MICROBIOLOGY TODAY

47:1 May 2020

75 YEARS

Why Microbiology Matters

We are celebrating our 75th anniversary by showcasing why microbiology matters and the impact of microbiologists past, present and future.

MICROBIOLOGY SOCIETY

Editorial

Welcome to *Microbiology Today*, which has a new look. This issue is the first of two special editions of the magazine to be published in the 75th anniversary year of the Microbiology Society. As we look back and celebrate during 2020, we are also considering 'Why Microbiology Matters'. The longer you think about it, the more you realise how in so many ways it does.

Whole Picture

Since the first observations of microbes by Antonie van Leeuwenhoek in the 1600s, our understanding of how microbes underpin and impact our lives has advanced considerably. From discovering their life cycles and roles within various environmental niches to harnessing them in industrial processes, and, not least, our ability to utilise them for good, to vaccinate and treat diseases, with many diseases now known to be caused by microbes.

This edition offers a range of insights covering the gamut of the microbial world, with articles outlining why microbes matter for our environment, our health and even space exploration.

The first section is introduced by Lindsay Hall, who shines a spotlight on microbiomes. Lindsay focuses on how research on the interactions between microbial life and their environments has opened up a world of understanding. This section also highlights how our increasing knowledge of these interactions could lead to improved agricultural output and management, or even the creation of a microbial 'seed bank'.

In the next section, Laura Bowater considers the challenges we face when trying to understand bacteria. Laura provides context and outlines the scale of these challenges by discussing the issues related to antimicrobial resistance and the possible solutions. The articles in this section also provide insight into how new models of microbial culture can aid our overall understanding of microbes *in vivo*.

Moving on to our attempts to prevent disease, Norman Fry's section introduces us to vaccines and the global challenges faced in this arena. Reminding us of the many diseases for which vaccines are now available, the articles clarify the vital role vaccination plays in global health.

Public perception of microbiology can often focus on human health and disease, which can mean that the majority of microbes that have a host of other lifestyles and functions can be overlooked. The articles introduced here by Katherine Duncan describe some of these many microbes which can thrive in extreme conditions and are found in every niche around the globe.

Part of the reason for the success of microbes in these varied environments is their genetic plasticity. Charles Dorman introduces the next section on microbial genetics and the role it has played in advancing modern biotechnology. From the original discovery of restriction enzymes through to potential future uses for CRISPR-Cas, the articles presented give real insight into the significance of this area of research.

The advances in microbial genetics, taken alongside technological advances outside the field of microbiology, allow us to consider the role microbiology could play as we progress through the 21st century. Bryn McCulloch and Thorsten Allers discuss new frontiers being tackled by microbiology, alongside articles which help us to see where microbial life has come from, how we can study these complex communities and whether, in the future, microbes could support human space exploration by going where no microbe has gone before!

Given the pandemic spread of COVID-19 it is only too easy to see why virology holds such a central position in both microbiological research and in public perception. Nicola Stonehouse and Natalie Kingston introduce this section, highlighting both viral structures and the ways in which we can manipulate them for human benefit.

In these extraordinary times it has been heartening to see the wonderful responses from microbiologists working to help support the healthcare system. In this year of disastrous contagion which is changing all our lives in different ways, we hope these articles may provide some respite from the overwhelming flow of daily news, and give a broader outlook on microbiology than the one on which we all find ourselves focused at the moment.

Rowena Jenkins

Editor

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Unlocking the world of microbiomes: exploring microbial communities

This section considers some of the interactions between microbial life and their environments in this developing area of science.

Understanding bacteria and challenges in microbiology

This section highlights some of the many challenges we face understanding bacteria, with a focus on the global issue of antimicrobial resistance.

Vaccines: the global challenge for microbiology

This section describes the crucial role vaccination plays in health.

Microbes and where to find them

This section introduces some of the many microbes that thrive in niches around the globe and considers how microbes could exist outside of our world.

Microbiology and genetics

This section outlines some of the advances that have been made in modern biotechnology and the significance of this research to microbiology.

New frontiers in microbiology

This section considers the ever-growing tree of life, how we can study complex microbial communities to gain new insights and the possibility of discovering life on other planets.

Understanding viruses and challenges in microbiology

This section focuses on viruses, their structure and how we can manipulate viruses to benefit society.

Inside the gut – microbiome and human health. Chloe James

Features

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From the President

Our anniversary celebrations began at the start of the year when we launched the Why Microbiology Matters project, after a call to the community in 2018 to ask microbiologists to submit their ideas. This special issue of *Microbiology Today* focuses on the seven topics submitted and a range of microbiologists have shared their thoughts and research.

The vibrancy and diversity of our community is clearly represented when looking through the answers to the question "Why does microbiology matter?" We are working in areas that impact people at all points of their lives.

Now, more than almost any other time in recent history, as I sit in my makeshift home office looking at an empty street, it must be clear that microbiology really does matter. Due to the spread of SARS-CoV-2, the cause of COVID-19, we were unable to meet at our Annual Conference. However, we will not lose all of the exciting planned programme. For example, the special anniversary Fleming Showcase day planned for this year will now take place at Annual Conference 2021 in Birmingham. I look forward to meeting you there. The President's Roadshow will also be postponed until next year. I hope to see you at a future event if you are able to attend one, to share your research and network.

Do take advantage of the opportunities the Society offers and progress your career, promote your science and consider ways to engage with your community by sharing information about your research.

You can do this as part in our 75th anniversary celebrations, by submitting your images to the Microbiology Images project. Submitting your images, so they can be shared with the public and wider microbiology community, is a great way to promote your science and get involved with the Society. Find out more on our website: **microbiologysociety.org/MicroImages**.

The Society's Policy team is collating case studies on three key areas (antimicrobial resistance, soil health and the circular economy) for the A Sustainable Future project to illustrate the importance of microbiology in helping to address the United Nations Sustainable Development Goals (SDGs). Contact **policy@microbiologysociety.org** if you would like to contribute. The Policy team would especially like to hear from members who have developed interdisciplinary collaborations, worked with industry, non-governmental organisations (NGOs) or policy-makers, or those that have made a novel discovery which impacts the SDGs.

As part of our ethos to ensure your research is seen by as many people as possible, the Society's journals launched 'Publish and Read' at the end of 2019. It has been taken up by institutions across the world. Check to see if your institution has the package in place and take advantage of fee-free open access by visiting our journals platform: **microbiologyresearch.org/fee-free-open-access**. If your institution isn't yet signed up, find out how they can: **microbiologyresearch.org/publish-and-read**. The Society has also temporarily removed the paywall from our journals' platform **microbiologyresearch.org** until further notice due to the global efforts made to curb the spread and impact of SARS-CoV-2. This should help microbiologists away from their workplaces to access resources.

I would like to take this opportunity to request nominations for the 2021 Prize Lectures and 2022 Prize Medal. The prizes reflect our community so please nominate someone you feel deserves recognition and please don't assume someone else will. Anyone can nominate. Submit your nomination: **microbiologysociety.org/prizelectures**. The ballot for those nominated to Council, Committees and Divisions will soon open in June. Details can be found on the website: **microbiologysociety.org/elections**.

I hope you enjoy reading this issue. The Why Microbiology Matters topics cover some of the pivotal subjects affecting both science and society and underpin our future research focuses and those of generations to come. Microbiology holds the answers that will secure society's future, and our role as microbiologists is more vital than ever.

Judith Armitage
President

president@microbiologysociety.org

From the Chief Executive

This is a special year for the Microbiology Society as we celebrate our 75th anniversary. Unfortunately, our plans to celebrate have been knocked off course by a microbe – cancelling Annual Conference because of the spread of the virus that causes COVID-19 was an extremely difficult decision for Council. It underlines why microbiology matters.

At the very first meeting of the Society, on 16 February 1945, the founding President, Alexander Fleming, together with Marjory Stephenson, Muriel Robertson and about 200 others, emphasised the breadth and importance of microbiology. Fleming stressed, "the common links which united the various branches into a whole". He also set the culture of the Society as a welcoming community.

Although many things have changed, these ideals remain central to the purpose of the Microbiology Society.

From the early days, the Society has aimed to be a strong voice for our membership and the wider microbiology community. Fleming's inaugural address, for example, included trenchant observations on the organisation of the British university system. This theme also continues strongly in our work. Science Foundation Ireland (SFI), the largest single funder of scientific research in the Republic of Ireland, recently consulted on its future strategy. We surveyed our Irish members, drafted a discussion paper to stimulate debate and held a series of workshops with members in Ireland. The level of engagement from members was extremely high and resulted in our position statement, released earlier in the year. This considers what further steps we can take to ensure that the wider issues of funding microbiology get sufficient attention.

Microbiology deserves more attention because it is important – and this is shown with abundant clarity in our Why Microbiology Matters project. During the anniversary, we are shining a light on the role of and value of microbiologists working to resolve important global issues, and we are generating new content based on your work. We asked you to nominate the discovery or event that best showcases why microbiology matters, and how it affects almost all aspects of our lives. From those submissions, we designed new collections of themed digital material, collating members' stories in one place for the first time. In this issue of *Microbiology Today*, we delve further into these areas – to help foster understanding of how microbiology addresses global challenges and to reinforce the importance of the discipline in 2020 and beyond.

Among the content that is brought together in Why Microbiology Matters is of course research published in the Society's journals. Fleming and the other founders of the Society were frustrated that they could not start a journal straight away, because there was a shortage of paper and restrictions on its use in 1945. But they set up a group at their first meeting to prepare the ground and, within two years, the long tradition of publishing had begun, with the first paper of the first issue of *Microbiology* being by B. N. Singh of Rothamsted, on *Myxobacteria*. Things in the field of publishing have changed a great deal since then (we do not use hard copy journals anymore, so paper is no longer important!) but it is still a huge part of the Microbiology Society's purpose to publish the best research. Our new Publish and Read deal, which gives researchers at participating institutions unlimited fee-free open access publishing in the Society's titles, is one manifestation of that ongoing commitment to the ideals of our founders.

The response of the Society's members to Council's painful decision to cancel this year's Annual Conference proved to me that the vision of our founders is now an established reality – a strong and diverse community dedicated to using microbiological knowledge for the common good.

It is a great privilege to be working at the Society in its anniversary year, looking back over 75 years, and a great responsibility as we look forward. Annual Conference will be back bigger and better than ever next year!

Peter Cotgreave

Chief Executive

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News

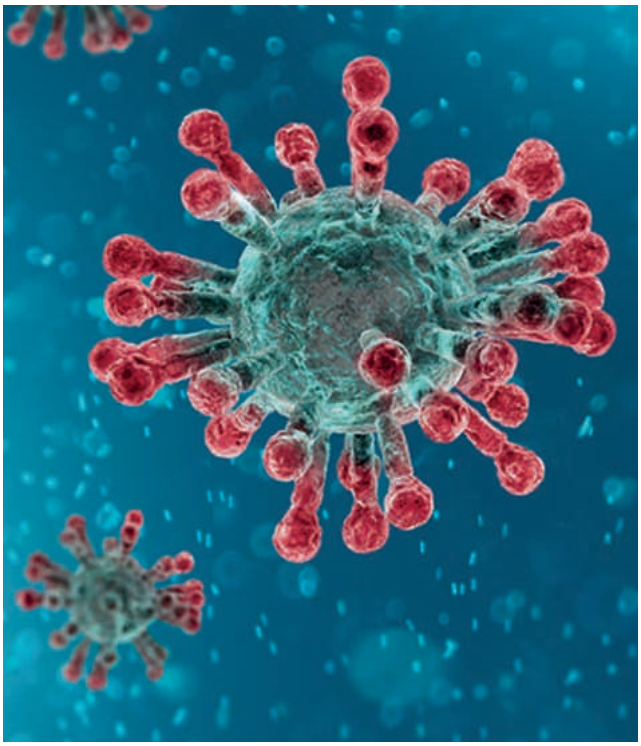
Society events 2020

This year, the Council of the Microbiology Society, as Trustees of the Society, took the difficult decision to postpone all events in the organisation's programme for the remainder of 2020, due to the continued spread of SARS-CoV-2, the cause of COVID-19.

This has meant the cancellation of the Society's flagship Annual Conference that was scheduled to take place in Edinburgh and the deferral or cancellation of its Focused Meetings, Roadshow and wider programme of events.

The Society's meetings are at the very heart of what we do to develop, expand and strengthen the networks available to our members so that they can generate new knowledge about microbes and ensure that it is shared with other communities. However, the wellbeing of our members, delegates, speakers, staff, exhibitors, contractors and local communities clearly remains our priority and the key reason behind the decision to indefinitely postpone all our events for this year.

Further details about the Society's exciting events – scheduled from 2021 – can be found on our website (**microbiologysociety.org/events**).



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A Sustainable Future: call for case studies

The United Nations Sustainable Development Goals (SDGs) are a collection of 17 global goals which aim to produce a fairer, more prosperous and more sustainable world by 2030. The Microbiology Society has decided to act in its A Sustainable Future project (**microbiologysociety.org/SDGs**). We believe that major policy decisions needed to set us on this journey require knowledge of relevant microbial activities and how these can be channelled for the greater benefit.

Microbiology is essential to achieving the SDGs and we have selected three areas in which the contributions it can make are most critical: antimicrobial resistance, soil health and the circular economy. We are looking for case studies within these three areas.

Case studies (400–800 words) will be published throughout 2020 on the project webpage, promoted on social media and may be edited for inclusion in the reports. We are particularly interested in narratives where microbiologists have worked with other stakeholders (e.g. other scientists, farmers, industry, etc.), developed interdisciplinary collaborations or made a novel discovery which impacts the SDGs. If you have an interesting story to tell, please contact the policy team: **policy@microbiologysociety.org**.

News

Get involved

The Society is celebrating its 75th anniversary this year and there could not be a better time for members to get involved. Participating in Society activities helps build on existing experience and knowledge and offers the chance to develop new skills. It is a great way to give something back and make a difference. Find out more about current opportunities to get involved with Society activities on the website (**microbiologysociety.org/membergetinvolved**).

Microbiology Outreach Prize and Prize Lecture nominations

Nominations for the Microbiology Outreach Prize, the 2021 Prize Lectures and the 2022 Prize Medal are now open. Nominations are welcome from any member of the Microbiology Society, regardless of membership period or category, by 10 June 2020. Find out more and submit your nomination on our website (**microbiologysociety.org/prizesandcompetitions**).

Elections

Following implementation of a new Governance structure in support of our organisational structure, there are three new Committees to govern the strategic objectives of the Society, along with the Finance Committee and the Early Career Microbiologists' Forum Executive Committee:

- Building Communities Committee
- Impact and Influence Committee
- Sustainability Committee

There are vacancies for positions commencing in 2021, for Elected Members on Council, the Building Communities Committee, the Impact and Influence Committee and the Sustainability Committee and on the Early Career Microbiologists' (ECM) Forum Executive Committee. There are also roles for specific areas of expertise across the Eukaryotic, Prokaryotic, Irish and Virology Divisions.

Nominations are now closed, but voting will open in June. Check the website (**microbiologysociety.org/elections**) for more information.

Grant deadlines

Date	Grant
1 June 2020	Travel Grant – for eligible members wishing to present at conferences or attend training events taking place between 1 July and 30 September 2020.
1 September 2020	Travel Grant – for eligible members wishing to present at conferences or attend training events taking place between 1 October and 31 December 2020. Careers Conference Grant – to support Undergraduate Student members wishing to attend the Royal Society of Biology Bioscience Careers Day.
30 September 2020	ECM Forum Event Fund – for ECM members requiring sponsorship for local events.
1 October 2020	Education and Outreach Grants – for eligible members requiring support for projects to communicate or teach microbiology. International Development Fund – for eligible members wishing to contribute to the development of microbiology in low- and lower-middle-income countries. Research Visit Grants – for eligible members wishing to make a research visit to a collaborator.

For more information please visit the website (**microbiologysociety.org/grants**).

Connect with the Microbiology Society on social media:

@MicrobioSoc

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MICROBIOLOGY

Publishing for the community

The Society's flagship journal, publishing high-quality international research continuously since 1947.

microbiologyresearch.org

@MicrobioSoc
#MicrobioJ

Publishing is stressful enough… so why place financial burdens on authors?

For postdocs mapping out a future career as well as principal investigators (PIs) who support them, their grant applications and their university's Research and Excellence Framework (REF) prospects, the publishing stakes have never been higher.

Gaynor Redvers-Mutton

A successful research career rests on three simple accomplishments: 1. research, 2. publish your research, 3. apply and get more grant funding to continue to research…(rinse and repeat). Let's look at each step in the cycle and find out why frontline researchers get so stressed.

Research by its very nature is for the curious. It may lead to unexpected – but useful, and sometimes fascinating – discoveries. It may lead to a particularly productive project with more collaborations and more publishing opportunities than had been expected originally. It may also run to the more prosaic, null or negative results. The point is the endgame is rarely predictable, and so the next step is not always obvious.

Publishing your research and getting your article into a journal with a high impact factor used to be the over-riding aim. This REF round, the first consideration is to publish Open Access (OA), and universities are being strongly discouraged from making hiring or tenure decisions based on the impact factor of the journal in an author's bibliography. The argument runs that this proxy is no assurance of the actual quality or impact of a piece of work. Submission and peer review are not for the faint-hearted; the process for getting published is necessarily rigorous. Reviewers and Editors take their responsibilities seriously. If you make it through to acceptance, it is time to rejoice. However, unless you know for sure that OA funds are ring-fenced for you, the OA payment process can be a real worry.

Applying for grant funding is heavily based on track record; the more OA articles under a researcher's belt, the better the chance of successful grant applications, and universities will find a postdoc more attractive leading into the next REF cycle, the more visible their work is. In effect, more OA articles are likely to attract more funding.

One of our members, Cardiff University postdoc Helen Brown, gave us a personal example of the situation:

> *"I have a side project that I have developed over the last few years. This is my way of showing independence and quality and I hope this work will be the basis for future fellowship/lectureship applications. I've had a couple of small grants to get the work going but when I applied for larger grants to progress the work, the feedback from the review panel was that I needed to show a track record in the area before I was fundable."*

Mind the gaps

OA publishing fees in the UK are often covered by block grants which are paid directly from UK Research and Innovation (UKRI) to universities, allowing for centralised administration and payment of OA fees covered by the research councils. This was devised as a way to remove the burden of paying for OA from researchers. However, block grants run out (at unpredictable times during the year) and if you miss out you need to tap into another pot of gold.

Grant funding that doesn't stretch is a very common problem because research output (the number of articles) will not be known at grant application time. Often, researchers inherit the project and will have no control whatsoever over how much was calculated for publication costs. Examples of articles that commonly fall outside the grant remit are independent research, small seedcorn or summer/student projects and collaborations, outreach

and pedagogy, and null and negative results. All this research adds value to our science, should be published and is rarely funded.

The simple three-step research cycle is easily disrupted and can lead to costly headaches. Removing this friction fed into the Society's decision to address an increasingly burdensome problem that affects early careerists disproportionately; finding the funds to publish OA.

Open science initiatives such as OA publishing have been pursued by the Society as a strategic goal for many years, hence the establishment of two full OA journals, *Microbial Genomics* and *Access Microbiology*. Until now, the only business model to underwrite OA was to charge authors an article processing charge (APC). From the start of 2020, a new model called Publish and Read will help fund OA out of institutional funds, using the block grant system, but tapping into it upfront and so avoiding the pitfalls of the current pay-down system.

Helen Brown at Cardiff University:

"Publishing is stressful enough without the added demands of not knowing where the money to publish is going to come from. At least now (with Publish and Read) we have a way to help ECRs trying to get a foot in the door."

Re-wiring subscription spend

The Society's subscribing institutions are now offered the option to include publishing OA along with access rights to content within one annual fee. Designed to be administratively light, as simple for authors as it is for librarians, Publish and Read passes the responsibility for paying for research to be published from researchers to their employers; from an individual's pocket to a centrally administered transaction pot that can be managed and monitored by an institution on behalf of their researchers.

Gaynor Redvers-Mutton

Head of Business Development and Sales

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Are you eligible to publish OA fee-free? Check our journals platform (**microbiologyresearch.org/fee-free-open-access**) to see if your library has signed up for Publish and Read.

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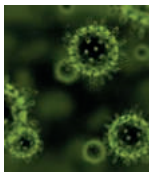

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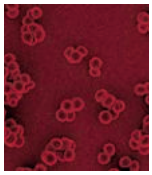

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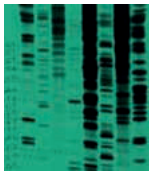

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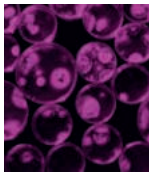

ACCESS MICROBIOLOGY
acmi.microbiologyresearch.org
#AccessMicro

We hope that you're finding these articles useful. If there is a topic you would like us to address, email us at **journals@microbiologysociety.org**.

Celebrating the Society's 75th anniversary

We would like to say a big thank you to all our members for making the Society what it is today: a vibrant and welcoming home for everyone, everywhere, who has an interest in microbiology. This year we are celebrating the 75th anniversary of our founding with activities dedicated to demonstrating the impact of microbiologists past, present and future – bringing together and empowering communities that are helping to shape the future of microbiology.

Why Microbiology Matters

Alongside this special anniversary issue of *Microbiology Today*, we are launching new collections of digital content to celebrate our 75th anniversary, under the heading 'Why Microbiology Matters'.

From the submissions received from throughout the microbiology community, we have created a series of digital content hubs, each examining an important theme in detail, including testimony from our members and microbiologists working in each area to share a wealth of rich and interactive content. We will continue to add new content to the hubs as it becomes available; therefore, our list of resources will expand and be available beyond our anniversary year, as a lasting resource for the microbiology community. The digital content hubs will be released throughout the year.

Visit **microbiologysociety.org/WhyMicroMatters** to see the topics released to date and follow **#WhyMicroMatters** on Twitter.

Celebrating the impact of microbiologists past, present and future

We will be holding our Fleming Showcase event, a day dedicated to the legacy of Fleming Prize winners which will demonstrate the impact of both established and up-and-coming scientists in addressing important global challenges, at next year's Annual Conference in Birmingham.

Visit **microbiologysociety.org/FlemingShowcase** and follow **#FlemingShowcase** for an overview of the event.

A special anniversary issue of *Microbiology Today* will be published this October, focusing on the Fleming Prize winners and their legacy.

Microbiology Images

You can get involved in our Microbiology Images project, which highlights how microbiology answers big questions by giving us knowledge of very small things. We welcome images of your science, nature, people, places and events that will inspire, inform and demonstrate how the study of microbes helps us to understand our world and our place within it.

Visit **microbiologysociety.org/MicroImages** for details on how to submit images and follow **#MicroImages** on Twitter to see the submissions we have received so far.

A Sustainable Future

We continue to work on our policy project, A Sustainable Future, demonstrating the value and raising the profile of microbiology in addressing the world's biggest challenges.

Throughout 2020, we will convert our complete journal archive into the modern format, improving the visibility and reusability of our archive, and preserving our content for the long term.

Visit **microbiologysociety.org/SDGs** for more information about the project and follow **#MicroGlobalChallenges** on Twitter.

Microbiology Book Club

In March, to coincide with World Book Day 2020, we launched a new activity to celebrate microbiology in literature. This project is inspired by member Jo Verran, who runs the Bad Bugs Book Club.

Find out more about how you can be involved by visiting **microbiologysociety.org/BookClub** and follow **#MicrobioBookClub** on Twitter.

If you are interested in getting involved in any of the 75th anniversary activities, please email **getinvolved@microbiologysociety.org**.

Look out for further updates on our website, or via Twitter using the hashtag **#MicrobioSoc75th**

75 years on: a brief update on the history of the Microbiology Society

In 1995, former President John Postgate wrote a history of the Society for General Microbiology entitled *50 Years On* which covered the founding of the SGM, as it was usually referred to, and he described in some detail many of its activities. The members voted to rename the Society in 2015, and in 2020 the Microbiology Society celebrates its 75th anniversary.

As part of those celebrations, we asked former President Nigel Brown to dig into the archives, speak to long-standing colleagues and make new friends, as he uncovered the history of the Society over the last 25 years.

"The Microbiology Society is not an end in itself," says Nigel, "It is a membership organisation, so if you want to understand the Society's history, you need to look at what it has meant for some of its members. Most of us know the journals, meetings and grants, but these have all changed markedly since 1995."

The Society's activities

Journals

The Society's journals are an important part of our vision, as well as being a valuable source of income. In 1995, there were just two titles, *Microbiology* (which had changed its name from the *Journal of General Microbiology* in 1994) and the *Journal of General Virology*. In 1997, the Society successfully bid to publish what became the *International Journal of Systematic and Evolutionary Microbiology*, the journal of record in microbial taxonomy. From January 2004, the Society took over publication of the *Journal of Medical Microbiology* from the Pathological Society.

The Society launched two new open access journals: *Microbial Genomics* in 2015 and *Access Microbiology* in 2019. This last journal is an important development, allowing, among other benefits, publication of repetition studies, negative or null results, additions to methods, posters, and Case Reports. Interestingly, publishing a journal on genomics was first suggested to Council in 1997, but was not acted upon at the time. A second suggestion in 2011 was taken forward.

Although the majority of our journals have Editorial Boards of experienced microbiologists, *Access Microbiology* is unique in using early career microbiologists, mentored by an experienced editor. This will help develop the next generation of editors and hopefully help to ensure the sustainability of our publishing activities for the future.

Journal publishing remains the largest single source of income for the Society. As Nigel Brown points out, "It allows us to make grants and contribute to conference expenses for speakers and student attendees. In 2013, one university instructed its staff to publish only in a certain subset of journals. Sadly, the Society's journals were not among them. As President at the time, I wrote to the Vice-Chancellor enquiring whether the university intended to replace the Society's funding for its PhD students' attendance at conferences. I never received a reply."

Meetings

Prior to 2001, three scientific meetings were held each year, and different interest groups of the Society would organise sessions in one or more of these meetings around New Year, Easter and Autumn. In 2001 this was reduced to a Spring and Autumn meeting. "These meetings were held in universities, where older members could relive their lost youth by staying in student accommodation!", comments Nigel. Only in 2008 was the first meeting held at a conference centre.

In 2013, the decision was made to move to a single Annual Conference in the spring, with additional Focused Meetings on specific topics suggested by members. Although they were initiated on a trial basis, these Focused Meetings have proved to be popular and have been retained. In addition, the Early Career Microbiologists' Forum now organises its own Summer Conference, the first being in 2018.

"One of the attractions of campus university meetings was that nearly everyone met in the bar in the evening," says Nigel, "and that is not possible in conference venues". Consequently, there has been a deliberate attempt to foster interactions. Early career members can attend a social event the evening before the conference programme starts. "They also meet with some senior microbiologists," says Nigel, "and discover that we are all interested in microbiology, irrespective of apparent status!"

Recent changes to the Conference agenda include having early career microbiologists act as co-chairs for the scientific sessions, the provision of crèche facilities for members with young children, and inclusion grants for those with carers' responsibilities, allowing them to attend the Conference. At each Conference since 2016, delegates have been asked to make suggestions on what the Society should start doing, stop doing or keep doing. This has provided useful feedback and has been acted upon.

Microbiology Today through the years.

When we moved from Reading to London in 2014, the Society initially decided to try outsourcing much of the organisation of the Annual Conference. "This didn't really work," Nigel commented. "Something as important to the identity of a Society as its Annual Conference cannot be produced by outsiders, however good they are."

Communication with members

As a membership organisation, the Society needs to be able to communicate with all its members. In 1995, there were about 5,000 members, the number fell in the late 1990s and then more than recovered, so now it is nearer to 6,000. In the early days, communication with members was in print – through letters and a magazine, *The SGM Quarterly*, which had been running since 1973. In 1999 the magazine became *Microbiology Today*, and it continues to provide information about the Society and about microbiological issues to members. It has won prizes for design and content as a house/membership magazine.

The Society's first website was in 1997, and the current version is now an important source of interaction with members – it had over a million hits in 2019.

A Twitter account was opened in 2009 and a Facebook account in early 2011. Twitter was used from 2013 to 2016 to discuss papers appearing in the Society's journals. The Society's Twitter account (now **@MicrobioSoc**) started with 180 followers and currently has over 44,000!

Communication with the public

The Society's mission is "Advancing the understanding and impact of microbiology by connecting and empowering communities worldwide". Nigel wisely points out, "This cannot be met by only talking to ourselves". Members are encouraged to engage in outreach and resources are available to assist them. A summer school for teachers was first run in 2002 and microbiology practicals for schools were developed with the help of a research assistant at the University of Nottingham. Subsequently, a PhD student was funded at Manchester Metropolitan University to develop novel laboratory-based microbiology activities. The Society also supports the Microbiology in Schools Advisory Committee (MiSAC), which celebrated its 50th anniversary in 2019.

Nigel recalls, "To bring the importance of microbiology to a wider audience, the Society attended the Chelsea Flower Show focusing on plant–microbe interactions, winning Silver medals in 2005 and 2006 and a Silver Gilt medal in 2012". We

The Society stand at the RHS Chelsea Flower Show in 2012.

also highlighted the problem of antimicrobial resistance, and a play, *Stopping the Spread of Superbugs*, was produced in 2012. We worked with a US-based initiative, leading to a four-year programme (2014–2018), 'Antibiotics Unearthed', in which 17 universities liaised with local schools on projects looking for new antibiotics. In 2018, the Eden Project invited the Society to take an Antibiotics Unearthed Citizen Science event to its *Invisible Worlds* exhibition.

The Society's communications team have good interactions with the media, and we are approached on a regular basis by TV and newspaper reporters to comment on microbiological topics of public interest. Nigel commented, "Issues such as antibiotic resistance, TB, Ebola and 'flu have received significant input from members, but none more so than COVID-19!" Arcane topics, such as the microbiological hazards associated with spa baths, mattresses or handshakes have also been covered!

External communications on policy

The external activities of the Society have taken many forms in addition to communication with the public, particularly communication with policy-makers. The Microbiology Awareness Campaign (MAC), started in 2002, aimed to promote the understanding of microbiology and the important role of microbiologists to parliamentarians, opinion-formers, and policy-makers. The Society also produces two-page briefing documents on topical microbiological issues, such as TB, measles, polio, swine 'flu, antimicrobial resistance and the role of micro-organisms in climate change. In 2011, an expert panel was recruited to develop a *Position Statement on Food Security and Safety*. Once published, this led to a meeting with the Government Chief Scientific Adviser organised by the Food Standards Agency. A policy statement on sexually transmitted infections was launched at the House of Commons in March 2014. "Our hosting MP, Dr Julian Huppert, tabled an Early Day Motion to highlight the research challenges raised in the document," says Nigel. An associated play for schools about condom use, entitled *If it's not on, it's not on*, was specially commissioned by the Society. In January 2018, the Chair-Elect of the Policy Committee gave oral evidence to the House of Lords Select Committee on Science and Technology about the Life Sciences Industrial Strategy.

Working with other societies

The Society has had many interactions with other societies over the years. The overarching body representing all biologists in 1995 was the Institute of Biology (IoB), to which the SGM was affiliated. In due course, the Society became a Member Organisation of the Society of Biology (now Royal Society of Biology).

The Society has been a member of the Federation of European Microbiology Societies (FEMS) since the latter's foundation in 1974, and has supported FEMS directly for several decades, hosting the FEMS office until it moved to Delft in 1998. In 2001, the Society joined the Federation of Infection Societies and has supported and helped organise its conferences since 2005.

Member benefits

In addition to our publications, conferences and meetings, there are several benefits that membership of the Society confers. Some stories of the effects that membership has had on individuals appear in this and the next issue. "These are personal benefits that came up in my conversations with some of our successful microbiology colleagues", says Nigel, "However, even those who do not go on to a career in the discipline may benefit from the opportunities to give poster presentations or talks, to network with their peers or to understand work on policy or public engagement.".

Grants

There is a number of grants available to members to attend conferences and meetings, to travel to collaborators, to supervise summer students and to undertake outreach or education activities. Conference grants are available for Postgraduate Student and Full Concessionary Members. More recently, Society Conference Grants have been made available for members with childcare or caring costs. In the mid 2000s, over 350 grants were given annually to attend the Society's two meetings. Currently about the same number are awarded to attend the Annual Conference, with a high success rate

for applications. Grants are also available to attend our other meetings, other conferences or even to organise conferences. Eligible members can also apply for FEMS grants. Science teaching or science promotion can be supported through Education and Outreach Grants. "Members who are research supervisors can apply to take a summer student into their lab on the popular Harry Smith Vacation Studentship scheme," says Nigel, adding, "the Vacation Studentships were renamed in 2011 to honour my predecessor, Harry Smith, who was President from 1975–1978."

Prizes

Prizes are available to members, and others, at several career stages, including a young microbiologist's prize and prize lectures awarded to distinguished microbiologists. In 1995 these awards were known as Named Lectures and have since been re-designated as Prize Lectures. Until 2007, it was possible for members to self-nominate for a Prize Lecture. All Prize Lectures are selected by a sub-committee of Council and given at the Annual Conference. Prior to 2013, the lectures were distributed across the Society's meetings. There have consistently been only a small number of nominations for these prizes, and a prize will not be awarded if no suitable candidate is found. Since 2018, members of Council cannot nominate individuals for prizes, thus reducing potential conflicts of interests.

The Sir Howard Dalton Young Microbiologist of the Year competition is run before the AGM in September when finalists, selected from the poster presentations at the Annual Conference and an Irish Division Meeting, each give a short talk. The talks are judged by a small group from the Professional Development Committee and the Divisions. This originated from the Young Life Scientist of the Year competition, run across several societies, with an internal selection competition. This was subsequently sponsored by and named after the company, Promega, which changed the rules in 2002. The Society's competition became the Young Microbiologist of the Year. In 2009, the competition was named after Howard Dalton, a former President.

The first Prize Medal awarded to Stanley Prusiner in 2009.

Further reading

Society for General Microbiology – Fifty Years On. microbiologysociety.org/50yearson

Microbiology Society Journals. microbiologyresearch.org

Microbiology Today. microbiologysociety.org/microbiologytoday

Microbiology Society Strategy 2018–2022. https://microbiologysociety.org/strategy

Microbiology Society grants and prizes. microbiologysociety.org/grants

Member stories

The Microbiology Society does not operate in isolation. It is a membership organisation, overseen by and driven by its members. So, as an adjunct to this brief history, this is a section to highlight some members and stories of how the Society has supported their careers.

David Blackbourn (joined 1987). As a PhD student, the Society funded him to attend a *Bacillus* conference at Asilomar, California, where he met Roy Doi. This opened up a postdoctoral opportunity working on simian immunodeficiency virus at University of California (UC), Davis, leading to six years' work on HIV and KSHV with Jay Levy at UC, San Francisco. The Society has been very supportive of him, his students and postdocs. David was on Council from 2007 to 2013, serving as General Secretary from 2009, which taught him a lot about leadership and administration. He worked with Simon Festing

on a new strategy for the Society in 2012, and with Hilary Lappin-Scott and Nigel Brown on making significant changes to the Society, including the move to London from Reading.

Laura Bowater (joined 2008) has been a member of both the Education Committee and the Communications Committee, and was previously Editor of *Microbiology Today*. These roles allowed her to build her network of national and international contacts and helped her to develop a career as a teaching-focused academic. Her editorial duties improved her editing skills and made writing easier, but also helped her establish her reputation en route to becoming Professor of Microbiology Education and Engagement. Laura's work was also recognised by the Society when she was awarded the 2019 Peter Wildy Prize.

Nigel Brown (joined 1974) remembers sitting next to Professor Pat Clarke FRS at a meeting and her being interested in discussing his PhD work. As a new lecturer, he presented his early research results at a Society meeting in 1980 and received excellent feedback. In a more senior role, meetings were an opportunity to catch up with colleagues and also enabled his students to present their work. When at the BBSRC, he discussed the BBSRC Review of Microbiology with the Society's Chief Executive. The Review was instrumental in the reorganisation of the Scientific Conferences infrastructure. After leaving BBSRC, he served the Society on a Division, on Council and as President.

Tadhg Ó Cróinín (joined 1999) has found the Society to be a huge source of support throughout his career. From his first presentations at an Irish Division meeting as a PhD student, to watching his own students get the same opportunity years later, he's been impressed by how supportive members are of each other and particularly of early career microbiologists. The Society funded undergraduate summer projects in his laboratory and provided a meetings environment where he could meet others at the same career stage, developing collaborations, celebrating success (and occasionally drowning sorrows). Meeting more senior and experienced colleagues was inspirational and knowing they faced similar challenges in their careers was helpful. The sense of community and generosity between members is the main reason he is proud to be a member and to support the Society in any way he can. This led him to seek the position of Chair of the Professional Development Committee and member of Council. He considers the Society's dedication to supporting its members' personal and professional development and the vibrancy of the community that it has built to be its greatest strengths.

Amy Pickering (joined 2012) received a Society Research Visit Grant during her PhD, which allowed her to visit a lab in the US for three months, giving her valuable insight into a different working environment. The Society also supported her attendance at a conference at which she was nominated to organise and co-chair a Gordon Research Seminar in August 2019. Amy was a founding member of the ECM Forum, serving as its first Conference Representative and is currently Chair (2019–2021).

Ian Roberts (joined 1985) was a member of Council 2001–2004 and Treasurer 2017–2020. He won the Fleming Prize in 1994 and has said winning has had a significant positive influence on his career, as did being on the Editorial Board of the then *Journal of General Microbiology*. Members first embarking on their careers, including Ian at the time, were involved in organising sessions in meetings, which enabled the development of skills outside the lab.

Karen Robinson (joined 2000) was an elected member of Council 2009–2012 and was the Chair of Scientific Conferences Committee 2016–2017. Karen's experience on Council allowed her to understand more about committee structures, which proved helpful when utilising her skills later chairing the Nottingham Medical School Postgraduate Research Committee.

Nicola Stonehouse (joined 2000) started her research career as a technician undertaking a part-time PhD on tooth enamel development and inorganic crystal growth. She moved from inorganic crystals to structural biology of bacteriophages and moved into virology as a postdoc, MRC Career Development Fellow, lecturer and professor. As a member of the Virology Division, she met and interacted with a new group of virologists, but also met other microbiologists, deepening and broadening her understanding of microbiology. She still believes that the Annual Conference is the place to meet colleagues across UK virology, consolidate existing collaborations and explore new ones. The Society funded an outreach grant, allowing her to set up teaching resources in Bangladesh, which is an ongoing activity. She has found her service on Council (2016–2019) and interaction with Society staff to be both rewarding and enjoyable.

Unlocking the world of microbiomes: exploring microbial communities

Research into the microbiome has evolved over time, allowing us to study microbial communities, genes and proteins in more depth. This section considers some of the interactions between microbial life and their environments in this developing area of science.

Microbial communities

Lindsay Hall

We live in a microbial world. Rather than living in isolation, the vast majority of microbes reside within communities, i.e. microbiomes, which play crucial roles in their 'home' environment. Thus, as microbiologists we are in a unique position to explore and seek answers to many different global challenges. We can look inside us to understand how our resident microbes impact our health and also look out to the microbes that influence the food that we eat and the environments that animals and crops inhabit. We can study the environmental microbes that reside within the places we live, work and play; at a global level we can focus on how microbes modulate our climate and the planet that we call home; and even further afield, to boldly go where no microbiologist has gone before. Focusing on how bacteria,

'Guardians of the Gut'. Lindsay Hall

viruses, fungi, archaea and microscopic eukaryotes interact with each other, their niche and their 'host' has opened up new avenues for microbiologists to explore, innovate and have impact in. The microbiome field has welcomed with open arms other disciplines within science and the humanities, as well as those working within healthcare, industry, policy and agriculture settings, together with the wider public, whose thirst for knowledge on microbiomes seems insatiable. Like our microbial friends, scientists (and microbiologists!) do not live in isolation, but rather thrive within supportive and dynamic communities. It's been 75 years since the Microbiology Society was founded, with some key 'microbiome' discoveries made throughout this period driving real impacts, like the introduction of faecal microbiota transplants to treat *Clostridioides difficile* infection. Here's to the next 75, and further exciting encounters within a world of microbiomes.

Lindsay Hall

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Lindsay Hall is a Microbiome Group Leader and Wellcome Trust Investigator. Her team study the early life gut microbiota–host interactions, with a particular focus on *Bifidobacterium*. Lindsay obtained a BSc in Microbiology from the University of Glasgow, then a PhD in Microbiology and Immunology from the University of Cambridge and was a Postdoctoral Fellow at University College Cork, Ireland, before returning to the UK to work at the University of East Anglia and the Quadram Institute Bioscience from 2015.

Why does microbiology matter?

Microbes are all around us – and play hugely important roles in all aspects of our lives. It's pretty amazing that things so small have such significant impacts, and therefore why being a microbiologist is so exciting, as we can really strive to make a difference.

Please tell us a little about the education and outreach activities you undertake in your role

As well as our lab and clinical work, the team is also passionate about wider public engagement. One of our larger projects involved working with artists and creators to develop a giant walkthrough interactive gut to convey the importance of our gut microbes. We have also more recently developed an exciting new primary school resource which is aimed at introducing children to their 'Guardians of the Gut', a project which has been supported by the Microbiology Society.

Understanding and harnessing the wild microbiome

Jack A. Gilbert

When and why did I become known as a 'microbiome researcher'? To be honest I cannot remember when, but it was probably because 'microbiome' became the new zeitgeist that helped us to get funding. I have always considered myself a microbial ecologist, studying the world of microbe–microbe interactions, and how these are shaped by the environment, be that an ocean, soil or human gut. Microbiome research is relatively field agnostic; for example, I currently reside in the Department of Pediatrics and Scripps Institution of Oceanography at University of California, San Diego. I guess that makes me the world's first paediatric oceanographer, or oceanographic paediatrician? Unfortunately, neither of these epithets is supported by my CV, but they do extol the breadth of my research interests. Of course, I would consider my research interests quite narrow – I really only study how microbes interact within a given ecosystem, and how that shapes who grows and who dies – competition, mutualism, parasitism and commensalism; but I have the opportunity to apply that to any environment, including human bodies, plant roots, industrial factories and even buildings.

Industrial microbiology

Historically, the study of microbes has been dominated by those that cause disease, but if we strip away that 50,000 lb gorilla, we are left with the study of microbes of utility to industry and exploration of their role in environmental

ecology. Industry-focused research has been dominated by microbial fermentation of foods for preservation, food spoilage and agriculture – with attempts to harness microbial chemistry in industrial processes relegated to the Holy Grail bin. Mind you, that is not to say that we have not been able to harness microbial chemistry in industrial processes, just that the number of successes is greatly outweighed by the number of failures, much like science generally, I suppose. The basic premise for discovery of novel functionalities across all industrial and agricultural practice has been to look for microbially mediated processes in natural systems, including extreme natural environments, food and soils, and attempts to isolate those organisms that perform the observed activities. For example, the discovery of yeasts as agents of fermentation, demonstrated by Pasteur (actually the work of many different scientists over many decades), led to the isolation of yeasts and the development of an industry using yeasts and their products, which is still flourishing today. The sheer number of ways in which microbial chemistry has been harnessed for industrial processes is not worth listing here, but it is exciting to note that new techniques are being derived all the time to augment our microbial toolbox. The application of metagenomic and metatranscriptomic sequencing, for example, is being used to mine the genomes of microbes across the planet for important enzymes – the diversity of coding both at the nucleic acid and amino acid level means that new variants of enzymes and chemical transformation pathways can now be catalogued, synthesised in the lab, transformed into heterologous expression models and even integrated into a synthetic organism and used to augment an existing chemical strategy. Coming up with new ways of producing nutrients in the lab, or improving the productivity, disease resistance and stress resilience of crops and animals, could help bolster food security with a growing population and the threat of climate change. Work to capture those microbes that grow on our pollution (e.g. oil spills, plastics, chemical dump sites) and harness them to clean up our mess is also a critical need. These applied approaches require further funding to tackle the worst pollution problems facing our planet – including carbon dioxide and methane production: identifying microbes that can store or transform these pollutants would be transformative.

Environmental microbiome

Since the father of modern ecology, G. Evelyn Hutchinson, identified the ooze at the centre of his dynamic food webs,

Louis Pasteur, famous for the discovery of yeasts as agents of fermentation. Illustration from 1894 stock illustration. suteishi/iStock

we have been interested in how microbes shape our visible ecosystems. The history of environmental microbiology is long and detailed, and in many ways, while ostensibly a basic science with no obvious translational impact, it has influenced the industrial and medical microbiology fields far more than most people expect. Demonstrating that most microbes in most environments are centrally important to the proper functioning of an ecosystem helped to instill in people the concept that non-pathogenic microbial metabolism may be important in agricultural and clinical settings. With the ground-breaking technical advances pioneered by Carl Woese and the intellectual contributions from scientists like Jo Handlesman, we have launched environmental microbiome research into a new era. My own contribution, the Earth Microbiome Project (EMP), provided the impetus to leverage techniques developed through pioneering efforts from Julie Huber and Mitch Sogin to catalogue the world's microbial diversity. The study, which is in fact a massive-super collaboration, has now generated data on more than 100,000 environmental samples and an equal number of human samples. It has demonstrated the

ubiquity of microbial distribution, supporting the preposition that everything has the potential to be everywhere, but the environment selects for traits, resulting in environment-specific adaptations that can also propagate throughout the global ecosystem. The concept of a global 'seed bank' which was proposed by Jay Lennon in 2011, and further supported by the EMP in 2017, creates a framework for modelling and predicting how the Earth microbiome will respond to a changing climate and land use. That's the next frontier, leveraging the ever-growing body of data to allow us to better steward the planet by giving us forewarning of impending doom, as well as potentially the tools to address it.

Biobanking for the future

Of course, our efforts to use microbes in industry and agriculture, as well as the potential to manipulate the environmental microbiome to effect changes in the equilibrium that could benefit our survival, may be moot if we cannot access the necessary microbial diversity. That is why myself and my colleagues are building a vision to install a microbiome seed bank in non-sovereign territory that could hold examples of the Earth's microbiome. Guided by the data from the EMP, we are identifying samples of whole ecosystems, including soils, water, air, plants, animals, etc. that can be stored in a viable but dormant state, with the aim of resurrecting these genomic resources when we need them most. The Microbiota Vault will be a repository of the planet's microbial heritage that could be our saviour if we are unable to halt global destruction.

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Jack Gilbert is a Professor of Paediatrics. He helped establish the Microbiota Vault and works on the American Gut Project and Earth Microbiome Project. He began his career as an ecologist at the Natural History Museum in London before undertaking his PhD at Nottingham University, a postdoctoral position at Queen's University in Ontario, Canada, and a directorship at the University of Chicago's Microbiome Center working on the Home Microbiome Project and Hospital Microbiome Project before moving to San Diego in 2019.

Why does microbiology matter?

Quite simply, microbiology is the study of the lifeblood of our planet. If we can fathom the depth of knowledge that microbes possess, we could reshape medicine, revolutionise farming and industry, colonise barren worlds and hopefully limit the damage we are inflicting on our own planet.

What do you love most about your job?

Diversity. I love that I get to work with so many unique and brilliant people and engage on a plethora of wonderful projects. Working on microbial ecology, I can be at the bottom of the ocean, in the beating heart of a hospital or on a rocket to mars. Nothing is off limits.

Microbiomes underpinning agricultural systems

Sharon Huws

Microbes associated with crops, livestock and agricultural environments are essential for food security and food safety. For example, microbes in and around plant root systems, the rhizosphere, play a role in plant growth, nutrient absorption, disease resistance and soil structure. Microbes associated with food production, storage and transport can be implicated in food spoilage and the spread of pathogens. Livestock gastrointestinal tract microbes also contribute substantially to host production, health and environmental impact of livestock agriculture. In particular, the rumen microbiome is known to influence feed efficiency, quality of ruminant products and the extent of nitrogen and methane released to the environment (Fig. 1). Indeed, the influence of microbes on agricultural

systems and food production has been known for many years.

Microbiomes and 'omic technologies

The advent and rapid growth of 'omic technologies in the past few years have increased our understanding of microbe diversity and function and have led to the terminology 'microbiome' being developed to describe microbial diversity and function in a biome. Arguably the most used terminology in the world of microbiology in the past decade is the term 'microbiome'. The Nobel Laureate, Professor Joshua Lederberg, is often quoted as being the person to coin the term in 2001 to describe a collection of microbes living within a biome. Nonetheless, a small number of publications pre-dating this use the term 'microbiome' to denote the same meaning. Irrespective, how has the coining of this term underpinned by developments in 'omic technologies helped us advance science? For many years post the advent of the first nucleic acid sequencers, studies on agriculture-related microbiomes, as well as microbiomes in general, were largely focused on metataxonomy-based studies, i.e. sequencing rRNA to assess microbial diversity within a biome. Monitoring diversity alone can be argued as being akin to stamp-collecting as it does not give us information on the function of the microbiome. Nonetheless, metataxonomical approaches are cheaper than function-based 'omic technologies and software is now available allowing a broad inference of function from 16S rDNA information. The lack of standardisation and use of controls in these studies in the past have also meant that comparing between studies has been challenging due to the number of variables in protocols. This also leads to our inability to come to conclusions on a global level. Consequently, it could be argued that few of these metataxonomic studies have moved the field on substantially, although baseline information of the underlying microbial diversity in these biomes has aided our understanding of the 'core' microbes, which are always found in these biomes. One such study is the global rumen census study, which provided metataxonomic information for rumen-faecal microbiomes from 768 samples taken from a range of ruminants and has allowed the definition of the 'core' rumen/faecal microbes across the various geographical locations.

More recently published articles using multi-omics (metagenomics/metatranscriptomics/metaproteomics/metabolomics) and system-biology-based approaches have provided a major step-change in our understanding of microbiome function. For example, these approaches aid on-farm antimicrobial resistance (AMR) risk management strategies and define target genes/proteins for animal production/health/environmental impact purposes. These multi-omic approaches also allow us to prospect for useful compounds and enzymes in agriculture-based biomes,

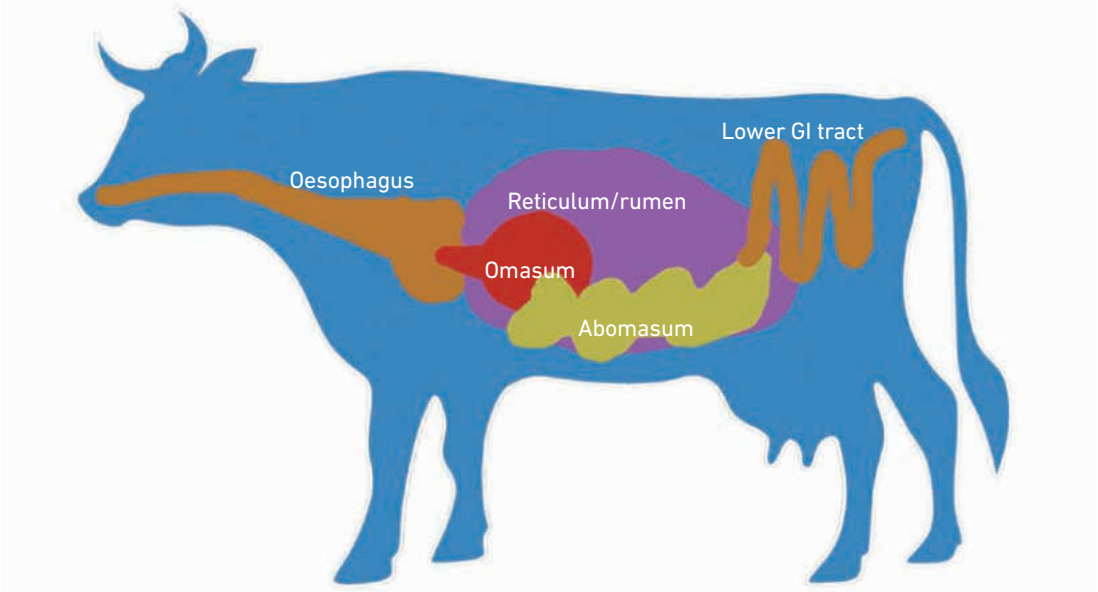

Fig. 1. Ruminant gastrointestinal tract. Most of the microbes (bacteria, archaea, fungi, protozoa and phage) inhabit the large fermentative rumen, resulting in effective digestion of dietary material. Sharon Huws

for further characterisation and commercial development. For example, a number of novel glycosyl hydrolases (carbohydrate-active enzymes) have been discovered within livestock gastrointestinal tract microbiomes which have a plethora of industrial uses, e.g. bioethanol production.

Metagenomically-assembled genomes and culturomics

Sequencing technologies were largely used to circumvent the challenges associated with isolating representative bacteria using culture-based techniques, the so called 'great plate anomaly'.

However, until recently it was not possible to isolate and construct genomes from metagenomes, which meant that assigning functions was challenging, as well as locating genes within a bacterial genome. More recently, tools have also been developed to allow these genomes to be constructed, and these are referred to as metagenomically-assembled genomes (MAGs). This represents a further major step change in our understanding of microbiomes. In the context of the rumen microbiome, there are now 4,941 MAGs available, representing a major resource for enhanced understanding and for compound/enzyme mining purposes.

Agricultural microbiomes: what does the future entail?

Of course, while the field has progressed substantially, it is important that we don't 'oversell the microbiome', a concept used by Dr Jonathan Eisen (University of California, Davis), in which he awarded prizes on social media for publications that did exactly that. This is largely a response to correlative studies and wild statements resulting from those publications without definitive proof. Certainly, in the agricultural setting, there is a need for a major push towards causative, rather than correlative studies, as few studies are available that can actually show causality. Developments in MAG isolation also provide a mechanism to move towards causality, as they provide information on the likely biochemical needs of a bacterium, allowing more informed culture-based technologies to be developed. Ultimately, having availability of pure cultures is crucial to develop hypotheses to confirm causality and the recent surge in culturomic-based activity is highly commended. In conclusion, the explosion in 'omic technologies and datasets available for agriculture-based microbiomes has been somewhat overwhelming in recent years. The lack of standardisation or controls used in studies makes comparisons between studies difficult and ultimately decreases our ability to look at global datasets using meta-analyses to increase the power of observations across geographical locations. While standardisation is challenging between laboratories in different geographical locations, the use of controls is critical for the future as we move from correlative studies to defining causality.

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Why does microbiology matter?

Most metabolic processes in nature are underpinned by microbial activity and industrial processes are enabled by the actions of microbes and their enzymes. Therefore, microbiology has always been and always will be at the core of most scientific endeavour, with few disciplines having such vast interdisciplinary importance.

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

I would say don't worry if you take some jagged routes to your final destiny. My path into microbiology has been a somewhat jagged one, and this jagged route is not one I regret as it's helped to develop systems-level thinking beyond the discipline. I'd also say take time to think – while it may seem an impossible thing to do in the 'race' towards qualifications, publications and obtaining a permanent position early in your career. Obviously, this is a utopian ideal and many scientists have other responsibilities, such as having a family, but it gets much more challenging as your career develops, therefore, make the most of this time.

Find out more about this topic on our website:
microbiologysociety.org/WhyMicroMatters

Understanding bacteria and challenges in microbiology

Bacteria are found in every habitat on Earth and there are approximately 10 times as many bacterial cells as human cells in the human body. This section highlights some of the many challenges we face understanding bacteria, with a focus on the global issue of antimicrobial resistance.

Combatting antimicrobial resistance: alternative technologies?

Laura Bowater

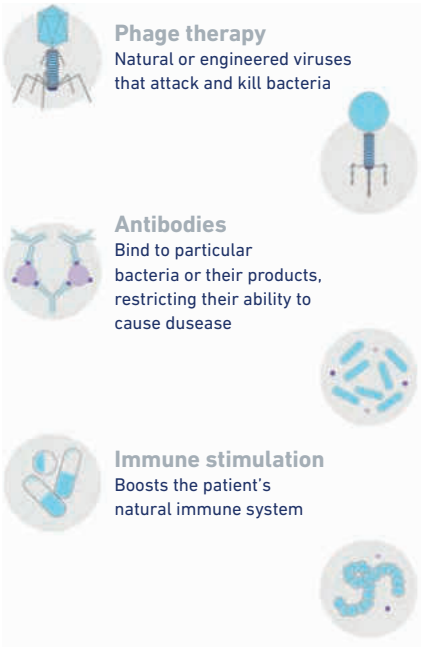
The problem of antimicrobial resistance is one of the most significant threats facing global health, wellbeing and food security. As of June 2019, only 42 new antibiotics, with the potential to treat serious bacterial infections, are in clinical development and only one in five is likely to gain approval. The seminal O'Neill report on antimicrobial resistance, released in 2016, emphasised the need to develop new antibiotics but gave a compelling argument for the need to develop new solutions and treatments to replace our antibiotic reliance.

So, what are these alternative solutions? Some are well established pharmaceutical products such as immunotherapies that are effectively treating other diseases and may be able to treat or prevent bacterial infections. Others are new therapies. For example, lysins are hydrolytic enzymes derived from bacteriophages that target and disrupt bacterial cell walls and are currently being trialled against Gram-positive and recently Gram-negative pathogens. Other solutions include virulence inhibitors, such as products that disrupt the cooperative social behaviour of bacteria, alleviating their pathogenic threat to patients, or products that replace harmful bacteria with 'healthy' bacteria. It is reassuring to see that there is still a keen interest in hunting down novel bacterial targets. One example is oligonucleotide transcription factor decoys (TFDs), molecules that resemble the binding sites for essential bacterial transcription factors. When delivered on nanoparticles into bacterial cells they act as decoys, preventing expression of the genes needed for the bacteria to survive and cause infection.

The good news is we currently have 29 alternative candidates in clinical development compared to the 42 new antibiotics in current pipelines. The bad news is most non-traditional products are only active against a limited range of pathogens and the establishment of regulatory guidelines for their approval is still in its infancy. Nevertheless, the hunt continues...

ALTERNATIVE PRODUCTS TO TACKLE INFECTIONS

A selection of alternative products that are under development, which could be used for prevention or therapy



Review on Antimicrobial Resistance

Further reading

The Pew Trust. Assessment of nontraditional products in development to combat bacterial infections; 2019. https://www.pewtrusts.org/pt/research-and-analysis/issue-briefs/2019/09/assessment-of-nontraditional-products-in-development-to-combat-bacterial-infections [accessed 30 January 2020].

Köhler T, Perron GG, Buckling A, van Delden C. Quorum sensing inhibition selects for virulence and cooperation in *Pseudomonas aeruginosa*. *PLoS Pathog* 2010;6: e1000883. DOI:10.1371/journal.ppat.1000883

Procarta Biosystems. https://www.procartabio.com [accessed 30 January 2020].

AMR Review. Tackling drug-resistant infections globally: final report and recommendations. https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf [accessed 30 January 2020].

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Laura Bowater is currently Academic Director for Innovation and a Professor of Microbiology Education and Engagement. She was previously Associate Dean for Enterprise and Engagement in the Faculty of Medicine and Health. Laura graduated from the University of St Andrews with a BSc in Biochemistry with Microbiology then moved to the University of Dundee to study for an MSc and PhD in Microbiology. After a four-year career break to raise her family, she took up a postdoctoral post at the John Innes Centre, attained an MA in Education from the University of East Anglia, worked for the Open University and then moved to the University of East Anglia to focus on teaching, science communication and public engagement.

Why does microbiology matter?

Because almost every aspect of life as we know it relies on the intricate relationship we have with the microbial world.

In your opinion, which areas of research are likely to have the greatest impact on tackling antimicrobial resistance in the future?

There are a lot of research areas to choose from. In my mind, I think it is vital that we begin to refill our pharmaceutical cupboards that are starting to look uncomfortably bare. Therefore, searching for new antimicrobial compounds would be a top priority for me.

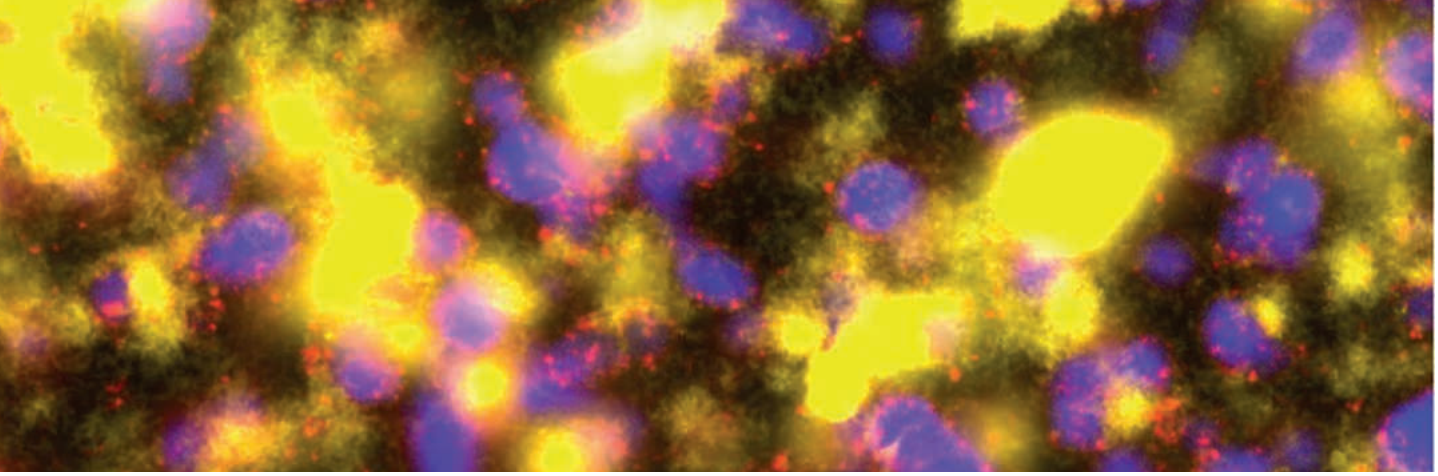
The world of biofilms

Thomas James O'Brien and Martin Welch

Bad news folks; ever since modern microbiology emerged as a distinct discipline in the latter part of the 19th century, it looks like we've been studying the wrong thing. Those colonies on your agar plates or flasks of liquid culture in your orbital shaker are about as physiologically relevant as the medium which you're growing them in. That's because it turns out that *most* bacteria spend *most* of their time doing things differently – they live out their lives either stuck to one another or attached to the debris and organic matter floating around them. This realisation is somewhat ironic, especially given that microbial communities attached to solid surfaces (teeth) were among the very first things to be described by Antonie van Leeuwenhoek using his prototype microscopes in the 17th century. However, it wasn't until the 1930s that Arthur T. Henrici pushed the point home by commenting: "it is quite evident that for the most part water bacteria are not free-floating organisms but grow attached upon submerged surfaces". The expression 'biofilm' was born shortly afterwards. If you think that this would have catalysed rapid progress, you'd be wrong. Although most 'environmental microbiologists' had been wittingly studying biofilms for decades, the field did not emerge from its lag phase within mainstream microbiology until the mid-1980s. The most likely reasons for this are two-fold. First, scientists hate mess. We like to work with pure axenic cultures grown from isolated colonies, cultured in defined laboratory media. Why would we possibly want to add bits of floating detritus (as biofilm substrata) to these pure, defined cultures? Second, it wasn't until the mid-1980s that the link between biofilms and chronic infection was first proposed. But *that* was a game changer...

The formation of biofilms

It turns out that there is a loose, but nevertheless compelling, link between growth mode and infection severity/type. Acute



Biofilm Battleground: Confocal laser scanning microscopy image taken of a co-culture of *Pseudomonas aeruginosa* PA01 (yellow cells) and *P. aeruginosa* PA04 (blue cells). Propidium iodide labelling of compromised cells (red spots) reveals that PA01 kills off PA04 cells present within the mixed species biofilm. Dr Nuno Miguel Oliveira, Department of Applied Mathematics and Theoretical Physics, University of Cambridge

infections are generally associated with the planktonic growth mode, whereas chronic infections are generally associated with biofilm formation. By definition, chronic infections (such as those associated with cystic fibrosis or endocarditis) are poorly resolved by the immune system and/or antibiotic intervention. This is partly because biofilms are poorly permeable to some antibiotics, and partly because the slow-growing cells in the biofilm's centre are less susceptible to these agents. More insidiously, the high density and close proximity of micro-organisms in biofilm communities promotes the horizontal transfer of antimicrobial resistance (AMR) determinants, particularly through contact-dependent mechanisms such as conjugation. These realisations have driven an explosion in biofilm research over the last two decades. Indeed, a simple PubMed search reveals that the number of articles mentioning the word 'biofilm' remains on an exponentially increasing trajectory, with well over 5,000 publications last year alone. But we're getting a bit ahead of ourselves here – what exactly are biofilms and why should we care about them?

The physiology of biofilms

Biofilms are essentially quasi two-dimensional assemblages comprising one or more microbial species, held together by a self-produced extracellular polymeric 'glue' (termed matrix). As outlined above, such aggregates may be anchored to a solid (or semi-solid) substratum, or they may form free-floating assemblies called flocs. Environmental biofilms (and some clinical biofilms too) are more often than not polymicrobial (i.e. containing more than one species) and can reach cell densities as high as 10^{11} cells (g wet weight)$^{-1}$. Living cheek by jowl in the centre of such a densely packed community does pose several problems, not least the fact that your cousins at the surface will quickly consume all the oxygen and nutrients before you get a look-in. Therefore, it is not surprising that biofilm physiology changes rapidly with increasing depth and the individual cells comprising the structure are exceptionally heterogenous. The self-organised structural heterogeneity in biofilms is abundantly clear in laser scanning confocal microscopy studies, which reveal that biofilms are comprised of spatially separated heterogenous sub-populations, called microcolonies. The complex spatial organisation and accompanying chemical gradients strongly promote genetic diversity within the population, as no single species is perfectly adapted for every available environmental niche.

Biofilms and AMR

As mentioned earlier, biofilms are very much at the forefront of microbiological research these days, because of their role in AMR. In addition to their phenotypic and genetic heterogeneity, another reason biofilms remain resistant to antimicrobial agents is because the polysaccharide matrix itself forms a physical protective barrier against environmental stressors. The matrix also limits the diffusion of extracellular molecules away from the population, allowing for the sharing of public goods and a division of metabolic labour.

Thankfully, biofilms are not always bad news. As far back as 1860, engineers were inadvertently using the biofilms associated with sand particles to clean up wastewater in sewage treatment plants. In a similar vein, biofilms play a key role in the bioremediation of industrial effluents and environmental pollutants, including dairy industry waste and marine oil spills, respectively. More recently, this field has seen a resurgence of interest, with anode-associated biofilms used in microbial fuel cells and several high-value bioproducts being made by exploiting the unique catalytic potential of biofilms. Ongoing research into the complex world of biofilms is aimed at developing novel treatments for the removal and prevention of biofilm growth in problematic scenarios, as well as unlocking and harnessing their full potential in industrial applications. But don't hold your breath; it is unlikely that there will be a universal Achilles heel to target. Biofilms have been around for billions of years (try Googling 'stromatolites') and, as pointed out earlier, they represent the default growth mode for *most* bacteria *most* of the time. Just as many roads lead to Rome, it is highly likely that there are *many* ways to make a biofilm.

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Thomas James O'Brien is a PhD student and Research Assistant in the Department of Biochemistry at the University of Cambridge. His research aims to develop an *in vitro* polymicrobial model to recapitulate and study the complex microbial communities associated with cystic fibrosis airway infections. He is particularly interested in interspecies communication and microbial ecology at the community-wide level. He has been a member of the Microbiology Society for three years (since the start of his PhD) and has found the support given by the Society to be an invaluable resource throughout his studies.

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Martin Welch was born near Cambridge, and studied biochemistry at Oxford. He studied for his PhD at the Weizmann Institute of Science in Israel, and followed this with a short postdoc in Toulouse where he learned how to solve x-ray crystal structures. Now back in Cambridge, his laboratory currently focuses on understanding the link between bacterial metabolism and virulence/lifestyle choices. In his spare time, Martin enjoys cooking and horse riding. He is also passionately interested in local history and natural history.

Why does microbiology matter?

Thomas: Micro-organisms are the most versatile and abundant life-form on the planet, inhabiting every known environmental niche – no matter how treacherous or desolate. Not only are they truly fascinating organisms to study at the molecular level, but they play a focal role in undertaking and modulating natural biochemical processes that occur across the entirety of the Earth's surfaces and within our own bodies, especially as micro-organisms outnumber our own cells 10 to 1! Whether the action of these micro-organisms is positive or detrimental, fully understanding how they work and what regulates these will allow us to harness and adapt the power of micro-organisms for our own benefit and better tackle infectious disease, especially with the worrying rise of antimicrobial resistance.

How did you enter this field?

Thomas: I first became interested in microbiology when studying 'general biology' at college. I was fascinated by the ability of microscopic, and seemingly inconsequential, organisms to eventually adapt to and overcome any therapeutic or environmental challenge they may face – especially in the context of infectious disease. As such, I chose to enrol in a microbiology course for both my undergraduate and master's studies at the University of Leeds. Here, my fascination grew as I began to learn more and more about the truly endless world of microbiology, cementing my desire to enter the world of research at the academic level. Hence, I pursued several lab-based projects throughout my studies in order to prepare myself for undertaking a PhD and hopefully I will be able to continue working within this amazingly diverse field as my studies begin to draw to a close.

Bacteria in industry: microbial bio-factories for a sustainable future

Anna Trego and Vincent O'Flaherty

Often, bacteria carry a bit of a *bad rap* – being commonly associated with spoiled food and infectious disease, when in fact, fewer than 1% of the known microbial species on the planet are pathogenic. Moreover, we rely on many different bacteria, archaea, fungi, yeasts and moulds for the biochemical conversions that are part of their natural genetic machinery. Indeed, microbial cells are essentially miniature bio-factories, producing a wide range of useful products. Evidence suggests that over 6,000 years ago, micro-organisms were used by humans

to make bread, wine, beer and cheeses. People didn't understand the fermentative processes which they were exploiting, and fermentation wasn't linked to microbial metabolism until 1857 when Louis Pasteur discovered that yeast cells were responsible for the conversion from sugar to alcohol.

Microbial potential

Since then, our use of microbial metabolism has rapidly expanded and has completely revolutionised food production, healthcare, chemical production and waste treatment. Advancements in genetic engineering in the 1960s and 1970s saw the rise of numerous medical biotech companies using microbial cells to produce helpful biological substances – an industry estimated to be worth over 700 billion by 2025. These companies often use genetic engineering to patent bacterial super-strains which quickly pump out a wide range of specialised enzymes, hormones, probiotics, antibiotics and vaccines, providing treatments for a number of medical conditions such as diabetes, tuberculosis (TB), AIDS, various cancers and systemic lupus erythematosus (SLE). The outlook and potential for such industries is boundless. Indeed, it is now proposed that Earth may be home to as many as one trillion different species of microbes – 99.99% of them are yet to be discovered, meaning that the untapped microbial metabolic potential is enormous.

While the past few decades have unleashed a flood of biotechnological advancements with a strong industrial focus on combating disease, there are other challenges facing humanity – specifically, global population increase coupled with climate change. Increased pressures in food production are to be expected, waste generation will increase, water will become scarcer and energy consumption will increase. We are going to need innovative solutions to address such challenges. Could sustainable solutions be hidden in the genetic makeup of micro-organisms?

Microbes for sustainable food production

Traditionally, bacteria and yeasts are important for the direct manufacture of a variety of food products including chocolate, coffee, wine, beer, bread, meat products such as sausages, dairy products and pickled goods such as sauerkraut, pickles and olives. Recently, however, a somewhat controversial concept has been revisited for the sustainable production of protein with a low environmental footprint. Traditional plant- and animal-based protein sources are quickly becoming unsustainable and scientists are turning to bacteria, algae, yeasts and fungi for the production of protein-rich feed or food additives as a more sustainable option. This microbial protein (MP) can be developed for human consumption, or as a microbial alternative for the protein supplements added to agricultural feed. For example, FeedKind®, developed in Norway and for sale in the EU, is a fish feed (for fish farming) produced by *Methylococcus capsulatus* from natural gas. In comparison with traditional soy- and fishmeal-based feeds, its production has much lower land and water requirements. Alternatively, for human consumption, fungal production of MP has been successful. Quorn™, a mycoprotein meat alternative, produced by *Fusarium venenatum*, has expanded into the global market and expects to be a billion-dollar business by 2027. The success of these emerging MP-based industries will likely generate growing interest in sustainable, microbial food additives.

Microbes for sustainable wastewater treatment, resource recovery and energy production

Microbiology and microbial industrial technologies are key for environmental sustainability. In natural environments, such as soils and oceans, micro-organisms are the major drivers of biogeochemical and elemental cycles that maintain the biosphere. Their extraordinary metabolic diversity is also exploited in environmental engineering systems, such as wastewater treatment plants. Microbiology will play a key role in how society achieves the UN Sustainable Development Goals. A growing human population, particularly in urban areas, will produce more wastewater, which requires treatment before being safely discharged into the environment – but clean water and sanitation are still not available to millions. Generally, wastewater treatment involves a biological component – where active micro-organisms metabolise and remove organic pollutants. There are several approaches to this. Traditionally, aerobic treatment facilities were implemented and have been highly successful all over the world, but they have important drawbacks associated with cost, energy and scalability. By comparison, the alternative anaerobic microbial treatment process is low-cost, more energy efficient and can meet all criteria for water protection. Furthermore, anaerobic treatment, which is underpinned by a complex consortium of micro-organisms from various trophic groups, can completely convert complex organic compounds into a combustible biogas in the form of methane – a renewable energy source. This technology, which took off in the 1970s, has expanded from lab-scale

research to full-scale industrialised bioreactors all over the world. According to a recent report, the global anaerobic digestion industry is projected to grow to over $16 billion by 2026. But it's no longer just about securing water sources and generating energy; there is an increasing focus among researchers and industry alike, in not just *removing* nutrients from wastewater, but in using bacteria and archaea to *recover* valuable sources of nitrogen and phosphorus – both principal components in fertilisers.

Outlook

Not only do microbes provide the foundation for many billion-dollar businesses spanning multiple industrial sectors, but they also likely contain the genetic power to provide us sustainable solutions to the growing pressure on Earth's finite resources. As Louis Pasteur said so many years ago, microbes really will have the last word.

Further reading

Leroy F, De Vuyst L. Lactic acid bacteria as functional starter cultures for the food fermentation industry. *Trends Food Sci Technol* 2004; 15:67–78. DOI:10.1016/j.tifs.2003.09.004.

Matassa S, Boon N, Pikaar I, Verstraete W. Microbial protein: future sustainable food supply route with low environmental footprint. *Microb Biotechnol* 2016;9:568–575. DOI:10.1111/1751-7915.12369

McKeown RM, Hughes D, Collins G, Mahony T, O'Flaherty V. Low-temperature anaerobic digestion for wastewater treatment. *Curr Opin Biotechnol* 2012;23:444–451. DOI: 10.1016/j.copbio.2011.11.025

O'Flaherty V, Collins G, Mahony T. The microbiology and biochemistry of anaerobic bioreactors with relevance to domestic sewage treatment. *Rev Environ Sci Bio/Technology* 2006;5:39–55. DOI: 10.1007/s11157-005-5478-8

van Lier JB, van der Zee FP, Frijters CTMJ, Ersahin ME. Celebrating 40 years anaerobic sludge bed reactors for industrial wastewater treatment. *Rev Environ Sci Bio/Technology* 2015;14:681–702. DOI:10.1007/s11157-015-9375-5

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Anna Trego, a native Californian, graduated from the University of Arizona with a bachelors degree in Environmental Science, before serving two years with Teach for America as a chemistry and physics teacher. She then completed her MSc in Sustainable Resource Management at the University of Limerick and the NUI Galway. She recently completed her PhD at NUI Galway – studying microbial community development of biofilms used for biological wastewater treatment. She now works with Professor Vincent O'Flaherty as a postdoctoral researcher in microbial ecology.

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Vincent O'Flaherty is Professor of Microbiology at the National University of Ireland, Galway. His expertise is in the field of microbial ecology and bioprocess research. To date, three start-up companies have been formed arising from research in his laboratory. He teaches and learns about microbiology and environmental biotechnology with students at all levels.

Why does microbiology matter?

Anna: Microbiology matters almost inherently. Not only are our bodies filled with microbes – indeed we are just now starting to uncover how important the human gut microbiome is to our overall health and wellbeing – but as far as we know, micro-organisms are the most evolutionarily ancient life forms on the planet. They can be found in even the most inconceivable of environments: hot, cold, salty, anoxic, acidic, you name it, there's a microbe that can make it work. Understanding the structure and function of micro-organisms and microbial communities can help unlock the secrets of the evolution of life on our planet, can help us live healthier, longer lives and can potentially provide the basis for sustainable solutions to increased pressure on natural resources.

On a typical day (or week) in your job what do you do?

Anna: I am a Postdoctoral Researcher at the National University of Ireland, Galway. On a typical day I can be found in the microbial ecology lab where, together with my colleagues, I study mixed microbial communities, how they respond to changing environmental conditions, how they interact with one another, and how we can apply their natural functions for the sustainable production of energy, biopolymers or valuable industrial chemicals. One of the most challenging parts of our work is that the micro-organisms that we study are anaerobic, meaning that oxygen is toxic to them. We have to create special, completely enclosed environments with no oxygen in order to study them.

Vaccines: the global challenge for microbiology

Vaccines are made from microbes that are dead or inactive, and these microbes stimulate an immune response to protect against disease. Not only do vaccines protect those inoculated, but they can also provide herd immunity. This section describes the crucial role vaccination plays in health.

The vital importance of vaccines

Norman K. Fry

As the media headlines increasingly remind us, the prevention, control and elimination of vaccine-preventable diseases (VPDs) do indeed present global challenges. Recent reports of outbreaks of measles in Samoa, the battle to regain polio-free status of several countries, and the enormous efforts to make one of the world's deadliest diseases (Ebola) preventable and curable, all illustrate the vital importance of vaccines.

After clean water, vaccination is the most effective public health intervention in the world for saving lives and promoting good health. In 2019, The World Health Organization (WHO) re-affirmed its commitment to the prevention and control of communicable disease, including the VPDs. In the WHO's list of 'Ten threats to global health in 2019', VPDs, vaccines and factors which can confound their successful delivery feature in most of them.

The success of vaccination over the last century in reducing death and disease caused by infectious diseases has been dramatic. Many viral and bacterial infections which historically disproportionally affected infants and children have been significantly reduced thanks to national immunisation programmes. However, we cannot afford to be complacent. Conflict leading to the breakdown of health service infrastructures and delivery systems, mass migration, movement of displaced persons (dramatically illustrated by the Rohingya refugee crisis in 2017), vaccine misinformation and hesitancy can all undermine the control of VPDs.

This issue contains articles on human papillomavirus (HPV) vaccination and herd immunity, and vaccine development and production. In the UK, the HPV vaccine has been offered to all girls in school Year 8 for over ten years and has continued to achieve very high vaccine coverage despite concerning declines in uptake in other European countries. From September 2019, the programme was expanded, with Year 8 boys now offered the vaccine alongside girls to help accelerate protection of both boys and girls from HPV-related cancers.

Innovative technologies are now playing an essential role in the development of new vaccines, and the hope for the future is that more diseases will become vaccine preventable across all age groups.

Further reading

Nature News. Make Ebola a thing of the past': first vaccine against deadly virus approved; 2019. https://www.nature.com/articles/d41586-019-03490-8 [accessed 14 February 2020].

National Health Service. HPV vaccine overview; 2017. https://www.nhs.uk/conditions/vaccinations/hpv-human-papillomavirus-vaccine/ [accessed 14 February 2020].

Public Health England. Why vaccinate?; 2014. https://publichealthmatters.blog.gov.uk/2014/05/01/why-vaccinate/ [accessed 14 February 2020].

Wellcome Trust. This is the decade we made one of the world's deadliest diseases preventable and curable; 2019. https://wellcome.ac.uk/news/decade-we-made-one-worlds-deadliest-diseases-preventable-and-curable [accessed 14 February 2020].

World Health Organization. Thirteenth general programme of work 2019–2023; 2018. https://www.who.int/about/what-we-do/thirteenth-general-programme-of-work-2019–2023 [accessed 14 February 2020].

World Health Organization. Ten threats to human health in 2019; 2019. https://www.who.int/emergencies/ten-threats-to-global-health-in-2019 [accessed 14 February 2020].

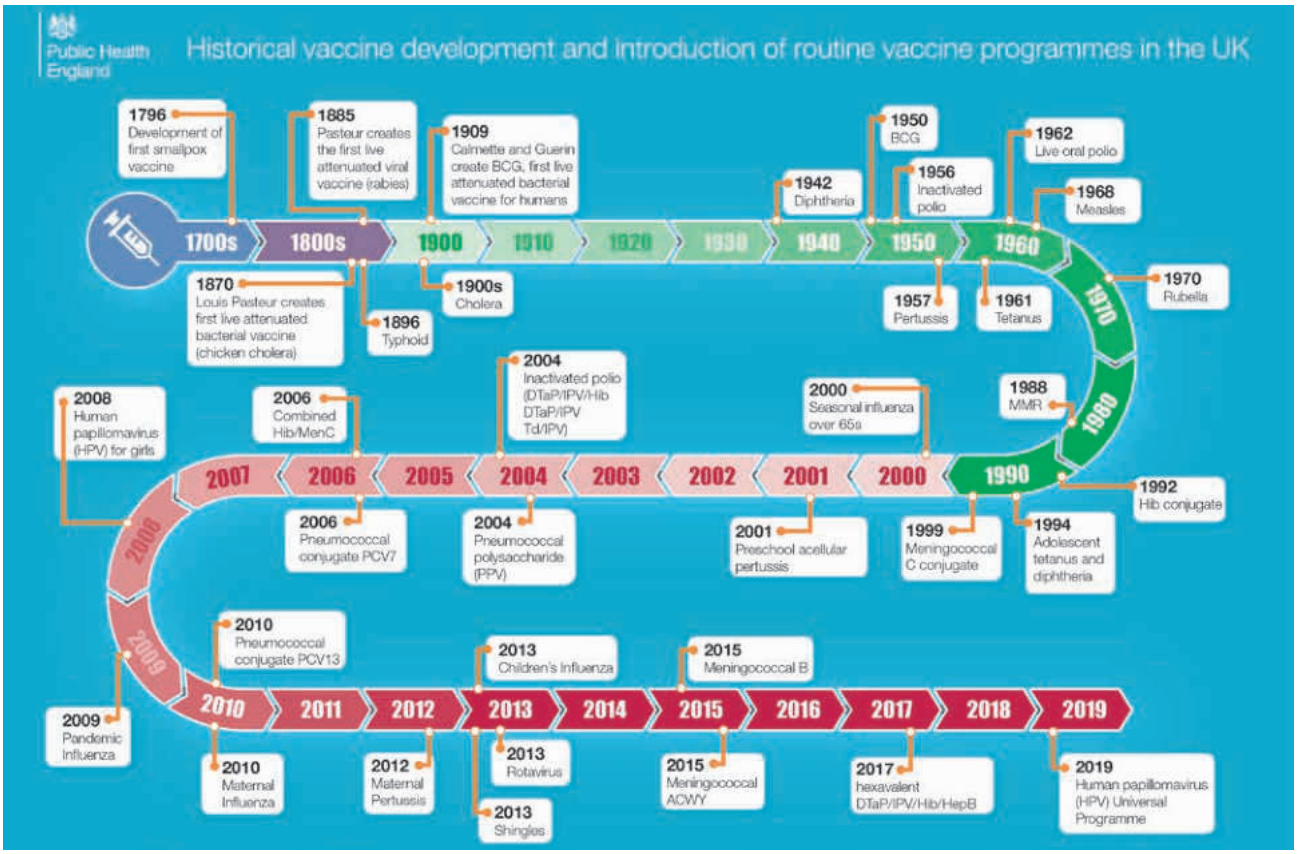

Fig. 1. The figure shows the historical development of vaccines and the introduction of routine vaccine programmes in the UK. By kind permission of Public Health England

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Norman Fry is a Consultant Clinical Scientist and Laboratory Surveillance Lead for Vaccine Preventable Bacteria in the Immunisation and Countermeasures Division, Public Health England – National Infection Service, London. He is Head of the Vaccine Preventable Bacteria Section which hosts the National Reference Laboratories for *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Bordetella pertussis* and diphtheria. His laboratory also hosts the World Health Organization Collaborating Centre (WHO CC) for *Streptococcus pneumoniae* and *Haemophilus influenzae* (Heads: N.K. Fry and D. Litt) and the WHO CC for diphtheria and streptococcal infections (Head: Prof. A. Efstratiou). Norman is also Co-Editor-in-Chief for one of the Microbiology Society journals, the *Journal of Medical Microbiology*.

Why does microbiology matter?

Since this article was written, a novel coronavirus (later named SARS-CoV-2) was found to be responsible for a pneumonia outbreak that started in Wuhan City, Hubei Province, China. Due to the rapid spread of this virus the World Health Organization (WHO) declared a Public Health Emergency of International Concern and later made the assessment that the disease this virus causes, termed COVID-19, can be characterised as a pandemic.

If ever there was an answer to the question of why microbiology matters, this is certainly one. However, we should also not forget about the other infectious diseases, especially the ones for which we currently have vaccines for, and we should continue to maintain good vaccine uptake for those.

How are you striving to monitor the effectiveness of vaccination in the hope that it can control disease?

We work closely with our colleagues in Public Health England and the National Health Service (including scientists, epidemiologists and consultant medical microbiologists) to define outbreaks, describe the epidemiology of circulating strains and identify transmission pathways. We also collaborate with academia and other public health organisations, nationally and internationally, and are actively involved with several European laboratory and epidemiology networks. To monitor the effectiveness of vaccination nationally, it is essential to have both high-quality laboratory and epidemiological data. These data are also used to inform any potential changes to vaccine policy, following the approval and recommendation by the Joint Committee on Vaccination and Immunisation (JCVI), an independent departmental expert committee and statutory body which advises UK health departments on immunisation.

HPV vaccination and herd immunity

Kate Cuschieri and Heather Cubie

Papillomaviruses (PVs) are ancient and intriguing viruses. Biologists have been fascinated, challenged and perplexed by warts for centuries. In 1842, Dr Rigoni Stern, a Veronese physician, commented on the difference in cervical lesions in Catholic nuns compared to married women. Of course, at that time the transmissible element to cervical cancer was unknown, but the observation was astute. However, it was not until Harald Zur Hausen and his team discovered the fundamental links between certain human papillomavirus (HPV) types and cervical cancer, for which he later received the Nobel Prize, that this became more than a niche interest. Indeed, establishment of a viral aetiology to nearly all cervical cancers paved the way for one of the most influential, global public health interventions in modern history: HPV immunisation.

HPV vaccines: the building blocks

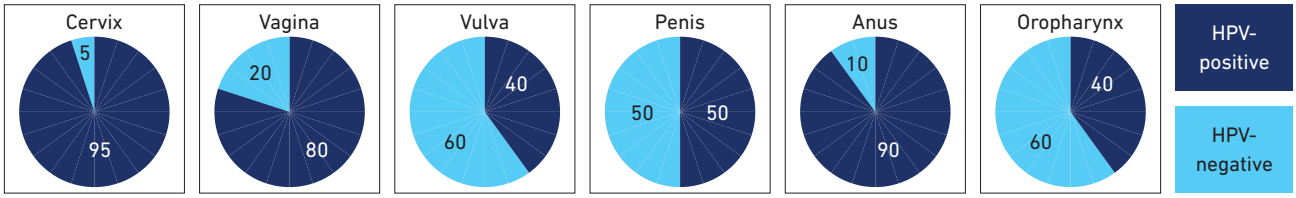
It has been known for several decades that virus proteins can self-assemble into virus-like particles (VLPs), either naturally or synthetically through expression, providing an invaluable delivery system for vaccines. VLPs are essentially empty shells which 'look the part' to the immune system. They produce a strong neutralising antibody response, considerably more potent than responses elicited by natural infection, but are incapable of replication. The discovery in 1990 by Jian Xhou and Ian Frazer in Brisbane that the two structural proteins of HPV could self-assemble into VLPs was a huge breakthrough and quickly led to investment in the development of HPV vaccines.

Initially, single valency vaccines containing only HPV 16 VLPs were trialled. These preceded the bivalent (Cervarix from GSK) and quadrivant (Gardasil 4 from SPMSD) vaccines which both confer protection against HPV 16 and 18, types associated with around 70% of cervical cancers. Gardasil 4 also provides protection against HPV 6 and 11 which cause around 90% of genital warts. Cross-protection has been demonstrated against non-vaccine HPV types, most notably by Cervarix for HPV 31, 33 and 45. More recently a nonavalent vaccine (Gardasil 9 from SPMSD) was licensed which confers protection against HPV 16, 18, 31, 33, 45, 52 and 58 as well as HPV 6/11 and is anticipated to directly protect against 90% of the types that cause cervical cancer. HPV 16 has a proven aetiology in non-cervical cancers, namely those of the vagina, vulva, penis, anus and oropharynx (Fig. 1), so clearly the vaccines have a reach for cancer protection beyond the cervix.

Introduction and evolution of HPV vaccine within national programmes

Since 2006, 115 countries have introduced HPV immunisation as national pilots or full-scale programmes and the vaccine is now listed as an essential medicine by the WHO. Uptake has varied and depends on resource, competing healthcare priorities and perceptions of harm relative to benefits. Australia was the first country to offer a national HPV immunisation programme in 2007, with several countries following suit, including the UK in 2008. Initially, most programmes were female only, but increasingly males are also offered the vaccine. Gender-neutral vaccination has not been universally lauded, particularly where female uptake is high, and especially with global vaccine demand outstripping supply. Proponents contend that vaccinating boys accelerates and sustains herd immunity.

Fig. 1. Attributable fraction of HPV in cervical, vaginal, vulval, penile, anal and oropharyngeal cancer. Cuschieri & Graham: taken from *Molecular Microbiology* – a guide to microbial infections 19th Edition, Eds Greenwood *et al.* Prevalences are based on Plummer *et al. Lancet Glob Health* 2016; 4: e609-16 and represent a global perspective



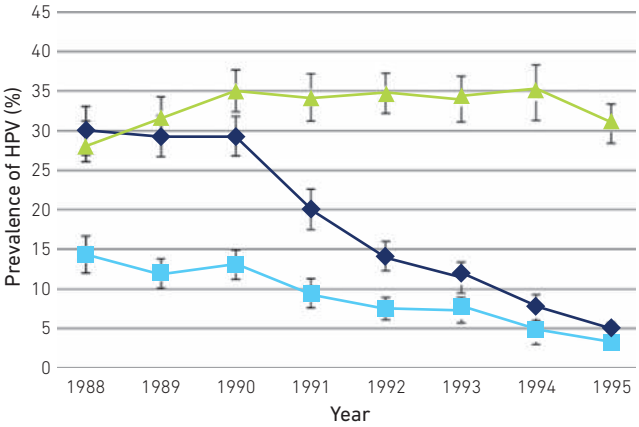


Fig. 2. Type-specific prevalence of HPV in women attending for their first cervical smear in Scotland stratified by birth cohort showing reductions in vaccine-type infection and cross-protective types. Females born in 1988 and 1999 were largely unvaccinated; from 1991 the majority of females were vaccinated. ◆, HPV16/18; ■, HPV 31/33/45; ▲, HR HPV other. Created by Kate Cuschieri from data available in Kavanagh *et al.* DOI:10.1016/S1473-3099(17)30468-1

Furthermore, in addition to genital warts, males also shoulder a burden of HPV-associated cancer of the penis, anus and oropharynx. While these cancers are not common, they have a high morbidity and, importantly, are rising in incidence.

Data from the first randomised clinical trials (RCTs) of HPV vaccines were based on three-dose regimens and became the norm for implementation programmes. Now two-dose 'prime-boost' schedules are common, and, based on bridging studies that showed antibody levels after two doses were not inferior to those associated with clinical effectiveness, have been recommended by the WHO since 2014. More recently, analysis of the RCTs indicates that even a single dose may be protective against HPV infection, and prospective trials are underway to investigate this more comprehensively. Given the challenges of vaccination, particularly in low- and middle-income countries (LMIC) where 80% of the disease burden is manifest, this is a timely and exciting endeavour.

The effectiveness of HPV vaccines at the population level

The impact of HPV immunisation has been profound. In the UK, a 90% reduction of HPV type-specific infection (Fig. 2) in women who received the vaccine aged 14 was mirrored by an equivalent ~90% reduction in high-grade cervical lesions.

Impact is also being observed in the clinic, where the number of procedures required to remove cervical lesions has reduced over time in the vaccination era. We are now tantalisingly close to showing reduction, not just in disease but in invasive cancers.

Herd protection

Evidence of herd protection has accumulated for both quadrivalent and bivalent vaccines. One of the first key signals was reduction in genital warts in heterosexual males as a consequence of the then female-only vaccination programme in Australia. In Scotland, where vaccine uptake rates have been 80–90% since 2008, HPV vaccine-type infection and high-grade disease in girls aged 20, *offered* the HPV vaccine when aged 13–14 is the same, irrespective of immunisation status. As with any immunisation programme, high uptake should be encouraged to ensure maximal population-level benefits. Furthermore, men who have sex with men (MSM) are much less likely to gain herd protection from female-only programmes yet are at additional risk of HPV-associated disease compared to men who only have sex with women. Some countries have therefore introduced opportunistic programmes for MSM, including the UK in 2017, with monitoring systems in place to assess impact.

New technologies to address global challenges

There is a global shortage of all HPV vaccines, with new production facilities under construction. Yet HPV vaccine remains one of the most expensive vaccines ever developed, and in some LMIC, especially in Africa and Asia, HPV types beyond HPV 16/18 contribute significantly to the cancer cases, suggesting not all vaccines will have equivalent efficacy in different countries. New technologies are required, and quickly, if the world is to respond to the WHO call for co-ordinated global action to eliminate cervical cancer [*Dr Tedros Ghebreyesus, WHO Director General; 19 May 2018*]. China and India have HPV vaccines under trial which should provide alternatives and bring down costs. Innovative collaborations between companies in developing countries and more established vaccine manufacturers will create further opportunities and competition.

Conclusion

As a result of immense efforts in producing, delivering and monitoring impact of HPV immunisation and herd immunity in high-income countries, global elimination of cervical

cancer could be on the horizon, but it will require large-scale investment to provide high coverage of HPV vaccine to pre-sexually active girls and probably boys; political will and global action to address the United Nations Sustainable Development Goals (SDGs) of health for all and gender equality; and increased global investment in cervical screening for women over 30 to achieve high population coverage for at least the next two decades.

Further reading

Drolet M, Bénard É, Pérez N, Brisson M (on behalf of HPV Vaccination Impact Study Group). Population-level impact and herd effects following the introduction of human papillomavirus vaccination programmes: updated systematic review and meta-analysis. *Lancet* 2019;394:497–509. DOI:10.1016/S0140-6736(19)30298-3.

Kavanagh K, Pollock KG, Cuschieri K, Palmer T, Cameron RL *et al.* Changes in the prevalence of human papillomavirus following a national bivalent human papillomavirus vaccination programme in Scotland: a 7-year cross-sectional study. *Lancet Infect Dis* 2017;17:1293–1302. DOI:10.1016/S1473-3099(17)30468-1.

Plummer M, de Martel C, Vignat J, Ferlay J, Bray F *et al.* Global burden of cancers attributable to infections in 2012: a synthetic analysis. *Lancet Glob Health* 2016;4:e609–616. DOI:10.1016/S2214-109X(16)30143-7.

de Sanjose S, Brotons M, LaMontagne DS, Bruni L. Human papillomavirus vaccine disease impact beyond expectations. *Curr Opin Virol* 2019;39:16–22. DOI:10.1016/j.coviro.2019.06.006.

Schwarz E, Freese UK, Gissmann L, Mayer W, Roggenbuck B *et al.* Structure and transcription of human papillomavirus sequences in cervical carcinoma cells. *Nature* 1985;314:111–114. DOI:10.1038/314111a0.

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Kate Cuschieri is a Consultant Clinical Scientist and current Director of the Scottish HPV Reference Laboratory. She is also lead for the HPV research group and Scottish HPV Archive, University of Edinburgh. She has been involved in monitoring the impact of the HPV vaccine on infection and associated disease in the UK.

Heather Cubie

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Heather Cubie was a Consultant Clinical Scientist in Virology. She was Founder Director for the Scottish HPV Reference Laboratory and Scottish HPV Archive, retired in 2014 and is currently Senior Advisor to the Global Health Academy, University of Edinburgh. She also devotes much time to involvement in programmes of cervical cancer reduction in Malawi.

Why does microbiology matter?

Kate: From a clinical perspective the control of infection remains of extreme relevance for global health, including prevention through immunisation and public health interventions. Recent infectious outbreaks in the first part of the 21st century continue to emphasise this. Diverse microbiological expertise is needed to address the challenges imposed by infections, including basic scientists who can delineate mechanisms of pathogenicity, epidemiologists who can map infection and outbreaks – and health care scientists and clinical microbiologists who can support affected patients through laboratory testing and direct care.

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

Kate: Currently, I am Director of the Scottish Human Papillomavirus (HPV) Reference laboratory, where we offer a national specialised service for testing of HPV. I am a consultant clinical scientist so in terms of qualifications I have a PhD, became state registered with the Health and Care Professions Council (HCPC) and then gained FRCPath by publication. As the laboratory acts as a hub for both testing and also advice on 'things-HPV', contemporary knowledge of the subject area is clearly required. In addition, I am lucky to be able to interact and collaborate with various multi-disciplinary groups that interface with HPV, including those involved in cervical screening, public health immunisation teams, clinical oncologists, quality assurance experts and academics/basic researchers. I also manage staff on the NHS and university side and support in the training and development of students and staff within and outside the microbiology sphere. Other required skills are the initiation and delivery of appropriate audit and research, the ability to contribute to national exercises that relate to the management of HPV infection and associated disease and finally (but importantly for a service laboratory!) the application of quality management systems to support clinical laboratory testing.

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Vaccine development and production

Vanessa Terra and Brendan Wren

Vaccines have been one of humankind's great successes in terms of combatting infectious diseases. However, despite their proven success, vaccines continue to be unavailable for most bacterial pathogens. Alarmingly, this includes the multi-antibiotic resistant ESKAPE group of pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacter* species). Also, there is a pressing need for emergency response vaccines after natural disasters or civil strife (e.g. *Vibrio cholerae*) and for biothreat agents that could be released for nefarious purposes (e.g. *Francisella tularensis, Bacillus anthracis* and *Burkholderia pseudomallei).* Even if vaccines are available, such as glycoconjugate vaccines that prevent meningitis and pneumonia, they are often too expensive to be used in the low-resource settings where they are desperately needed.

Glycoconjugate vaccines for bacterial diseases

Current marketed vaccines include a number of different formulations that are effective in most high-income countries. These include component vaccines (tetanus and diphtheria), outer membrane vesicle-based vaccines used in the prevention of meningitis group B (e.g. Bexsero), live attenuated viral vaccines (such as the MMR vaccine) and glycoconjugate vaccines (*Neisseria meningitidis*, *Streptococcus pneumoniae* and *Haemophilus influenzae* b). The latter are most desirable where glycans (e.g. O-antigens and capsules) are covalently linked to carrier proteins. They induce T-cell dependent responses that are long-lasting and are highly effective in infants and the elderly, with a remarkable safety record. Such vaccines are endorsed by the World Health Organization who recommend the development of glycoconjugate vaccines for more bacterial diseases. However, the use of the current carrier proteins (diphtheria and tetanus toxoids), means that new carrier proteins need to be developed to avoid cross-competition between different glycoconjugate vaccines.

Chemical conjugation

The development of new glycoconjugate vaccines continues at a pace. For example, TypBar-TCV and Zydus Cadila vaccines that protect against enteric fever caused by *Salmonella typhi* were licenced in 2013 and 2017, respectively. Both vaccines chemically conjugate the Vi capsule to tetanus toxoid and are effective in infants. Alternative strategies include the production of polysaccharides independent of the host pathogen including chemical and enzymatic synthesis of polysaccharides. Organic synthesis has been used to produce sufficient bacterial oligosaccharides for new vaccines against *H. influenzae* b (Quimi-Hi) and *Shigella flexneri* serotype 2a, which are currently in phase I clinical trials. Automated glycan assembly is another method used to generate polysaccharides independent of handling the pathogenic bacteria. This approach coupled to glycoarrays has been instrumental in the identification of epitopes from polysaccharide antigens that have been used to determine optimal oligosaccharide epitopes from serotypes excluded in current *S. pneumoniae* glycoconjugate vaccines. An alternative approach to producing a polysaccharide is by enzymatic assembly. Irrespective of how the polysaccharide is generated, all of these approaches require the need for chemical

conjugation to the carrier protein. The disadvantages of the chemically synthesised glycoconjugate vaccines are that they are expensive to manufacture (due to multiple quality control steps), they don't always fully cover strain/serotype variation and lack flexibility in the coupling of alternative carrier proteins to glycans.

Bioconjugation

An alternative to chemical conjugation is protein glycan coupling technology (PGCT) or bioconjugation that produces recombinant glycoconjugate vaccines in *Escherichia coli* cells that act as mini-factories for the single-step production of purified vaccines. The recombinant production of glycoconjugate vaccines in *E. coli* has many advantages including (i) no requirement to handle pathogenic bacteria, (ii) flexibility in the design of carrier protein/glycan combinations for tailor-made glycoconjugate vaccines and (iii) simplicity of the process means it is low-cost. Reduced production costs make this affordable for low-resource countries and the simplicity of the manufacturing process means that PGCT-derived vaccines can be produced within these countries, further driving down the cost of vaccines where demand is greatest.

Current PGCT-based vaccines in development include the refinement of *S. pneumoniae* vaccines with new carrier proteins from the host organism and further serotype coverage, new vaccines for *F. tularensis, B. pseudomallei*, Group A *Streptococcus, K. pneumoniae*, *S. aureus*, *Shigella* and *E. coli*. Some of these have been tested in phase 2 clinical trials and shown to be safe and effective. More recently, PGCT-derived vaccines have been developed for livestock (e.g. poultry, pigs and ruminants) where low-cost is paramount. Glycoconjugate vaccines have not previously been used in animals, so in an ironic twist, with over a billion glycoconjugate vaccines administered to humans annually, we have acted as the 'guinea pigs' for animals.

With the imminent post-antibiotic apocalypse, more than ever vaccine development is an obligation. In contrast to humans, vaccine development for animals has lagged. Appropriate vaccines for livestock have several advantages including disease prevention in animals (and humans for zoonotic pathogens), economic prosperity and a reduction in the use of antibiotics for animals. This means that the research, development and production of new human and animal vaccines is a timely pursuit and will continue to be a global imperative.

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Brendan Wren gained a PhD in Biophysical Chemistry at the University of Leicester and published seminal papers on the effect of ionizing radiation on DNA. He then took a postdoctoral position in medical microbiology and has been at LSHTM for the past 20 years. He researches glycosylation in bacterial pathogens and developing a 'glycotoolbox' for glycoengineering; comparative phylogenomics and the evolution of bacterial virulence; and mechanisms of bacterial pathogenesis. This research has been used to develop glycoengineering to apply to the construction of affordable recombinant glycoconjugate vaccines.

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Vanessa Terra is a biochemist trained in Portugal. She obtained a PhD at the University of Leicester, working on pneumococcal interactions with mucin. Then she moved to the LSHTM and started working on vaccine development; more specifically protein glycan coupling technology (biological conjugation). Vanessa concentrates mostly on developing veterinary vaccines (PGCT), but also has an interest in the development of pneumococcal vaccines.

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

Brendan: Follow what interests you and don't be frightened of new research topics.

Vanessa: The most valuable advice I think I can give is to be passionate, be curious, be observant, be stubborn and don't be afraid to explore – most important discoveries were made when we were looking for something else!

Why does microbiology matter?

Brendan and Vanessa: Microbes are the great survivors and occupy most niches on the planet, from deep-sea vents to hot springs. Understanding how and why they thrive is a true voyage of discovery.

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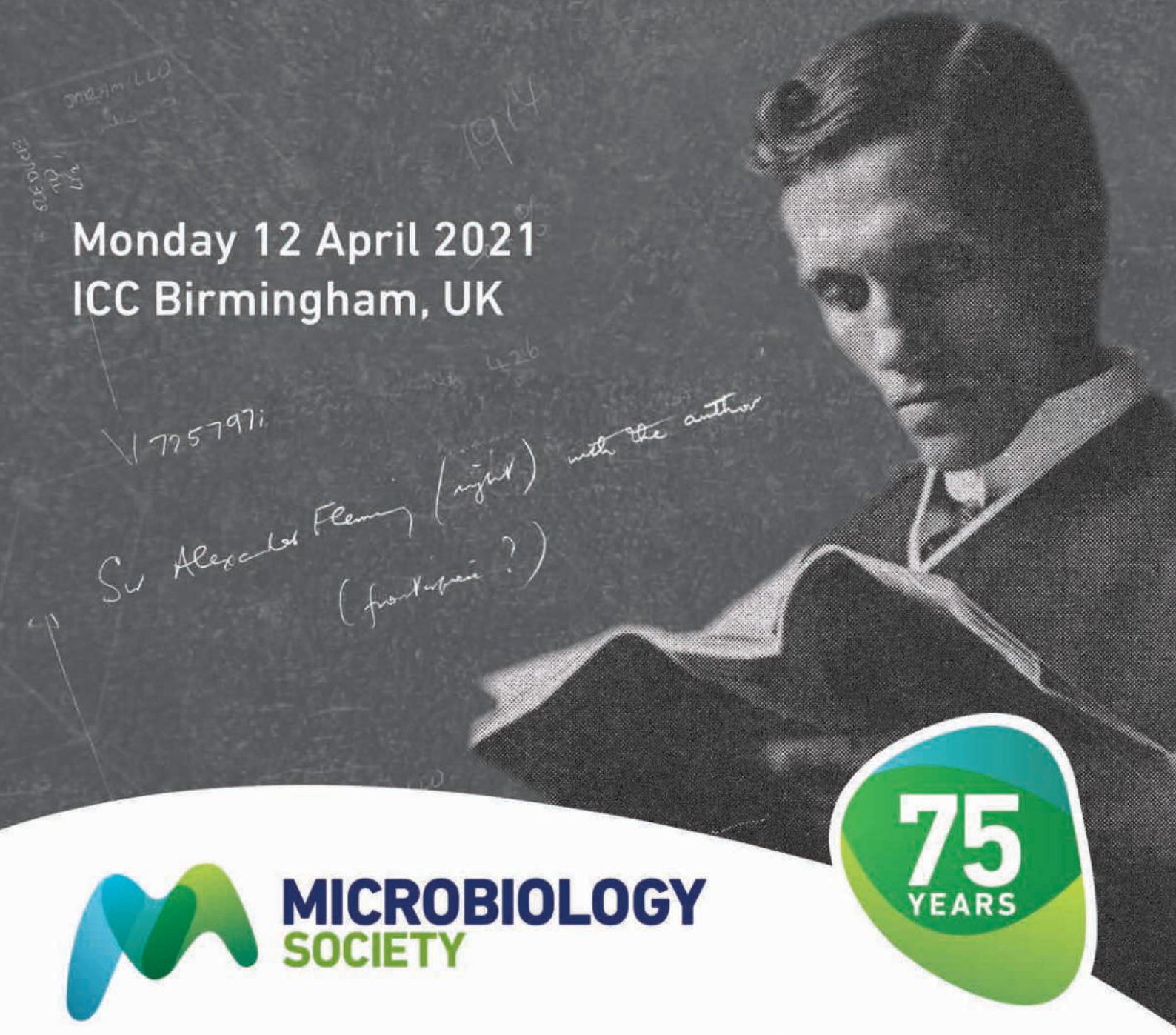

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The Antarctic marine environment. K. R. Duncan

Microbes and where to find them

Microbes are found in a diverse range of environments and contribute to many essential environmental processes. This section introduces some of the many microbes that thrive in niches around the globe and considers how microbes could exist outside of our world.

Microbes at extremes

Katherine Duncan

Antarctic ice-sheets and ancient geological rocks from other planets are examples of fascinating and extreme ecosystems used to study life. However, when considering the breadth of physical and chemical parameters, almost any environment can become extreme by tweaking even one variable. These extreme microbial environments can include thermophiles thriving in compost heaps, bacteria under enormous pressure on the sea floor, our own microbiota at low pH in the stomach, heavy-metal-adapted strains in mines and fungi surviving extreme radiation in Chernobyl.

Understanding the boundaries in which life can not only exist, but thrive, can aid our understanding of microbial adaption through genomic and metabolic processes. Although the environments are extreme, understanding these processes can have wide-ranging applications. Some examples include understanding anthropogenic impacts on the environment, improving biotechnological processes and studying the evolutionary mechanisms that lead to new biological and chemical diversity.

Microbes living at the extremes are testing out possibilities and carving out a niche to survive. These microbial pioneers are pushing limits; as a microbiologist the questions are exciting, challenging and represent a fascinating world of discovery.

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Katherine (Kate) Duncan has completed an MChem (Scotland and Florida), PhD (Biomedical Sciences, Canada) and two postdoctoral fellowships (Marine Biomedicine, University of California, USA, and Scottish Marine Institute, UK) all focused on marine natural products. In 2016, she started her research group, combining genomics and metabolomics to understand the chemical language of marine microbes and what influences it. Kate is a member of the Society's Prokaryotic Division (environmental microbiology).

Why does microbiology matter?

Micro-organisms are a fundamental component of every ecosystem on the planet.

What qualifications did you obtain before starting this role?

I have a master's degree in Chemistry (MChem, University of Aberdeen) with an international placement (Florida) focused on marine natural products. Following this, I decided to learn molecular biology and microbiology and completed a four-year PhD in Biomedical Sciences (University of Prince Edward Island, Canada). I then completed two postdoctoral fellowships, the first in Marine Biomedicine at Scripps Institution of Oceanography, University of California San Diego, and a second in Marine Biodiscovery at the Scottish Marine Institute.

Extreme bacteria in supporting human space exploration and the future of habitats on the Moon and Mars

Mara Leite

As we celebrated the 50th anniversary of the Moon landing this past year, another historical milestone for humanity is on the horizon. Different space agencies are preparing for long-term human presence on other planetary bodies. There are several convincing arguments to pursue this goal. Among these are technological advances and scientific knowledge, economic interests, as well as human ambition and curiosity.

Due to their proximity to Earth, both the Moon and Mars are the main targets for the establishment of permanent human colonies. The European Space Agency (ESA) has already expressed interest in building a moon village, and, more recently, the National Aeronautics and Space Administration (NASA) has created the Artemis program, aiming to take humans back to the Moon in the next decade, followed by crewed missions to Mars in the 2030s. Furthermore, countries such as China and Russia, and private companies, like SpaceX, are also expanding their space programs with similar intents.

Human settlement in space

The first steps of a human settlement involve the construction of habitats that can protect crew members from high doses of radiation and significant temperature fluctuations, while simultaneously providing a breathable atmosphere. Proposed designs have included a variety of materials. Some ideas incorporate inflatable subterranean modules, ice houses, and 3D printed structures using thermoplastics and local regolith (a mixture of dust and broken rock present on the surface of terrestrial planets and moons). The use of local (lunar and Martian) resources, also known as *in situ* resource utilisation (ISRU), is gaining momentum.

One of the biggest challenges in deep-space exploration is the cost related to the number and mass of consumables needing to be transported from Earth. Adapting to using native resources and recycling these resources will be pivotal in reducing mission costs. Habitats will be supplied with life-support systems – a combination of instruments that can provide an artificial Earth environment. These systems will rely on extreme bacteria to recycle human waste into valuable products, such as oxygen and water.

Extremophiles as model organisms

Extreme micro-organisms live in environments that are inhospitable to humans. Notable examples of these habitats include hot springs and hydrothermal vents. Extremophiles, as they are commonly known, are classified according to the environmental parameters in which they thrive. These parameters range from physical to chemical, and cover temperature, pH and radiation, among others. For instance, thermophiles, such as *Thermus aquaticus*, proliferate in high temperatures, while *Thiobacillus acidophilus* and other acidophiles flourish in acidic environments.

NASA / Science Photo Library

In the field of astrobiology, extremophiles are used as model organisms for extraterrestrial life. They can identify the range of conditions where life can be found and pinpoint locations that might potentially harbour micro-organisms. In this discipline, extremophiles can also help us to understand how life emerged and assist humans surviving in hostile conditions, like the ones present on the Moon and Mars. The rise of oxygen during the Great Oxidation Event is attributed to cyanobacteria; a popular example of the importance of these organisms in shaping Earth's atmosphere and, consequently, its terrestrial biosphere. Due to their ability to convert carbon dioxide and sunlight into carbohydrates and oxygen, cyanobacteria and other photosynthetic microbes have been suggested for engineering the Martian atmosphere through a process known as terraforming.

Extremophiles are also gaining biotechnological notoriety. Their enzymes are capable of withstanding stressful conditions, including those present in industrial processes. Two industries in which they are being exploited are mining and biofuels. In biomining, valuable minerals and metals are extracted by micro-organisms that interact with rocks. Species of fungi, acidophiles and thermophiles have proven to be efficient in this process. Thermophiles are also being studied in the production of biofuels. Locally produced biofuels could help alleviate the challenge of transporting propellant from Earth.

Secondary metabolites and valuable properties

Furthermore, microbes also secrete products with proven value in the food industry, medical field and agriculture. Some species of cyanobacteria and algae are known for being rich in vitamins, antioxidants and other compounds with nutritional value. Additionally, a wide range of extremophiles produce secondary metabolites with pharmaceutical properties that can be used to fight infections and other maladies. Moreover, some strains produce bioplastics which can be 3D printed into a variety of objects.

In agriculture, metalophiles, known for growing in high concentrations of metals, can be utilised to detoxify the Martian soil through bioremediation, while nitrogen-fixing bacteria can serve as soil fertilisers.

Lastly, the biomass of some micro-organisms has the potential to serve as renewable feedstock to other microbes that rely on organic sources to grow, expanding the spectrum of microbial applications in human space flight.

Sustainable solutions

Sustainability in deep-space missions is vital. It can dictate the success of a mission and, more importantly, the survival of astronauts. Technological innovation and sustainable solutions developed for future settlements could also help us navigate through a climate and resources crisis here on Earth.

Through utilisation and recycling of local resources, extreme microbes can assist in all aspects of human life, from medical applications to the production of oxygen, opening the doors to a new era of space exploration.

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Mara Leite completed a BSc and MSc in Microbiology before working at the University of Washington in Seattle, WA, USA. She is currently pursuing a PhD in Astrobiology in London at the University of Westminster under the guidance of Dr Lewis Dartnell (**lewisdartnell.com**). She is interested in the applications of micro-organisms for space missions, with a particular focus on the production of bioplastics and 3D printing.

Why does microbiology matter?

I find microbiology to be one of the most important disciplines because it studies the main inhabitants of our planet, the microbes. Micro-organisms hold a crucial part in maintaining life on Earth. One of microbiology's most critical aspects is sustaining human survival by fighting pathogens and providing probiotics. The study of microbiology also extends beyond medicine, with applications in the food industry, industrial processes and other areas, consequently improving our everyday lives and making microbiology an incredibly valuable field as a whole.

How do you see this field changing in the future?

These are thrilling times in the field of microbiology. The tools available have improved and will continue to do so for years to come. Many of the time-consuming procedures are now being automated. Genome sequencing is becoming more accessible, which allows for increasingly rapid identification of organisms and characterisation of new species. Areas that are expected to see growth are human microbiome research, synthetic biology and pharmaceutical research. Advances in human microbiome research can help us to gain a better understanding of how the gut microbiome can influence our health, as well as the effectiveness of drugs and treatments. Synthetic biology is also growing and it can broaden microbiology's applications. Finally, antibiotic-resistant superbugs are currently one of the biggest threats to human health, and are increasing the urgency for the development of improved pharmaceuticals. This will hopefully create a new golden age in the field of microbiology.

Microbes in climate change and recycling

Penny Hirsch

Soil is a complex environment that supports the largest, most diverse and resilient microbial community on the planet, essential for nutrient cycling and plant growth. The expanding human population means that exploitation of land for agricultural and industrial use is increasing, raising concerns about long-term sustainability and impact on the major biogeochemical cycles. The earth has finite resources, and without soil microbe activity, many essential elements would not be available to plants. Likewise, without carbon and energy supplied by photosynthesis and detritus from animals (directly or indirectly sustained by plants), soil would consist mainly of inorganic mineral particles from weathering of rocks. Together, plant, animal and microbial activity provides the organic components that bind mineral particles into aggregates, give soil structure and make it fertile.

The soil microbiome has an estimated 10^9 bacterial cells and 10^4–10^6 species (or 'operational taxonomic units' – OTUs) per gram (g) of soil in temperate climates. Soil archaea and fungi are less abundant and diverse than the bacteria but are also essential for nutrient cycling. The soil microbiome can fix atmospheric carbon and nitrogen, solubilise minerals (P, K, S, Mg, Ca, Fe and a range of trace element micronutrients) to aid plant nutrition and degrade organic residues to release nutrients, cycling them between abiotic and biotic pools. These nutrient transformations can be divided into functions common to many diverse organisms and more specific activities performed by defined groups of specialists.

The carbon cycle

The majority of soil micro-organisms return carbon (C) to the atmosphere as carbon dioxide (CO_2) via aerobic respiration, often measured as a proxy to estimate soil microbial biomass. In contrast, methane (CH_4), a major greenhouse gas more potent than CO_2, is produced during anaerobic respiration and fermentation by a narrow range of methanogenic archaea. Wet, organic C-rich soils (wetlands, rice paddies) generate more CH_4 than methanogens in animal rumens and wastes. Emissions are predicted to rise as global warming thaws permafrost. Some specialist methanotrophic bacteria and archaea can oxidise CH_4.

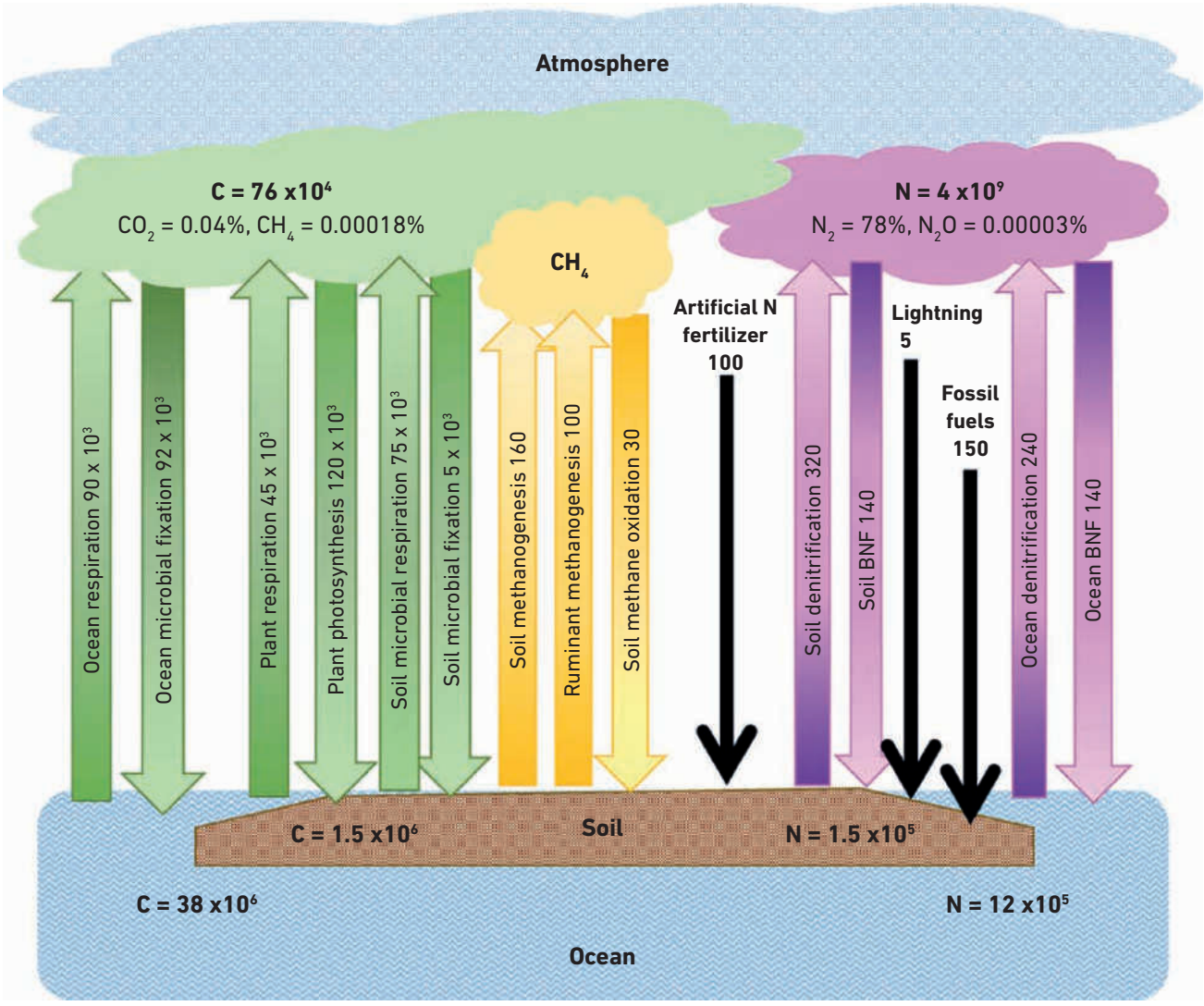
Although plants provide most organic C to the soil pool, many phototrophic and autotrophic bacteria and archaea also fix atmospheric CO_2. Further organic C is released to soil by fungi that decompose plant polymers containing lignin,

cellulose and hemicellulose, their hyphae efficiently colonising plant litter and woody residues. Diverse soil bacteria, belonging to the *Proteobacteria*, actinomycetes, *Firmicutes* and *Bacteroidetes* also produce enzymes that degrade such residues. This ability to oxidise complex organic polymers enables many of these bacteria and fungi to decompose xenobiotic pollutants such as phenolic rings.

The nitrogen cycle

Nitrogen gas (N_2) is 78% of the atmosphere and N is an essential component of all living organisms. Only certain bacteria and archaea possess nitrogenase that can reduce the triple bond in N_2 to ammonia. Some N_2 is reduced by lightning, but the major natural source is biological N fixation (BNF) in soils and a similar amount in oceans. Burning fossil

Fig. 1. **The most important steps in the global N and C cycles, leading emissions of the greenhouse gases carbon dioxide (CO_2), methane (CH_4) and nitrous oxide (N_2O). Fluxes shown in the arrow are teragram (Tg) year^{-1}; pools in atmosphere, soil and ocean are Tg (1 Tg = 10^{12} g). The green arrows show CO_2 fixation and losses, the yellow arrows show CH_4 fluxes and the purple arrows show N_2 fixation and the return of gaseous N (both N_2 and N_2O) by denitrification. The biotic drivers are microbiological except for plant photosynthesis and respiration. The abiotic inputs of N are shown as black arrows. Compared to CO_2, CH_4 has 28x and N_2O has 265x more global warming potential over 100 years.** Intergovernmental Panel on Climate Change 2014 Synthesis Report (ipcc.ch/site/assets/uploads/2018/02/SYR_AR5_FINAL_full.pdf); Penny Hirsch



fuels releases oxides of N which are ultimately deposited on soil and in oceans, increasing since the industrial revolution with adverse effects on air quality and human health, contributing to global warming. Since the early 20th Century, industrial production of N fertiliser using the Haber-Bosch process to reduce atmospheric N_2 has enabled increased agricultural productivity and now provides a similar input to soil as BNF. Without artificial fertilisers or recycled manures, farming relies on leguminous plants (e.g. soybean, clover) that form symbiotic associations with rhizobia (mostly *Alphaproteobacteria*) in root nodules that provide a protected niche rich in organic C and energy for efficient BNF. Other BNF bacteria are important in marine/aquatic systems and soil crusts (e.g. *Cyanobacteria*) and in associations with plants other than crops, e.g. *Frankia* (*Actinobacteria*).

Ammonia (NH_4^+) in soil may arise from BNF, artificial fertiliser, animal wastes or decomposition of organic matter by many bacteria and fungi. It is subject to nitrification by specialist chemoautotrophs that derive energy from oxidation reactions: first to nitrite (NO_2^-) by ammonia-oxidising bacteria and archaea, then to nitrate (NO_3^-) by nitrite-oxidising bacteria. As NO_3^- is more mobile that NH_4^+, it is more readily lost from soil in water run-off and leaching, and it is also a substrate for denitrification, a function of at least 5% of soil bacteria. Denitrification is a problem in anoxic conditions when bacteria switch from aerobic respiration to using nitrite and nitrous oxides as terminal electron acceptors. Ultimately, conversion to N_2 completes the N cycle but the intermediate nitrous oxide (N_2O), a potent greenhouse gas, is released in significant quantities. Soil emissions are worst in warm, wet conditions where N and organic C are plentiful.

Looking forward

Soil microbes are essential for healthy soil and food production, releasing nutrients from minerals and organic matter and contributing to soil organic C and soil structure. Some form symbiotic associations that enhance mineral uptake by plants (mycorrhizal fungi) or provide N (rhizobia), beneficial associations that are exploited to improve sustainable agriculture. Adverse effects arise from the release of CH_4, N_2O and other greenhouse gasses: terrestrial and aquatic metagenomes reveal many microbes with the capacity to generate these products, and others that can mitigate (e.g. by oxidising CH_4 or reducing N_2O). Therefore, in managed systems, it is important to avoid conducive conditions, such as by improving drainage and avoiding excessive N fertiliser use. Taking care of soil is key to a greener future.

Further reading

Ciais P, Sabine C, Bala G, Bopp L, Brovkin V *et al.* Carbon and Other Biogeochemical Cycles. In: Stocker TF, Qin D, Plattner GK, Tignor M, Allen SK *et al.* (eds). *Climate Change 2013: The Physical Science Basis. Working Group I Contribution to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change.* Cambridge, UK and New York, USA: Cambridge University Press; 2013. pp. 465–570.

Fowler D, Pyle JA, Raven JA, Sutton MA. The global nitrogen cycle in the twenty-first century: introduction. *Philos Trans R Soc Lond B Biol Sci* 2013;368:20130165. DOI:10.1098/rstb.2013.0165.

Hirsch PR. Microorganisms cycling soil nutrients. In: van Elsas JD, Trevors JT, Rosado AS, Nannipieri (eds). *Modern Soil Microbiology,* 3rd edn. Portland, USA: P. Taylor & Francis Inc; 2019. pp. 179–192.

Hirsch, PR. Soil microorganisms: role in soil health. In: Reicosky ED (ed). *ManagingSoil Health for Sustainable Agriculture*. Cambridge, UK: Burleigh Dodds Science Publishing; 2018. pp. 169–196.

Schimel JP, Schaeffer SM. Microbial control over carbon cycling in soil. *Front Microbiol* 2012;3:348. DOI:10.3389/fmicb.2012.00348.

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Penny Hirsch has worked on the microbiology of crop plants and soils for many years. She is now an emeritus scientist and, until recently, she led a group investigating microbiome diversity and activity at Rothamsted Research, a major centre for strategic agricultural science.

Why does microbiology matter?

Microbes underpin all life on earth: without them the planet would have remained abiotic and we would not be here. We have to understand them to comprehend the functioning of ecosystems on all scales.

What parts of your job do you find most challenging?

Trying to explain to non-experts why it is essential to study things we cannot see and often describe only by identifying DNA and RNA sequences, and how we can deduce their functional significance from this information.

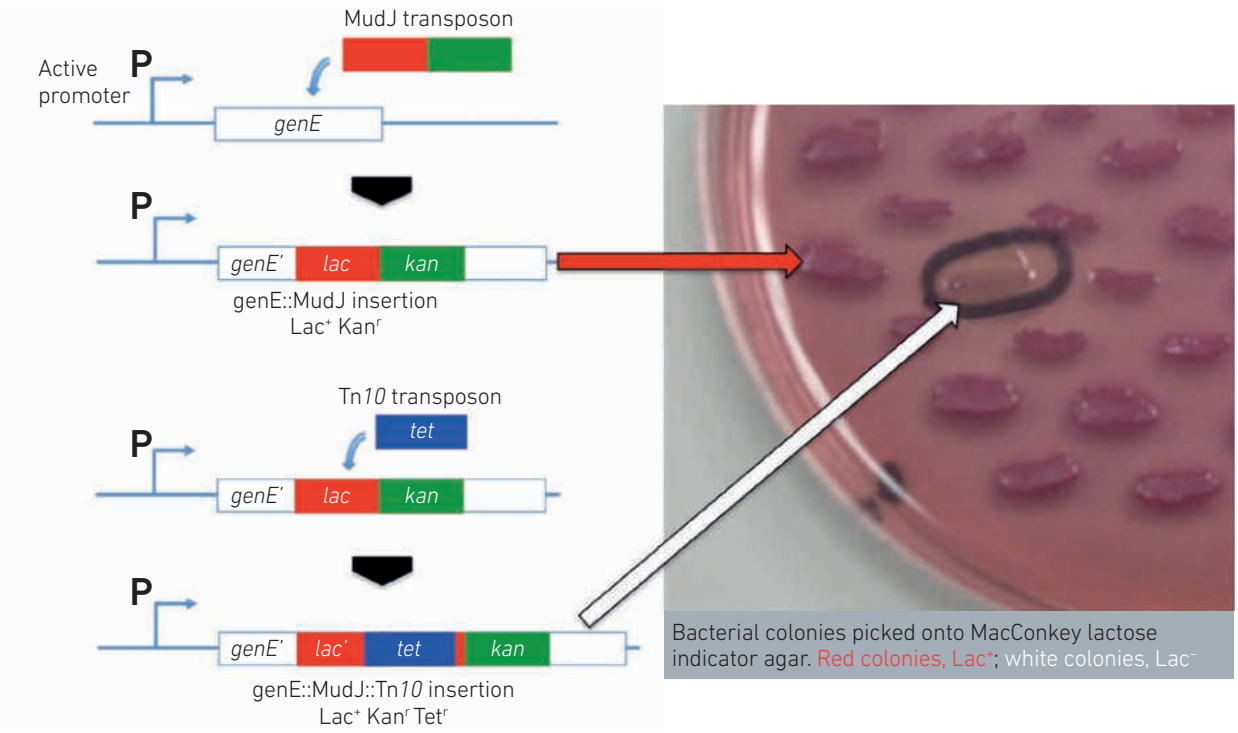
Microbiology and genetics

The genetic plasticity of microbes enables their survival. This section outlines some of the advances that have been made in modern biotechnology and the significance of this research to microbiology.

Genetics in microbiology

Charles J. Dorman

Much of our understanding of mutation, genome rearrangement, DNA repair, DNA recombination mechanisms, DNA replication, DNA transfer, gene regulation and much more has come from fundamental research in microbes. Their short life cycles have allowed microbes to be used in studies of evolution that have elucidated many of the underlying molecular processes. During World War Two, studies in a bacterium (*Pneumococcus*) identified DNA as the agent that could transform the phenotype of a living cell. Over sixty years ago, the first genetic switches to be characterised were in bacteria, and we continue to learn about bacterial gene regulation mechanisms and about genome-



Bacterial colonies picked onto MacConkey lactose indicator agar. Red colonies, Lac⁺; white colonies, Lac⁻

A simple experiment in bacterial genetics exploiting 'jumping genes' to create gene fusions and genetic mutations. A gene of interest in *Salmonella*, *genE*, is tagged with a *lac* reporter gene using a modified Mu bacteriophage , MudJ. Insertion of the modified phage by transposition is selected on kanamycin-containing agar plates followed by screening for the presence of the desired *genE-lac* fusion on MacConkey lactose plates where these form red (Lac⁺) colonies. The *genE* promoter, **P**, is responsible for expression of the Lac⁺ phenotype and any signals affecting its activity can now be studied in living bacteria that harbour the *genE-lac* fusion. The *lac* reporter gene is next interrupted by insertion of a Tn*10* transposon, producing colonies that are white (Lac⁻) on MacConkey lactose indicator plates. This proves that the *lac* gene is required for the red Lac⁺ phenotype. The structures of the modified genes are confirmed by polymerase chain reaction amplification followed by DNA sequencing. Charles J. Dorman

wide, collective control of gene expression. This both informs our understanding of naturally occurring microbes and guides developments in synthetic biology. Microbial and viral genetic switches are exploited as logic gates in biological computers, blurring boundaries between biology and information technology. Simultaneously, advances in conventional computing power allow us to interpret unprecedented volumes of genetic information, facilitating new approaches to infectious disease surveillance, prediction, prevention and therapy.

Modern biotechnology is founded on microbial systems. Recombinant DNA methodology ('cloning') began with bacterial plasmid vectors into which foreign DNA was introduced deliberately. Cloning exploits bacterial restriction enzymes, proteins that 'restrict' the replication of bacteriophages (viruses) in bacteria. Bacterium-specific DNA methylation patterns are epigenetic features that protect their genomes from restriction. The polymerase chain reaction (PCR) is based on the heat-resistant polymerases found in archaea from high-temperature environments. PCR is now in routine use in molecular biology and in forensic laboratories. The public has become accustomed to descriptions in the news media of CRISPR-Cas as a 'gene editing tool'. In fact, it is an adaptive immunity system used by bacteria to identify and to destroy invading DNA molecules, including viruses.

Combining microbial genetics with single-molecule and single-cell techniques, together with advances in imaging such as super resolution microscopy, is providing understanding of molecular processes at unprecedented levels of detail. The future for genetics in microbiology is a very bright one indeed!

Further reading

Dorman CJ. *Structure and Function of the Bacterial Genome*. Hoboken, NY, USA: John Wiley and Sons; 2020.

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Charles J. Dorman joined the Microbiology Society in 1982. He has held the established Chair of Microbiology at Trinity College Dublin in Ireland since 1994, having previously been a lecturer in biochemistry at Dundee University in Scotland, where he also held a Royal Society University Research Fellowship.

Why does microbiology matter?

Studying the relationships that microbes have with one another, with non-microbial organisms and with the wider environment provides humans with useful insights into how these transactions can be conducted successfully and sustainably. They may be much smaller than us, but microbes face problems of resource discovery and management, energy deficits, transport and manufacturing, waste production and recycling, political interactions involving cooperation and antagonism, economic cycles of boom-and-bust and much more that is eerily reminiscent of our own experiences.

What inspired you to become a microbiologist?

Two things. (1) Discovering that a study of bacteria opened the door to an investigation of gene regulation in biological systems that are experimentally tractable. (2) Discovering an undergraduate degree course that allowed me to win enough prize money each year to cover the following year's tuition fees (unlike the UK in the 1970s and early 1980s, Ireland charged for tuition, making university education difficult to access for people from my social group).

Restriction enzymes

Qaiser I. Sheikh and David P. Hornby

Restriction enzymes, or endonucleases, have been at the core of molecular biology for over 50 years. This is perhaps somewhat surprising, in view of the esoteric nature of the work that led up to the discovery of these enzymes, which was famously recognised by the award of the 1978 Nobel Prize in Medicine or Physiology to Werner Arber, Daniel Nathans and Hamilton O. Smith. The practical translation of an enzymatic system, referred to both genetically and functionally as 'restriction and modification', represents a landmark in the close interplay between

biological genome processing and the laboratory manipulation of genes. In many prokaryotes, restriction and modification form part of a struggle for supremacy between bacteria and bacteriophages. The restriction enzyme attacks and destroys unmodified DNA (the bacteriophage) while the modification enzyme protects the host genome from restriction.

Restriction enzymes have been centre stage in molecular biology for around 40 years, providing the first route to molecular cloning of genes in prokaryotes. The type II restriction enzymes (often considered by aficionados to be the boring relations in this fascinating family of endonucleases, which are categorised with respect to their genetic and biochemical properties) are among the most enduring and valuable tools for molecular biologists. These homo-dimeric enzymes typically recognise a short (4–8 base pairs) DNA duplex within a genome or plasmid and introduce a precise cut across the symmetry axis, producing either two 'blunt' DNA fragments, in a sequence such as that shown below:

```
5′ ... G A T ▼ A T C ... 3′
3′ ... C T A ▲ T A G ... 5′
```

or a staggered cut, in a palindromic sequence of the type shown below:

```
5′ ... G ▼ A A T T C ... 3′
3′ ... C T T A A ▲ G ... 5′
```

In the laboratory, any 'compatible' DNA fragments can be joined using, for example, a DNA ligase enzyme. Restriction enzymes are given names that reflect their biological origin and the chronology of their discovery, hence *Eco*RI (from *Escherichia coli* strain R, recognising the duplex GAATTC) and *Bam*HI (from *Bacillus amyloliquefaciens* strain H, recognising the palindromic sequence GGATCC). Restriction and modification enzymes play key roles in safeguarding the host genome in many microbial genomes, deriving their name from their function in restricting the growth of invading bacteriophages.

The golden age of restriction enzymes

During the 'golden age' of restriction enzymes in molecular biology, they were essential for not only cutting and pasting genes, but were central to the development of DNA diagnostics – some of you may remember RFLPs (restriction fragment length polymorphisms) and for the construction of plasmid and later genome maps. Ten years after the first commercial development of restriction enzymes, pioneered by New England Biolabs in the late 1970s, the emergence of thermostable DNA polymerases took centre stage, as the polymerase chain reaction began to drive the development of many molecular biology protocols. However, there remain today many situations, such as analytical gene and plasmid mapping and the general manipulation of DNA fragments, that enable these two powerful technologies to exist side by side.

The first steps to CRISPR-Cas9

In a similarly serendipitous discovery, a series of clustered, regularly interspaced short palindromic repeats discovered in prokaryotes 15 years later led to the development of the contemporary field of gene and genome editing. Unlike restriction enzymes, the recognition sequences are derived from prior phage infection and genome recombination events. However, the first step in the CRISPR-Cas9 (in one well used example) process is a sequence-specific DNA cleavage, in a manner related to the endonuclease activity characteristic of restriction enzymes. Biologically, this is used to fend off subsequent phage invasion by the original phage, but the ability to harness this phenomenon for any specific gene has led to its emergence as one of the most important techniques in genomic medicine as well as molecular biology research.

Restriction (and modification) enzymes have not only powered biological and medical research and diagnostics since their discovery, they have also shed light on the fundamental molecular events associated with DNA recognition. Starting with the publication of the structure of *Eco*RI and *Eco*RV in the 1990s, the diversity of recognition strategies, including DNA twisting, kinking and flipping (discovered first in the modification partner of *Hha*I restriction enzyme), have paved the way for our molecular understanding of many genetic transactions. Moreover, the growth of microbial genome sequences has revealed that restriction and modification genes are present in around 90% of those genomes sequenced to date. In my view, this fascinating class of genes has many more secrets to reveal.

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Qaiser I. Sheikh studied in Pakistan and Japan before moving to the University of Sheffield for a PhD and postdoctoral research fellowships. He then worked as Postgraduate Support Officer and then as a lecturer in the Department of Molecular Biology and Biotechnology, and developed the current Molecular Biology and Biotechnology MSc course, of which he is Programme Leader.

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David P. Hornby obtained a BSc (Biochemistry and Chemistry) and a PhD (Biochemistry) from the University of Sheffield. He undertook postdoctoral work in Sheffield, Leeds and Basle, followed by a Fellowship at EMBL and work at the Scripps Research Institute. He was appointed to a Lectureship at Sheffield in 1990 and became Director of Enterprise in Life Sciences in 2008. He was Sabbatical Visitor (2012–2013) at the LSTM and Director of Research and Innovation at the Liverpool Life Science UTC (2013–2015). He is currently working with school students in association with the Northern Schools Trust.

Why does microbiology matter?

David: I used to place a high value on microbiology because it made biochemistry more tractable: a somewhat simplistic and rather selfish perspective, but this was because I spent much of my research career purifying and characterising enzymes and later recombinant enzymes. Many years later, as I develop new multidisciplinary science lab classes for schools based around insects and simple catalysts, I have become fascinated by the concept of the microbiome and the evolution of early microbes. Microbiology matters to me now because it helps us not only understand how life originated on Earth, but how microbes continue to play a key role in the evolution of all higher organisms through a diverse range of mutually beneficial interactions.

What is the most rewarding part of your job?

David: Being able to continually educate myself and then finding a way to pass the ideas and concepts on to young scientists of all abilities.

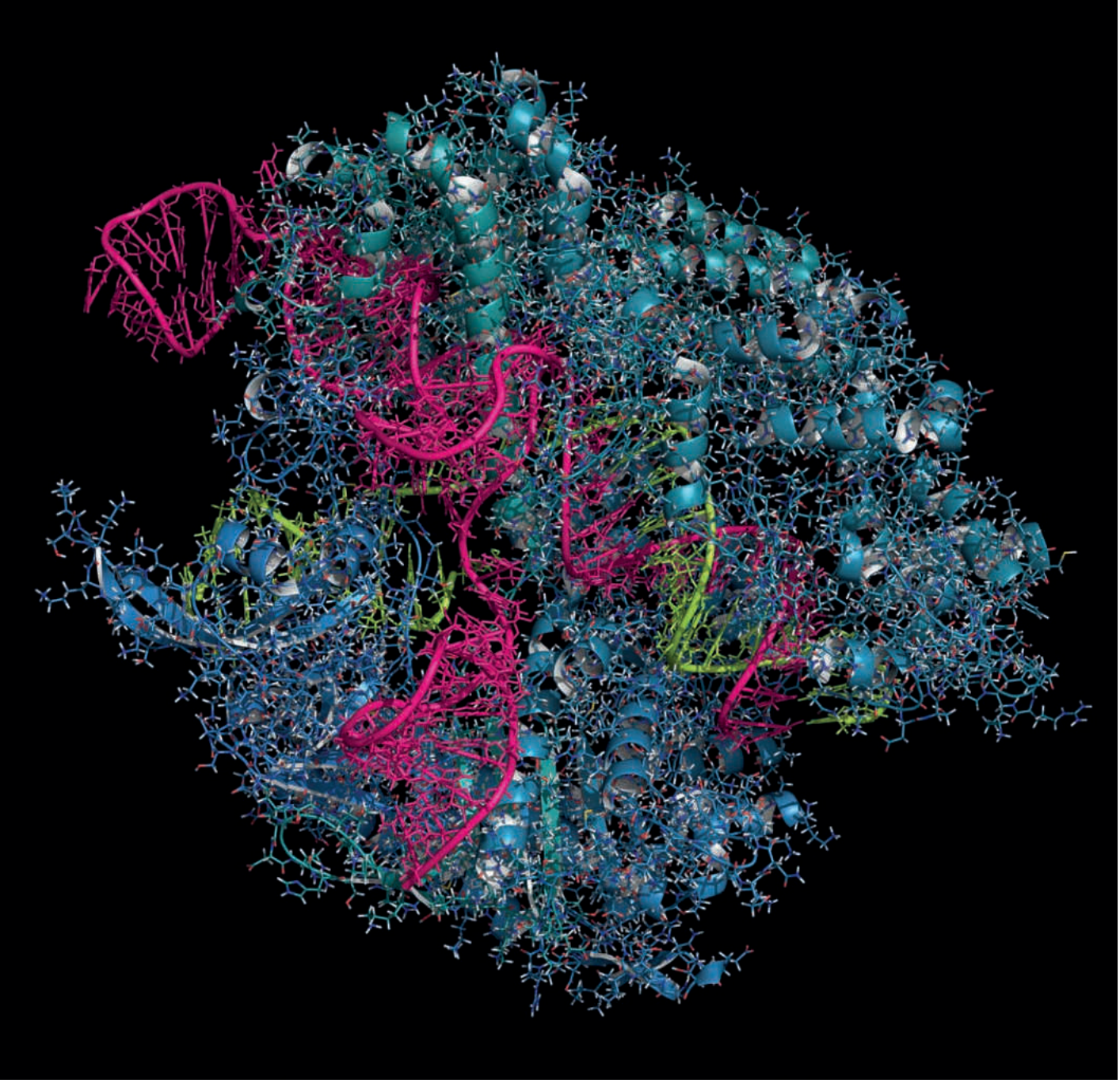
CRISPR-Cas: Cunning Research Investigating the Science of Prokaryotes Results in Challenges and Applications for Society

Peter C. Fineran and Nils Birkholz

It has been a common theme in recent years: just before the Nobel Prize winners are announced, the #CRISPR (clustered regularly interspaced short palindromic repeats) Twitter feeds are buzzing with debates. Which heroes and/or heroines of the field will be awarded? October 2019 was no different. And even though all expectations went unfulfilled once more, everyone agrees that a CRISPR Nobel is a question of when not whether. Who should the Academy pick, and for what? The characterisation of CRISPR as a sophisticated form of bacterial immunity? The discovery that the enzyme Cas9, involved in this immunity, could be harnessed for gene editing purposes? One of the many CRISPR-based technologies developed since? The impact of CRISPR is not only founded in the tremendous research output, however. If, within a decade, a scientific discovery rises to a global issue worthy of dedicated documentaries, the impact of this discovery is going to be profound – not only for academia but for society as a whole. How did it come to this?

CRISPRs and Cas

It is a beautiful example of the serendipity of fundamental research leading to unexpected potential in diverse applications. It all started with some peculiar repetitive sequences in a bacterial genome, more than 30 years ago.



CRISPR-CAS9 gene editing complex from *Streptococcus pyogenes*. The Cas9 nuclease protein (blue) uses a guide RNA (green) sequence to cut DNA (pink) at a complementary site. Molekuul/iStock

It took decades to figure out that these sequences, now known as CRISPRs, provide an immune memory – storing small bits of DNA from past invaders, such as viruses, to facilitate their recognition upon subsequent attack. Scientists from all over the planet have now elucidated more details of how bacteria update and use these memories, as well as CRISPR-associated (Cas) proteins, to detect and destroy their enemies. Cas9 attracted particular attention after it was shown to be a single programmable nuclease – it can be supplied with an artificial memory and target any desired sequence which will then be cleaved. The researchers envisioned that this capacity would enable the application of Cas9 for gene editing.

The use of CRISPR-Cas

Bacteria possessing an adaptive immune mechanism – a feature long thought to be exclusive to higher organisms – was a spectacular discovery in its own right, but the easy programmability of Cas9 really got the 'CRISPR Craze' rolling. Not long after, CRISPR technologies were applied in fields such as agriculture, where plants can be enhanced to withstand drought or increase yield, and diverse model and previously 'non-model' organisms are being genetically modified with ease. The possibilities of the technology appear endless. Why not apply it to human genomes to rid them of disease-causing mutations? Indeed, multiple clinical trials involving medical applications of genome editing are being pursued.

This is exciting – but CRISPR–Cas9 is not flawless. For example, Cas9 not only targets the programmed sequence but can sometimes cause damage to other genomic locations too. To make precise changes in the genome, researchers can supply a repair template, but this is not always efficient. Newer variants of the technology aim to address these challenges. One approach is to use a Cas9 variant that can target but not cleave DNA, and couple this with another protein that performs a certain task at the desired location. For example, base editors can alter a single DNA base without cutting the double helix – useful, as many genetic diseases are caused by a single faulty nucleotide. The recently developed technique of prime editing utilises Cas9 fused to a reverse transcriptase enzyme for a find-and-replace approach.

Ethics and prohibitions

While we are getting closer to mastering the technical challenges of gene editing, many other aspects require consideration before it can be widely applied. With the rapid development of CRISPR technologies, ethics, public acceptance and legislation have a hard time catching up. A striking demonstration of this was the announcement in late 2018 by a Chinese scientist who claimed to have used Cas9-mediated genome editing on twin embryos to protect them against HIV infection. Although many countries prohibit human germline modifications, the outrage that followed the announcement highlighted the lack of adequate controls and regulations. Some leading scientists have called for a moratorium, while others consider this a waste of time or question the feasibility: it would be difficult to monitor and not all countries might care equally about prohibitions.

Reaching consensus is paramount, not only for genome editing but for other CRISPR-based innovations too, as the latter might be jeopardised if scepticism against CRISPR arises. For example, Cas9 and other CRISPR-associated proteins, such as Cas12 and Cas13, can be utilised for the detection of viral infections or identifying antibiotic-resistant bacteria – important applications in times of devastating viral epidemics and failure of common antibiotics. Things need to be handled transparently for CRISPR technologies to unfold to their full potential. Yet more innovations are certain to be discovered – and with them, yet more discussion for the yearly Twitter Nobel debates.

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Peter C. Fineran heads a research team interested in bacterial defence systems, including CRISPR-Cas and bacteriophage biology. He obtained his PhD from the University of Cambridge, UK, and a BSc (Hons) in Biochemistry from the University of Canterbury, NZ. He has been a Microbiology Society member since 2002 and was the recipient of the 2019 Fleming Prize.

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Nils Birkholz is a PhD candidate working on interactions between bacteria and bacteriophages in Peter Fineran's research group. He obtained his BSc and MSc degrees from the Technical University of Braunschweig, Germany.

How does CRISPR benefit the average person?

Peter: Well, if you had yoghurt this morning then you probably had some dairy that has been fermented using strains that have been naturally adapted (using CRISPR) to phages that can spoil fermentations in the dairy industry. So, it is already having an application there. More generally, the tools are leading to massive advances in our ability to do fundamental science and to understand disease processes. We are also heading in the direction of being able to use CRISPR in different therapies and diagnostics.

Why does microbiology matter?

Peter: Although invisible, microbes are everywhere and important for so many things, from the environment, to health and industry. For me, I love that microbiology is such an incredible experimental system. That is actually why I got interested in microbial genetics; it's kind of like solving a puzzle. You can just play around with the components and then actually work out how systems work. For example, you can just take out a gene, see what happens; put a gene in, see what happens. It's because of this simplicity that microbiology is such a powerful system for answering biological questions.

New frontiers in microbiology

As we have progressed through the 21st century, we have expanded and developed our understanding of how microbes are related to and interact with each other. This section considers the ever-growing tree of life, how we can study complex microbial communities to gain new insights and the possibility of discovering life on other planets.

The ever-growing tree of life

Bryn McCulloch and Thorsten Allers

Genealogical research can yield some unexpected surprises. The tree of life shows the relationship between all organisms based on their common ancestry. Until 1977, it had two major branches: prokaryotes and eukaryotes. Then Carl Woese suggested that life could be categorised into three fundamental domains: Eukarya, Bacteria and Archaea. Notably, Archaea and Eukarya are more closely related to each another than to Bacteria.

The discovery of new archaeal groups has included DPANN – archaea with extremely small cell and genome sizes that appear to be obligate symbiotes – and Asgard – a recently cultivated group found at deep sea vents. Including Asgard archaea in phylogenetic analyses has uncovered a strong affiliation with eukaryotes, leading to the proposal for a two-domain Tree of Life: this time, the Eukarya branch originates from *within* the Archaea. In this scenario, eukaryotic cells originated from a symbiosis between an Asgard-like host cell and a proteobacterium, which later became a mitochondrion.

As with any genealogical research, the two-domain versus three-domain tree has been a topic of debate within the scientific community, but new evidence is making a two-domain tree appear more promising. Tom Williams and colleagues at the University of Bristol analysed more than 3,000 gene families in Archaea and Eukaryotes and consistently found Eukaryotes to have originated from within Archaea and that an Asgard lineage called *Heimdallarchaeota* is the closest archaeal relative to the Eukarya.

The tree of life continues to expand with the discovery of new life. This could come from previously unexplored environments, such as the growing field of astrobiology, but also from the ability to create synthetic life. Expect plenty more unexpected surprises!

Further reading

Imachi H, Nobu MK, Nakahara N, Morono Y, Ogawara M *et al.* Isolation of an archaeon at the prokaryote–eukaryote interface. *Nature* 2020;577:519–525. DOI:10.1038/s41586-019-1916-6.

Williams TA, Cymon JC, Foster PG, Szöllősi GJ, Embley TM. Phylogenomics provides robust support for a two-domains tree of life. *Nat Ecol Evol* 2020;4:138–147. DOI:10.1038/s41559-019-1040-x.

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Bryn McCulloch graduated with a first class BSc (Hons) in Biology at Edge Hill University, working on extremophiles from salterns in Cabo Verde, and is now completing a master's in Thorsten Allers' lab, working on growth conditions of Archaea and the corresponding effects on DNA repair and replication.

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After a PhD at the University of Edinburgh and a postdoctoral fellowship at the National Institutes of Health (NIH), USA, Thorsten Allers was awarded a Royal Society University Research Fellowship to establish his laboratory at the University of Nottingham. His group uses the model species *Haloferax volcanii* to study the genetics of DNA replication, repair and recombination in Archaea.

Why does microbiology matter?

Thorsten: Microbiology with model species helps us to understand the rules of life and where we come from. We were all microbes once upon a time!

How did you enter this field?

Thorsten: I have always worked on micro-organisms; I did my PhD with the bacterium *Escherichia coli*, my postdoc with the eukaryote *Saccharomyces cerevisiae*, and my own research group works on the archaeon *Haloferax volcanii*.

Microalgae, bacteria and vitamins: three key players in aquatic microbial communities

Andre Holzer, Shelby Newsad, Nhan-An Tran, Ellen Harrison and Alison Smith

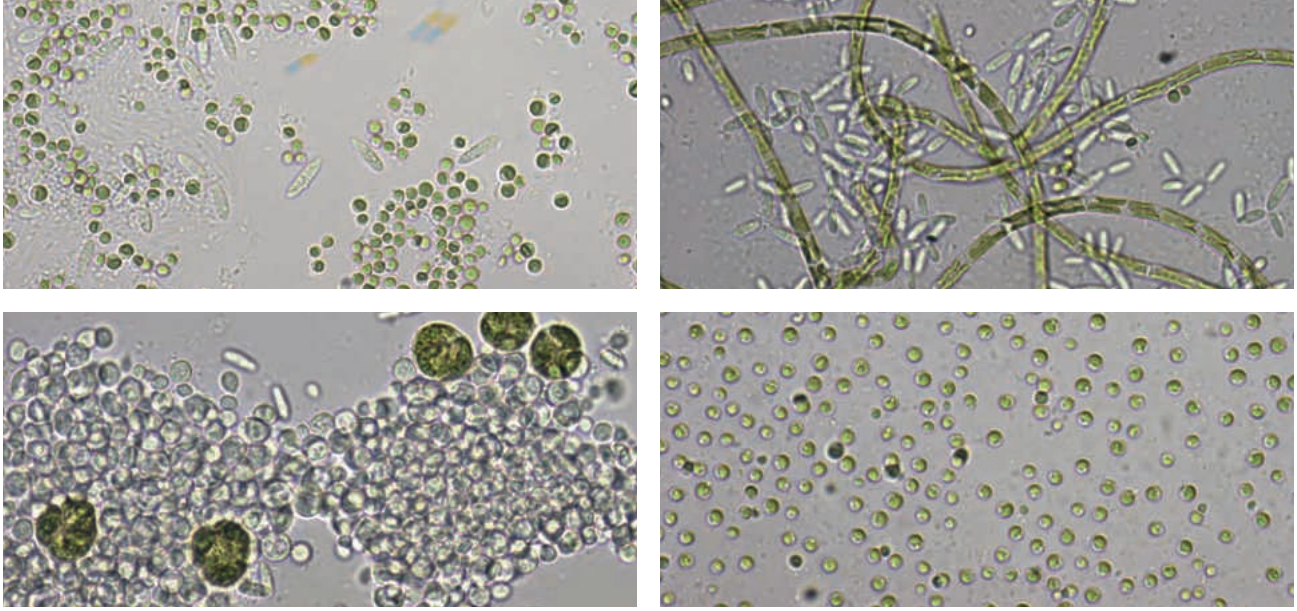
Micro-organisms are ubiquitous and form complex communities whenever they inhabit the same environment. Well-known examples of microbial communities include the human gut microbiome, but equally important to life on the planet are those in the aquatic environment. These are made up of photosynthetic algae and bacteria as well as many other protists, and are responsible for 50% of global carbon fixation. However, it is only recently that modern sequencing-based approaches have opened up the possibility of studying these aquatic microbial communities and their metabolic dependencies in exquisite detail.

Evolution of life began in the aquatic environment and so too did the formation of microbial communities. Today, diverse groups of microbes are found in every ocean and continent, ranging from temperate to extreme environments, and encompass members from all kingdoms of life (bacteria, archaea, protists and fungi). Whilst every teaspoon of seawater is filled with millions of these organisms, entangled in complex networks of interactions, from mutualistic to commensal (neutral) to parasitic, each community's composition is unique to the environment in which it lives. Understanding these microbial communities is of major importance, as they form the base of the ocean's food web, and their metabolic interplay is responsible for approximately 50% of total global carbon fixation.

What shapes these communities?

Open water communities of microbes are shaped by a patchy distribution of nutrients and other abiotic factors such as temperature and salinity. Research into aquatic microbial communities has highlighted the importance of nutrient availability in determining microbial community dynamics in both the freshwater and marine environments. Besides the major inorganic macro- and micro-nutrients such as nitrogen, phosphorus and iron, scientists discovered that the availability of many organic micronutrients, or vitamins, co-limits phytoplankton growth and determines its composition. It has been shown that B-vitamins in particular influence community composition, by favouring the succession of some species over others. In fact, research has revealed that many interactions within aquatic microbial communities are underpinned by the exchange of B-vitamins. This is because vitamin B_1 (thiamine), vitamin B_7 (biotin) and vitamin B_{12} (cobalamin) are required in different combinations by 60–70% of all microalgae. But what exactly are microalgae and where do algae obtain the vitamins from if they can't make them themselves?

Microalgae are a diverse group of largely unicellular photosynthetic eukaryotes, and their photosynthetic activity makes them responsible for primary production, which contributes significantly to the carbon fixation capacities of the ocean microbiome. A common misconception about microalgae, however, is that they are completely autotrophic, needing only simple nutrients, sunlight and carbon dioxide (CO_2) for growth. But with over half of all microalgae dependent on vitamin B_{12}, which is synthesised only by bacteria, this underlines the importance of metabolic exchange in defining ecological interactions between micro-organisms.



Images of algae communities from the Antarctic. Monika Krolikowski

How can microbial communities be studied?

To gain a mechanistic understanding of interactions, it is necessary to break down complex interaction networks by focusing on single model systems that can be co-cultured under controlled laboratory conditions. Direct demonstration of vitamin exchange came from studies with *Ostreococcus tauri*, an important picoeukaryotic microalga in oligotrophic waters, which has been shown to require B_{12} and B_1, and the bacterium *Dinoroseobacter shibae,* which requires vitamins B_3, B_7 and a precursor of B_9 for growth. The microalgae and bacteria can support each other's growth while in co-culture in the laboratory in a stable mutualism by fulfilling the vitamin requirements of the other species. Other studies of environmental samples looking at 16S rRNA gene sequences found that the *Rhodobacteraceae* family of bacteria, of which *D. shibae* is one example, are often found to co-occur with microalgae, suggesting that vitamins shape microbial interactions in the aquatic environment.

Recent advances in next-generation sequencing provide much more extensive possibilities to study interactions within microbial communities by identifying the entire metabolic capability present in an environment. One of the most important large-scale attempts applying such a strategy has been Tara Oceans. "The largest DNA sequencing effort ever done on ocean science" (Patrick Wincker, Genoscope, France) allowed identification of species in various communities and resulted in an extension of the tree of life by more than 30,000 species. With around 40 million mostly novel genes identified in the marine environment, this study provides a key resource that is now available to investigate species interactions in diverse aquatic communities by looking at co-occurrence of organisms in combination with their metabolic abilities.

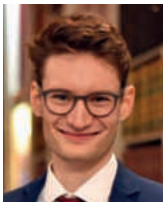
How can this knowledge be used?

As sequencing data becomes more readily available and species identification of microbial communities improves, it is now possible to infer more complex interactions and further investigate the importance of abiotic factors such as vitamins in regulating communities. Nutrient requirements can be inferred from the genetic or transcriptomic information and interactions can be tested in laboratory settings, experimentally validating co-occurring, metabolically compatible species. Increasingly, gene expression profiles can be generated to look for significant changes in the nutrient dependencies of microbes in different environmental conditions. This will be of great importance as climate change will continue to alter the pattern of nutrients in the ocean and so will change the species that can occur, especially with regards to the formation of harmful algal blooms.

Besides advancing our understanding of aquatic ecology, insights into microbial communities are key for a range of biotechnological applications. Industrial production of microalgae for feed and food applications or production of high-value compounds is often challenged by contamination issues. These may be overcome by the use of designed microbial consortia rather than using monocultures, since the former are likely to be more resistant to contamination. Moreover, vitamins have been shown to repress gene expression in microalgae, by both vitamin-responsive promoters and riboswitches. These genetic elements have the potential to be added to the synthetic biology toolkit, to engineer strains with more targeted production of high-value compounds. In future, we look forward to more breakthroughs, to move on from metabolic fitting to understanding more complex regulatory dynamics in both industrial and natural microbial communities.

Further reading

Kazamia E, Helliwell KE, Purton S, Smith AG. How mutualisms arise in phytoplankton communities: building eco-evolutionary principles for aquatic microbes. *Ecol Lett* 2016;19:810-822.



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Andre Holzer is a Gates Cambridge Scholar and PhD candidate. Andre completed a BSc degree in Molecular Biotechnology before he focused on computational biology during his MSc. After graduating from Heidelberg University in 2017, he started his PhD at Cambridge, where his research is investigating open questions in the evolution of B-vitamin dependencies and microbial interactions by applying multi-omics approaches. In parallel, he is co-leader of the citizen science project PuntSeq (**puntseq.co.uk**) which is employing novel real-time DNA sequencing to monitor microbial composition of freshwater sources.

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Shelby Newsad is a Cambridge Trust Scholar and PhD candidate. Shelby graduated from Ohio State University with a BS in Biochemistry. After graduation, she worked at the National Institutes of Health, then undertook an MPhil in Bioscience Enterprise where she decided to refocus her research efforts on sustainable systems. Shelby started her PhD at Cambridge in 2018 with her project investigating vitamin-dependent gene regulation and algae–bacteria symbioses.

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Nhan-An Tran is a Cambridge Trust Scholar and PhD candidate. Nhan-An completed a BSc in Marine Biology with Honours in Environmental Science at the University of Technology, Sydney. She started her PhD in Plant Sciences at the University of Cambridge in 2019, where her research focuses on exploring the interactions between microalgae and bacteria to improve large-scale microalgal production systems.

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Ellen Harrison is MELiSSA POMP II PhD Candidate. Ellen graduated from the University of St Andrews with a BSc in Marine Biology. Then she completed an MRes at the University of Plymouth in association with the Marine Biological Association, investigating nutrient sensing in diatoms. Ellen started her PhD in 2018, investigating how bacteria and algae in co-culture can provide vitamin B_{12} for human consumption on long space missions.

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Alison Smith is Professor of Plant Biochemistry. After studying Biochemistry at the University of Bristol, and then a PhD followed by a postdoc at Cambridge, Alison Smith was appointed to the academic staff in the Department of Plant Sciences in Cambridge, where she has been a Professor since 2007. Her research interests are understanding algal metabolism to facilitate exploitation of these organisms for food/feed, waste remediation and production of high-value compounds.

Why does microbiology matter?

Joint answer: Micro-organisms are invisible to our eyes but essential for all life on Earth. By studying micro-organisms, the field of microbiology helps us understand how life on our planet evolved, how health of single species, including humans, can be maintained as well as how whole ecosystems are shaped. Besides this, the field of microbiology has made significant contributions to many fundamental questions in molecular biology and allows industrial use of micro-organisms for biotechnological applications, including the production of high-value compounds like pharmaceuticals.

What is the most rewarding part of your job?

Joint answer: Multidisciplinary teamwork is the most rewarding part of the job. Like bacteria and algae living and working together, our collaborations and joint projects make science fun and exciting. Just as the organisms we study do not live in a silo – we do not work alone and depend on each other for different knowledge and expertise. Though we don't exchange vitamins, sometimes help forming a hypothesis or seeing your data from a different angle can be just as valuable.

Bugs in space: astrobiology and the search for life outside our planet

André Antunes

Are we alone in the universe? This question has haunted our minds and imaginations since the dawn of mankind and is arguably one of the final frontiers of science. Microbiology is bringing us closer than ever to finally getting an answer. The search for life outside our own planet is the object of astrobiology – a relatively recent cross-disciplinary research field bringing together bio-, geo- and planetary scientists, which is heavily linked with microbiology and the study of extreme environments.

From canals to exooceans

The dry and barren landscape of the Martian surface shown by the Viking Lander missions in the 1970s is contrasted with the romantic views of canals across its surface envisioned by Percival Lowell in the late 1800s. As part of the enthusiasm for exploring other planets was fueled by the expectation of finding little green men, public interest fizzled. Later, the end of the Space Race eventually reduced the rate of new space exploration missions and findings.

The wheels have turned once again, and we are currently witnessing a new wave of missions. The last few years have seen renewed interest in the search for extraterrestrial life in our Solar System. On one side, we now have a better understanding of the limits for life and its uncanny resilience on our own planet, and also a better knowledge of the conditions on other planets and moons.

The presence of liquid water – which is seen as an essential condition for life to exist – is now seen as certain for Mars and for a few of the icy moons of the outer solar system which seemingly have global-scale, salty (exo)oceans larger than the ones on Earth (Fig. 1). Surprisingly, Enceladus (and possibly Europa) appear to have hydrothermal activity, with geyser-like seawater projecting into outer space, which will facilitate their study.

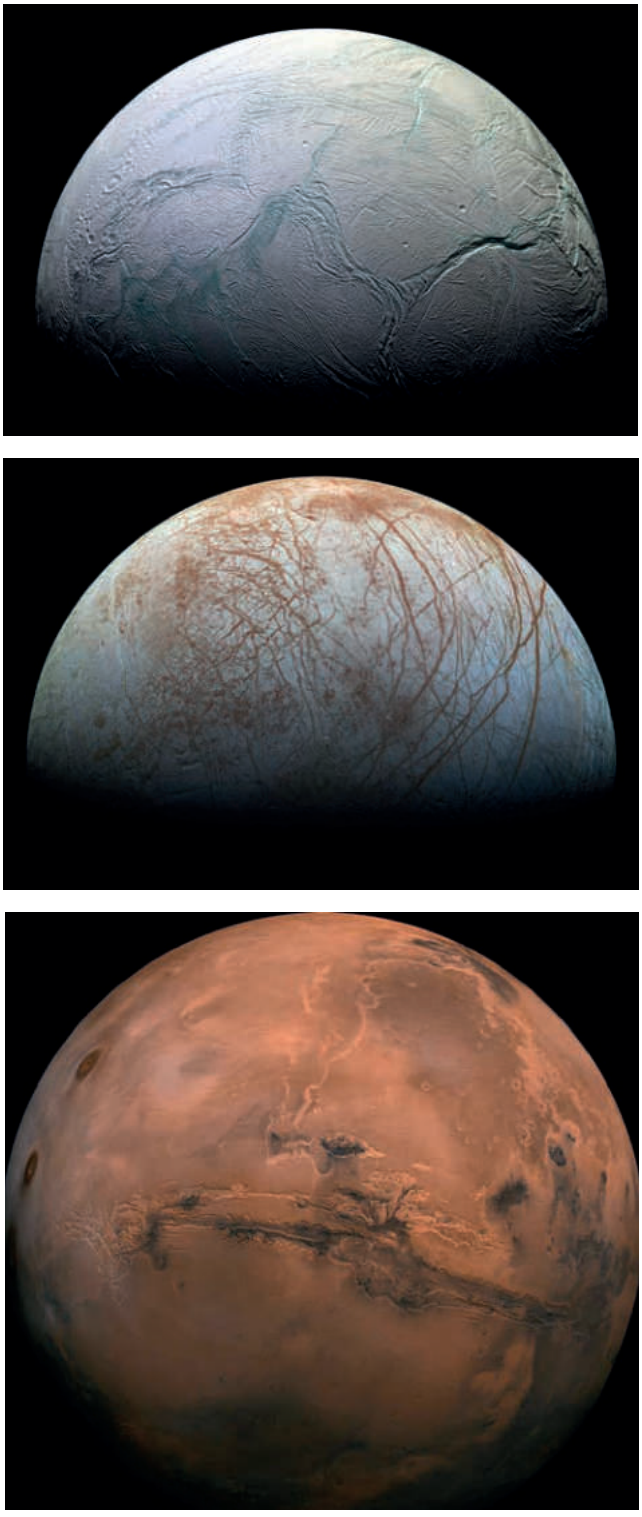

Fig. 1. Enceladus, a moon of Saturn (top), Europa, a moon of Jupiter (middle) and Mars (bottom) are currently the main targets for the search of life outside our planet. NASA

Fig. 2. **Examples of terrestrial analogue sites.** Top left, **Qaidam, China;** top right, **Pedra de Lume, Cape Verde;** bottom left, **Lake Tirez, Spain;** bottom right, **Qaidam, China.** A. Antunes, X. Yi

Terrestrial analogue sites

Despite increased technical capabilities and increased interest in retrieving samples from other bodies of our solar system for astrobiological studies, we are still years away from reaching this milestone. For the time being, our ability to study the feasibility of life's existence outside our planet is anchored on research that is done on terrestrial samples.

The search for life's limits is obviously linked with the exploration of the microbiology of different types of extremes on our own planet. The harsh conditions present on the aforementioned celestial bodies, which were once seen as impeditive for life, are not very different from some extreme environments on Earth which are teeming with microbes.

The comparison and extrapolation of these results are particularly useful when the conditions of the selected terrestrial environment more closely match conditions present on other parts of our solar system. Such environments, which include a wide range of locations across the globe (from deserts, to polar regions and deep-sea locations), are thus used as terrestrial analogues (Fig. 2).

Planetary protection

The increased likelihood of finding evidence of life on other parts of our solar system brings increased concerns when planning space missions. Given that several microbes have been reported as being able to survive space travel, we need to make sure that control measures are adequate to prevent contamination of other planets with terrestrial microbes (forward contamination). Such microbial hitchhikers could seriously compromise experiments looking for evidence of life (providing false positives) and their proliferation under hospitable conditions might lead to the collapse of entire alien ecosystems before we even know that they are there. Likewise, future sample-return missions also need to take into consideration mitigation measures of the potential risks associated with bringing over potential extraterrestrial microbes (backward contamination).

The discussion of these issues – normally referred to as 'planetary protection' – is a hot topic and involves regular collaborative efforts and discussions between all major space agencies.

Studies in astrobiology

Research in astrobiology is heavily anchored on the study of extremophiles. Several studies also focus on the survival of microbes during space travel or in conditions on other planets. We have seen considerable efforts in testing different types of microbes in exposure experiments (e.g. simulation chambers, high-atmosphere conditions or even outer-space) and in impact experiments. Results from this research hint at possible interplanetary transfer of microbes and likely survival of microbes on other planets.

The search for biosignatures – traces of biological activity of past or present life on Earth and elsewhere – is also a vital area of research. The distinction between biotic and abiotic is not as easy as it might seem, and long-term preservation of biosignatures can also prove problematic. However, these will be essential when analysing rocks, water or gases from other planets.

Astromycology and astrovirology

In addition to the ongoing effort to study bacteria and archaea within the context of astrobiology, the two most recent topics in this field revolve around fungi and viruses.

Several fungi are known to be incredibly sturdy or even to thrive under extreme settings. Fungi are frequently seen as either a blessing or a curse in the biology of space. On one side, their wide range of applications is vital for future breakthroughs in space biotechnology and even in supporting future manned missions. On the other side, controlling the proliferation of mould across surfaces of the International Space Station is a major and costly issue, due to its quick proliferation and detrimental effect on several types of materials.

At the edge of life, viruses are biological entities which are much simpler and more resilient than cells (which they largely outnumber). Some studies hypothesise that they might have been an early form of life, with critical relevance in the origin and evolution of life. They have been found to thrive in many extreme environments, including several astrobiologically relevant ones. Despite this, their role as potential biosignatures remains mostly unexplored.

Conclusions

Astrobiology is an exciting new field of research and one of the newest frontiers of microbiology. We are slowly starting to lift the veil from these amazing new worlds and opening a new age of major breakthroughs and discoveries.

Further reading

Merino N, Aronson HS, Bojanova DP, Feyhl-Buska J, Wong ML *et al.* Living at the extremes: extremophiles and the limits of life in a planetary context. *Front Microbiol* 2019;10:780. DOI:10.3389/fmicb.2019.00780.

Moissl-Eichinger C, Cockell C, Rettberg P. Venturing into new realms? Microorganisms in space. *FEMS Microbiol Rev* 2016:40:722–737. DOI:10.1093/femsre/fuw015.

Preston LJ, Dartnell LR. Planetary habitability: lessons learned from terrestrial analogues. *Int J Astrobiol* 2014;13:81–98. DOI:10.1017/S1473550413000396.

Rettberg P, Antunes A, Brucato J, Cabezas P, Collins G *et al.* Biological contamination prevention for outer solar system moons of astrobiological interest: what do we need to know? *Astrobiology* 2019;19:951-974. DOI:10.1089/ast.2018.1996.

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André Antunes is an Associate Professor and team leader of astrobiology at China's State Key Laboratory of Lunar and Planetary Sciences at Macau University of Science and Technology (MUST). He is an expert in microbiology of extreme environments, having specialised in deep-sea and high-salinity locations.

Why does microbiology matter?

We live in a microbial world! Microbes rule our planet, conditioning global geochemical cycles and sustaining all other life-forms, and rule our bodies, where they outnumber our own cells. They are increasingly seen as the solution to major issues that we face by helping us to feed, heal and fuel the world. Microbiology is also increasingly relevant in helping us to find whether we are alone in the universe or not. Microbiology is connected with pretty much everything that surrounds us, and we've only just started to scratch the surface of how amazing microbes are and the full scale of their impact.

What are the most important skills you need for your current role?

Passion, perseverance, curiosity and flexibility. I think this is valid for any field of research: you need to love what you do, be naturally curious and follow the opportunities that come along. Being a good communicator (and a good listener) also take you a long way!

Understanding viruses and challenges in microbiology

Virology holds a central position in both microbiology and public perception, never more than now as we face the challenge of a new viral pathogen. This section focuses on viruses, their structure and how we can manipulate viruses to benefit society.

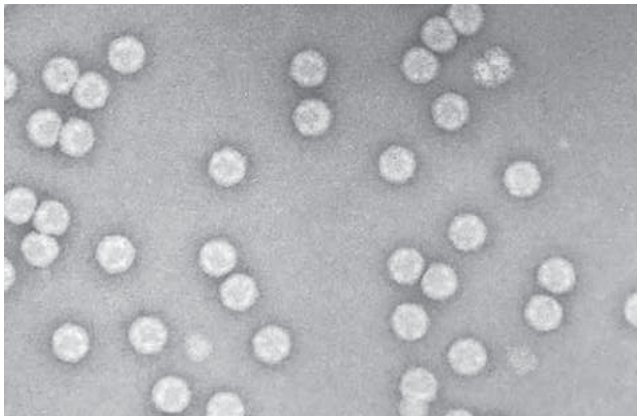
Virology and viral disease

Nicola J. Stonehouse and Natalie Kingston

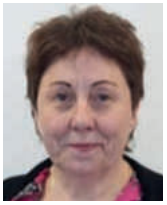
Viruses infect all forms of life, and while they can be extremely variable, the survival and propagation of all viruses is dependent upon living host cells. At their simplest, they are protein shells, with a nucleic acid centre. The shells (called capsids) protect the nucleic acid and serve to deliver this to new cells in order to spread infection. It is the nucleic acid that initiates disease. Cells can therefore become factories for the production of new viruses that then go on and infect other cells within the same host or infect new hosts.

Although it is viruses such as Ebola and Zika that make the headlines, information from studies of a range of viruses is what informs the development of prophylactic vaccines and therapeutic treatments. Indeed, understanding such details of virus structure and lifecycle has revealed parallels in simple viruses that infect bacteria and yeast with those that infect plants and mammals. However, small changes can have big consequences in terms of both severity of infection and susceptibility of the host. Furthermore, new viruses are always emerging. This is mainly due to the speed at which the viral genomes are copied and the errors that can be introduced as a result. This ability to change quickly can mean that viruses can 'jump' to infect new species.

Ongoing research is essential in order to better understand viruses, and to be in a position to respond rapidly to new and re-emerging viral disease.



Transmission electron micrograph of human rhinovirus, the main causative agent of the common cold. Nicola Stonehouse



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Nicola Stonehouse was awarded a PhD in 1992 on dental enamel development. She then moved from studies of inorganic crystals to protein crystals and structural studies on RNA bacteriophages. Postdoctoral studies took her to Uppsala and Leeds and, in 1997, she was awarded an MRC Career Development Fellowship. Her research moved from phage to picornaviruses, maintaining a strong interest in RNA. She was appointed Lecturer in Leeds in 2001, then promoted to Senior Lecturer and to Chair of Molecular Virology in 2013.

Natalie Kingston

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Natalie Kingston completed a PhD at Monash University, Australia, in 2017. Her research focused on the generation of chimeric virus-

like particle vaccines against *Plasmodium*. She then moved to the University of Leeds where she currently works on the characterisation of enteroviruses and the development of enterovirus vaccines with Nicola Stonehouse and David Rowlands.

What is the best career decision you've ever made?

Nicola: After my PhD, I moved fields to start working on viruses. At the time, this allowed me to translate my skills to a new biological problem, which was bacteriophage structure. But this opened up the world of viruses to me and I'm still fascinated by the virus lifecycle and of finding new antiviral strategies.

Natalie: Moving to Leeds and changing specialisation to molecular virology. This change has opened up new research areas for me that continue to be both exciting and have the potential to improve vaccine design.

Why does microbiology matter?

Nicola: Microbes are everywhere and affect almost all aspects of our lives. Harnessing the power of microbiology can therefore bring health, environmental, social, cultural, industrial and economic benefits to our society.

Viruses: the good, the bad and the useful

Hollie French, Elizaveta Elshina, Emmanuelle Pitre and Aartjan te Velthuis

Viruses are the most abundant and perhaps most diverse biological entities on Earth. They are simple life forms and are entirely dependent on hijacking host cells to replicate their genomes. However, contrary to common belief, not all viruses cause disease, since some are beneficial. By studying viruses, we can learn about the biology of host cells and organisms, develop strategies against viral disease and manipulate viruses for our own purposes.

Some viruses are only a single self-replicating gene, while others can encode almost a thousand proteins and be the size of a bacterium. Life cycles also vary among viruses, with some lasting millions of years and others less than an hour. Yet, in spite of vast structural and molecular differences, all viruses need to gain entry into a cell, find a site to replicate, and spread.

Binding and entry

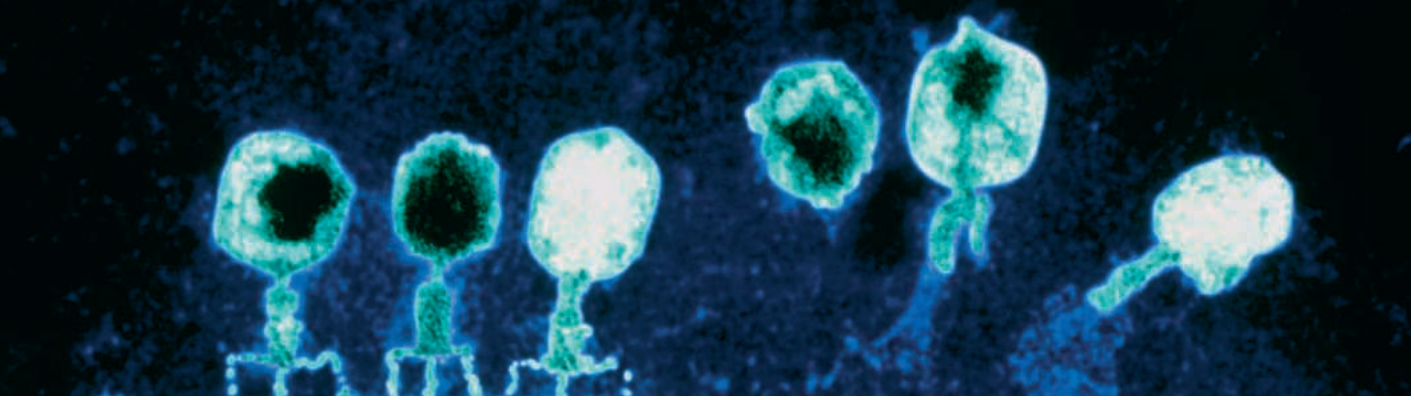
Virus entry can only occur if a cell expresses surface proteins that a virus can bind to. Because this is not always the case, virus infections are restricted to specific cell types, organs and organisms. Knowledge of a virus' tropism is important for estimating the potential that a virus emerges from a reservoir population and causes an outbreak in another species. For instance, a recently discovered bat influenza virus can enter human cells via the same receptor that it uses to enter bat cells, suggesting that bat flu might spill over into the human population.

Once inside a cell, viruses move their genetic material to sites of replication. Researchers can follow that movement by tracking single, fluorescently labelled viruses using a microscope. Studies of the interaction of the virus with the host have revealed how viruses use the cytoskeleton and intracellular membranes for viral translocation and replication, but also the importance of these host components for normal cellular signalling, movement and immunity.

Some viruses depend on the machinery in the nucleus and thus need to cross the nuclear membrane as well. To do this, influenza viruses and HIV-1 mimick host cell signals and employ cellular importins to carry their genome into the nucleus. In the nucleus, retroviruses express their genes by integrating them into the host genome. Such integration events can lead to cancer, but also shape animal evolution. One striking example is the 'domestication' of the retrovirus HERV-W envelope protein, now known as syncytin, as a component for placenta formation in mammals.

Replication and adaptation

Whether they replicate in the cytoplasm or nucleus, all viral genomes are copied by a polymerase. X-ray crystallography



Bacteriophage T4. Eye of Science / Science Photo Library

and electron microscopy techniques have enabled researchers to reveal the structure of these enzymes and develop drugs that frustrate viral replication. Some antiviral strategies can also exploit the high mutation rate of some viruses by pushing the error rate even higher, ultimately causing the viral population to collapse.

To prevent viruses from stealing their resources, cells express sensors that can identify viral genomes and proteins. The activation of these sensors triggers signalling, prevents virus spread and clears the infection. Many viruses encode proteins that can suppress or prevent these innate immune responses, but their function needs to be adapted to a host. Emerging viruses thus often trigger stronger responses than adapted viruses.

Vectors and spread

When new copies of the viral genome are ready to leave the host cell, some viruses fuse the infected cell with a neighbouring cell to allow faster spread. Other viruses condense their genome inside a protective protein shell with the right receptors to get the new virus to the next cell. To condense their genome, some herpesviruses and bacteriophages use a powerful molecular motor that can build up a pressure of 50 atmospheres!

Ultimately, a virus may need to spread between organisms. It can then rely on the natural behaviour of the host or a vector, such as a tick, or manipulate its host's behaviour. The rabies virus, for instance, uses a snake-venom-like compound that makes animals aggressive and froth at the mouth with virus-laden saliva in order to increase the chance that a bite will spread the virus. Similarly, some baculoviruses can turn caterpillars into 'zombies' that climb up to high leaves and burst, spreading infectious virus particles to healthy caterpillars below.

Although viruses use their host, they are also incredibly useful. Molecular biology uses viral enzymes to manipulate RNA and DNA. Moreover, we can now alter viral receptors to re-target viruses to specific cells, such as cancerous cells. In addition, we can create attenuated viruses that can only proliferate in cancer cells, which often lack antiviral sensors; we can lyse tumours and keep healthy tissues, which are still able to control the infection, unharmed.

Viruses are masters at infecting cells, utilising life's diverse abundance of molecules, systems and behaviours for their propagation. By studying them, we are learning from their expertise about ourselves and other organisms. This knowledge, combined with advances in other scientific fields, is enabling us to re-engineer viruses for our own purposes. Viruses may not only be the most abundant and diverse biological entities, but also some of the most useful.

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Hollie French is a Research Assistant. She holds a BA in Natural Sciences (University of Cambridge) and now works on flu aberrant replication and innate immunity at the University of Cambridge. Her interests are in infectious disease virology and public health. She was previously an intern in the Global Polio Eradication Initiative (WHO, Geneva). Hollie has been a member of the Microbiology Society since 2017.

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After completing a BSc in Infectious Diseases at the University of Edinburgh, Elizaveta Elshina worked in preclinical vaccine development at the University of Oxford. She started to work on influenza virus during her MSc at the University of Zurich and is currently researching erroneous activity of influenza virus polymerase for her PhD. She has been a Microbiology Society member since 2018.

Emmanuelle Pitre

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Emmanuelle Pitre graduated with a master's in Fundamental Virology from Sorbonne University and the Pasteur Institute. She is now

working towards a PhD at the University of Cambridge, on influenza viruses' replication mechanisms.

Aartjan te Velthuis

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Aartjan te Velthuis is a Henry Dale Fellow and Group Leader at the Department of Pathology of the University of Cambridge. He is interested in influenza virus replication and how aberrant viral RNA triggers innate immune responses. His research is funded by the Wellcome Trust, the Royal Society and NIH/NIAID.

Why does microbiology matter?

Joint answer: Microbiology has impacted human lives since the dawn of history. For centuries, it has played a key role in how we grow, prepare, flavour and preserve our foods. We used yeast for making beer before we knew how to make clean water and learnt to add salt to foods to prevent microbial growth. We also depend on microbiology to understand how viruses, bacteria and fungi cause disease, and how we can fight pathogens. In particular, the discovery of penicillin, a product of a fungus that can kill bacteria, has saved many lives. But microbiology is equally important for our future. It is helping us find ways to break down oil and plastic, to develop alternatives for other harmful products and to find (and possibly survive on) a habitable planet. Microbiology is without a doubt one of the most important research fields today.

What is the most rewarding part of your job?

Joint answer: In our lab, we study how influenza viruses replicate in human cells, how the viral genome is mutated, and how the efficiency of viral replication contributes to disease. It is extremely exciting to study this virus and being one of the first to uncover unknown molecular mechanisms. It feels like being an explorer discovering a new country or navigating a new mountain top. But one of the most rewarding aspects of our work is showing others how interesting microbiology is, either by presenting our work or using games such as our 'virus roulette' table to teach children (and adults) how infections and antibodies work.

Understanding viruses at the atomic scale: a history of virus structure research

David Bhella

As a PhD student in the crystallography department of Birkbeck University of London, I was struck by the proud heritage of that institution. Among the pioneers of structural biology from that department, J.D. Bernal, Rosalind Franklin and Aaron Klug made extraordinary contributions to structural virology. As a young researcher entering the field, a sense of walking in the footsteps of such towering historical figures was awe-inspiring. Over the intervening 25 years, I have been equally astounded by the technological developments in structural biology that have propelled the field forwards. In particular, the evolution of cryogenic electron microscopy (cryoEM), which has become a powerful tool for high-resolution structure determination, particularly suited to large macromolecular assemblies such as viruses.

Viruses are fascinating targets for structural biology research, being simultaneously the smallest (and most abundant) life-forms on the planet and the largest of macromolecular assemblies to be understood at the atomic level.

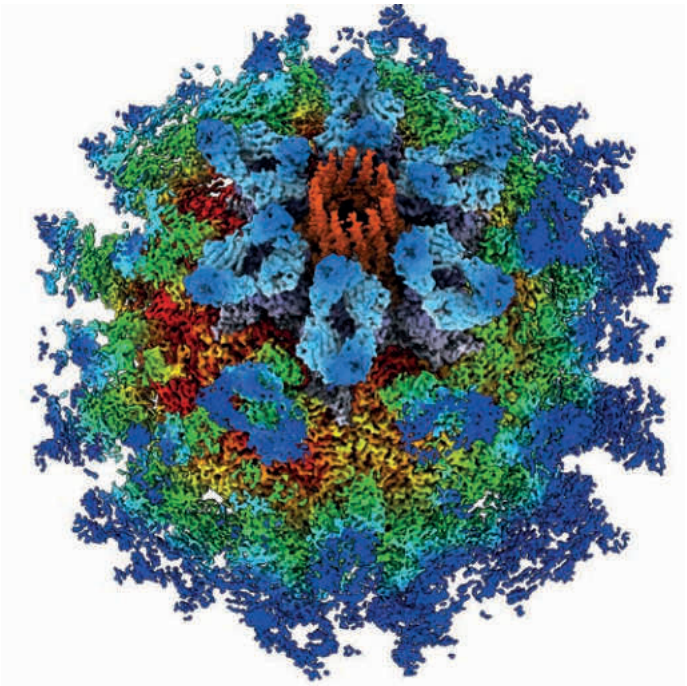
The shape of viruses

Our earliest insights into the shapes of viruses came when Helmut Ruska imaged plant and animal viruses for the first

time in the transmission electron microscope (TEM). These images were published in 1939. At this time, J.D. Bernal and Isidor Fankuchen were beginning to work on X-ray diffraction of concentrated preparations of plant viruses, including tobacco mosaic virus (TMV) and tomato bushy-stunt virus (TBSV) – showing the former to be a long filamentous structure and the latter to be a spherical one.

The work started by Bernal was continued at Birkbeck college, where he recruited Rosalind Franklin to study the detailed structure of TMV. She showed it to be a helical assembly and defined the spatial arrangements of protein and RNA. Based on the work of Franklin's collaborator and friend Don Caspar, Crick and Watson proposed that spherical viruses assemble with icosahedral symmetry. Using delightfully anachronistic language, these viruses were said to be likely to resemble a 'rather symmetrical mulberry' assembling from 60 protein subunits.

Initial theories of icosahedral symmetry in spherical viruses were insufficient, as many viruses were shown to form larger assemblies comprising many hundreds of capsid proteins. Don Caspar and Aaron Klug addressed this by formulating their theory of quasi-equivalent packing in icosahedral viruses. Building on emerging knowledge, they set out how larger capsids might be assembled by the introduction of small variations in bonding relationships between protein subunits.



Asymmetry in icosahedral viruses – the calicivirus VP2 portal structure.
https://www.ebi.ac.uk/pdbe/entry/emdb/EMD-0056

Atomic modelling and structure

The first atomic model of a spherical virus was calculated for TBSV by Steve Harrison *et al.* in 1978, revealing a shell comprising 180 copies of the major capsid protein. This was followed by structures of two small RNA-containing viruses that infect humans: rhinovirus, solved by Michael Rossmann and colleagues, and poliovirus solved by Jim Hogle *et al.,* both published in 1985. These studies revealed a common fold in the capsid proteins of these plant and animal viruses: an eight-stranded β-barrel known as the β-jelly roll.

The potential to use electrons rather than X-rays to determine virus structure was demonstrated in 1968 when David DeRosier and Aaron Klug calculated low-resolution 3D density maps of the contractile tail of phage T4 from TEM images. Exploiting the helical symmetry of the assembly allowed the density to be reconstructed from single images of phage particles stained with a heavy metal salt. A method to determine the structures of icosahedral objects followed, developed by Tony Crowther and colleagues. Many aspects of TEM were severely limiting, however, and the first step towards overcoming these challenges came with the invention of cryogenic methods for imaging biological material in the TEM. In 1985, Marc Adrian and colleagues published methods for the preparation of virus particles suspended in thin layers of vitreous ice. The absence of stain and chemical fixative meant that cryo-EM yielded images of macromolecular assemblies in a close to native state. Several technical advances in cryo-EM were required to move from early density maps at 30–40 angstroms resolution to where we are now – where 3D reconstructions at better than 4 angstroms resolution allow the construction of reliable atomic models.

Technological advances

The introduction of the first generation of digital cameras for TEM brought about a technological revolution in cryo-EM, facilitating the development of automated data collection and electron tomography (cryo-ET). Cryo-ET allows structure analysis of morphologically unique entities, by rotating them in the electron microscope and recording a tilt-series of images. These data may then be processed to compute a 3D

reconstruction at intermediate resolution. A notable application of this method led to the calculation of an atomic model of the HIV capsid in the laboratory of John Briggs at EMBL Heidelberg.

For much of the first decade of the 21st century, virus structure research combined intermediate-resolution cryo-EM maps with X-ray data to yield pseudo-atomic models of, for example, complexes of viruses and host proteins such as antibodies. The first *ab initio* atomic model built into a single particle cryo-EM map of a virus was that of cytoplasmic polyhedrosis virus published by the laboratory of Z. Hong Zhou in 2008. The cryo-EM resolution revolution has since transformed this method to the point that atomic models of icosahedral virus capsids may be rapidly calculated. At the time of writing there are 175 capsid structures in the protein data bank solved by cryo-EM at better than 4 angstroms resolution. Notable recent achievements include high-resolution structures of two very large viruses: herpes simplex virus and African swine fever virus.

Recent developments in image reconstruction software have allowed investigators to probe asymmetry in viruses, revealing instances where deviating from symmetry is critical for the viral life cycle. One recent example from my own laboratory is our discovery that the calicivirus minor capsid protein VP2 forms a portal at a unique three-fold vertex following receptor binding. We believe that this is the mechanism by which the virus injects its genome into the cell.

Looking to the future of virus structure research, both X-rays and cryo-EM offer the tantalising prospect of viewing virus behaviour within the cell. Cryo soft X-ray microscopy is emerging as a powerful tool for imaging whole cells, revealing organelle rearrangements associated with virus infections. Cryo-ET of virus-infected cells is allowing researchers to analyse virus structures *in situ*, providing valuable biological context to structure data and promising that in the not too distant future it will be possible to solve structures of viruses in their natural habitat.

Harnessing structural biology in a crisis

In January 2020, SARS-Coronavirus 2 emerged in the Chinese city of Wuhan and has rapidly spread across the world, causing severe illness and deaths. This has led to the widespread lockdown of cities and whole nations. The scientific community has mobilised to address this crisis, including structural biologists. A testament to the significant advances in both X-ray crystallography and cryo-EM is the speed with which researchers have solved atomic structures for critical viral proteins. At the time of writing (20 March 2020), 29 protein structures for SARS-CoV-2 have been deposited in the Protein Data Bank, including the protease Mpro bound to several inhibitors, the S protein that mediates attachment and entry, and a complex of the S-protein's receptor binding domain and the virus' cellular receptor ACE2. These data will inform the development of antivirals and vaccines and are a major contribution to the global effort to defeat COVID-19.

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David Bhella is Professor of Structural Virology at the Medical Research Council – University of Glasgow CVR. He is also Associate Director of the CVR and Director of the Scottish Centre for Macromolecular Imaging (SCMI). David started his career working as a diagnostic virologist at the Royal London Hospital before undertaking a PhD with Professor Helen Saibil FRS at Birkbeck College. He then moved to Glasgow's MRC Virology Unit where he developed his programme of structural virology research.

Why does microbiology matter?

Microbiology impacts many key elements of human endeavour. Understanding microbes as primary drivers of the planet's ecosystems, disease-causing agents, irreplaceable components of our own biological processes and as tools is a vital scientific need. Investigating the biology of micro-organisms has the potential to allow us to prevent and treat infectious and metabolic diseases, as well as feeding ourselves while minimising our ecological impacts.

What is the most rewarding part of your job?

For much of my career the primary driver has been the sheer thrill of discovery. That moment when your experiments lead to a new insight into the biology of an important virus is so often unexpected and startling. For a moment you are the only person in the history of humanity to know something important. Recent events have reminded me why I first chose to become a virologist. Understanding viruses at the molecular level is key to preventing serious diseases and saving lives. Microbiology is a worldwide endeavour and I am proud to play my own small part in this.

Annual Conference

Fleming Showcase 2021
Monday 12 April
International Convention Centre (ICC), Birmingham, UK

Following this year's disappointing cancellation of Annual Conference, the Society is delighted to confirm that the Fleming Showcase element of the meeting will be retained in full at next year's Annual Conference 2021 in Birmingham.

Sir Paul Nurse and the wider Fleming Committee were keen to recognise the incredible support and hard work from everyone involved in the project and were determined to ensure that this important event went ahead as originally conceived.

As a result, the Fleming Showcase has now been formally re-scheduled to take place on **Monday 12 April 2021** at the start of the Society's Annual Conference week. The event will be followed by the standard four days (Tuesday–Friday) of scientific sessions.

The Microbiology Society's Fleming Prize is awarded each year to an early career researcher who has achieved an outstanding research record within 12 years of being awarded their PhD. As before, the Fleming Showcase will offer an opportunity to hear the legacy of some of these past Fleming Prize winners and will focus on the influence of both established and up-and-coming scientists in addressing global challenges.

The day will feature presentations from a global speaker line-up, including:

- **Luke Alphey** Pirbright Institute, UK
  Genetic control of mosquitoes
- **Stirling Churchman** Harvard University, USA
  Orchestrating gene regulation across the genome and across the cell
- **Eddie Holmes** University of Sydney, Australia
  The expanding virosphere
- **Grant Jensen** CalTech, USA
  Visualising bacterial nanomachines in situ *by electron cryotomography*
- **Mark Pallen** Quadram Institute, UK
  Palaeomicrobiology: what ancient DNA can tell us about pathogens from the past
- **Liz Sockett** University of Nottingham, UK
  Predatory Bdellovibrio *bacteria – 58 years of understanding them as allies against AMR infections*

The day is designed to provide value to everyone within the microbiology community. Early career scientists will be able to attend the Fleming Showcase for free when registering for Annual Conference. The day costs £60 for all other delegates. Further information about the day can be found on the Annual Conference 2021 website (**microbiologysociety.org/microbio21**).

ImagesofBirmingham.co.uk

Annual Conference 2021
Monday 12 April–Friday 16 April
International Convention Centre (ICC), Birmingham, UK

Preparation is now well underway for Annual Conference 2021, which will see the Society return to Birmingham's International Convention Centre.

The agenda is currently in production with our scientific committees who work across the broad range of microbiology topics and its various disciplines to deliver an exciting and cutting-edge programme. Check the event website (**microbiologysociety.org/microbio21**) for further information.

Abstracts

Conference provides an excellent platform to showcase emerging scientific research, so make sure you submit your microbiological work.

Abstract submission open:	**from the week of 17 August 2020**
Submissions deadline:	**14 December 2020**
Notifications of acceptance:	**from 11 January 2021**

Destination Birmingham

Birmingham is a dynamic, creative city that is constantly evolving. As the UK's natural meeting place, Birmingham is also a crossroads for culture, and diverse cultural influences are easy to spot everywhere in the city.

With a compelling and varied arts scene, Birmingham is home to inspirational organisations and venues right across the cultural spectrum. With its growing reputation as a foodie haven, critically acclaimed independent festivals and a year-round calendar of world-class sporting events, it offers a unique visitor experience.

Visit **visitbirmingham.com** to find out more about our 2021 location.

Accommodation

The ICC Birmingham is easily accessible from around the UK and abroad and has plenty of hotels and restaurants within walking distance.

Visit our website (**microbiologysociety.org/microbio21**) for a link to our booking agent – First Choice Conference and Events. First Choice have secured rates at local hotels to suit a range of budgets and will be able to accommodate single occupancies, double rooms, group bookings and family rooms.

Please ensure you register at Conference before you arrange your accommodation to avoid disappointment.

Programme

The Microbiology Society Annual Conference is the organisation's flagship event and is the UK's largest annual gathering of microbiologists.

As always, Annual Conference is designed to cover the breadth of microbiology research, and its comprehensive scientific programme has over 30 sessions taking place over four days in a range of formats, including symposia, virology workshops, eukaryotic and prokaryotic forums and professional development sessions.

Registration

Registration opens for Conference in August. Ticket prices are heavily subsidised by the Society to ensure that the meeting remains of value to our broad microbiology community.

The following items are included in your registration fee:

- access to an electronic abstracts book
- access to CPD points
- access to the Conference app
- admission to all scientific sessions
- certificate of attendance
- delegate bag and conference material
- full access to scientific poster sessions
- full access to the trade exhibition
- hard-copy Conference programme guide
- hot buffet lunch
- tea and coffee breaks
- two drinks during the drinks receptions each evening

Spotlight on Grants
Harry Smith Vacation Studentships

Last summer, University of Cambridge BA Natural Sciences student Eliza Walker was awarded a Harry Smith Vacation Studentship by the Society, where she worked under the supervision of Dr Nerea Irigoyen at the Department of Pathology, University of Cambridge.

During her project, Eliza compared the infectivity of an African strain of Zika Virus (ZIKV-Dak84) with an American strain (ZIKV-PE243) in human brain cells.

She started her project by performing a time-course and competition assay before attempting to construct the infectious clone. At this stage, Eliza had to depart slightly from the original plan and was only able to successfully insert one of the six fragments of the ZIKV Dak84 genome into the disease vector.

The results obtained indicated that the African ZIKV strain had a greater level of infectivity compared to the American strain. Eliza found these results intriguing, as infections in humans by the African strain are generally thought to be mild or asymptomatic. By contrast, the American strain can cause severe neurological and gestational problems. This shows that there is still much to learn about the differences in pathologies of these two strains.

Eliza said that "performing Zika virus infections was really exciting, knowing I was working with a live infectious pathogen. It was also a great opportunity to practice and improve my aseptic technique.

It was great to come into the laboratory every day and be working towards a goal, getting results and problem-solving as issues came up. This was really different to my experience in the teaching laboratories at university and truly gave me a taste of the life of a research scientist. As well as giving me a sense of respect for the resilience and ingenuity of researchers, my studentship has also re-enforced my passion for pathology, and I am excited to pursue further study within this field."

Dr Irigoyen is a recently appointed Junior Principal Investigator and Eliza was the first student she directly supervised on a daily basis, helping her with the experimental planning, set-up and data interpretation.

Dr Irigoyen said that the studentship "has been a very enriching experience in which I have learnt a lot in managing people and time. I have really enjoyed the task of teaching such an enthusiastic student and transmitting part of my knowledge to her. I presume that this will help me a lot in supervising my latter students, and also in managing the start-up of my own laboratory".

Eliza (front) and Nerea (back) after doing a Zika infection in the Biological Safety Laboratory 2+ in the Division of Virology. Nerea Irigoyen

Dr Irigoyen's lab hope that the characterisation of the African reverse genetic system will be shortly published in a scientific journal and shared to a wider community of researchers.

Applications for the Harry Smith Vacation Studentship open in December each year.

To find out more about the wide range of grants to support Microbiology Society members, visit the grants area (**microbiologysociety.org/grants**) of our website.

Kirti Mistry

Grants and Professional Development Officer

k.mistry@microbiologysociety.org

Careers Focus: Scientific entrepreneurship

As a scientist, the prospect of transitioning your research into a commercially successful product or service can be a new and exciting career opportunity. It can also mean exploring unfamiliar areas of work and implementing important steps to ensure you're headed in the right direction. Here are a few things you might want to focus on when starting your business.

Rachel Asiedu

A great idea

Once you have identified an idea of research that serves an untapped need or want in the market, you will need to ensure you protect your intellectual property. Before doing so, some research into what is already on the market is essential. After the necessary research and once your idea has been transformed into a product or process, it's important to take steps to patent it. This will provide you with exclusive rights, which is very attractive to investors.

Bear in mind, your idea or research may not be published but it might already be patented by someone else.

Olivier Le Moal/iStock

Funding

There are a variety of funding options available to new start-ups and innovative ideas. Competitions are a great way to gain funding and will also help you to gain experience in pitching for future investors. There are also various funding schemes such as the UK Government's Innovate UK (**gov.uk/apply-funding-innovation**).

Build a team

Being surrounded by a good team can help you compensate for your weaknesses and compliment your strengths. Perhaps you need a commercial expert, someone to review your data or a mentor to strengthen your business proposal. Working with people you can trust to help build your business is important, and while you're an expert in the science, it can be helpful to delegate business tasks.

With a great idea, the right resources and hard work you can find success as a science entrepreneur. The process of transitioning your research into a business may take time; however, the outcomes can be both economically rewarding and personally enriching.

Rachel Asiedu
Professional Development Manager

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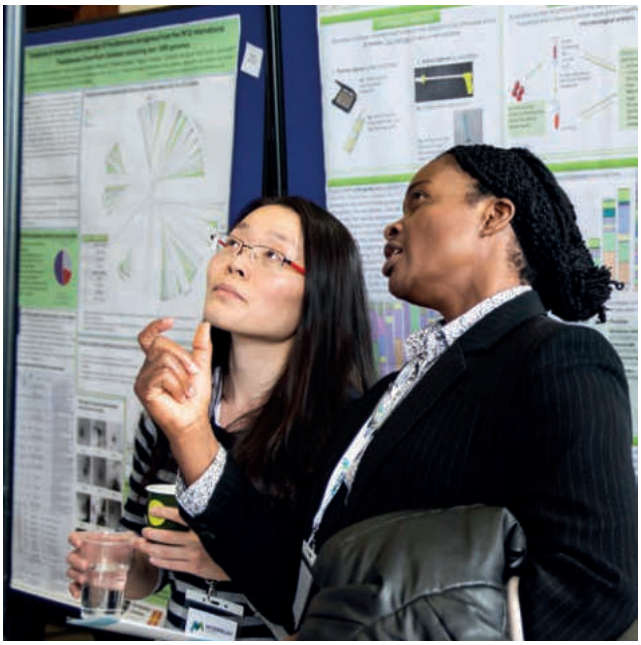
Early Career Microbiologists' Forum Update

I'm Robert Will, the Early Career Microbiologists' (ECM) Forum Communications Representative for the next two years. I am a PhD student in my second year at the University of Cambridge, researching bacterial disease using genomics, and am really excited to continue Rebecca Hall's work as part of the Executive Committee, to represent early career microbiologists throughout the Society and beyond.

Robert Will



I hope you have been enjoying this issue of *Microbiology Today*, highlighting the many ways microbiology matters. I want to use this theme to discuss the ways that early career microbiologists matter, especially to the field itself. In the not-too-distant future, current ECMs will be the leaders of our field, running their own academic research groups, flying high in industry and making social change as policy-shapers, to name just a few potential career paths. The challenges we face as a discipline are as large as they've ever been; we need to address the climate crisis, ensure our food security and tackle the rise of antimicrobial resistance. Thanks to the Society's *A Sustainable Future* project, we have seen how microbiology can impact almost all the United Nation's Sustainable Development Goals, and it will be incredibly interesting to see the ideas and projects than spin out of the initiative. A lot of this research will be carried out by ECMs, so never doubt the impact you could have!

The Society has made great efforts integrating ECMs into its governance, having them present on all Society Committees and Council. This means that no matter what decisions are being made, early career viewpoints are included to make sure the Society is listening to and benefiting everyone.

As an early career researcher, there are many benefits of being part of the Society's ECM Forum, not least the ECM Forum Event Fund. This awards up to £500 to ECMs, covering a variety of activities that benefit early career microbiologists. This could include inviting a speaker to give a talk, a careers advice session, or holding a symposium, workshop or small conference. The format is very much up to you as an organiser, with support from the Society. The next closing date will be 30 September, so there's still plenty of time to dream up a great event that not only helps ECMs around you, but also promotes the field of microbiology.

Finally, we are all dealing with the large changes brought about by COVID-19. This has meant the cancellation of all Microbiology Society events in the near future, which, while extremely sad, I think we can all agree is the right decision. We, as a field, should be leading the way, showing and educating the wider public as best as we can. Please stay safe and healthy, follow the expert advice, and help those that need it. Take care everyone!

Robert Will
Communications Representative, ECM Forum Executive Committee

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Member Q&A: Arno Fricke

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

Where are you currently based?

I'm currently working between labs in the Microbiology Department at University College Cork and the Environmental Research Institute, here in Cork in the south of Ireland.

What is your area of specialism?

Microbial biotechnology.

And more specifically?

My PhD is part of a wider interdisciplinary project called Newtrients. This project focuses on a circular economy approach for dairy processing wastewater. My role is to generate volatile fatty acids from raw wastewater and later convert these to bioplastics (polyhydroxyalkanoates) using a mixed microbial approach, driven by selection rather than genetic optimisation. We try to utilise waste streams and reduce energy costs associated with sterilisation in pure culture fermentations in an effort to supplement global research to make bioplastics more competitive with current plastics.

Tell us about your education to date.

I finished my undergrad in biology at the University of Marburg (Germany). During that time, I focused mainly on microbiology and, following a field trip to a major biotech company, I realised that my future would involve more applied research in biotechnology. This plan came into action with my master's at the University of Münster (Germany) and, since 2017, with my PhD here in Cork.

Where did your interest in microbiology come from?

The first line from our microbiology professor during my undergrad was, "Bacteria rule our world". In the next few lectures, he showed us how true this statement is and how we can work together with bacteria to solve problems we face.

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

Working in the lab by yourself can feel very lonely. I'm a very sociable person and need a certain amount of human interaction to enjoy my days. I think I'm not alone with that and therefore joined the postgraduate committee to organise events for PhD students to bring people together and create a more open and interactive environment for everyone.

What is the best part about 'doing science'?

One of my professors told me his three-year PhD was to sequence a single gene, which is less than a day's work today. It is amazing to be part of this global network that makes the impossible possible.

Who is your role model?

I don't have a specific role model, but I am constantly influenced by the people surrounding me.

What do you do to relax?

When I moved to Ireland I fell in love with the landscape and coastline of this beautiful island. So most of my hobbies include different aspects of it, either during a trail run across the mountain ranges, kayaking on the River Lee or cycling in the harbour area.

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

My camera, to capture moments happening around me. If somebody finds it later they will be able to see the story of my time on the island.

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

The top two priorities on my bucket list are to drive a flying car and to go to space once. (Shout out to all the scientists working out there at the moment to make this dream come true one day.)

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

Graphic designer. Maybe I will be able to combine the two jobs in the future in the form of science communication.

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

Why should scientists care about policy?

Experiences from the Microbiology Society Science Policy Workshop for Microbiologists.

Alice Fletcher-Etherington

I'm a PhD student from the University of Cambridge, where I'm using classical laboratory-based research techniques to study immune evasion by human cytomegalovirus (HCMV). My aim is to gain insight into the interactions between virus and host in order to develop therapeutics that would prevent the virus from overcoming cellular defences. Despite the vital importance of basic research, I am sometimes disheartened that the direct translation of my work into benefits for society is not always obvious. This led me to consider science policy as a means to increase the impact of my research, and to attend the Microbiology Society's **Science Policy Workshop for Microbiologists**. The workshop was held in partnership with the Society for Applied Microbiology (SfAM) on 25 November 2019 in London.

Dr Chris Brown from the House of Commons Science and Technology Committee.

Outline of the day

Science in Parliament and Government

The morning started with a presentation by Dr Chris Brown (House of Commons Science and Technology Committee) who gave an insightful introduction into science policy. Science policy involves the integration of scientific expertise with an understanding of government and policy-making to ensure that legislation and policy have a sound evidence base. Dr Brown highlighted the two areas in which research scientists can have an impact: '**policy for science**' and '**science for policy**'. This was nicely followed-up by Dr Grant Hill-Cawthorne from the Parliamentary Office of Science and Technology (POST), who spoke about the differences between Parliament and Government, and the roles of the House of Commons Libraries, Select Committees and POST in bridging the gap between research and policy. Rebecca Asher then spoke about Sense about Science, an independent charity that aims to improve the use of science and evidence in informing public policy. They do this through a number of initiatives which encourage discussions about evidence between scientists, policy-makers and the public. As a scientist who is sometimes demoralised by current political debates that lack an evidential basis, I found it encouraging to hear about an organisation trying to tackle this issue!

Rebecca Asher presenting on behalf of Sense about Science.

Eva Scholtus, Policy Manager at the Microbiology Society.

Engaging in science policy

The next session featured a range of speakers from non-governmental organisations working at the interface between science and policy. Dr Daniel Rathbone spoke about the role of the Campaign for Science and Engineering (CaSE) in ensuring that the UK has the skills, funding and policies to enable science and engineering to thrive. Next, Wellcome Trust Policy Officer Dr Ben Bleasdale explained how to communicate with, and make our research accessible to, policy-makers (see 'Take-home messages', below). Dr Bleasdale structured his talk on the principles of an article by the Chief Medical Officer Professor Chris Whitty: 'What makes an academic paper useful for health policy'. Finally, Eva Scholtus and Lucky Cullen spoke about the role of the Microbiology Society and the Society for Applied Microbiology (SfAM) in science policy, through education of their members and informing policy through governmental consultations and policy briefings.

Activity: translating research into policy

In the afternoon we split into groups and were given the chance to talk about our own research and its policy implications. I was motivated by the fact that, although the majority of attendees were working on topics with clear links to policy (such as antimicrobial resistance), everyone was extremely receptive to my research on HCMV. This was followed by a group task that encouraged us to think about how to effectively communicate research to policy-makers: by considering the scientific evidence, its impact on society, the target audience and the desired outcome of any policy changes.

Take-home messages from the workshop

The workshop highlighted a number of useful points for researchers looking to get involved in science policy:

1. How can I contribute to science policy?

- Look out for opportunities to give evidence at **Select Committee evidence sessions**, via the Parliament Knowledge Exchange Unit (Twitter: **@UKParl_Research**); they also offer 'Parliament for Researchers' training.
- **Contact an MP directly**. Back bench MPs with a previous interest in your topic are more likely to be responsive.
- Get involved with **Sense about Science** through their **Voice of Young Science** programme for early career researchers.

2. How should I interact with policy-makers?

- The main priority of an MP is their constituents. Think about how your area of research **impacts society**, and how potential policy change would have a positive impact.
- Explain what **actions** you want them to take.
- Use **concise** and **accessible** language.
- Be **transparent** about the evidence and don't hide any limitations – help foster an environment where evidence can be trusted.
- Recognise your biases and remain **neutral** – let the evidence speak for itself.

Many people choose to become researchers to make a contribution to society, and, in the case of microbiology, to improve health. Engaging with policy allows scientists to maximise the impact of their research and in turn influence the policies that affect the scientific research landscape. The workshop provided a valuable opportunity to interact with like-minded researchers and policy experts in a welcoming and encouraging atmosphere. Best of all, I met some incredibly engaged and intelligent researchers who I hope to see at future Microbiology Society or SfAM events. I encourage all early career researchers to take advantage of similar opportunities provided by the Microbiology Society and to think about the policy implications of their research – even if you work on the most under-studied pathogens!

Alice Fletcher-Etherington
University of Cambridge

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@Alice_F_E

Reviews

Read excerpts from the latest book reviews below. To read the full reviews, and for more reviews, please visit our website: **microbiologysociety.org/MTMay2020Reviews**

Protozoan Parasitism: From Omics to Prevention and Control

Edited by Luis Miguel de Pablos Torró and Jacob-Lorenzo Morales
Caister Academic Press (2018) £159
ISBN 978-1-910190-83-8

Protozoan parasites are responsible for many serious diseases around the world including Chagas disease and leishmaniasis. This short, edited volume aims to provide a background and historical context to the current treatments for many of these diseases and investigate how genome-wide approaches are helping to develop new therapeutics.

Jack Sunter Oxford Brookes University, UK

Forensic Microbiology

Edited by David O. Carter, Jeffery K. Tomberlin, M. Eric Benbow and Jessica L. Metcalf
John Wiley & Sons Ltd (2017) £94.75
ISBN 978-1-119062-55-4

Forensic Microbiology was published as part of the Forensic Science in Focus series, a joint venture between the American Academy of Forensic Science and Wiley. This book provides a comprehensive overview of the forensic applications of microbiology associated with pathology, taphonomy, anthropology and trace evidence analysis.

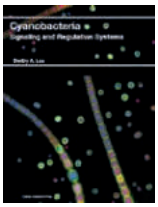
Magdalena Karlikowska University of Warwick, UK

The Power of Plagues (2nd Edition)

Written by Irwin W. Sherman
ASM Press (2017) £30.50
ISBN 978-1-683670-00-1

A fascinating guided tour through a museum of infections, showing us some of the major influencers of societal change; *The Power of Plagues* tells us the story of how the emergence and spread of infectious diseases have in turn caused humans to change and adapt in both biology and culture.

Andrew Bosworth Public Health England, UK



Cyanobacteria: Signalling and Regulation Systems

Written by Dmitry A. Los
Caister Academic Press (2018) £259
ISBN 978-1-910190-87-6

The role of cyanobacteria in oxygenating Earth's atmosphere and producing as much oxygen as plants sets the microbe apart in Earth's evolution and biogeochemical cycles. In this book, the author, Dmitry A. Los, focused on stress response and various regulatory mechanisms in cyanobacteria to combat such stress

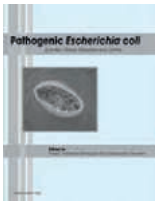
Arindam Mitra Adamas University, India

Methylotrophs and Methylotroph Communities

Edited by Ludmila Chistoserdova
Caister Academic Press (2019) £199
ISBN 978-1-912530-04-5

Methylotrophs and Methylotroph Communities is a new text that aims to provide an overview of the topic of methylotrophy, including the significant updates that have occurred in recent years.

Michael Macey The Open University, UK



Pathogenic *Escherichia coli*: Evolution, Omics, Detection and Control

Edited by Pina M. Fratamico, Yanhong Liu and Christopher H. Sommers
Caister Academic Press (2018) £159
ISBN 978-1-910190-77-7

This book provides a timely update on the potential of novel methodologies for the development of efficient prevention and treatment strategies against pathogenic *E. coli* infections.

Stephanie Schüller University of East Anglia, UK

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MICROBIOLOGY SOCIETY

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12–16 April 2021
ICC Birmingham, UK

Abstracts open:
17 August 2020

Abstract submission deadline:
14 December 2020

Grants deadline:
14 January 2021

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