemother.* 2014; 69: 881-891. **8.** Spigaglia P "Recent advances in the understanding of antibiotic resistance in Clostridium difficile infection". *Ther Adv Infect Dis.* 2016; 3(1): 23-42. **9.** Summary of Product Characteristics. Chloramphenicol capsules. Last revised 16/10/2015. Chemidex Pharma Ltd. **10.** Fluit, AC *et al.* "Epidemiology and susceptibility of 3,051 *Staphylococcus aureus* isolates from 25 university hospitals participating in the European SENTRY Study". *Journal of Clinical Microbiology.* 2001; 39(10): 3727-3732. **11.** Weigel LM *et al.* "High-Level Vancomycin-Resistant *Staphylococcus aureus* Isolates Associated with a Polymicrobial Biofilm". *Antimicrob Agents Chemother.* 2007; 51(1): 231-238. **12.** Poilane I *et al.* "Interest of the disk diffusion method for screening *Clostridium difficile* isolates with decreased susceptibility to antibiotics". *Pathologie Biologie.* 2007; 55(8-9): 429-33. **13.** European Food Safety Authority. "The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2014". EFSA Journal. 2016; 14(2): 4380

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Editorial

Welcome to the first of the 2018 issues of *Microbiology Today*. In this February edition we are going to take a closer look (no pun intended) at one of my favourite techniques in microbiology: imaging. Initially established by some of the best known names in microbiology, such as Antonie van Leeuwenhoek, advances in microscopy and associated techniques, such as fixing and staining, now provide us with the opportunity to see what is going on within the invisible world that we work with. In this issue, the authors discuss a series of specialisms in the field of imaging and explain how visual cues can fundamentally change our understanding of our own research.

Whole Picture

We start off with a fascinating article from Pippa Hawes, who gives a view of microscopy and its use to enhance our knowledge of some of the most devastating livestock diseases found across the globe. She explains how microscopy can help advance developments of new antiviral treatments and describes some of the complications encountered when using microscopy to observe microbes that require high containment facilities.

Next Chris Bartlett discusses super resolution microscopy, giving us the ins and outs of photo-activated localisation microscopy and stochastic-optical reconstruction microscopy, and how these imaging techniques can provide new information for the researcher. This is especially true in the case of viral biology, where comprehensive information provided by these methods allow access to information at a scale far below the scope of conventional microscopy. Research into hepatitis C is given as an example of the work being undertaken with these techniques, revealing just what types of information can be gained.

Moving on, we come to the use of glowing microbes and how they can be used to provide a new perspective on how bacteria organise themselves. Jessica Mark Welch paints a picture of how, by using fluorescent tags, we can explore the localisation, structure and organisation of bacteria within communities, and how this might impact our understanding of the role of microbes in health and disease.

Gail McConnell, Brad Amos and Liam Rooney are up next discussing the Mesolens, a new type of microscope which has been developed to enhance resolution. This microscope takes a step away from the traditional model, with a new design harnessing both high resolution and a wide field of view. This new, wider outlook can help capture large fields of view at high resolution. In doing so it can be used for observing a variety of different biological situations, for example, large-scale spatial arrangements between bacteria, pin-pointing rare events and highlighting biological patterns.

Then, providing insight on microscopy and its use in neuroscience, Michele Darrow and Karen Marshall outline how microscopy can used in the case of protein misfolding diseases such as Huntington's and Alzheimer's. Imaging can help researchers better understand how misfolded proteins cause cellular disturbances, with cryogenic electron microscopy giving detailed images for analysis. Michele and Karen address, how, once you have the images, someone needs to consider what they show, and they explain how they are engaging with citizen science to try and speed up the analysis of large, complex data.

Our Comment piece has been provided by Bruno Martins and James Locke, and takes us into the world of movies, where dynamic processes can be captured through time-lapse imaging. The article gives a perspective on how you can go about making these types of film, the benefits of investigating single cells and how advances in technology mean microfluidic chips can allow us to see how microbes respond to environmental changes in real time.

Rowena Jenkins
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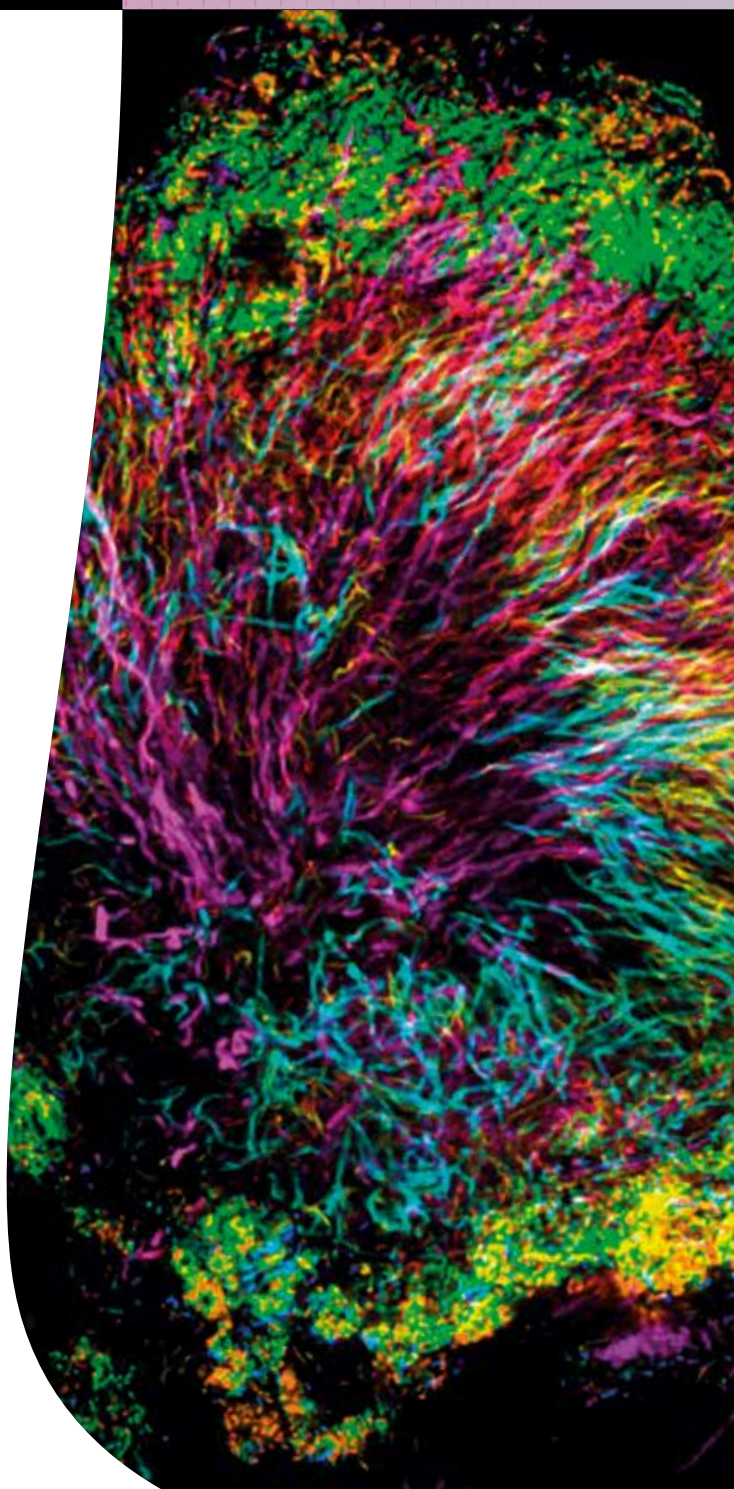

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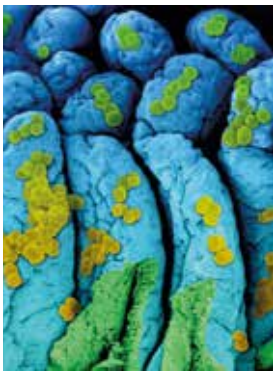

FSC Logo

Coloured scanning electron micrograph of *Staphylococcus aureus* bacteria (round) on the surface of small intestine villi. Dennis Kunkel Microscopy/Science Photo Library

MICROBIOLOGY SOCIETY

Council 2018

Executive Officers

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From the President

When I was first a student of microbiology, this field was introduced to me as the biology of 'invisible organisms' – i.e. the study of microbes, which are below the resolution of the human eye. Strictly speaking that definition has never really been accurate, but it is true that the science of microbiology was born when Antonie van Leeuwenhoek made a first microscope capable of resolving bacteria, and it has progressed in no small measure by generations of inventions that expanded the ways in which we can image microbial cells. This issue is devoted to the science of imaging.

In my office I have a golden *mu* (μ) symbol, which I used use in teaching our Access course to symbolise the scale for microbiology – thousandths of a millimetre. As a very crude rule of thumb, and with exceptions, I will tell students taking their first class of microbiology that viruses are on the sub-micron scale, bacteria have a diameter of around a micron, and eukaryotic microbes are often around 10 microns in diameter. It is claimed that the most acute human eyes can resolve about 576 megapixels and, at best, see something as small as 20 μm in diameter. Mine can't! However you estimate the performance of the eye as a lens, microbiologists need microscopes.

The advances in imaging technologies in the last decades have been astonishing. Coupled with the creation of fluorescent proteins, dyes, antibodies and other ways of labelling individual components of the cell, we can now see microbes like never before. The repertoire of imaging technologies that are now available allow us to bridge the scales of life, from the molecular to the cellular to the colonial. We can watch cells grow and divide, respond to stimuli, or die in response to an antibiotic or the expression of a conditional mutation. From the human end of a lens we can now drill down to observe, in real time, the molecular events that drive the metabolism, growth, movement, behaviour, multiplication and cell division of viruses and cellular microbes. In this issue you will find fascinating articles that introduce technologies such as high containment microscopy, single molecule localisation microscopy, fluorescence *in situ* hybridisation (FISH), Mesolens, cryogenic soft X-ray tomography and single-cell time-lapse microscopy.

It is not only light microscopes that have been revolutionised. Since the electron microscopes first resolved the fine structure of tobacco mosaic virus, ultrastructural imaging has also undergone a constant series of advances. We can now use high pressure freezing to instantly immobilise microbes to generate superb representations of fragile and intricate subcellular structures. Tomography can be used to render 3D images of nanometre scale features of the cell, and cryo-electron microscopy is complementing X-ray crystallography to enable detailed models of the molecular machines of life to be resolved. The area of imaging has therefore been one of sustained interdisciplinary invention – on par with the extraordinary advances in DNA sequencing and other -omic technologies. As microbiologists, limited by the resolving power of images that fall on the human retina, we have benefited more than most from these technologies, and, indeed, since necessity is the mother of invention, microbiologists have contributed significantly to the set of imaging technological revolutions. I hope you will enjoy this issue.

It is now the start of 2018 – and 2017 was a good one for the Society – with a new Strategic Plan in place to guide the way forward. I think we have gone a long way to showing that we can be bigger and also better, wider in our vision, but not forgetting and passionately empowering our members individually. 2018 will prove to be yet another step forward for you and for us.

Neil Gow
President
president@microbiologysociety.org

From the Chief Executive

What an exciting year 2018 is for the Microbiology Society – it is the beginning of our new five-year strategy, which has two crucial features. First, it recognises that for microbiology to play its full part in addressing the world's opportunities and challenges, we must be extremely ambitious. Second, it re-emphasises that the Society's role in these opportunities is helping to unlock the potential of the knowledge of you, our members. Your expertise is a unique resource with huge potential, and by being part of the Society, you are helping to get the subject the attention it deserves.

We are already doing many things to turn this ambition into reality. Some are straightforward – such as expanding the Conferences Team so we can take advantage of more of your ideas for inspiring scientific meetings. Others are behind-the-scenes things that affect the efficiency with which the staff can serve the microbiology community.

All of the things we are doing aim to support you in your careers, and one of the most important will be the appointment of a new Member Engagement Officer to ensure that you have easy access to all of the opportunities the Society offers in publishing, professional development, policy, communications and other areas.

As we redouble our efforts to ensure that your expertise has the maximum impact, it will be imperative that we focus our efforts on those areas that really matter. The Early Career Microbiologists' Forum is already giving a voice to microbiologists who are setting out on your careers, and we are now looking to make sure that mid-career researchers are also heard. A new working group, chaired by Tadhg Ó Cróinín from University College Dublin, has started looking at this and we would welcome views from any mid-career members.

Another important development will be a major project to define the 'state of microbiology'. Many members say that the discipline of microbiology is becoming harder to recognise in labs, but many of you also report that there is more microbiology than ever going on – it's just sometimes called something else. The Society is welcoming to anyone interested in microbes, whether or not they call themselves a microbiologist, and we hope that the new project will in time provide a stimulating and interactive way for members to see where you sit in the overall microbiology landscape, and what exciting routes may be open to you.

The Microbiology Society is one of the few societies that still publishes its own journals, ploughing all the income back into science, so we are also investing in our publishing activities. Just as our grants and conferences programmes provide you with the first opportunity to apply for funding or present your work in friendly and supportive ways, our journals do the same for your published papers.

Looking forward to the Society's 75th Anniversary in 2020, it is interesting also to look back at what the Society's founders set out to do. At their first meeting, they wanted to "link up the interests" of people studying different aspects of microbiology, they wanted to "learn a lot by meeting other types" of scientists, and to "enable researchers of different types to meet and talk and get to know one another". These days, we encapsulate the same thoughts in our mission statement: "advancing the understanding and impact of microbiology by connecting and empowering communities worldwide".

Communication is the key to doing this effectively – communication among the members, communication between the members and others such as policy-makers or the public, and communication between the membership at large and the staff, Council and Committee members.

I have no doubt that when we come to review our progress at the end of the five years of the new strategy, we will be proud of the impact members of the Microbiology Society are having on scientific, environmental, economic, social and medical aspects of life. Please get in touch and let me know how you want to make that happen.

Peter Cotgreave
Chief Executive
p.cotgreave@microbiologysociety.org

News

Unlocking the Microbiome report published

The Society launched its latest policy report, 'Unlocking the Microbiome', at the Royal Society in November 2017. Over 60 experts in research, funding and policy-making attended the launch event to discuss progressing the rapidly developing field of microbiome science. The report makes recommendations for how the scientific community can address the opportunities and challenges for microbiome research through collaboration between different sectors and disciplines. The Society is also publishing three in-depth briefings exploring developments in microbiome science relevant to human health, agriculture and food, and the environment and biotechnology. The report was informed by Society members and other experts, including the Expert Working Group, chaired by Professor Julian Marchesi. The report, briefings and summary of the launch event are available on our website: **microbiologysociety.org/microbiome**. Contact **policy@microbiologysociety.org** with any enquiries.

New Honorary Member: Dr John Schollar

The Microbiology Society is delighted to welcome Dr John Schollar as an Honorary Member. Dr Schollar has been working with the Society since 2001, and has taught basic microbiology techniques to teachers, helped to develop many of our educational resources, and trained teachers over the summer for our Antibiotics Unearthed project.

Microbial Genomics trial in ScienceOpen

The Society is currently running a trial Launchpad (**microb.io/2AMu0tW**) for our youngest journal, *Microbial Genomics*, on the research and publishing network ScienceOpen (**www.scienceopen.com**). ScienceOpen offers next-generation indexing and marketing services, aggregating published content from across open access sources to build context and promote collections, with the aim of bringing the journal's content to a wider audience. If the trial is a success, we will be extending this service to other journals in the Society's portfolio.

ECM Forum Summer Conference

The Early Career Microbiologists' (ECM) Forum Conference planning group are delighted to announce the inaugural ECM Forum Summer Conference. Bringing postdocs together to share their research with undergraduate members, this will be a fantastic opportunity to bring members of the ECM Forum together and learn from each other. To find out more, see the website: **microb.io/2C1bZEQ**.

Hilary Margaret Lappin-Scott OBE

Congratulations to past president of the Microbiology Society, Professor Hilary Margaret Lappin-Scott, on her OBE for services to Microbiology and the Advancement of Women in Science and Engineering.

Vacancies on Council, Committees and Divisions

Serving on a Committee or a Division enables you to make a real contribution and impact to the microbiological community, and public benefit. From January 2018, we have vacancies on Council, most of our Committees, and on all of our Divisions. We are seeking engaged, innovative and dedicated members with the relevant skills and expertise to join these bodies, and really contribute to the work we do while nurturing their own professional development.

If you perhaps feel you do not yet have the necessary skills or experience to put yourself forward for a Committee or Council position, then consider getting involved with the Society's Early Career Microbiologists' Forum (**microbiologysociety.org/ecmforum**).

We also offer a shadowing scheme for eligible members to gain insight into our Council's activities (**microbiologysociety.org/shadowingscheme**).

Further details will be available on the website in April 2018.

Grant deadlines

Date	Grant
1 March 2018	Travel Grants – to support members presenting their work at conferences between 1 April and 30 June 2018.
1 April 2018	Research Visit Grants – to support members visiting collaborators from 1 June.
	Education and Outreach Grants – to support members' teaching public engagement activities from 1 June.
	International Development Fund – to support members working to develop microbiology in low-income countries from 1 June.
18 April 2018	Microbiology in Society Award – to recognise members conducting high impact public engagement activities from 1 June.

Applications for Society Conference Grants to support members presenting at Focused Meetings are also open – check the website for details (**microbiologysociety.org/grants**).

Council Member Professor Steve Oliver wins Yeast Genetics Meeting Lifetime Achievement Award

The Microbiology Society would like to congratulate Council Member Professor Steve Oliver for winning the Genetics Society of America's 2017 Lifetime Achievement Award, for his contributions to the field of yeast genetics and outstanding community service. Professor Oliver, who won the Microbiology Society's Marjory Stephenson Prize in 2016, will be presenting a lecture at the Yeast Genetics Meeting in August 2018 (**microb.io/2Bz65vW**).

Society events for 2018

Throughout 2018, we are once again hosting an excellent array of Focused Meetings, with topics ranging from emerging zoonoses to testate amoeba research. It's also not long until the Annual Conference, which is taking place in Birmingham this year. Find out more about all of our upcoming meetings on page 30.

Would you like to organise your own Focused Meeting? The next deadline for proposals for 2019 events is 12 June 2018.

Alternatively, apply for a Society-Supported Conference Grant to help support invited speakers' costs for your microbiology-related event. The application deadline for the next round is 11 June 2018. Visit our website for more information: **microbiologysociety.org/events**.

Cork Conference Ambassador Awards honours ISSY33

The Cork Convention Bureau's annual Cork Conference Ambassador Awards, which took place in December last year, paid special tribute to 33 ambassadors for placing a spotlight on the city over 2017. The Society would like to congratulate Council Member Dr John Morrissey, also formerly the Eukaryotic Division Chair, who accepted an award on behalf of the organising committee for the International Specialised Symposium on Yeasts (ISSY33). The meeting, which took place in June 2017 at University College Cork, was a great success and attracted over 250 delegates from around the world.

Anita McBride & John Morrissey at Cork Conference Ambassador Awards ceremony.

Contributions and feedback

The Society welcomes contributions and feedback from members. Please contact **mtoday@microbiologysociety.org** with your ideas.

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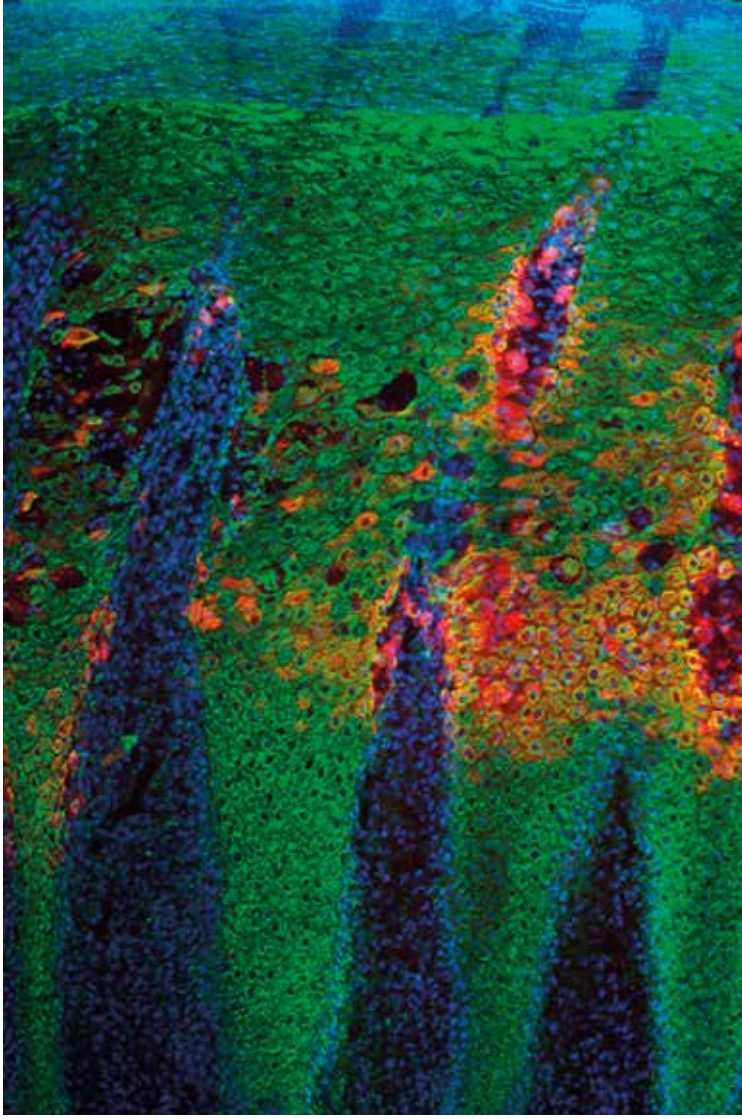
How do you image an exotic virus?



Bovine tongue epithelium, infected with foot-and-mouth disease virus, imaged using a confocal laser scanning microscope. The virus is labelled in red, and the green shows the skin protein, keratin. Cell nuclei are shown in blue. The surface of the tongue is uppermost in the image. The Pirbright Institute

Pippa Hawes

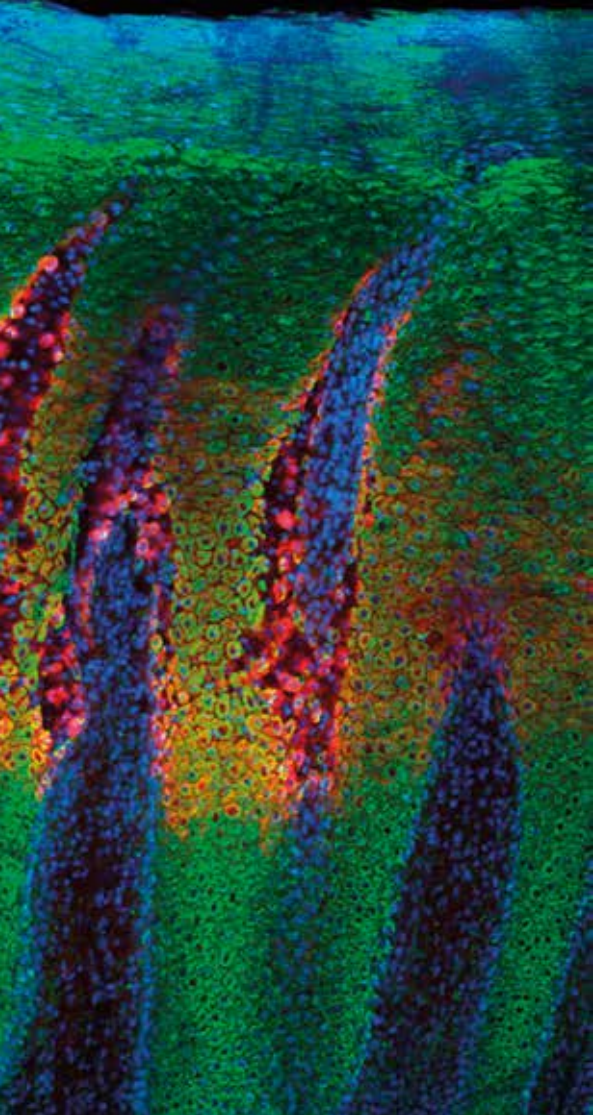
The internationally unique bioimaging facility at The Pirbright Institute enables us to explore the biology of animal diseases, and see how some of the world's most devastating livestock viruses function on a microscopic scale.

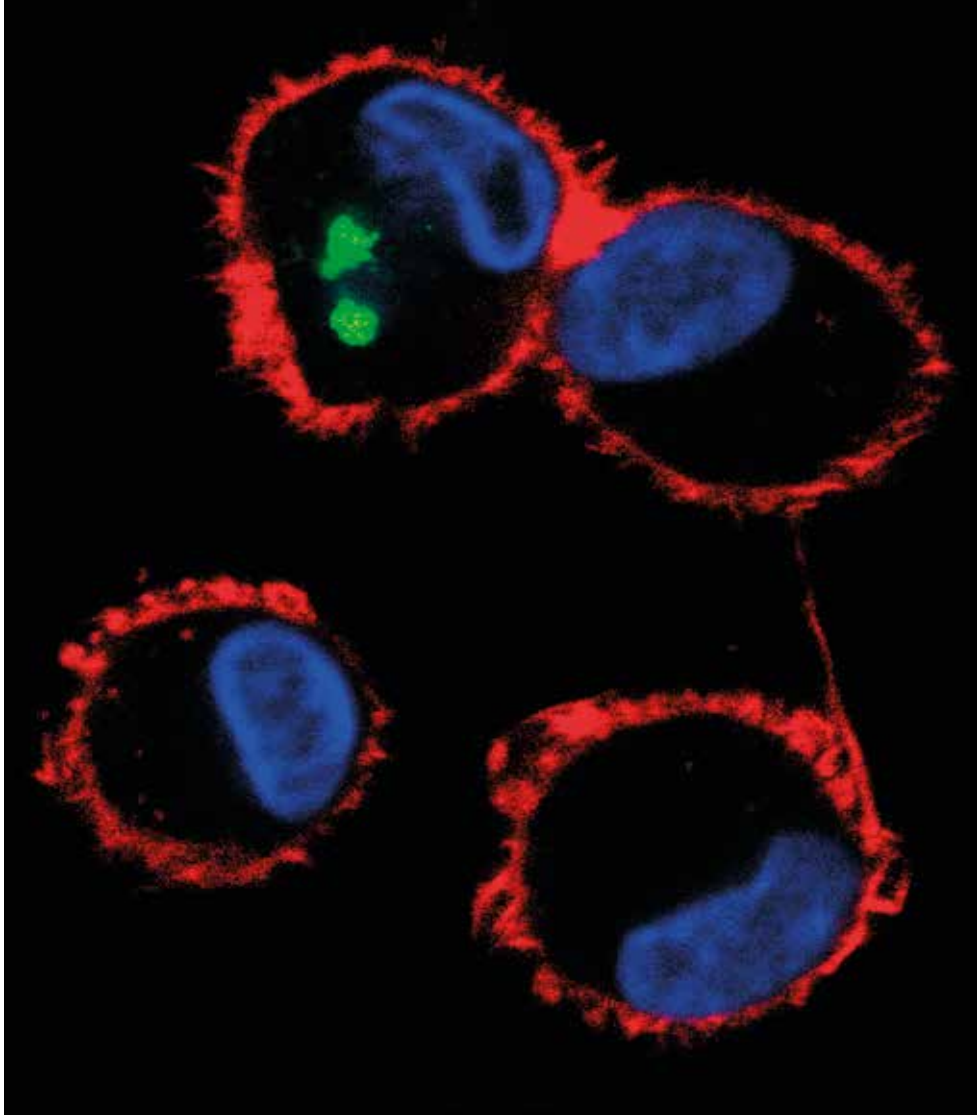
Disease outbreaks in livestock have a major impact on economies, health and food security globally every year. This is particularly true in poorer areas where diseases are endemic and communities rely on livestock for survival. With little money available for research and few vaccines available for prevention, eradication of disease is challenging.

Countries that are disease free are still susceptible to virus incursions, the cost of which can escalate rapidly when knock-on effects such as restrictions on trade and movement are taken into account. For example, the 2001 foot-and-mouth disease (FMD) outbreak in the UK is estimated to have cost over £8 billion.

The threat of virus outbreaks is always present and can occur from illegal movement of animals, interaction of domestic herds with wild animals or spread by vectors via insect or tick bites. Border control authorities keep a close eye on imports; however, wildlife and vector species know no borders. This has been brought into sharp relief in recent years with the importation of African swine fever virus into the Republic of Georgia in 2007 and its subsequent spread across the Russian Federation, Eastern Europe and into the European Union. Taking into account that this disease causes up to 100% mortality rate in domestic pigs and there is currently no effective vaccine, other countries including China, home to half the world's pig population, are preparing for the worst.

The North Sea provides a corridor of protection for the UK, although this





Alveolar macrophages infected with African swine fever virus, labelled with an antibody against a viral protein (green) and stained for the actin cytoskeleton (red). The cell nuclei, containing DNA, are coloured blue. This image was taken using a confocal laser scanning microscope.
The Pirbright Institute

is not infallible. In 2007, the bluetongue virus outbreak across continental Europe reached UK shores as clouds of small biting midges carrying the virus were blown over the Channel, arriving in Suffolk in August. A successful sheep and cattle vaccination programme eradicated this virus from the UK within a year.

Given the devastating effects an outbreak can have at a national and personal level, it is imperative that effective vaccines are developed and used to either stop an outbreak in its tracks or, better still, prevent it from happening in the first place. The work here at The Pirbright Institute is focused on research into new vaccines, diagnosis, and reporting of global outbreaks and prediction of future threats to the UK.

Why use microscopy to study viruses?

In order to produce an effective anti-viral treatment, the basics of how a virus infects a host animal, how it replicates and how it spreads must be identified. This is where microscopy comes into its own. A combination of high-resolution light microscopy and electron microscopy can give protein localisation and ultrastructural information that other molecular laboratory techniques cannot. The majority of projects using microscopy at the Institute seek to answer the age-old question of how does a virus infect a cell and take over its machinery to reproduce? If those pathways are defined in detail then the possibility of blocking one of the processes, and therefore infection, can be investigated and the data ultimately used to produce a vaccine.

Sounds easy, doesn't it?

As with all research, there are challenges associated with delivering results. However, there is an added layer of complexity at The Pirbright Institute because our confocal and electron microscopes are located within a high containment facility. The Biotechnology and Biological Sciences Research Council National Virology Centre: The Plowright Building accommodates laboratories within a restricted access area where we can research live

veterinary viruses that are exotic to the UK. These labs are designed for the use of SAP04 (Specified Animal Pathogen Order level 4) viruses, the most well-known and economically important of which being foot-and-mouth disease virus (FMDV). In practical terms, anything that goes into these labs cannot leave without being fully decontaminated. Air is passed through double HEPA filters before leaving the building, effluent is treated on site, waste is autoclaved or fumigated out, and staff have to take a full shower before leaving. The labs are kept under negative pressure so that air is sucked in, never blown out. This leads to some interesting practices, not least of which is that the first thing you do after arriving at work is take your clothes off! Luckily, the second thing you do is put on some blue scrubs before accessing the laboratories.

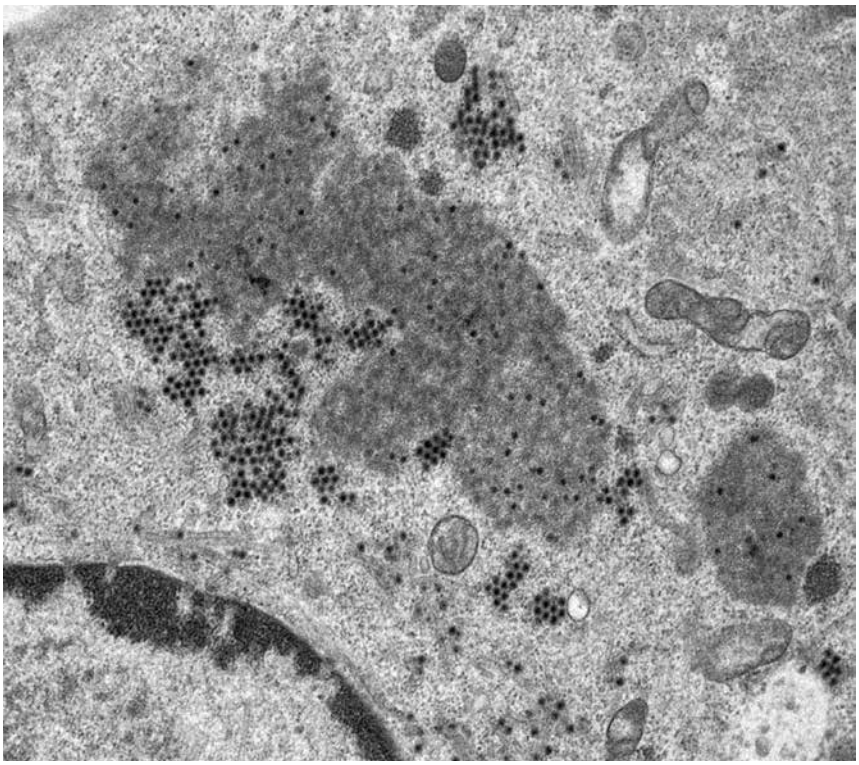
The Bioimaging Suite in the restricted area houses confocal and super-resolution microscopes, and two transmission electron microscopes (TEM), plus there are areas for tissue culture, sample preparation and image analysis. The challenges of running highly complex equipment within a containment building are many, and it takes years of experience to understand and apply the biosafety regulations to all that we do. Top of the list of considerations is decontamination. How do we effectively decontaminate complex equipment to comply with the stringent terms of our SAPO licence? To address this, all possible situations are risk assessed and protocols are written so that users know what to do, should the situation arise. For example, we have procedures in place to follow if:

1. A microscope needs cleaning.
2. A microscope needs maintaining by a contract engineer.
3. There is a small virus spill on the confocal microscope stage or inside the TEM column.
4. A part needs to be sent away for repair.
5. Parts are broken and need to be disposed of.

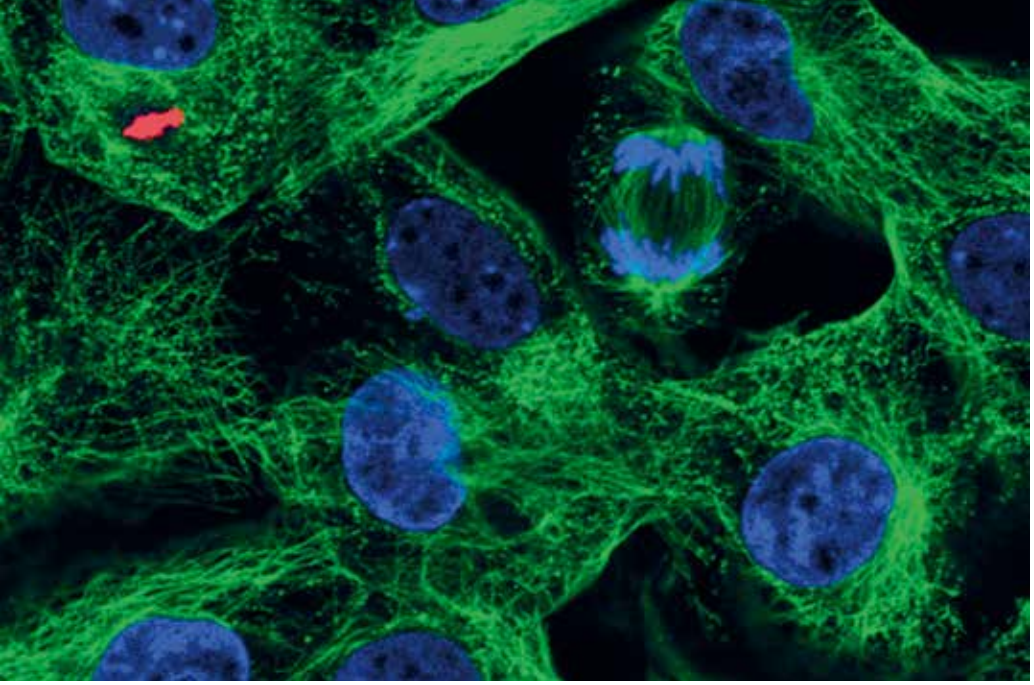
Procedures include wiping with disinfectant, fumigation with formaldehyde gas (without the use of ammonia as a neutralising agent) and gassing with chlorine dioxide in the case of the TEM vacuum system. It is rare that parts are decontaminated and sent out for repair. If that does happen, the serial number of each particular part is recorded so that we can make sure the same part is returned. Parts will more usually be replaced by manufacturers, which of course adds a premium to the cost of our instrument service contracts.

Many preparation techniques for both confocal and electron microscopy involve the use of aldehyde fixatives, which deactivate viruses. These samples can be imaged with no further biosafety concerns. However, certain imaging methods require live samples, for example live cell imaging in the confocal microscope. Each method is risk-assessed, and procedures are put in place which minimise or eliminate the risk of live virus becoming uncontrolled.

It is generally accepted that preparation techniques for the electron microscope that eliminate the use of fixatives provide more accurate information about your sample. These modern cryo techniques are essential in any EM lab, but lead to biosafety



A cell infected with bluetongue virus, and then prepared for the transmission electron microscope. New progeny virus appears as small, black dots in the cell cytoplasm. Part of the cell nucleus can be seen in the lower left-hand quadrant of the image. The Pirbright Institute



Confocal laser scanning microscope image of cells in culture infected with African swine fever virus, labelled with an antibody against a viral protein (red), an antibody against microtubules (green) and stained for DNA (blue). A dividing cell can be seen in the top right quadrant of the image. The Pirbright Institute

complications. One technique calls for live, infected samples to be frozen at a pressure of 2,100 bar in order to preserve the fine ultrastructure, and cryoTEM techniques dictate that live virus samples should be plunged into liquid nitrogen-cooled ethane and imaged at a very low temperature in the TEM. In order for us to carry out these essential preparation techniques safely, and in compliance with our licence, each has to be thoroughly risk assessed and additional steps incorporated to eliminate the potential for uncontrolled virus.

Is it worth it... really?

Of course! Being able to contribute to improving the health and well-being of livestock, and the people who rely on livestock, on a global scale is hugely rewarding. Vaccines that are developed by scientists at The Pirbright Institute have a proven impact. For example, in 2010 the UN Food and Agriculture Organization (FAO) confirmed the global eradication, through the use of vaccines developed at The Pirbright Institute, of rinderpest, a disease that had devastated domestic cattle populations in Europe, Africa and Asia for centuries.

The day-to-day challenges of running a multi-user advanced microscopy facility in a high containment building are numerous, but they are not insurmountable given access to the right infrastructure and expertise. After all, if it were easy, everyone would be doing it!

Now if you'll excuse me, I'm off for a shower...

Pippa Hawes

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An experienced, qualified microscopist with an established track-record in imaging virally-infected animal cells and tissue, **Pippa Hawes** has specific expertise in confocal and electron microscopy, and its application to the study of virus–host interactions. Pippa is regularly invited to speak at residential courses and events in the UK and further afield. Well known within the microscopy community, she is a member of the Council of the Royal Microscopical Society and an active supporter of microscopy networks, such as EM-UK and BioimagingUK.

What inspired you to become a microbiologist?

My career path has been slightly different from that of a classic scientific researcher. During my first degree at Royal Holloway, University of London (BSc Zoology), I was lucky enough to use their electron microscopes. I enjoyed the intricacies of specimen preparation and the challenge of coaxing the best possible images out of the microscopes, but mostly I became fascinated with looking at cells, the building blocks of all living things. After my degree, the opportunity arose for me to do a MSc in Biological Electron Microscopy at Aberystwyth University, which defined my career. I began working at The Pirbright Institute in 2001 as a microscopist, with very little experience in microbiology. Since then, I have completed my PhD, and learnt a lot about viruses along the way – but I wouldn't call myself a virologist!

What is the most rewarding part of your job?

I still enjoy using our microscopes to investigate how viruses interact with host cells, but now I get more satisfaction from discussions with our scientists about projects that include microscopy, and the questions that can be answered. We have a unique facility here, so there are almost endless opportunities to add value to projects. If I had my way, everyone would have a microscopy element in their research!

Keep PALM and STORM on

Christopher Bartlett

Scientists have long depended on microscopes in order to observe and understand biology, particularly when the organisms under investigation are smaller than the human eye can see. The earliest observations using microscopes date to the 17th century with Antonie van Leeuwenhoek and Robert Hooke, who were the first to observe micro-organisms.

Technological advances have continued to improve how much detail can be seen, one of the most powerful being fluorescence labelling of pre-defined targets for the direct visualisation of cellular processes. However, higher image magnification does not equate to an improved image resolution at small length scales because of the interactions of light as it passes through the microscope optics. As a wave, light is subject to diffraction – the bending of a wave after it interacts with an obstacle or object – and this causes the image of a point object to blur into a finite-sized spot.

Seeing is believing

This was first described by Ernst Abbe in 1873, and its relation to image resolution defined by Lord Rayleigh in 1879. In a fluorescence microscope using visible light (λ = 550 nm) and a high numerical aperture (NA = 1.4) lens, for two objects to be resolved as separate they must be positioned ~240 nm apart. This is considerably larger than much of the subcellular architecture that constitutes a cell. Therefore, the molecular details of objects are obscured by this blurring as the signals of thousands of fluorescently labelled targets overlap and merge together.

In 2014, Eric Betzig, Stefan W. Hell and William E. Moerner jointly shared the Nobel Prize in Chemistry for the development of super-resolved fluorescence microscopy. These advances in optical engineering and photochemistry led to the development of a number of fluorescence microscopy techniques which bypass the diffraction barrier. These techniques can resolve biological samples using conventional fluorescence labelling strategies with

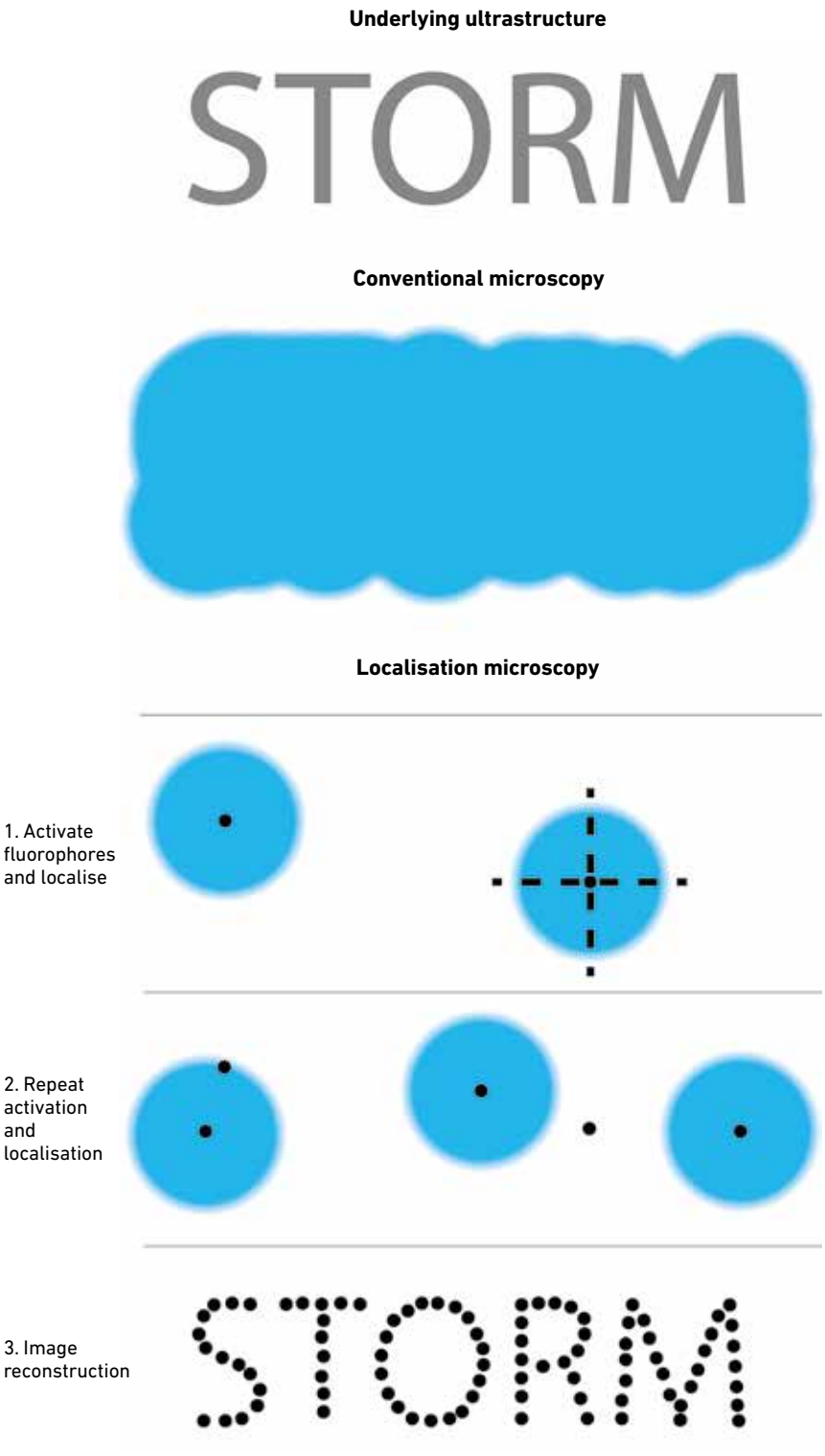


Fig. 1. Single molecule localisation microscopy. C. Bartlett

up to a 10-fold improvement in image resolution.

Bypassing the barrier

One type of super-resolution microscopy employs mathematical modelling to localise single fluorescent events with a precision better than the original diffraction-limited volume. Termed single molecule localisation microscopy (SMLM), these approaches rely on the ability to separate fluorescent events for individual labelled molecules such that only a subset are imaged at any one time (Fig. 1). This is achieved using different photochemical approaches but results in the successive blinking of fluorophores 'on' and 'off'. Sequential imaging and localisation of thousands of fluorophores that are spatially distinct can then be used to reconstruct a super-resolved image.

Since the initial development of these techniques, the field has become swamped in acronyms which each detail how the particular flavour of SMLM causes fluorophore blinking, or how fluorophores are localised. However, all approaches can ultimately be grouped into two main categories.

Photo-activated localisation microscopy (PALM) uses photo-switchable fluorescent proteins that are genetically tagged to the biological protein of interest. These proteins undergo a photoconversion, either by switching from one fluorescent state to another (e.g. from green fluorescence to red), or by activation from a dark state to a fluorescent 'on' state.

Stochastic optical reconstruction microscopy (STORM) on the other hand uses organic fluorescent dyes. These are placed into a 'dark' state under certain experimental conditions, and stochastic activation into the 'on' state is controlled by careful laser excitation (Fig. 2).

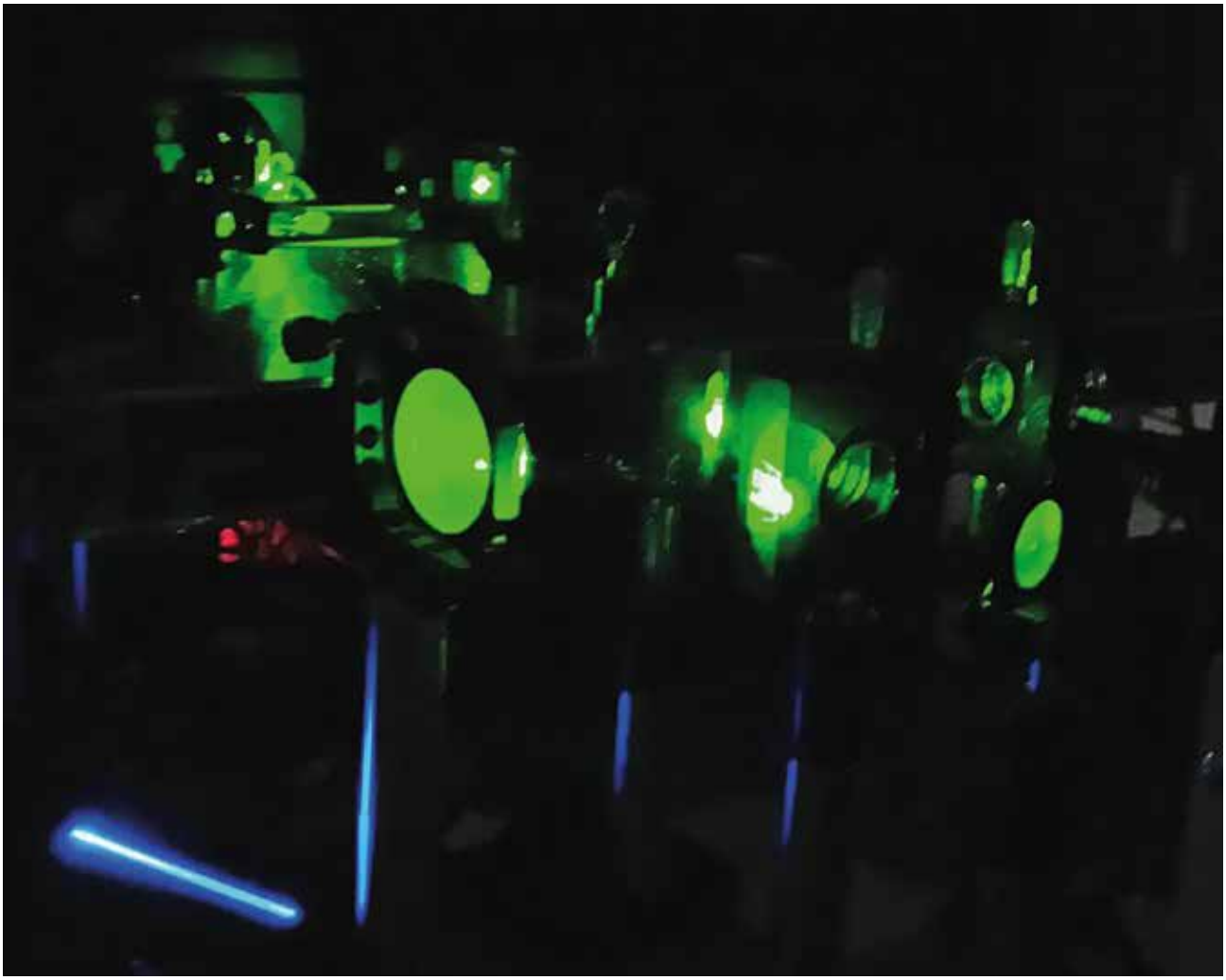
SMLM microscopy: bringing viruses into focus

Considering the similarities in size between virus particles and the resolution of a light microscope, it is surprising that there are but a few virological studies exploiting the resolution improvements of SMLM. However, the application of these specialised imaging techniques has begun to gain traction in the microbiology community and is providing novel insights into virus biology.

One such study directly visualised the precise organisation of tegument and envelope proteins within herpes simplex virus (HSV) particles. The authors combined the molecular identification strategies of fluorescence labelling, the improved resolution of SMLM, and particle averaging techniques used in electron microscopy to distinguish individual protein layers within the HSV virion. Similar approaches have been applied to human immunodeficiency virus (HIV) and have been of sufficiently high resolution to distinguish the conical morphology of the mature capsid and the internal architecture of HIV particles.

We at the University of Leeds have been using SMLM to investigate the molecular architecture of hepatitis C virus (HCV) replication factories. These are specialised sites for virus genome replication that are formed in a coordinated process that requires a number of viral and cellular proteins. Our investigations have resolved

Fig. 2. Lasers supplied to a fluorescence microscope. C. Bartlett



> **This is an exciting time to be a virology researcher; the advancements in fluorescence imaging now allow a direct visualisation of viruses and their intricate interplay with the host cell using conventional fluorescence labelling strategies. The meeting point between disciplines frequently proves fruitful for developing ever more impressive technical feats.**

differences in size as small as 10–30 nm in the distributions of two key proteins known to be involved in the establishment and maintenance of replication factories. This novel information is at a length scale far below what is achievable using conventional microscopy approaches.

SMLM as a quantitative tool

The power of SMLM, however, is not just in the ability to reconstruct high-resolution images from the coordinates of localised fluorophores. Information about the molecular stoichiometry, clustering behaviour and geometric features can be extracted from the mathematical relationship between the positions of localisation coordinates in space and time.

However, with great power comes great responsibility. The pointillist nature of SMLM data requires that sufficient testing of fluorophores from the sample is conducted such that the underlying biological structure is accurately revealed. For example, are gaps in a filamentous structure biologically relevant or a consequence of undersampling?

Conclusion

This is an exciting time to be a virology researcher; the advancements in fluorescence imaging now allow a direct visualisation of viruses and their intricate interplay with the host cell using conventional fluorescence labelling strategies. The meeting point between disciplines frequently proves fruitful for developing ever more impressive technical feats.

The application of these methodologies will continue to offer novel insights into often well-trodden topics. Looking forward, the next biggest challenge for virologists seeking to exploit SMLM is incorporating robust image analysis methods in order to correctly interpret the observations and ensure that seeing is believing.

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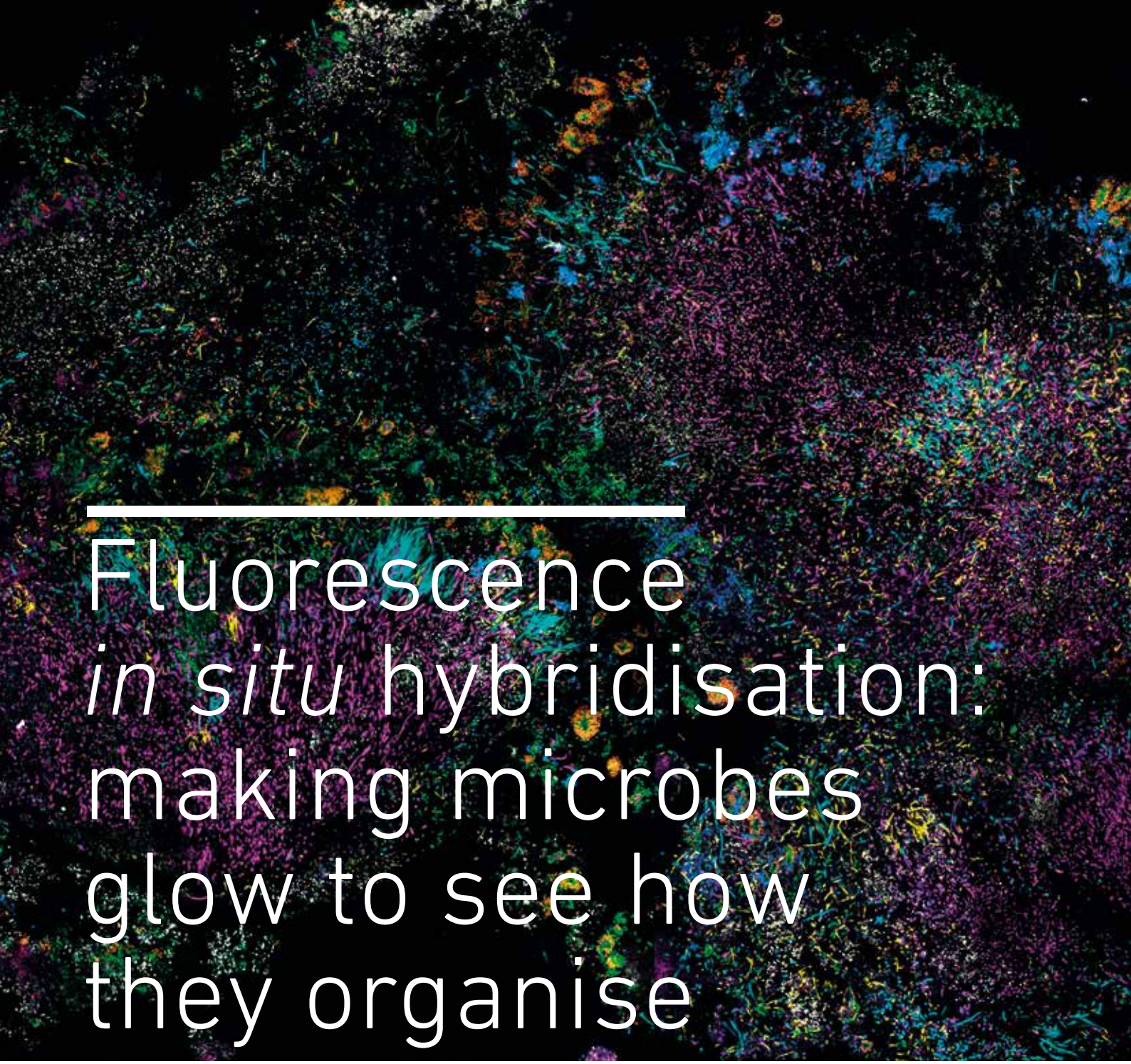
Christopher Bartlett is a molecular virologist with a specialism in advanced microscopy technologies. He achieved a first-class degree in Microbiology with Virology at the University of Leeds in 2012 before completing a PhD in Molecular Biology in 2017. Software engineering and image analysis methods are Christopher's current interests.

How did you enter this field?

I developed an interest in virology through my undergraduate studies in Microbiology at the University of Leeds. I then completed a PhD in Molecular Biology in the laboratories of Mark Harris and Michelle Peckham. My research focused on using PALM and STORM to study hepatitis C virus replication. I continued this project for a further year as a research fellow, where I established a greater interest in software engineering and image processing technologies.

What parts of your job do you find most challenging?

The super-resolution microscopy techniques produce fantastic, high-resolution images. The biggest challenge is the subsequent analysis and careful interpretation of these large data sets.

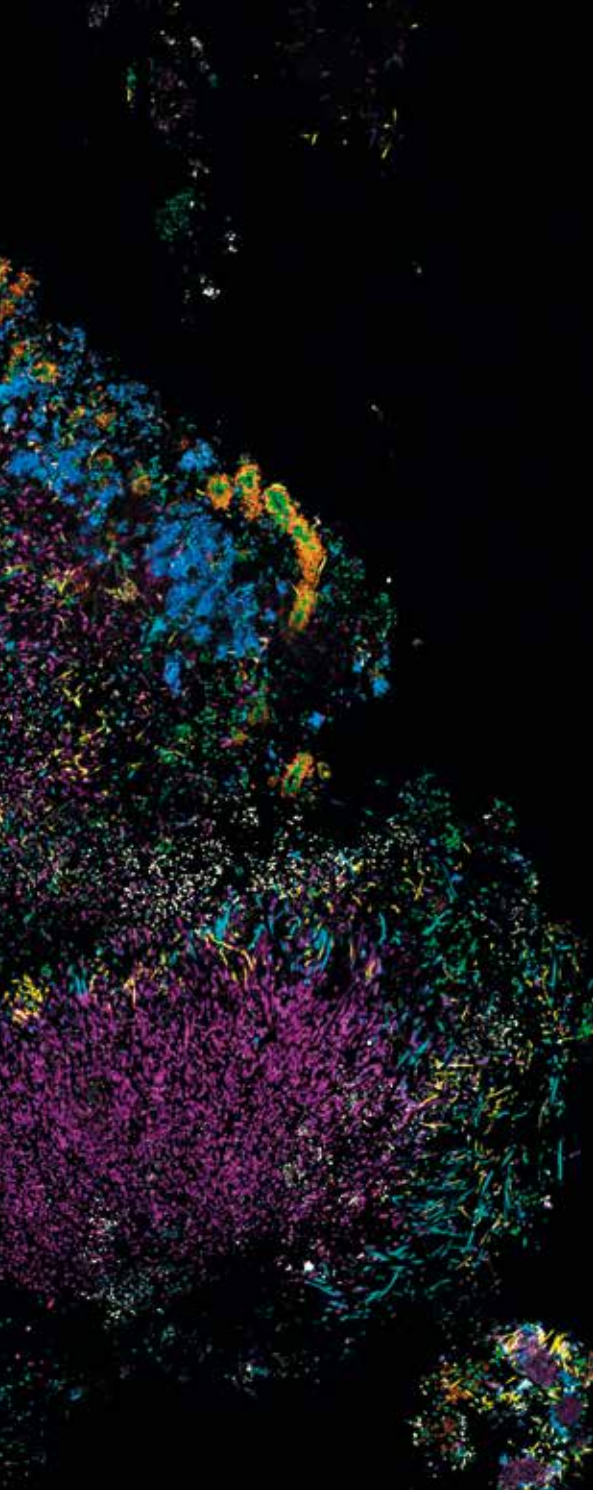


Fluorescence *in situ* hybridisation: making microbes glow to see how they organise

Jessica Mark Welch

Bacteria form distinctive, organised structures in human dental plaque.
Jessica Mark Welch/*Proc Natl Acad Sci* **113**, E791–E800

The microbial world is social, but we usually study it in monoculture. Most of what we know about the behaviour and properties of microbes comes from studying pure cultures, single cells allowed to proliferate into millions in the laboratory in sterile broth or agar.



But in the natural world, a microbe lives in a complex and variable environment. Its neighbours can cause it to change its metabolic profile, and a microbe embedded in a cluster of other microbes can have properties that it would not have on its own, such as the ability to survive in an aerobic environment or invade a host cell. If we want to understand the interplay of human and microbial in our own biology, or if we want to understand how microbes degrade toxins, help plants grow or drive biogeochemical cycles in the ocean, we have to understand how microbes behave within communities.

Micron-scale spatial organisation is key to understanding microbial community behaviour. Bacteria are micron-sized and frequently occupy habitats that are spatially heterogeneous at micron scales. Important features of the environment, from a microbe's point of view, can include inorganic material, plant or animal tissue, organic detritus, and the mucus and mucilaginous goo secreted by animals and plants, as well as other bacteria, all of which can provide surfaces for attachment and sources of nutrients. Understanding the structure of these habitats, and the localisation of microbes within the habitat at micron scales, is a first step in elucidating how the communities work.

Glowing reporters

Microscopy is a uniquely suitable technique for looking at microbial communities and learning about their structure and organisation. But with hundreds of types of bacteria in any given sample, and with only a few visible morphologies, such as spheres, rods, and filaments, many disparate bacteria look near-identical under a microscope.

This identification problem can be solved using fluorescence *in situ* hybridisation (FISH). FISH is a technique in which a probe made of DNA or RNA is used to locate a complementary DNA or RNA molecule in a cell by binding (hybridising) to it. Each molecule of probe is attached to a small fluorescent tag that can be detected by microscopy – a glowing reporter molecule that reveals the presence and the location of the target.

In medicine, FISH is commonly used as a diagnostic test for chromosomal abnormalities. Microbiologists use it in a different way – to visualise where the bacteria are in a sample, and also to identify bacteria using probes complementary to the ribosomal RNA of only certain groups of bacteria. FISH lets us track the subtle changes in localisation of bacteria, showing exactly where they are within the tissue of a host, for example, and how that localisation changes when we change some feature of the host.

FISH is instrumental in visualising individual microbial types and where they are. But for visualising interactions in natural communities, there is a mismatch between the complexity of the community and the number of different types that traditional FISH can see. FISH is usually done using a simple fluorescence microscope with bandpass filters that can differentiate three or four bands of emitted fluorescence – such as far-red, red, green, and blue wavelengths. For an experiment with several probes, the fluorophores for each probe have to be chosen so that their fluorescence emission spectra overlap as little as possible, so that each can be discriminated by a different filter. This requirement for minimal overlap usually

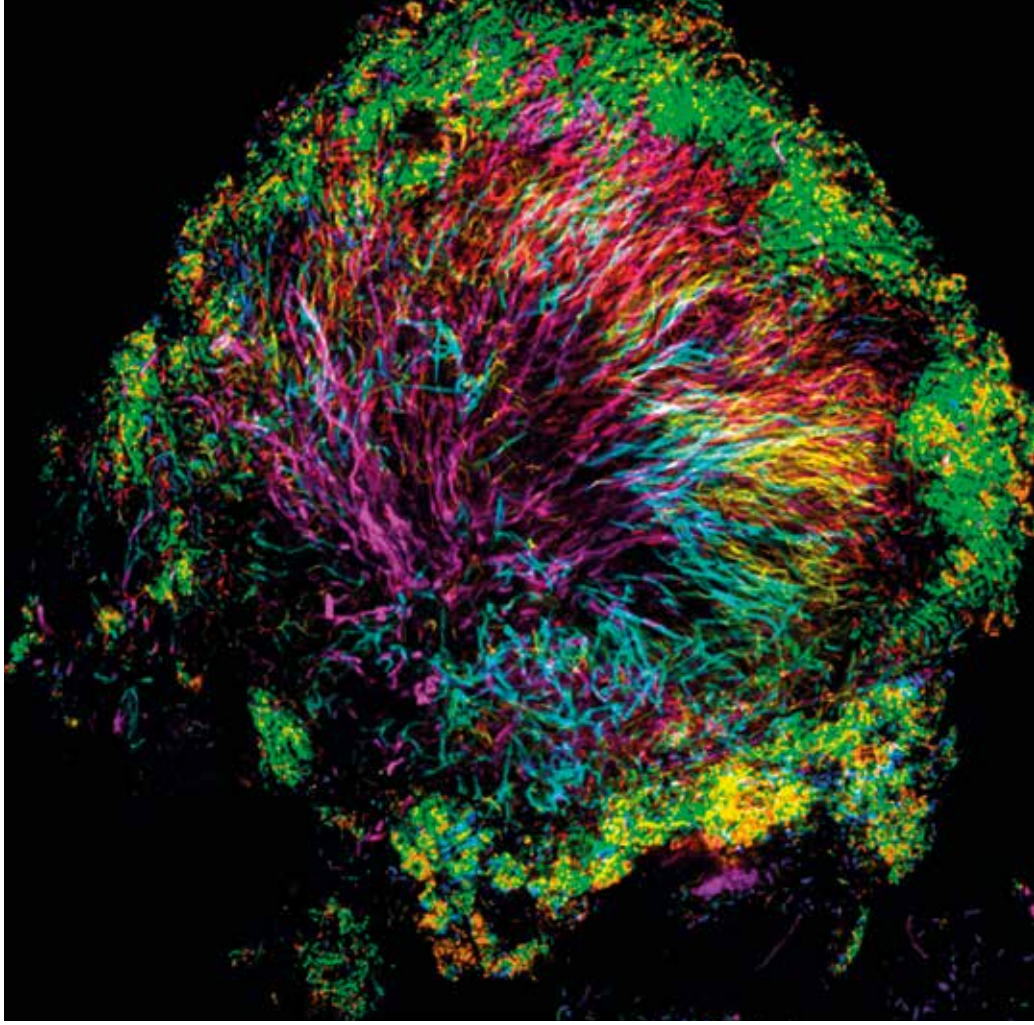
limits to three or four the number of signals that can be simultaneously imaged.

Hyperspectral imaging expands the palette

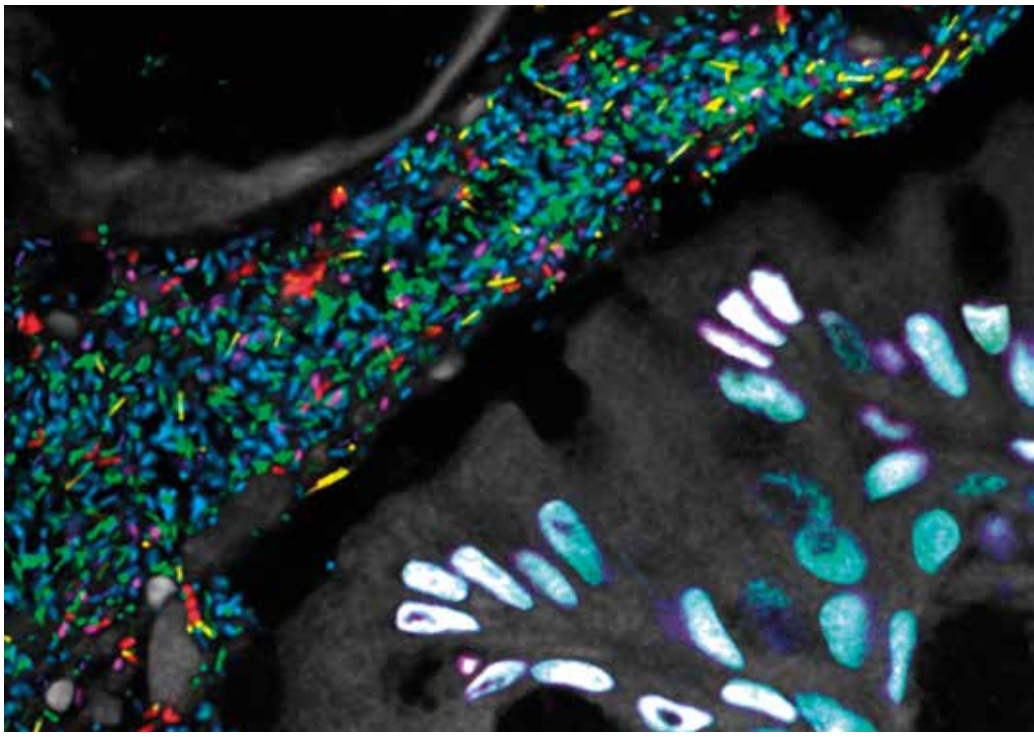
Hyperspectral imaging is a technology that leapfrogs the limitations of bandpass filters and brings the capabilities of FISH much closer to matching the complexities of a natural microbial community. With hyperspectral imaging, it is possible to read the fluorescence spectrum from every pixel in an image and differentiate fluorophore signals that overlap spectrally – making it possible to discriminate a dozen or more fluorophores. Using this technology, my colleagues, including Gary Borisy, Floyd Dewhirst and Alex Valm, and I developed a way to tag and image most or all of the major members of a microbial community simultaneously. We called it CLASI-FISH: combinatorial labelling and spectral imaging FISH, and with it, suddenly the structure of complex microbial communities, the spatial relationships of the bacteria to one another, became visible.

Amazing structure

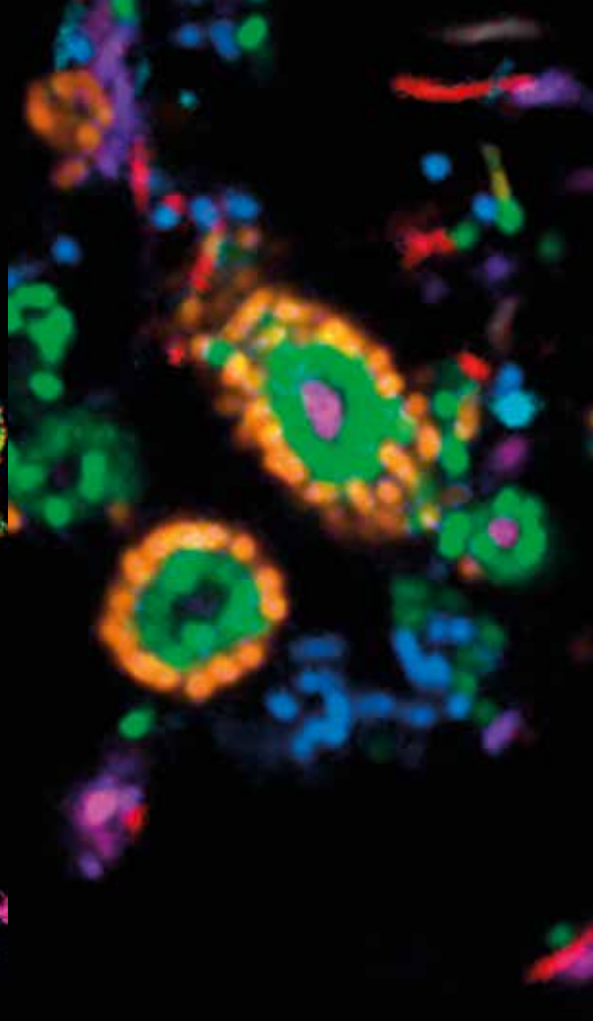
Using CLASI-FISH, we found an amazing microbial structure very close to home – on the surface of teeth. We scraped plaque from the teeth of volunteers, dropped it onto a slide, applied a set of probes, and saw an astonishingly complex and highly organised microbial community. Filaments of the microbe *Corynebacterium* clustered together and radiated outward, forming a clump or bush whose sometimes spiny appearance suggested the name we gave to this community: the hedgehog.



Radial organisation of bacteria in a 'hedgehog' structure from dental plaque.
Jessica Mark Welch/*Proc Natl Acad Sci* **113**, E791–E800



Mixed organisation of bacteria in the mouse colon. Jessica Mark Welch & Yuko Hasegawa



'Corncob' structures from dental plaque.
Jessica Mark Welch

The other microbes making up the hedgehog structure inhabited the *Corynebacterium* bush at characteristic positions. Oxygen-tolerant taxa such as *Streptococcus* bound to the tips of the filaments and formed a kind of outer shell, and anaerobes sheltered in a presumably low-oxygen band just inside this shell.

As we had hoped, seeing the structure immediately suggested hypotheses about function and the inter-relationships of taxa: which taxa form the physical scaffold on which the community is built; which appear to play a key role in modulating the biochemical environment; and which are localised in a strikingly specific way adjacent to one another, their physical closeness suggesting that they share an important biochemical interaction or a similar niche. But not every microbial community is organised in this way. Another habitat close to home – the gut – housed a microbiota with a structure that proved to be strikingly different, with less apparent spatial organisation and more micron-scale mixing.

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Jessica Mark Welch

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Jessica Mark Welch is an Associate Scientist at the Marine Biological Laboratory in Woods Hole, Massachusetts. In addition to her work as a scientist, she serves as host to a varied and structurally complex community of microbes.

Does seeing the structure of these microbial communities change how we think about them?

We know that different kinds of plaque coexist in the mouth and have different properties – for example, that plaque rich in filaments is more likely to form dental calculus than plaque rich in cocci. But whether the presence of either type of plaque makes the preservation of health, or a possible transition to disease, more likely we do not yet know. FISH and imaging, however, can sharpen our questions, focus our attention, and point out promising avenues for targeted investigation to define the role of the microbiome and its different conformations in healthy people.

What next?

I hope that the hedgehog is only the first in a long line of complex spatial structures we will discover with CLASI-FISH, so that we can begin to understand the common principles underlying diverse structures. Other fluorescence microscopy techniques provide exciting complementary approaches. As well as being used to identify cells, FISH can be tuned to detect single-copy genes and gene expression, moving us closer to an understanding of how individual microbes and the community as a whole react to changing conditions. Live imaging at high resolution provides an exciting window into community dynamics. All of these methods contribute toward the goal of being able to understand, predict, model, and manipulate the function of these complex and beautiful microbial communities.

Can the Mesolens help the microbiologist?

Gail McConnell, Brad Amos & Liam Rooney

The founders of microbiology, Pasteur and Koch, depended heavily on the optical microscope. Their key work in 1868–1882 coincided with the commercial availability of newly-invented immersion objectives.

Abbe realised that the ability of a lens to resolve fine detail was proportional to a quantity which he called 'numerical aperture' (NA) The NA = $n \sin \theta$, where n is the refractive index of the fluid (ideally 1.5, which can be achieved if oil is used to fill the space between lens and specimen) and θ is the angle to the optical axis of the extreme ray, i.e. one that is at such a high angle that it is only just captured by the lens. Abbe's NA is still the main figure of merit in choosing objectives for studying microbes but, even at the highest NA no detail can be seen within the cells of most bacteria. The objective lens forms an image, and the amount of detail in this image is proportional to the NA and inversely proportional to the magnification. If the magnification were too high, the image of a single bacterium might fill the entire field with a smoothly-blurred pattern with little detail.

For more than 100 years, the ratio of magnification to NA has been held at approximately 40:1 for all microscope objectives. This gives an image in which the detail is well-fitted to the human eye. Objectives of low power are designed to have a proportionally low NA, which makes them easy to design and cheap to manufacture. A typical microbiology microscope has an objective of ×100, NA 1.4 for looking at bacteria and a low-power objective, ×4 NA 0.1, for searching for an appropriate area on the slide for study.

A new perspective

With the introduction of 3D microscopes, such as the confocal laser-scanning microscope in the mid-1980s, this rule-of-thumb for designing microscopes was revealed as inadequate, in that the ×4 NA 0.1 lens had very poor discrimination of depth, smearing all detail in depth over a 30–60 µm along the instrument axis (usually referred to as the Z axis), so no useful confocal optical sectioning could occur.

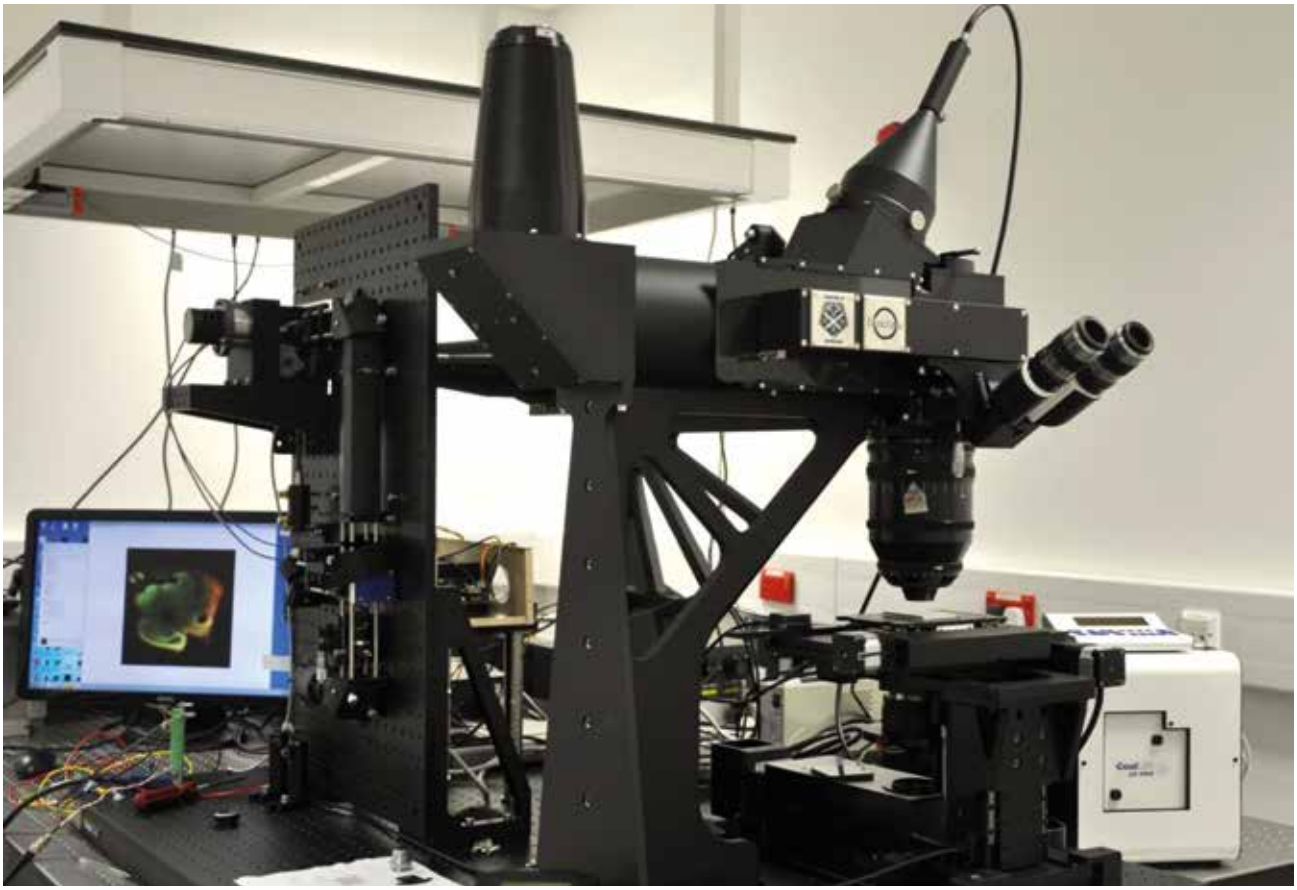
This has led to the abandonment of confocal microscopy for large specimens such as thick brain slices of rodent brain and the introduction of a thin, planar sheet of light to selectively illuminate a narrow section of the specimen, so that 3D information can be obtained from one level only within the large depth of field of the low-magnification lenses. Unfortunately, large specimens are still difficult to image because a basic optical limit (diffraction) prevents the formation of a thin enough sheet over a width of more than a millimetre or two in the XY plane. Also, cameras are now commonly available with an acuity exceeding that of the human eye, so there is now an incentive to improve the low-magnification objectives by increasing the NA. This cannot be done, for fundamental reasons, to the high-NA lenses, which are at a limit set by the nature of the lens materials and those surrounding the specimen.

A new type of lens

We and our colleagues have developed a new type of giant lens, the Mesolens, in which the magic ratio is 8:1 rather than 40:1, which is unprecedented for a fully colour-corrected microscope objective. The lens is too large to fit on a standard microscope, so the entire microscope is built around it and the whole setup occupies approximately one cubic metre (Fig. 1). The performance of this lens is such that one can resolve individual bacteria (resolution <1 μm) throughout a volume of more than 100 mm^3. The name Mesolens (a registered trademark of Mesolens Ltd) is chosen to signify that the lens is intermediate in properties between a microscope objective and a macroscopic camera lens, having the high resolution of the first and the wide field of the second.

An example of the wide field but detailed image in the Mesolens is demonstrated in Fig. 2, which shows a wide-field epi-fluorescence Mesolens image of a *Streptomyces coelicolor*

Fig. 1. The Mesolens imaging system. Gail McConnell



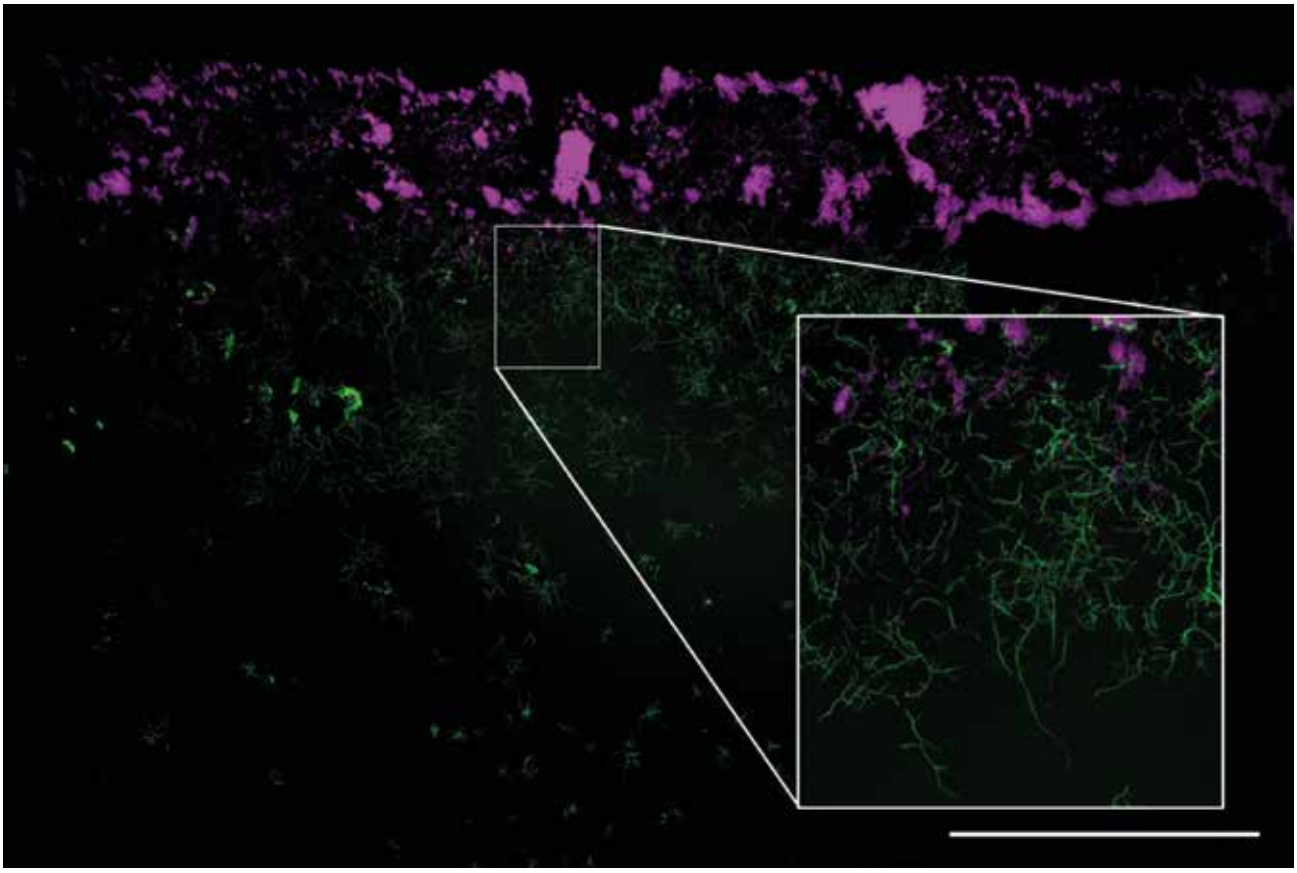


Fig. 2. Mesolens image of a *Streptomyces coelicolor* (M145) mycelium obtained using a high-resolution camera (Vieworks VNP-29MC, giving an effective pixel number of 250 megapixels in each image). Nascent peptidoglycan is stained with FITC-wheat germ agglutinin (green) and nucleoids are stained with propidium iodide (magenta). Fluorescence excitation was performed using high-brightness light-emitting diodes (CoolLED pE-4000). The insert, achieved by software zooming, shows a magnified region of interest from the Mesolens image, where individual hyphae are clearly resolved and sub-cellular detail can be observed. This level of detail is present across the whole 6 mm diameter field of the Mesolens. Bar, 1 mm. Liam Rooney

(M145) mycelium. Nascent peptidoglycan is stained with FITC-wheat germ agglutinin (green) and nucleoids are stained with propidium iodide (magenta). The insert, achieved by software zooming, shows a magnified region of interest from the Mesolens image, where individual hyphae are clearly resolved and sub-cellular detail can be observed. This level of detail is present across the whole 6 mm diameter field of the Mesolens.

We originally specified and designed the Mesolens for imaging 9–12 day-old rodent embryos, but we expect it to have much broader applications in biomedicine and materials analysis.

A closer view

How useful can the huge volume of capture be in microbiology? A single imaged plane comprises of voxels measuring approximately 0.5 × 0.5 by 6 µm for a complete single-channel image (e.g. single fluorescent stain), and a 3D volume imaged at full resolution contains up to 1,000 imaged planes. At first sight it seems that this is so much larger than a single microbe that it can be useful only with multicellular organisms. We believe that it has several potential areas of use:

1. Micro-organisms may exist in large-scale spatial arrangements. These include spacings and zonation in biofilms, and restriction to particular interfaces, e.g. that of *Thiovulum* and other organisms in a sulphide gradient. Dynamic pattern formation also occurs, as in *Tetrahymena*. Large-scale structures can be formed by association of amoeba, as in the grex of cellular slime moulds or the parallel association of ciliates.

> **Pathogens could be located even if present in sputum or body fluids at very low concentrations.**

2. The study of quorum sensing may benefit from an ability to image a volume of growth medium of hundreds of cubic millimetres, in which the response of individual bacterial cells can be seen as well as patterns of enhanced or suppressed growth.
3. Rare events, such as sporulation or cell division, could potentially be measured with good statistics because of the huge number of cells in the photometric volume. Pathogens could be located even if present in sputum or body fluids at very low concentrations.
4. In forensic applications, a vast amount of information might potentially be captured from evanescent samples such as blood films or wounds and viewed and analysed only if this was warranted.

Further reading

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Gail McConnell

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Gail McConnell is Professor of Biophotonics at the Department of Physics, University of Strathclyde, UK. Her research focuses on the design of new types of optical imaging instrumentation and methods and their application in cell biology.

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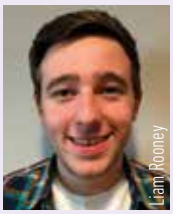
Brad Amos is a Visiting Professor at the University of Strathclyde, where he collaborates with Gail McConnell's research group. After a long career in cell motility research and confocal microscope development, he and Esmond Reid founded Mesolens Ltd in 2009 to design and manufacture the imaging system described here.



Liam Rooney

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Liam Rooney is in the second year of his PhD at the Strathclyde Institute of Pharmacy and Biomedical Sciences. His research involves using the Mesolens to study biofilm formation and dynamics, as well as using interference microscopy techniques to shed light on bacterial gliding motility.

What do you love most about your job?

Gail: I enjoy the luxury of freedom to work on areas of science that interest me and to have the opportunity to work with others who share my interests. It is very rewarding to build an optical imaging system that can show something that has before been unseen, and share this delight with others, particularly if it helps them to solve problems in their own research. It is also very enjoyable to teach students how to set up and use microscopes and witness their first view of the microscopic world!

What advice would you give to someone starting out in this field?

Gail: Don't be afraid to learn new things, especially outside of your own immediate field. I trained as an optical physicist but learning some cell biology and wet chemistry has transformed my research, and has opened up new and exciting collaborative research opportunities.

Using X-rays to look inside the cell

Michele C. Darrow & Karen E. Marshall

Protein misfolding disorders are a class of diseases associated with unchecked protein misfolding and aggregation. The two examples we focus on are Huntington's disease and Alzheimer's disease, which are both neurodegenerative, protein misfolding disorders and share common features.

Huntington's disease (HD) and Alzheimer's disease (AD) are disorders of the brain in which neuronal cells die, and are strongly associated with the aggregation of different proteins into amyloid fibrils (Fig. 1). In HD, mutations in the huntingtin gene lead to the production of huntingtin protein consisting of abnormally long stretches of the amino acid glutamine. There is a relationship between the length of the polyglutamine repeat and clinical onset; the longer the repeat, the earlier in life the disease will manifest.

Protein misfolding in disease

AD is associated with the misfolding of two proteins, amyloid-β and tau. Both are able to self-assemble; however, they have very different structures and functions. Amyloid-β (Aβ) is a relatively short (39–42 amino acids) peptide with no established function and exists in an unfolded, disordered conformation. Tau is a much larger protein and is known to be important for microtubule stabilisation. In AD brains, Aβ fibrillar aggregates are found in the extracellular space whereas tau aggregates are deposited intracellularly. Many lines of evidence suggest that Aβ misfolding is the trigger of AD that leads to downstream effects, including tau aggregation, synapse loss, and eventual neuronal cell death.

Although HD and AD have many similarities, they manifest differently, with HD being primarily a movement disorder and AD affecting memory. Although much is known about protein misfolding disorders (PMDs), precisely how protein misfolding leads to neuronal dysfunction and loss remains a pressing question in neurodegeneration research.

In both AD and HD, a number of systems are impaired in response to mutant huntingtin or misfolded Aβ including protein folding and degradation pathways, synaptic signalling, and mitochondrial function. Whether these dysfunctional effects of misfolded proteins are direct or indirect, which aggregated forms are the most toxic, and how the disturbances to different cellular functions interplay with or exacerbate each other is not clear at present.

Viewing the inside of the cell

Many of the functional disturbances occur in parts of the cellular machinery that can be visualised using various microscopy

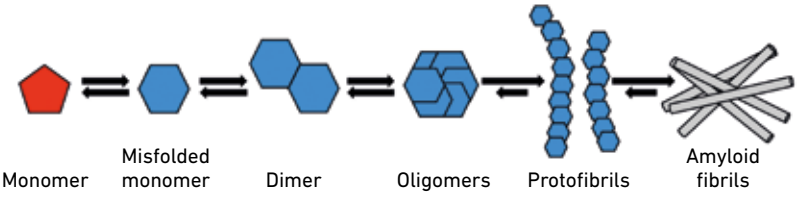

Fig. 1. The process of protein misfolding. Monomeric proteins or peptides can, under certain conditions, undergo conformational changes that lead to a higher likelihood of further aggregation. At the dimer or oligomer stages, a critical nucleus is formed that recruits additional monomers, leading to formation of protofibrils and eventually amyloid fibrils of the type observed in HD and AD brains. Karen Marshall

techniques, such as fluorescence light microscopy, resin-embedded serial-sectioning scanning electron microscopy (SEM) or transmission electron microscopy (TEM), and here cryo soft X-ray tomography. Mitochondria, lysosomes, nuclei, autophagosomes and synapses are all clearly identifiable subcellular compartments that may show structural alterations, providing enormous benefit to our understanding of disease pathogenesis. For example, autophagic vacuoles and lysosomes accumulate in neurons in AD brains, suggesting damage to the protein quality control network. Similarly, morphological changes both to organelles associated with protein degradation and mitochondria have been observed in HD. These observations can give clues as to how diseases are caused, the effects of protein misfolding on cells and the underlying molecular mechanisms of neurotoxicity.

A structural understanding of PMDs can provide functional context across multiple levels. Cryogenic electron tomography (CryoET) can be used to provide a limited cellular context of thin areas such as the edges of cells or the processes of neurons. The cells can also be processed to an appropriate thickness using cryo-sectioning or cryo-focused ion beam milling techniques. However, each of these techniques provide data of only limited areas of the cell. Cryogenic soft X-ray tomography (cryoSXT) alleviates this concern, but at the expense of resolution.

CryoSXT uses X-rays to visualise vitrified cells grown on TEM grids. Tilt series are collected and then reconstructed into a 3D volume representing the cell as it was when frozen. This sample preparation method does not use fixatives, stains or resin. In this way, it is possible to collect data through even the thickest part of the cell, at 30–50 nm resolution, using the inherent contrast of the sample.

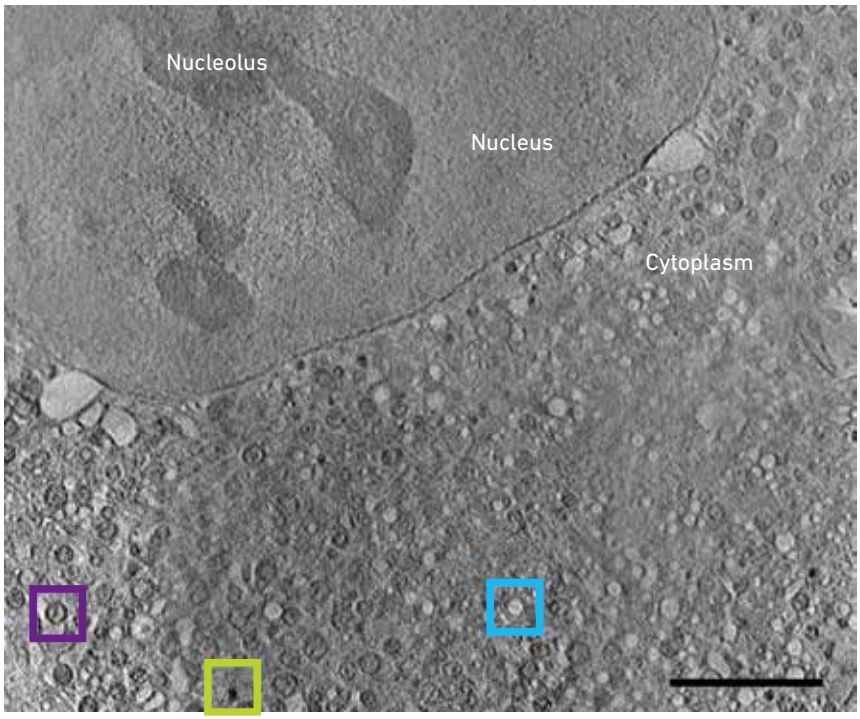

Fig. 2. CryoSXT of an intact mammalian cell expressing mutant huntingtin. Various organelles (lipid droplets, green box; empty vesicles, blue box; mitochondria, purple box) are identifiable due to their inherent characteristics. Bar, 5 µm. Michele Darrow

The power of X-rays

One area of interest, studied on Beamline B24 at Diamond Light Source, is the changes to mitochondrial structure and organisation during expression of mutant huntingtin fragments. Using cryoSXT, large regions of the cell, such as the nucleus, nucleolus and cytoplasm, are clearly recognisable (Fig. 2). The cytoplasm in this disease state cell is extremely crowded. Lipid droplets are easily spotted as dark black organelles (green box) and empty vesicles can be spotted as bright white organelles (blue box). Mitochondria can be recognised structurally due to the presence of cristae (purple box), making the study of their dysfunction here relatively straightforward. However, without further labelling, it is difficult to determine the identity of many of the other organelles.

To address this, if desired, fluorescence light microscopy (FLM) images can be acquired, while keeping the sample at cryogenic temperatures. This enables the specific localisation of events or areas of interest (Fig. 3). This was carried out in collaboration with the Serpell Group at the University of Sussex, to examine changes to lysosome structure and organisation during exposure to oligomeric forms of aggregated Aβ. To explore these intracellular changes, neurons were treated with green fluorescently labelled Aβ oligomers (top image), while lysosomes were fluorescently labelled red using LysoTracker (not shown). Cells were imaged using a cryogenic fluorescent microscope to identify the localisation and distribution of oligomers (purple boxes) and lysosomes (not shown) within the cell. Following this, the same cells were imaged using cryoSXT, revealing the cellular architecture at higher resolution. The overlay of fluorescent signals with X-ray data is critical in providing an annotated map of a neuron deteriorating in response to misfolded forms of Aβ.

People powered research

The greatest bottleneck in this pipeline is the segmentation and analysis of the data. Segmentation is the process of identifying and annotating areas or objects of interest. The current standard in the field is to trace the outlines of each object of interest, on each slice of the 3D data. This is usually a fully manual process, making it tedious, slow and variable. Recently, the development of a new software algorithm has led to the use of machine learning to reduce the amount of user time spent on this task. The user now provides a small amount of markings for each region of interest, which is then used as training data to teach the algorithms the characteristics of each region so that it can predict a full segmentation. Using these techniques, the time to fully segment a single, standard 3D volume has decreased from approximately one month to one week of person-hours. While this is a major improvement, it is still too slow when considered in the context of the experiment at hand. Multiple cells, from both the disease and wild-type state, should be quantitatively assessed to ensure a relevant biological finding, meaning this type of study would still take months of person-time to generate the segmented volumes. Even with this herculean effort, the output segmented volumes would still represent a single, subjective interpretation of the data.

To begin addressing this bottleneck, we have begun a project called Science Scribbler through Zooniverse (**http://microb.io/2FGSB2D**), an online platform

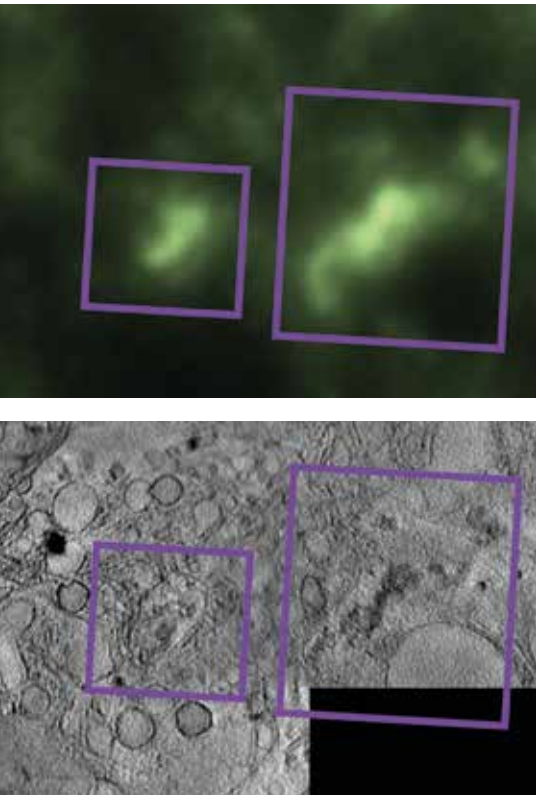

Fig. 3. Correlative imaging of aggregates. Fluorescently labelled Aβ oligomers within neurons can be observed using cryo-fluorescence microscopy (upper panel), providing limited-resolution localisation information. Imaging the exact same part of the cell using cryoSXT reveals they are located within membrane-bound vesicular structures (lower panel). Combining these methods gives an annotated cellular map showing how oligomers are distributed within the cell body. Matthew Spink from Diamond Light Source

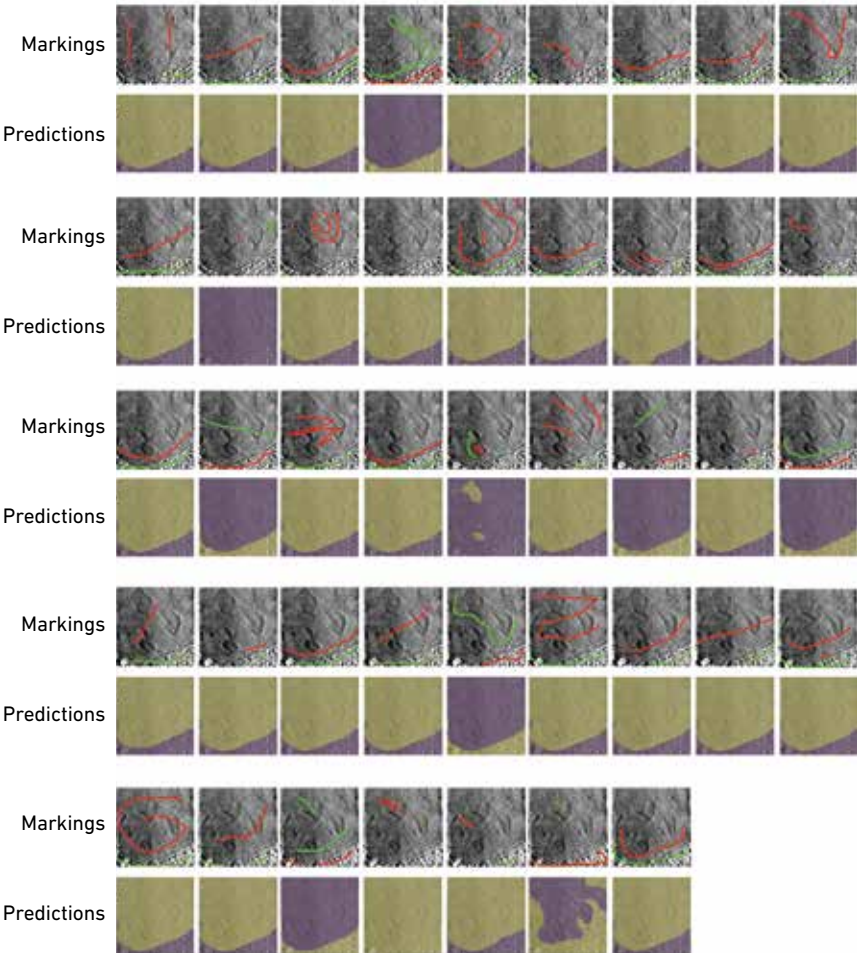

Fig. 4. Volunteers mark images to teach an algorithm to segment. In many cases, using these marks, the algorithm was able to correctly segment the two large regions (nucleus and cytoplasm) from each other. Michele Darrow

that uses citizen science to answer research questions. This model will allow us to collect manual input from multiple people to use as training data to create segmentation predictions. This will speed up the process of segmenting data, while also decreasing the subjectivity of the task by querying more people. We have recently tested one of the tasks during a public Inside Diamond Open Day at Diamond Light Source. Interested attendees were asked to make marks in each of the large regions in a 2D image (Fig. 4). From these marks, predictions were calculated for the 100 central slices of the 3D volume. In many cases, the predictions find and follow the boundary between the nucleus and cytoplasm quite well. Using these preliminary data, we can identify an ideal strategy for collecting and using segmentation data from citizen scientists. It will also pave the way for the application of deep learning strategies in the future because large amounts of data can be segmented in this way.

Using a lower resolution, but more forgiving, structural biology technique can provide important information about the structures present in various protein misfolding disorders *in vivo*, the interactions between these structures and other cellular components, and the overall disease state of the cell. Each technique has positives and negatives associated with it that will impact the sample preparation, imaging parameters, and processing decisions. However, across many imaging techniques, segmentation is the bottleneck, necessitating further development in this area.

Further reading

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Michele C. Darrow

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Michele Darrow is a postdoctoral research associate at Diamond Light Source. She received her doctorate from Baylor College of Medicine in 2015. Her research focuses on correlated imaging techniques and annotation for the purpose of studying interesting biological questions about protein misfolding disorders, and cellular infection and treatment.

Karen E. Marshall

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Karen Marshall is a postdoctoral researcher at the University of Sussex. She has a background in amyloid structure and protein misfolding and is currently interested in how misfolded proteins cause detrimental effects to cellular ultrastructure.

What skills are required in your position on a day-to-day basis?

Michele: Research science is very collaborative so time management and communication are important skills. In addition to the knowledge and skills gained from the study of your field of science, a questioning and imaginative mind, and willingness to discuss, debate and change your mind based on evidence are all useful.

Karen: Skills range from the technical – diligence, precision, a steady hand and good planning – to making sure experiments run smoothly. Good social and communication skills are crucial as research is collaborative and interactive.

What advice would you give to someone starting out in this field?

Michele: A good work-life balance is essential. Burnout and bullying are real problems in research science. You will have to be assertive and take steps to ensure your own happiness.

Karen: Make sure you are determined and have (or can develop) a thick skin. The peer review process can be quite defeating, but if you have a genuine passion and curiosity for your subject, research is a very rewarding job.

Annual Conference **2018** #Microbio18

Tuesday 10 to Friday 13 April ICC, Birmingham, UK

Annual Conference 2018 is almost upon us, and our programme offers a wide range of topics and talks to appeal to all microbiologists. The Conference this year includes over 100 invited speakers from around the world, and four days of presentations, networking and professional development. Don't forget that this year's Annual Conference runs from Tuesday to Friday, and because we sold out last year we urge you to register as soon as possible to secure your space, as well as book for our social events. Registration will close on Monday 19 March.

Ian Atherton

We have ensured that there is significant value to your Annual Conference ticket and it is worth knowing that all rates are subsidised for members, without compromising on what you get as part of your attendance. Below are just some of the highlights that are included in the ticket price.

Admission to all scientific sessions

Our daily programme is jam-packed with topics, talks and presentations throughout the day featuring top quality speakers from leading research institutions in the UK and around the world. You do not need to book for individual sessions, which means you are free to move between any sessions that interest you. Please note that every session does have a room capacity, so make sure you're in the right place at the right time to ensure you get a seat.

Full access to the trade exhibition

We have already sold all of the exhibitor stands, with the final spot taken up in November 2017, highlighting how important the Annual Conference is with major companies wishing to showcase their latest products and services. Exhibitors are a key part of the Conference, and it is highly recommended that delegates visit and speak to the exhibitors to find out about the latest opportunities in the field of microbiology.

Full access to poster sessions

The Annual Conference attracts hundreds of posters each year and this part of the Conference is a highly coveted opportunity to display your work on a large scale. Delegates get access to view posters and speak to presenters on a daily basis. There will be three poster prizes in 2018, read more on p. 44.

Hot buffet lunch, plus tea and coffee breaks every day

Conference consists of long days and requires a lot of concentration! So, to help you keep your momentum, we have ensured that you have access to regular refreshments and delicious hot buffet lunches and puddings! All of which are included in your daily rate.

Inclusive drinks vouchers

You will find two drinks vouchers inside your badge for each of your registered days at Conference, to be used at the evening poster and drinks receptions. Each voucher can be exchanged for a soft drink, a glass of wine or a beer while you are viewing posters and networking with speakers and other delegates.

Conference material

On arrival, you will receive a Conference Guide to help navigate the Conference, and identify which speaker you want to hear and what sessions you wish to attend. This guide works in conjunction with the online programme, allowing you to search for speakers and to add calendar updates to electronic devices. You can also view our poster abstract book and read speaker abstracts online.


ICC Birmingham

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

Annual Conference Social Programme 2018


Ian Atherton

Pre-Conference Networking Event

We are delighted to once again host this fabulous and important networking event. This event is aimed to assist new Conference delegates or refresh repeat visitors on how to make the most of the networking opportunities throughout the week. Join us for **£20** on **Monday 9 April** in **Hall 11 at the ICC** from **18:00–20:00**; includes dinner and refreshments.

Society Quiz and Games Night

Put your thinking caps on for the second annual Society quiz. Tickets are **£22.50** and the price includes an American-style buffet, a welcome drink and an additional drink ticket. The quiz will start from 20:00 and conclude around 22:00, but that is not the end of the night or the competition. You will have private access to the games in the bar, such as shuffleboard, table football and pool. Book your ticket on the Society website now to avoid disappointment.


Shooters Sports Bar Birmingham


The Bierkeller Bavarian Bar Birmingham

Conference Party

Don't miss your chance to celebrate the last night at the Conference with a fantastic Oompah band show. The amazing Bavarian Stompers will put on an action-packed show starting at 20:00, with real German bierfest music, and lots of comedy and audience participation. Guests will enjoy a Bavarian-style buffet dinner and refreshments. Tickets cost **£30** per person. Places are strictly limited, so book early to avoid disappointment.

Prize Lecture Winners

Peter Wildy Prize

Tansy Hammarton
University of Glasgow, UK

17:40–18:30
Tuesday 10 April


University of Glasgow Photographic Unit

Microbiology Society Prize Medal

Jill Banfield
University of California, Berkeley, USA

09:00–09:50
Wednesday 11 April


Roy Kaltschmidt

Fleming Prize

Sarah Coulthurst
University of Dundee, UK

17:40–18:30
Wednesday 11 April


University of Dundee

Marjory Stephenson Prize

Geoff Smith
University of Cambridge, UK

09:00–09:50
Thursday 12 April


German National Academy of Sciences Leopoldina

Unilever Colworth Prize

Sharon Peacock
London School of Hygiene & Tropical Medicine, UK

17:40–18:30
Thursday 12 April


UCL

Focused Meetings and Events update

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

Focused Meetings 2018 – Call for abstracts

We are delighted to announce that you can now submit an abstract for our Focused Meeting programme 2018. By submitting an abstract you could have the opportunity to present your work alongside some of the leading scientists in your field, either as an offered talk or as a poster. Below is a recap of this year's events. You can visit our website to find out more about each meeting and their topics.

Microbes and Mucosal Surfaces
O'Brien Centre for Science, University College Dublin, Ireland
Thursday 21 to Friday 22 June
microb.io/MMS2018

#MMS18

#BYGEV18

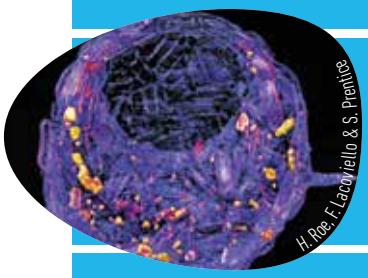
British Yeast Group: Embracing Variation
Stamford Court, University of Leicester, UK
Wednesday 27 to Friday 29 June
microb.io/BYGEV18

Emerging Zoonoses and AMR: A Global Threat
School of Veterinary Medicine, University of Surrey, UK
Monday 2 July
microb.io/EZAMR18

#EZAMR18

Molecular Biology and Pathogenesis of Avian Viruses
St Catherine's College, University of Oxford, UK
Monday 3 to Tuesday 4 September
microb.io/avian18

#AVIAN18



9th International Symposium on Testate Amoebae (ISTA9): Recent Advances and Future Research Priorities
Riddel Hall, Belfast, UK
Monday 10 to Saturday 15 September
microb.io/ISTA2018

#ISTA9

#MUA18

Microbiomes Underpinning Agriculture
The Kingsley Hotel, Cork, Ireland
Monday 1 to Tuesday 2 October
microb.io/MUA18

Future Focused Meetings

All meeting topics and the Society's programme of events are derived from proposals submitted by our members, and we are always looking for new opportunities that will enrich our programme and bring together communities to network and share knowledge and expertise. If you are planning an event or have an idea for a suitable meeting, why not get in touch with the Conferences Team at **conferences@microbiologysociety.org**, or complete our online proposal form for consideration? To ensure events are fully promoted, please send in your completed form by **Tuesday 12 June**.

Teaching in Higher Education: an Annual Conference satellite meeting

The Professional Development Committee will be hosting a special Annual Conference satellite symposium on teaching in higher education this April. The meeting will bring members who are active in teaching – from demonstrators to senior lecturers – together to share their teaching triumphs and woes, and hear from those who are pioneering novel teaching methods. The meeting will kick start a network of like-minded members, enabling the group to continue to share advances in microbiology teaching.

Teaching in Higher Education symposium

9 April 2018 11:00–18:00
Hall 11, ICC Birmingham

The higher education environment is constantly evolving; national initiatives, such as the Teaching Excellence Framework, and regular continuing professional development activities, such as maintaining accreditation with the Higher Education Academy, can mean that a lot is going on alongside keeping teaching material engaging and up-to-date. Added to that, the need to meet rising student expectations and keep up with the pace of innovative technology to incorporate into teaching makes a peer network a valuable resource to stay current and connected.

With sessions including the use of digital platforms and novel techniques (including the use of pantomime in the lecture theatre), this symposium will provide inspiration for delegates to take back and implement in their teaching. We have prioritised space for delegates to discuss their own teaching challenges, achievements and areas for improvement, and troubleshoot problems arising for other delegates.

Find out more about the symposium and speakers by visiting the Annual Conference event at – **www.microbiologysociety.org/annualconference**.

Abstracts for this session are now closed, but this event can be booked online.

The 6th Beneficial Microbes Conference 2017: Pre- and Probiotics for Lifelong Human and Animal Health

The 6th Beneficial Microbes Conference, organised by Bastiaanse Communication, took place in Amsterdam from 9–11 October 2017. Participants were mainly from European countries, and the conference considered how beneficial microbes are advantageous to the health of humans and animals.

Rising antibiotic resistance and the lack of promising new antibiotic candidates threatens clinical settings. As clinical trials can be prohibitively expensive and Big Pharma are not investing in the area, the focus has turned to beneficial microbes in the gut to boost immunity and increase host resilience to disease.

Probiotics are beneficial bacteria and yeast, and are given a variety of different labels – 'friendly', 'good' and 'helpful'. They may be subject to sweeping health claims. This conference aimed to investigate the hype and challenged this area as a pseudoscience.

We heard of ultra-low microbial gut diversity in critical illness, of the promising role of probiotics in re-establishing gut and overall health following long bouts of antibiotic use and in necrotising enterocolitis (NEC) of pre-term infants. Away from humans, examples included weaning piglets are benefiting from probiotics rather than antibiotics to prevent fatal *Escherichia coli* infections, and researchers are working with chicken gut models (CALIMERO) to consider health outcomes.

Alongside probiotics, prebiotics are non-digestible food ingredients promoting growth and/or activity of probiotic bacteria. Within these areas, we heard that we now eat 140g of fibre less per day than our ancestors. Due to this lack of dietary fibre, mucus degraders abound which can cause host mucus degradation and allow pathogens to cross an eroded mucosal barrier. In several presentations, glycans and human milk oligosaccharides (HMOs) cropped up as compounds shaping the microbiota and preventing dysbiosis.

I left with a strong underlying message that pre- and probiotics could be an alternative pathway to antibiotic use within a health and disease context.

Dr Lisa Crossman
Director, consulting, SequenceAnalysis.co.uk, Norwich, UK
Honorary Lecturer, University of East Anglia, Norwich, UK
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Three decades promoting the beauty and impact of transcription

The biennial Asian Conference on Transcription (ACT) covers a broad range of topics focused on the transcriptional regulatory networks of prokaryotes and eukaryotes. This year, the 15th ACT (www.asianconferencetranscription.com) was co-organised by the School of Biological Sciences, Universiti Sains Malaysia (USM), and the ACT committees in Jen Hotel, Penang, Malaysia from 31 July to 4 August 2017. There were 100 participants representing 13 countries. The Microbiology Society sponsored eight travel awards.

There were two keynote speakers: Professor Frans J. de Bruijn from France, who talked about the stress and environmental regulation of gene expression in bacteria; and Professor Thomas Gilmore from the USA, who described the key roles of NF-Kb with particular reference to the devastating effects of the pathogen *Vibrio coralliilyticus* in our warming oceans. Two *Journal of Medical Microbiology* (JMM) Editors delivered featured lectures, with Professor S. Karutha Panthian (Algappa University, India) speaking on the cAMP-mediated transcriptional regulation in group A streptococcal biofilms, and Dr Kim Hardie (University of Nottingham, UK) discussing the regulation of the AaaA autotransporter of *Pseudomonas aeruginosa*.

There were too many distinguished talks to mention everyone, but noteworthy were the elegant studies of G.V. Shivashankar (Singapore) on the mechanoregulation of chromosome intermingling and transcription; sigma factor regulatory networks in Actinobacteria (Jung-Hye Roe, Republic of Korea); quorum sensing-induced anticancer drug expression (Hyon Choy, Republic of Korea); and cancer drug repurposing (Cheong Sok Ching, Malaysia). Additionally, the presentations on tRNA modification in stress response in *Pseudomonas aeruginosa* (Mayuree Fuangthong, Thailand); oxidative stress induction of antibiotic resistance in *Stenotrophomonas maltophilia* (Nisanart Charoenlap, Thailand); cell-derived mammalian living models for synthetic biological approaches (Yoh-ichi Tagawa, Japan), characterisation of mosquito small RNAs in relation to dengue virus infection (Ghows Azzam, Malaysia); and mapping the 3D structure of the chromosome to identify the overlap between obesity and type-2 diabetes (Justin O'Sullivan, New Zealand) were of great interest. Sex-specific RNA splicing in mammals (Vincent Harley, Australia) and zygotic genome activation in zebrafish (Julia Horsfield, New Zealand) were also fascinating.

Six oral presentations showcased early career researchers (ECRs). Kwangbeom Hyun (Republic of Korea) won the JMM Best Oral Presenter Prize, followed by Vikas Malik (China) who won second prize, and Akshay Bhat (Singapore) with third. Narumon Thongdee (Thailand) received an honourable mention. All the other ECRs delivered a quick-fire two-minute oral presentation, applying the effective communicating skills learned from Professor Kalai Mathee and Dr Mahaletchumy Arujanan. The best poster award, sponsored by the Young Scientists Network-Academy Sciences Malaysia, went to Ananya Pal (Singapore). The following won the Microbiology Society-sponsored awards: Hyunjoo Ko (Republic of Korea) won second prize, Shruti Srinivasan (Singapore) won third prize, and Haroldo Rodriguez (USA) and Kogaan Anbalagan (Malaysia) both received honourable mentions.

A first for ACT this year was the Women in Science forum sponsored by L'Oréal Malaysia, which was chaired by Dr Mahaletchumy Arujanan, and featured Ms Jane Loh (Communications Director, L'Oréal Malaysia) and four accomplished women scientists on the panel. The discourse highlighted the benefit of a supportive work–life balance for all scientists and the need to advocate for those succeeding them.

As is tradition, the conference included a cultural visit to Penang and an impressive display of dance and music provided by USM staff. The evening included a presentation of the ACT's history by one of the founding organisers, Professor Changwon Kang (Republic of Korea), earmarking his retirement.

The next meeting will take place in New Zealand in 2019, so watch out for this opportunity to learn fascinating, high-profile science from excellent speakers in a collegial atmosphere.

Acknowledgements

Special thanks to members of the ACT international, scientific and local committees, and to our sponsors: Microbiology Society – Silver Sponsor; New England Biolabs; L'Oréal Malaysia; Young Scientists Network-Academy Sciences Malaysia; Malaysian Biotechnology Information Centre (MABIC); Genomax Technologies Ptd Ltd; Axon Scientific Sdn Bhd; and Prima Nexus Sdn Bhd.

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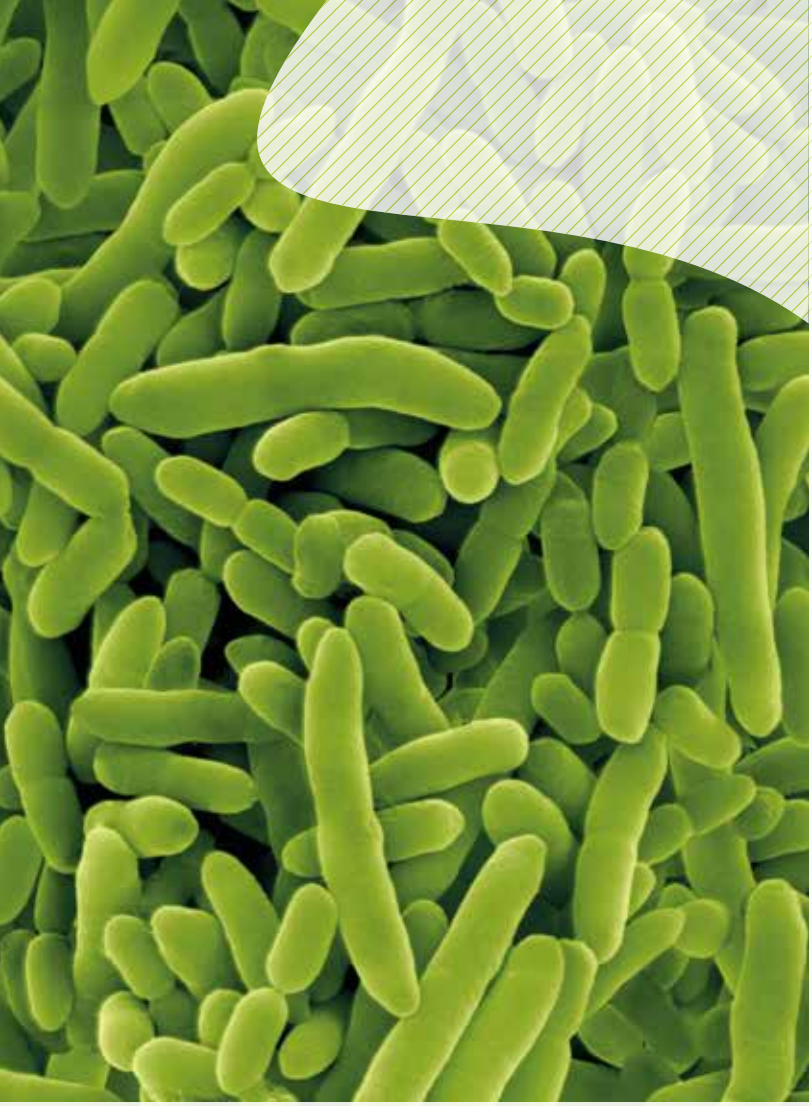
*This event was supported by the Society via a Society-Supported Conference Grant. Find out about other Society-Supported conferences taking place this year and how you could apply for a grant for your event: **www.microbiologysociety.org/grants**.*



Coloured scanning electron micrograph of *Pseudomonas putida*.
Dennis Kunkel Microscopy/Science Photo Library

16th International Conference on Pseudomonas

St George's Hall in Liverpool provided the stunning backdrop for the 16th International Conference on Pseudomonas, held in Liverpool, 5–9 September 2017. This was the first time that the conference had been held in the UK, and the Microbiology Society played a crucial role in making it possible, by sponsoring the event as a Focused Meeting.

The conference brought together more than 300 researchers from all over the world, and the presentations emphasised the importance of *Pseudomonas* as a versatile and widely used model organism and key pathogen.

The opening lecture by Søren Molin from the Technical University of Denmark emphasised the flexibility of the genus with an insightful overview of the complexity and challenges in *Pseudomonas* research, and multi-species biofilms with respect to both biotechnology and biomedicine. This brought together investigations of *P. putida* directed towards biocatalytic applications and studies of *P. aeruginosa* adaptation during chronic lung infections, with the observation that adaptation can be advantageous for biotechnology but a threat in the clinic.

In the 'Mechanisms: Signalling, Systems and Synthetic' theme, there were mechanistic insights into metabolic gene expression regulatory circuits (Victor de Lorenzo and Susanne Fetzner), signalling and communication systems (Jacob Malone and Miguel Cámara), virulence via novel secretion systems (Ina Attree), type VI secretion (Alain Filloux), and the assembly, function and disassembly of the type IV pilus motor (Lori Burrows).

In the 'Ecology, Evolution and Environment' theme, we heard about the study of evolutionary biology, gene transfer and adaptation (Mike Brockhurst), analysis of the adaptation of *P. aeruginosa* during chronic lung infections of cystic fibrosis (CF) patients (Jens Klockgether), and interactions between *P. fluorescens* and *Pedobacter* (Mark Silby). We also heard about adaptive and cooperative behaviour in relation to iron acquisition (Ashley Griffin), and the origin and evolution of a kiwifruit pathogen pandemic in New Zealand (Paul Rainey)

'Infections and Host–Pathogen Interactions' featured a range of topics including contact lens-associated eye infections (Suzi Fleiszig) and a clinical perspective on therapeutic approaches to the treatment of chronic lung infections of CF patients (Jane Davies). There were also talks on strategies for the treatment of chronic *P. aeruginosa* wound infections (Kendra Rumbaugh), and the role of type VI secretion as an anti-eukaryotic weapon (Sophie Bleves). Rob Lavigne switched the focus to the interactions between lytic phage and their bacterial hosts.

In the 'Antibiotics and Biofilms' theme, we were treated to a highly visual talk on explosive cell lysis (Cynthia Whitchurch) and work highlighting some of the fundamental issues pertaining to the relevance of model systems (Marvin Whiteley), while further talks focused on stress-inducible determinants of antibiotic resistance (Keith Poole), and the use of pyocins as protein antibiotics (Dan Walker).

The subject of 'Genomics' was covered with talks by Fiona Brinkman on the latest developments and tools associated with the Pseudomonas Genome Database (**pseudomonas.com**), and Roger Levesque on progress with the International Pseudomonas Consortium. There was also a crowdsourcing analysis of a mystery *Pseudomonas* genome, led by Nick Tucker, which ran throughout the conference and beyond.

With 20 excellent offered talks and 230 posters, the action-packed days of excellent science lived up to the grand setting.

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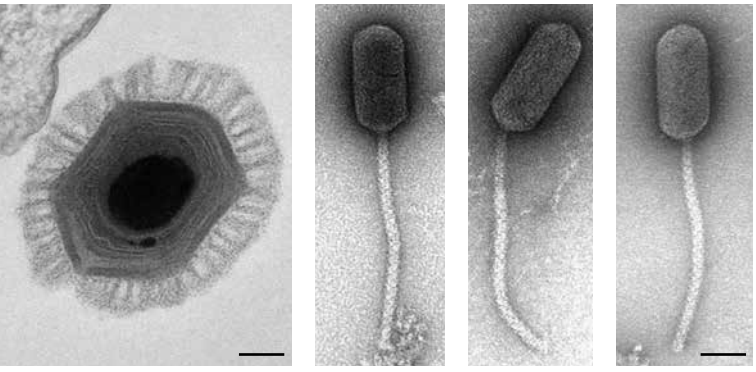
Why virus taxonomy is important

Classifying things was once the epitome of science. Nowadays many scientists think that taxonomy — the science of classifying and naming things — is an endless series of arguments about what things should be called; an unproductive, boring pursuit that is impossible to fund and a disaster if you want an academic career. Here is why this viewpoint is wrong.

The ordering, or classification, of organisms is based upon the premise that there is an evolutionary relationship among them. This does not mean that we cannot use a variety of characters (such as genetics, morphology, immunogenicity) in our classification system but, especially in the age of metagenomics and high-throughput sequencing, genetic characters have become predominant. Most depictions of evolutionary relationships are now 'phylogenetic trees' based upon analyses of DNA, RNA or protein sequences.

But having inferred a phylogeny, how do we group together (or cluster) the organisms; in our case, viruses? Some virologists would argue that the spectrum of genetic diversity for viruses is a continuum, so that any attempt to divide them into different categories will not be sustainable. Indeed, virus sequences obtained from metagenomics studies often occupy the gaps between previously described groups – such as species or genera – and some argue that current taxonomic distinctions will fade away as this type of work continues.

Other virologists, in contrast, believe that there are significant biological barriers to the exchange of genetic material between viruses. These barriers might include an inability to recombine or to co-infect the same host or cell type within that host. If such barriers exist, then groups of viruses that are more isolated from each other should be grouped separately and viruses that are less isolated, and more able to exchange genetic material should be grouped together.



The discovery of novel viruses provides a clearer picture of virus diversity but often presents formidable challenges to the taxonomist. Left **Transmission electron micrograph of *Megavirus chilensis*, a giant virus with a dsDNA genome of about 1.26 Mbp. Bar, 100 nm** (Chantal Abergel, IGS, CNRS-AMU). Right **Three images of the bacterial virus Lacusarx, which has a 130 kbp dsDNA genome that displays little similarity to other known bacterial viruses. Bar, 50 nm** (Lars Hestbjerg Hansen, Horst Neve).

This process of grouping is initially applied to the lowest level of virus classification: the species. Species are then collected into genera, and so on up through the levels of subfamilies, families and orders, currently the highest-level taxon permitted for viruses. However, as these groups of viruses become more divergent, or different from each other, it becomes increasingly difficult to base the classification on genetic characters alone, since comparisons between virus nucleotide and protein sequences contain more and more noise. Other characters then take on greater significance, for example, protein structure, gene order, the type of nucleic acid, strandedness and the translational polarity of the virus genome.

The result of this process is the current taxonomy of viruses, a framework that is continuously refined in response to taxonomic proposals made to the International Committee on Taxonomy of Viruses (ICTV; **www.ictv.global**) each year. This taxonomy groups together viruses that are similar to each other in a hierarchy of relationships and helps us to make sense of the virus world.

Taxonomy is important, but it is not fixed – changes are continually being made in response to new information on known and novel viruses. The mechanics of virus taxonomy are also changing, new and faster processes aimed at keeping up with the rate of discovery are being developed, as well as analytical methods based on genome sequences alone, which may eventually lead to automated classification.

The field needs young virologists who are interested in the origins, scope and impact of virus evolution and are willing to engage with the scientific discipline of virus taxonomy. This dynamic subject has an essential role to play in the future of theoretical and experimental virology. Come to the symposium below and find out more: *The global virome – the scope, causes and consequences of viral diversity*. Tuesday 10 April 2018 at the Microbiology Society Annual Conference, ICC Birmingham, UK. (**www.microbiologysociety.org/annualconference**).

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Schoolzone

Science, art and writing in schools

SAW Trust

Our members regularly engage with local schools or school-age groups, introducing them to the world of microbiology through many creative channels. The following is an example of a large consortium of mainly Microbiology Society members engaging children with the ideas of antibiotic resistance and hands-on science through the SAW Trust.

The senses of bacteria

The bacteria popped with colour,
Like rare exotic flowers,
Laying innocently on the grass.
The bacteria swam like splodges of paint,
Flicked clumsily by the infected.
The bacteria seemed so innocently beautiful.

The bacteria floated gently round in the Petri dish,
Like a beautiful lily floating around in a pond.
The beautiful white lily spun around,
Like a wild tornado, disturbing everything in its path.
The bacteria seemed to move so gracefully.

Eleanor, age 11

SAW Trust

Scientists from across Norwich Research Park have been working with the Science Art and Writing (SAW) Trust to deliver projects in schools on the theme of antimicrobial resistance (AMR). Children aged between 8 and 12 years old explored fundamental microbiology, and learned about the development of antibiotics and the current problems associated with increasing antimicrobial resistance. The scientists introduced the children to their research topics, which included looking in new places for antibiotic-producing bacteria; genome mining to unlock silenced antibiotic pathway gene clusters; and the development of new diagnostic tests for use in the surgery. The children also did some experimental work. In SAW projects, scientists team up with professional artists and writers who then use the science theme as a starting point to deliver poetry and visual arts sessions, giving the children opportunities to respond to the science through creativity.

The outputs of the projects have been brought together, along with examples of citizen science projects like the Microbiology Society's Antibiotics Unearthed project and Dr Adam Roberts' Swab & Send, and published in a new book entitled *SAW antibiotics*.

"I thoroughly enjoyed this stunning book. Educating children in such an interactive way is so important. I am passionate about addressing AMR, as are the researchers, and I hope this can help inspire future generations to engage in the efforts to save modern medicine."
Professor Dame Sally Davies, Chief Medical Officer

To purchase a copy of the book, find out more about working with the SAW Trust or to make a donation, please visit **www.sawtrust.org**.

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If you are a member and are currently doing work with schools, we want to hear from you! We are building up our resources on school–based activities and want to acknowledge our members that are doing this important work. Please email **education@microbiologysociety.org** *about your activities.*

Policy

Antimicrobial Resistance and One Health

Tackling antimicrobial resistance requires a coordinated 'One Health' approach involving human and animal health and environmental stakeholders. Participants at the Society's Focused Meeting on Antimicrobial Resistance and One Health discussed how to better inform One Health policy with science.

Participants at the Antimicrobial Resistance and One Health Focused Meeting policy session. Fiona Walsh

Antimicrobial resistance (AMR) is a common challenge for health, agri-food and environmental sectors. In 2016, United Nations member states agreed to develop "multi-sectoral national action plans, programmes and policy initiatives, in line with a One Health approach and the global action plan on antimicrobial resistance".

Better informing AMR policy with science

It is important that AMR initiatives and policies are informed by scientific evidence. Research grant applications usually require scientists to consider the potential wider impact of their research, stakeholder engagement, and measurable deliverables.

However, scientists and policy-makers often speak a different language and work to different timescales and priorities, which can make it difficult for both groups to communicate effectively with one another. Last year, at the Microbiology Society's Focused Meeting on Antimicrobial Resistance and One Health at Maynooth University in Ireland, a workshop involving researchers and representatives from funders and government agencies explored barriers and opportunities for translating research into One Health policy. Effective One Health AMR policy requires excellent scientific evidence and surveillance data across humans, animals and the environment. Research on these different components must be equally valued by policy-makers, and be supported with the necessary funding and infrastructure.

Better data for better policy

Workshop participants called for more international, multidisciplinary funding to support One Health AMR research. They also felt there was often a lack of coordination between research funders to link all three elements of One Health, although there have some positive examples of One Health funding calls, including under the European Joint Programming Initiative on AMR (JPIAMR).

However, when available data on AMR in a country is limited, for example,

to just surveillance in humans, it is very difficult for research to promote and inform effective One Health policies. One example is the European Antimicrobial Resistance Surveillance Network (EARS-Net) surveillance data for resistance in hospital-acquired infections. On these maps it is possible to identify countries with specific problems such as carbapenem-resistant *Enterobacteriaceae*, but it is not possible to identify if these resistant bacteria are present in livestock infections and in the environment via animal waste.

Participants also identified the need for experts across all sectors to better collaborate to agree common methods and standards for monitoring AMR in humans, animals and environments. Recent AMR action plans, including those published by Ireland and the European Commission, set out tackling AMR with a One Health approach. Hopefully, additional funding and coordination will improve surveillance data across all One Health areas, informing better agricultural and environmental policies to address the emergence and transmission of AMR in the food chain, and improved public health policies to minimise the transfer of novel AMR mechanisms into human pathogens.

Promoting interdisciplinary knowledge exchange

Participants also felt that the One Health focus of the conference at Maynooth University provided a unique opportunity for knowledge exchange between different sectors and stakeholders and a further need for such multidisciplinary meetings. They identified that different sectors and stakeholders need to better collaborate to develop shared priorities, methods and standards, for example, in how they monitor antibiotic use and conduct surveillance of AMR. We can all understand the commonality of AMR in each sector and learn from each other. Participants discussed common challenges for public health and agriculture, including working with the public and farmers to reduce usage of antibiotics, and the need to develop alternative therapeutics to antibiotics.

Supporting researchers to communicate their science

In addition to securing research funding, and conducting and publishing research, scientists are expected to effectively communicate their research to a wide range of stakeholders, from the public to policy-makers. Participants identified that professional bodies, learned societies and other intermediary groups have an important role to play bringing together the AMR research community's expertise to highlight funding and capacity needs to governments, and supporting scientists to effectively communicate and translate their research into policy. It is also important to appropriately communicate the risk posed by AMR for health and food security and safety, and the scientific evidence behind this to the public, raise awareness, to inform behaviour change and promote government and industry to take action.

Engage through the Microbiology Society

The Microbiology Society enables members to engage with and inform policy-makers about AMR and other microbiological issues. For example, responding to policy consultations, producing policy briefings and collaborating with the Learned Society Partnership on AMR (LeSPAR). We are always keen to hear from members working on AMR who want to inform policy to maximise the impact of microbiology.

Acknowledgements

We would like to thank the participants of the policy workshop at the AMR and One Health Focused Meeting.

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Journals update

Journal of Medical Microbiology

Since taking up the reins of *Journal of Medical Microbiology* in April 2017, we are now, more than ever, intensely aware of both the legacy left to us by our predecessors as well as our own commitment to build and improve on the journal during our term. We will also be celebrating 50 years of *Journal of Medical Microbiology* in 2018, as *Journal of Medical Microbiology* was officially separated from the *Journal of Pathology and Bacteriology* in 1968.

What have we been doing since we started as Editors-in-Chief?

At the Microbiology Society Annual Conference 2017, we co-led two scientific publishing workshops alongside the Professional Development Team at the Society. The two sessions 'How to review a scientific manuscript' and 'How to write a scientific manuscript for submission' were both well received at the 2017 Conference. We have also been chairing Editorial Board meetings and representing the journal by ensuring the visibility of the journal at conferences and Society-related events.

We have expanded the Editorial Board to better represent the international community that we serve, and revisited the journal scope leading to a revision of our Sections (and Section Editors) as follows:

- **Antimicrobial Resistance** Vincent Cattoir, France
- **Clinical Microbiology** Direk Limmathurotsakul, Thailand
- **Disease, Diagnosis and Diagnostics** Arunaloke Chakrabarti, India
- **Microbiome and Microbial Ecology in Health** Marcello Riggio, UK
- **Molecular and Microbial Epidemiology** Tim Inglis, Australia
- **One Health – Emerging, Zoonotic and Environmental Diseases** Roberto La Ragione, UK
- **Pathogenesis, Virulence and Host Response** Kim Hardie, UK
- **Prevention, Therapy and Therapeutics** Rikke Meyer, Denmark

For more information on the journal sections visit: **http://microb.io/2AZ2TIT**.

The full range of article types and submission criteria can be found on the journal website (**http://jmm.microbiologyresearch.org/about-us**).

Journal of Medical Microbiology as a presence:

To see what some of our Editors have been up to, have a read of the article on the 15th Asian Conference on Transcription 2017, Malaysia, in this issue on page 34.

It's never too early to get future conference dates in your diaries – you can get a full listing of forthcoming events at **www.microbiologysociety.org/events**. We would like to give a special mention about the Focused Meeting on Emerging Zoonoses and Antimicrobial Resistance: A Global Threat, taking place 2 July 2018 at the University of Surrey, UK, and organised by one of *Journal of Medical Microbiology*'s Section Editors, Roberto La Ragione.

Prof Kalai Mathee & Dr Norman Fry
Co-Editors-in-Chief

Call for papers: Arboviruses and their Vectors

Following the 2nd International Meeting on Arboviruses and their Vectors (IMAV) 2017 Focused Meeting, *Journal of General Virology* is inviting submissions of research papers and reviews for a new thematic collection: Arboviruses and their Vectors.

Curated by Professor Eng Eong Ooi (Duke NUS Medical School), Professor Alain Kohl (University of Glasgow) and Dr Esther Schnettler (Bernhard Nocht Institute for Tropical Medicine), the collection will present the latest advances in arbovirus research.

Articles are invited on the following topics:

- virus discovery and emergence
- virus–host interactions and evolution
- vector biology and ecology
- antivirals/vaccines

For more information on how to submit, please contact **jgv@microbiologysociety.org** using the subject line 'Arboviruses and their Vectors Collection' or go to the journal's homepage **jgv.microbiologyresearch.org**.

Microbial Genomics article processing charges

As an open access journal, *Microbial Genomics* introduced article processing charges (APCs) in January 2018. The Microbiology Society will partially subsidise these rates, which will be at the reduced price of £700 throughout 2018 (one-third of the full APC).

Any new manuscripts submitted will receive this discounted price, but free content such as invited reviews will remain free to publish. Any articles that were submitted before 1 January 2018 and are still under revision by this date will also not be charged an APC.

Microbiology Society Journals Author Survey 2018

Last year, the Microbiology Society surveyed over 350 authors to find out about their experience of publishing with a Society journal and we would like to share the results with our members.

The survey was conducted in June 2017, across the portfolio of Microbiology Society journals. The questions asked for feedback from researchers who had submitted an article to one of the journals in the past year. We wanted to find out about authors' experiences and learn where we could improve.

Would submit again and recommend to a friend

Once again, we are happy to announce that the response to the survey was positive overall. On a scale of 1–5 (1 being very poor; 5 being excellent), the response was 4 overall, with authors outlining that they would be 'submitting again' and 'recommending to a friend'. We are pleased that our responding authors have continued to have an experience that is 4/5 across the journals, in line with the 2016 results. We hope that the changes following feedback from last year's survey have made a difference to our authors.

Revised open access process

In response to feedback from 2016 regarding the open access process, we have fully implemented a streamlined online system with Copyright Clearance Centre, who handled the article processing charges for our open access papers.

Leading publisher in the field of microbiology

We asked our authors what the main reason was for submitting to their journal of choice. Across the journals, 1/3 of our respondents agreed with the statement that the Society is a 'leading publisher in the field of microbiology', followed by 'the scope of the journals'.

International reach

We are delighted that so many of our authors view the Microbiology Society's journals as leaders in their fields. Our Editorial Boards have a global reach and consist of experts within the broad scope of microbiology. We continue to strive towards continued author satisfaction and aim to remain a leader in the field of microbiology for our authors.

Peer review process and production

The overall peer review process and production were both rated as above 4/5. This result is in line with the 2016 survey and we will continue to listen to the feedback from our authors to ensure that the peer review experience is as positive as possible.

Continuous Publication

From the feedback of the 2016 survey, we have implemented a Continuous Publication model for our articles as 81% of respondents agreed on preferring the version of record being the first published form of article. This was implemented at the end of 2016.

Thank you to everyone who completed the survey, we really appreciate your feedback and hope that we can continue the success of the Microbiology Society's journals. If you have any queries or questions, please get in touch with **journals@microbiologysociety.org**.

Outreach

Member outreach activities

Microbiology Society members regularly do new and inspiring outreach activities supported by the Society. Through our grants, we have assisted many education and outreach activities including these two projects that took place in French Guiana and Sheffield, UK.

Microbiology Society members Dr Helen Brown and Michael Pascoe took an outreach programme, Science in Schools, to French Guiana to encourage interactive science learning in the region. Below is a summary from Helen and Michael about their trip.

During October, we participated in a week-long outreach programme in French Guiana, a tropical region of France nestled between Brazil and Suriname. The programme, dubbed 'Science in Schools', was a collaboration between the British Council and French Ministry of Education, which aimed to bring interactive science learning to the students living in the region. By teaching the students through the medium of English, the programme helped children to learn fundamental scientific concepts while practicing their language skills with STEM professionals.

In each session, we delivered three activities that covered the fundamentals of microbiology. The first activity consisted of taking swabs from various sources to see how prevalent microbes are. The children were particularly excited when they discovered they could test which toilets were dirtier: the girls' or the boys'! The second used Giant Microbes to introduce pupils to some of the most common disease-causing microbes in humans, as well as some which comprise our microbiome and contribute to health. The final activity was 'Blast-a-Biofilm', which uses water pistols and hair gel, and introduces the students to the concept of biofilms using the example of dental plaque. This also helped them to understand the role brushing teeth plays in preventing dental caries. In addition to interacting with pupils, we also ran a masterclass with trainee teachers at the Université de Guyane so that they could learn how to incorporate interactive learning methods into their own lesson plans.

Pupils from École des Citronniers in Cacao examining agar plates they prepared in the swabbing activity.
École des Citronniers

Over the course of the week, we travelled to five major areas of French Guiana, including Maripasoula, Cacao, Kourou, Cayenne and Saint-Georges-de-l'Oyapock. The communities in each of these areas had a distinct background including Creole, Hmong, Metropolitan French and native peoples, and demonstrated that French Guianan society was a true cultural mosaic. Reaching these isolated and economically deprived areas also required unusual transport arrangements. Maripasoula was an hour's flight over the Amazon in a very small plane (think *Indiana Jones*!) while the village of Trois Palétuviers was reachable only by catching a 45-minute ride downstream of Saint-Georges in a pirogue.

Transporting learning props to remote communities and finding a suitable parking space on the river added another layer of complication to the daily commute.

Although we've previously engaged in outreach in the UK, participating in Science in Schools was a uniquely challenging experience. As many of

Happy customers! Michael Pascoe

the students had limited English skills, we had to think carefully about the key messages that we wanted to convey and how to do that in the most simple terms. However, the satisfaction we both felt from teaching these children certainly made the experience one we will treasure and remember fondly for the rest of our lives.

We would like to thank the British Council for arranging our participation in the Science in Schools programme and funding the trip, the Microbiology Society for awarding the outreach grant to purchase many of the learning materials, and to Cardiff Institute of Tissue Engineering and Repair (CITER) for providing cloths, posters and badges. Special thanks go to all the pupils and teachers of the schools we visited, and especially the staff of Académie de Guyane for making us feel so welcome and ensuring we got to where we needed to be. If you are interested in finding out more about the British Council's Science in Schools programme, you can visit the website: **http://microb.io/2D5Up4b**.

The Horror Within

Society members Kirstie Rawson, Mel Lacey, Sarah Forbes, Emma Henly and Alex Andrews were part of a team who ran an event about the human microbiome with a 'spooky' Halloween spin. Below is a summary from Kirstie about how a Microbiology Society grant supported this great evening.

The human body has several unique ecological niches and is home to a plethora of diverse micro-organisms. From aiding in digestive processes to fighting off invading pathogens, this invisible community plays a significant role in maintaining the health of the human host. This project aimed to establish a new outreach exhibition with which to educate the public on the importance and multiple roles of their microbiome. To do this, we planned to build a light box to showcase many different Petri dishes with different selective agars and bacteria on, and show this at a small event at the local museum. The grant was originally awarded for an adult education evening but during the planning stages, we quickly realised we could make the event bigger and decided to run the event as a science-fuelled horror exhibition for Halloween. Colleagues at Sheffield Hallam University were successful in a subsequent grant application from the Royal College of Pathologists, which enabled us to provide a series of wet experiments throughout the event. The Horror Within was born: an adult-only, after hours, social event which was part of Millennium Gallery's Live Late series, hosted on Friday 27 October 2017.

A series of mini-lectures spanned the evening, covering a variety of topics from the importance of your microbiome at birth and the importance of poo, to the plague apocalypse and the horrors encountered in laboratory diagnostics. Running parallel to the lecture sessions were a number of experiments, including the extraction of DNA from cheeks and fruit, discovering parasitic worms and a "make your own poo" stall. The experiments were a massive success as they tied in nicely with our lectures, and people loved getting stuck in! There were also several exhibits, including our light box, which allowed a more informal, but more detailed discussion of microbiology.

The feedback from the event was very positive; those who attended gave us an average of over 4.5 out of 5 stars. On asking people what their favourite part of the event was, a selection of comments were: "agar plates looked super pretty and the bugs came from different areas of the body which was interesting!"; "about how small bacteria actually [are] and how [they] can affect the human body," and "all of it! It was brill." Interestingly, over 40% of those who visited the event hadn't visited a science museum, science festival or a laboratory in the last year, meaning that we engaged with many people who do not usually engage in science. We are delighted with this as it meant we achieved our goal of providing an evening that was not only educational, but interactive and enjoyable too. I would like to thank the Microbiology Society once more for supporting our vision, and we will be using the light box at many future outreach events.

Are you running any outreach events?

If you are running any education and outreach events, we want to hear about them. Please email **education@microbiologysociety.org**.

Early Career Microbiologists' Forum Update:

What's new for 2018? Committee members, networking events and the Summer Conference

The ECM Forum Executive Committee has been expanding! We have recently welcomed Grace Russell as our second Undergraduate Representative, after Amiee Allen stepped down in September. Grace hopes to use her one-year term in the role to develop a new network for undergraduate microbiologists where they can access career opportunities and enhance their university experience. Society Champion Colman Ó Cathail is now the new Finance and Operations Representative, and will be working closely with the Finance and Operations Committee to monitor the ECM Forum budget. In addition, Dr Helina Marshall has been selected as the first representative who will focus solely on Publishing, with Andy Day continuing his term working with the Policy Committee.

The Annual Conference in Birmingham is approaching rapidly and you should by now have found out whether you have been chosen to give an offered oral or present a poster. These are both fantastic opportunities to gain experience in communicating your work outside of your group or institution. It is worth remembering that you can use these presentations as your entry to the Sir Howard Dalton Young Microbiologist of the Year competition, an award that recognises excellence in science communication by a PhD student or postdoctoral researcher. The 2017 winner Daniel Hurdiss said that "it is a great feeling to have been chosen as the winner, especially given the calibre of the other finalists. Without the opportunities to present at the Annual Conference, I wouldn't be the confident public speaker I am today. Presenting your work to microbiologists with such broad scientific interests can be quite daunting, but luckily enthusiasm can be contagious." A selection of poster prizes will also be up for grabs so there is much to be gained from presenting at the Conference. The ECM Co-chairing scheme will also run this year, so keep an eye out for ECM Co-chairs.

We want to increase the ECM Forum's presence in Birmingham this year and so will be leading the popular pre-Conference networking event. This was a huge success last year and promises to be even better this time round! If 2018 will be your first Annual Conference or you have not yet attended the networking session then I really recommend joining us. You can mingle with fellow early career researchers, as well as senior Society members, in a semi-structured way. Refreshments are included in the ticket price so there is no excuse not to come down for an enjoyable evening! We are expecting the event to sell out so be sure to book when you register as soon as possible.

A large part of the Committee's schedule in 2018 is dedicated to organising the inaugural ECM Summer Conference. The aim is to provide undergraduates with an event where talks are given by invited early career speakers on a range of different topics in microbiology.

As always, do get in touch if you have any questions or suggestions, or indeed any microbiology-related events that you would like us to help publicise!

Rebecca Hall
Communications Representative,
ECM Forum Executive Committee

Membership Q&A

This is a regular column to introduce our members. In this issue, we're pleased to introduce Agah Ince.

A. Ince

Where are you currently based?

My main research and R&D station is in Acıbadem University, which is a relatively young thematic medical university in the heart of Istanbul, Turkey. I am a research scientist focusing on R&D initiatives on interdisciplinary Applied Microbiology projects. I am also responsible for international relations.

What is your area of specialism?

Microbial diagnostics and virology. I am currently focusing on synthetic biology and epigenetics.

And more specifically?

I am interested in developing simplistic, sensitive, on-site diagnostic tools and applications for using in the rapid diagnosis of diseases/pathogens. I can define myself as a cell/vector-farmer.

Tell us about your education to date.

I obtained my bachelor's in Biology and Science Education, and my master's in Cell Biology from Ondokuz Mayıs University in Samsun, Turkey. I then received a first PhD in Microbiology from the Karadeniz Tech University in Trabzon. This was followed by postdoctoral research at Wageningen University, Netherlands. I also have a second PhD degree in Virology/Biochemistry. I try to keep myself on the applied part of science as much as I can, so I had my sabbatical at the United Nations on the control of vector-borne disease agents. I am also directly involved in R&D infrastructure. I am a founder of two biotech companies active in medical diagnostics and work closely with related local industrial companies.

Where did your interest in microbiology come from?

From my grandmother who taught me how to make yoghurt, cheese and grape products. When I went to university I realised that I had learnt a lot of basic biology while living with her on the farm surrounded by nature in Arhavi (northeastern Turkey).

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

I observe various forms of discrimination (gender, age, nationality, race) in the scientific community. My personal opinion is that discrimination is sometimes unfairly used by people to gain control. Structuring an interdisciplinary and socially active team is challenging. To overcome these obstacles, I share my feelings and experiences with my colleagues and students, by accepting the risks and by continuing doing my work as decently as possible.

What is the best part about 'doing science'?

It is possible to create your own freedom and then help other people to reach their dreams. I also like the artistic part of science: the beautiful microscopic images, and the fact that you can understand mechanisms that can be used in an applied way, such as training cells to attack pathogens or misbehaving cells (cancer).

Who is your role model?

Mustafa Kemal Atatürk, because of how he was an interdisciplinary person combining: being an army officer; revolutionary statesman; writer (including the first geometry book in Turkish in which he defined all the fundamental mathematical and geometrical terms, and provided examples of basic axioms and theorems); and the first President of Turkey. He used scientific norms as a base in his management during a time in which dictatorship was in fashion. I think science and research would benefit from such a revolutionary mind nowadays.

What do you do to relax?

Swimming, playing squash, computer games, and brainstorming with people from different backgrounds. I also prefer to go into nature to find food by fishing or hunting.

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

Sufi music. Calm spiritual music with traditional instruments, such as the Ney. A water-resistant photo album that includes all of my loved ones.

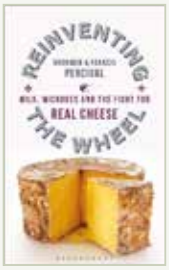
Tell us one thing that your work colleagues won't know about you.

That I have already found out how one virus can be infected by another virus. But seriously: my opinion about most conventional education systems, which are rudimentary and lack the power to give people self-confidence and vision for the future.

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

Being an astronaut was always my fantasy when I was a kid. I always wondered about the universe. But this is still in science. Outside science, I would be a good househusband, to help raise kids and take care of my family while running a farm.

Reviews



Reinventing the Wheel: Milk, Microbes and the Fight for Real Cheese

Written by B. and F. Percival
Bloomsbury (2017)
£16.99 ISBN 978-1472955517

Part manifesto, part history and part reference book, this summary of modern cheese-making will appeal equally to microbiologists, cheese aficionados, farmers and cheesemakers. With good humour, the two charming and well-informed authors (Bronwen Percival is the cheese buyer for Neal's Yard Dairy; her husband Francis is a food and wine writer) provoke debate about cheese, but also about the state of everything related to food, land use and modern consumption.

Chapters review the factors that govern production and quality of cheese, largely in northern Europe and the US. The Ecologies chapter sets the scene with today's re-assessment of the benefits, hazards and decline of microbial diversity in milk, and introduces the scientists whose work has challenged the predominant "destroy and replace" strategy for managing microbes in the dairy industry.

Setting out the current tensions in the market, and pondering the success of 'real' ale and bread, the authors state their ambition for "real cheeses made in the context of specific places". The biochemistry of cheese production leads into the source of the milk: the specifics of dairy cattle genetics is a re-evaluation of the utility of the ubiquitous black and white cows.

A recurrent theme is the problem of treating milk as a bulk commodity: market forces may now finally favour smaller scale producers. The Microbes, Risks and Cultures chapters are the heart of the book for microbiologists. The predominant species feature alongside those endowing particular flavours, and there is a thorough assessment of pasteurisation and dairy hygiene, and even difficulties with bacteriophages.

The authors firmly set out their stand for unique cheeses produced with characterful milk with as few inputs as possible – but must still ask, is it possible, after so much loss of expertise, to reinvent the wheel? To manage this scope and detail without clunkiness and errors is a tour de force.

Elinor Thompson
University of Greenwich

For more reviews, please visit the online issue of *Microbiology Today* at **microbiologysociety.org/microbiologytoday**

Comment

Every microbe matters: making movies of single cells

Bruno Martins & James Locke

The first time human eyes saw a microbe was through the microscopes of Antonie van Leeuwenhoek in the 1670s. His microscopes may have looked crude by modern standards, but were powerful enough to distinguish individual cells of fungi, protists and even bacteria. Van Leeuwenhoek's contemporaries were astounded by the existence of this world of tiny creatures with strange forms and going about on mysterious errands.

In the following centuries, microscopes were used to compile a basic natural history of microbes. They could not be used for much more. Many of the key discoveries that gave birth to microbiology in the 19th century, and to molecular biology in the 20th century, largely bypassed microscopy. Bulk-level studies of pure cultures, in which billions of cells from a single strain are cultured and assayed together, revealed a treasure trove of intracellular biochemistry. As a side effect, we also came to think there was a sameness about how individual microbial cells behave.

In recent years, advances in microscopy, such as increased automation of imaging, fluorescent proteins, computational analysis and microfabrication, forced us to revise our view and realise that microbial cells also have their own individual distinctiveness. At the same time, this distinctiveness can often enable decisions that work for the benefit of a colony as a whole. Static images, isolated snapshots of a particular moment in the life of the colony, offer glimpses of microbial individuality. Time-lapse imaging, or movies, of single cells bring this individuality into full view, tracking it regularly through the lifetime of a microbe. Our lab and others have been using microscopy movies to understand how single cells make decisions, and what lies at the origin of these decisions. They may owe to the microbe's internal state, or be due to extracellular circumstances, be it neighbouring cells or environmental cues.

How to be a movie-maker

The process of single-cell movie-making is straightforward, but each step presents technical challenges. First, live cells are laid in a support medium, where they continue to grow and divide, while sitting for hours or days on a microscope stage. An automated set-up snaps and stores pictures at regular intervals. Next, computer software analyses these pictures, creating maps that demarcate the boundaries of individual cells, and tracking which cell is which through consecutive movie frames. Typically, each microbe has been transformed to carry sequences of DNA coding for fluorescent proteins that glow under the appropriate wavelength of light. Finally, by superimposing this glow onto the cell maps, we can measure how much protein, or gene expression, there is in each cell over time.

What single-cell movies can tell us

Why bother measuring single-cell gene expression through time? The main reason is that by finding out what

individual cells are doing, we can discover cell behaviours that are hidden in population averages. Recently, our lab used single-cell movies to reveal how certain genes in photosynthetic bacteria are turned on twice every day. These genes are controlled by an internal 24-hour clock, which completes only one full cycle every day, as our own body clock does. It was therefore surprising that certain genes can complete two cycles per day, but, because each cell is not in perfect synchrony with its neighbours, the collective average masks this behaviour away. Ignoring the individuality of each cell causes us to see only one cycle, when in fact there are two.

Single-cell movies of fluorescent proteins can therefore reveal large variability from one microbe cell to the next, even for genetically identical cells in the same environment. At first, it was thought that this variability, or noise, was a nuisance caused by low protein numbers and the small cellular volume of microbes. However, it has become clear that this cell-to-cell noise can provide a function. We are only just beginning to understand the range of ways through which individual cell dynamics can shape population-level behaviours.

Single-cell individuality and collective function

Natural microenvironments change in unpredictable ways, and it may be impossible for any one microbe to respond (by activating the appropriate genetic programme) in time. For example, bacteria are often attacked with antibiotics. If the dose is high enough, all normal cells die. Yet, after the antibiotic is washed away, the population occasionally returns, in the clinic or in the lab. Time-lapse microscopy lays bare the strategy bacteria use to cope and survive. Just like any person taking an insurance, weighing a financial commitment in the present against the risk of catastrophic failure in the future, the bacterial colony survives by setting aside a small number of cells that enter a state called persistence, a kind of dormancy. These individual bacteria cannot grow, and therefore reduce colony yield, but at the same time, dormant cells can cope with antibiotic stress. Single-cell movies that have, by now, become classics show rare cells randomly entering, and later exiting, that dormancy state. When an antibiotic stress comes in, all other cells die, but persisters later emerge from dormancy, behaving like normal cells and quickly reproduce to regenerate the colony.

Greater control with microfluidics

Single-cell imaging is not just about microscopes and cells. One of the allures of the technique is the possibility of watching in real-time how individual microbes react to quick changes in their environment, like in the case of persister cells. To accomplish this, the skills of physicists and engineers have made way into the microbiology lab. One sign of this 'invasion' is the rise of experimentation in microfluidics. Microfluidic chips are small devices, made with a type of silicone polymer, of micrometre-size channels that have been designed to fit cells in a single layer. A liquid broth with nutrients or stress-inducing chemicals is flown continuously through the micro-colony, and can be swapped instantly with a broth with a different composition at pre-specified times. Many groups, including our own, employ a contraption that lets most cells be washed out with the flow, but retain some others in place. These cells can then be imaged for, in principle, an unlimited time. Rare events, or processes that develop over a long time, such as how single cells age, can be studied in unprecedented detail. Other groups are using special devices with wider chambers to study the treks of single cells, allowing us to understand how bacteria move away from threats or towards targets.

Time-lapse of a *B. subtilis* colony in a microfluidics chamber shows different individual strategies in response to a chemical stress (green cells turned a gene reporter on, dark cells kept the same gene reporter off). Darker shades in the background are structural features of the chamber. Christian Schwall, University of Cambridge

New frontiers

A major goal in the field of biology is, of course, to understand how cells function in real natural environments. In nature, many of our favourite microbes live in densely packed communities called biofilms, where they engage in behaviours not seen elsewhere and where cell-to-cell diversity is high. However, biofilms present a considerable challenge to single-cell time-lapse imaging. Cells can become aligned in any direction in 3D space, making their boundaries hard to map. Traditional wide-field microscopy illuminates the sample evenly and only scratches the surface of the biofilm. New computational techniques applied to confocal microscopy, which blocks out-of-focus light and can see through masses of cells, have just begun to penetrate into this secluded world of microbial individuality. As we keep pushing these and other boundaries, single-cell movies will continue to reveal the complex and dynamical lives of microbes.

Further reading

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Bruno Martins

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Bruno Martins was originally trained in Physics, before embarking on a PhD in Systems Biology at the University of Edinburgh. Later, he moved to the University of Cambridge, where he has been studying the cyanobacterial circadian clock using quantitative single-cell approaches, as well as synthetic biology.

James Locke

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James Locke is a group leader at the Sainsbury Laboratory at the University of Cambridge. His group is using movies to examine gene expression at the single-cell level in bacteria, cyanobacteria and plants.

What do you love most about your job?

James: Moving to the Sainsbury lab, where everyone tries to collaborate rather than compete, has been a revelation.

Could you describe a typical workday?

Bruno: On an ideal day, I organise my time around starting a microscopy movie. The microscope room remains a magical place for me. Every time I bring a sample into focus, I feel a rush of excitement in anticipation of what I might see. Time-lapse imaging is fully automated these days, so my attention is quickly drawn to making sure the computer scripts we wrote to control the microscope are correct. Once the experiment is running, I sit at my desk and analyse last week's experiment. Computer software processes the images and extracts the raw data. The real fun starts later, when I get to apply different mathematical tricks in search of patterns that may not be obvious at first sight. Our lab combines experiments with theory, and I have a background in physics myself. So, on a lucky day, the data will be intriguing enough to warrant finding a quiet room to start sketching some equations for a mathematical model. I simulate it on a computer the next day.

On an actual typical day, setting the time-lapse movie was easy enough, but I noticed a problem with last week's experiment, so its data is useless. Or maybe its results were inconclusive. Either way, it's back to the drawing board. Frustrated, I pick a paper from the backlog pile on my desk, go grab a coffee, and try again tomorrow.

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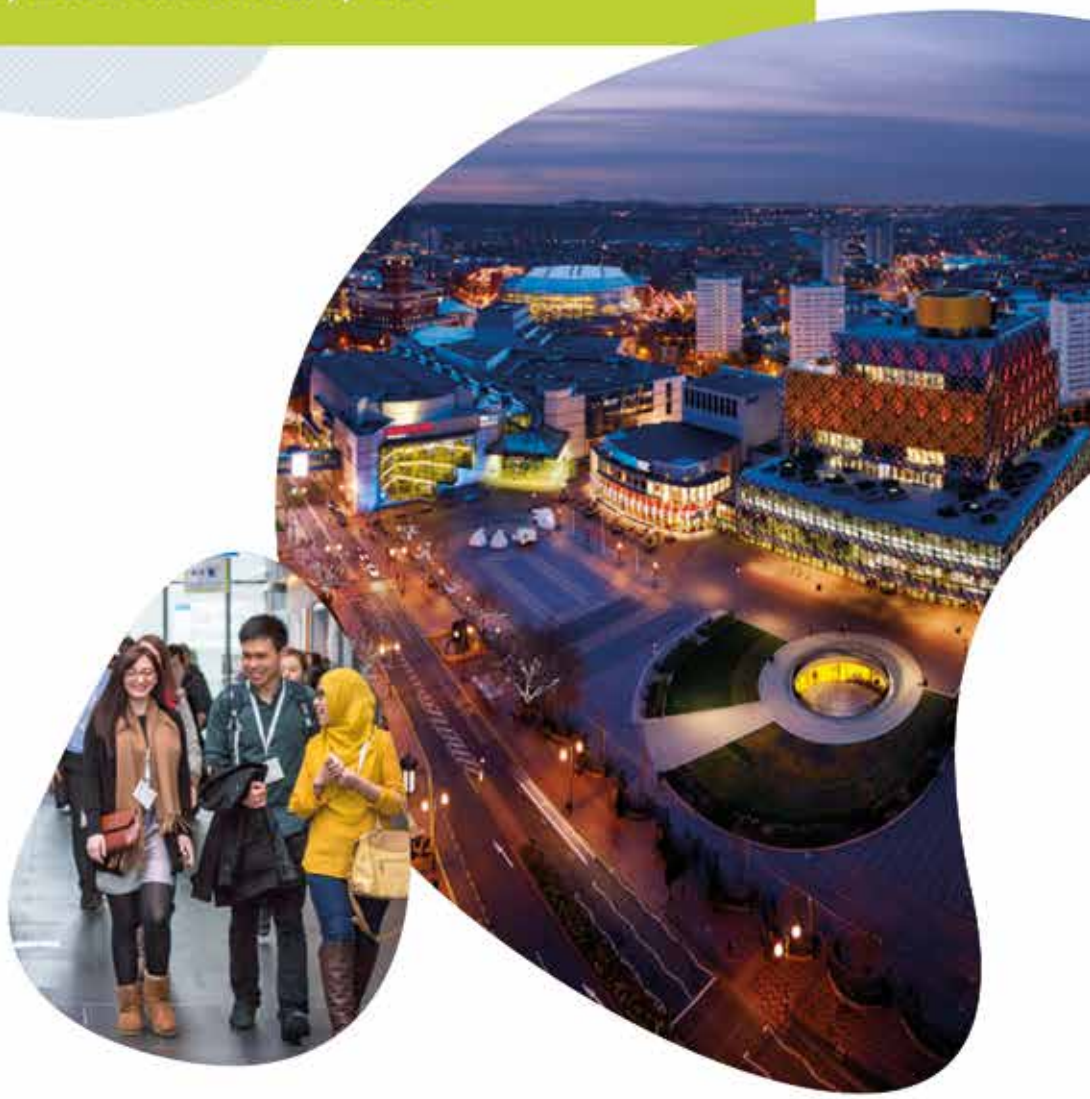

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