Microbiology TODAY

44:2 May 2017

The Microbiome

The microbiomes of things
Microbiomes and nutrient cycling
Beyond the gut
Microbial communities within the chronic wound
Microbiome–health associations

MICROBIOLOGY SOCIETY

CHLORAMPHENICOL

CAPSULES

Widely distributed throughout the body, including CSF[1]

Oral levels comparable to i.v. levels[2]

Rarely implicated with *C.difficile*[3,4]

Effective against serious infections including:

- *H. influenzae*[1,5]
- Typhoid[1,5]
- MRSA[2]
- VRSA[6]
- Neisseria[1,5]
- Legionella[1,5]
- Rickettsia[1,5]
- *C.difficile*[7-10]
- *E. coli*[1]

Abbreviated Prescribing Information
Chloramphenicol Capsules BP 250mg

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

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

References:
1. Martindale: The Complete Drug Reference. Chloramphenicol. [Online]. Available from: http://www.medicinescomplete.com [22nd of November 2016]. **2.** Fluit, A.C., Wielders, C.L.C., Verhoef, J., and Schmitz, F.J. Epidemiology and susceptibility of 3,051 Staphylococcus aureus isolates from 25 university hospitals participating in the European SENTRY Study. Journal of Clinical Microbiology. 2001; 39(10): 3727-3732. **3.** Kelly, C., LaMont. Patient information: Antibiotic-associated diarrhea caused by Clostridium difficile (Beyond the Basics).June 2015. **4.** Bartlett J.G. Antimicrobial agents implicated in Clostridium difficile toxin-associated diarrhea of colitis. Johns Hopkins Med J. 1981; 149(1): 6-9. **5.** Feder. H, Chloramphenicol: What we have learned in the last decade. Southern Medical Journal. 1986; (79)9: 1129-34. **6.** Weigel LM *et al.* High-Level Vancomycin-Resistant Staphylococcus aureus Isolates Associated with a Polymicrobial Biofilm. Antimicrob Agents Chemother. 2007 Jan; 51(1): 231–238. **7.** Ensminger, P., Counter, F., Thomas, L., Lebbehuse, P. Susceptibility, resistance development, and synergy of antimicrobial combinations against Clostridium difficile. Current Microbiology. 1982; 7: 59-62. **8.** Poilane, I., Bert, F., Cruaud, P., Nicolas-Chanoine, MH., Collignon, A. Interest of the disk diffusion method for screening Clostridium difficile isolates with decreased susceptibility to antibiotics. Pathologie Biologie (Paris). 2007; 55(8-9): 429-33. **9.** Cattoir, V., Ould-Hocine, ZF., Legrand, P. Antimicrobial susceptibility of Clostridium difficile clinical isolates collected from 2001 to 2007 in a French university hospital. Pathologie Biologie (Paris). 2008; 56(7-8): 407-11. **10.** Brazier, JS., Levett, PN., Stannard, AJ., Phillips, KD., Willis, AT. Antibiotic susceptibility of clinical isolates of clostridia. Journal of Antimicrobial Chemotherapy. 1985; 15(2): 181-5.

EG/CH/NOV/2016/02a

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ALLIANCE: 065995
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Editorial

I would like to welcome everyone to the latest edition of *Microbiology Today*, which addresses one of the most fascinating topics in microbiology: the microbiome. Research surrounding the microbiome has always been both complex and interesting, and with recent advances in technology we have been able to generate more insight into complex communities than ever before. As research interest in this area has grown, we have seen significant interactions between microbes, environment and the host. This has given us a fresh understanding about how they impact on every aspect of life, sometimes in the most unexpected of ways.

Whole Picture

The first article, written by Professor Julian Marchesi, outlines how microbiome research has developed and evolved, highlighting how access to a new type of information has allowed us to ask different questions. The article emphasises how an increasing understanding of microbiomes has the potential to impact on how we see and deal with not only human health, where the focus has traditionally been, but also multiple microbiomes within the environment, that when combined together support life on Earth.

Dr Thorunn Helgason has written the second piece, which delves into the importance of microbiomes within soil and how they can affect food production and the ability to support human population growth. The global need for more food means it is essential we understand how the microbiome of soil can help lead to increased crop production. Conversely, it highlights how poor understanding and management of soil can potentially lead to poor crop production, water run-off and flooding. The technology available is now being used to investigate which parts of the soil microbiome are integral to 'good' soil, and how different land management practices impact on these microbiomes.

Following on from this, Dr Melissa Dsouza and Professor Jack Gilbert have given an overview of how improvements in sequencing technology and statistical bioinformatics has given us a new insight into the complexity of both environmental and human microbiomes. They have then suggested ways in which this improved understanding of the interactions and relationships within microbiomes could be used to help us preserve and restore ecosystems across the globe.

In the fourth piece, Dr Sarah Maddocks examines the role of the microbiome in wound healing, outlining how a small shift in the composition of microbial populations within wounds can be the difference between timely and delayed healing. She discusses the latest ideas around the complexity of these systems, and how the diagnosis and treatment of wounds might be influenced by these findings in the future.

Professor Paul O'Toole talks us through through how variation in the microbiome of humans can lead to vastly different outcomes in terms of human health and disease. Again, the great strides forward in technology have allowed questions to be asked, not only about which microbes are present, but also which genes they carry and how that might affect the host. Much research has focused on how the variation within the gut microbiome can impact a whole range of disease, while still leaving plenty of questions about how exactly those effects come about. There is evidence that, as our understanding of the intricacies of microbiomes improves, the findings may be of increasing clinical value.

For our last piece, Professor James Prosser gives a balanced outlook describing how increased accessibility to molecular technology has and can continue to influence research studies, but also reminding us not to forget that all technology has limitations. He observes that, despite advances in sequencing technology and increased access to large data sets, more data doesn't necessarily mean improved understanding. It is essential that robust research questions are asked, to make meaningful use of the information being generated.

It is clear that this fascinating subject area is likely to produce exciting new findings as the research moves forward. This collection of articles begins to show just how significant the interactions between different microbiomes can be, and how understanding the interactions is critical to understanding the impact they might have.

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Contents

Microbiology
TODAY

Articles

44:2 May 2017

Features

Regulars

Address **Microbiology Society, Charles Darwin House, 12 Roger Street, London WC1N 2JU** T **+44 (0)20 7685 2683** E **mtoday@microbiologysociety.org**

Design **Ian Atherton, Corbicula Design** (www.corbiculadesign.co.uk)

Printed by **Charlesworth Press, Wakefield**

 ISSN 1464-0570

FSC Logo

Coloured scanning electron micrograph of various bacteria found in a sample of human faeces. Steve Gschmeissner/Science Photo Library

MICROBIOLOGY SOCIETY

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From the President

My own schedule has taken me to five symposia and the Microbiology Society Annual Conference already this year, and I have enjoyed being in the audience for a wide range of types of presentation, from fungal immunology to public health and tropical disease. The topic that has been a common denominator of every major meeting I have been to recently is the microbiome, and dozens of new papers are published each day on this topic.

Around 80% of the metabolites in our bloodstream are derived from the microbes in our gut and so it is perhaps not so surprising that the intestinal microbiome influences not only our local gut health, but impacts our human physiology, systemically affecting our immune responses and potentially even our behaviour and mood. It is therefore appropriate that the Microbiology Society is undertaking a major policy review of this topic (see article by Isabel Spence and Paul Richards, page 88). This issue of *Microbiology Today* also contains a series of other important articles on the microbiome in a variety of contexts. Read the overview by Julian Marchesi, the article on the microbiome of wounds by Sarah Maddocks, health-associated microbiomes by Paul O'Toole, and the microbiome beyond the gut by Melissa Dzousa and Jack Gilbert. We know that environmental microbiomes are also critical for the major nutrient cycles that drive the ecology of our planet (see the article by Thorunn Helgason) and that collectively the microbiomes of the world represent the major metabolic engines of life. The Comment article, 'Advances in the study of the microbiome', by Jim Prosser is also key to understanding the future aims in this field. The microbiome underpins so many aspects of biology and so the Schoolzone article by Hannah Forrest on teaching the microbiome provides a useful resource for those introducing this topic into the biology curriculum.

The microbiome was also a topic at the forefront of the Annual Conference in Edinburgh. We tried to ensure that the richness of the scientific buffet at Edinburgh was accompanied by plenty of local flavours, including a ceilidh, a quiz night and other entertainments. But with over 900 abstracts received this year for the event, it was a bumper feast and I hope all enjoyed the variety of microbial science on offer.

In this edition of *Microbiology Today* you can read the second official report from our newly established Early Career Microbiologists' (ECM) Forum that has been set up to empower our community of students, postdocs and non-tenured microbiologists. We have already received great input to Council meetings and we wish to grow this initiative to capture the aspirations and needs of ECMs, and to include bespoke elements that speak to this community within our main meetings.

Microbiology Today has proved to be immensely popular with our members for many reasons. The articles are pitched so that topics are explained to an interested but non-specialist audience, and it also provides Society news and updates that we hope keep you informed with all aspects of Society business. This issue also has useful information about our portfolio of journals, which we aim to expand in the coming year (see page 82) and other Society titbits from our Communications' captain Benjamin Thompson. There are also a number of book reviews to help guide your reading of the newest tomes, treatises and theses on our science, both in the issue and online, and I hope you will enjoy these. Also, don't be shy about suggesting topics we might want to consider for future issues of *Microbiology Today*. The *Microbiology Today* staff (**mtoday@microbiologysociety.org**) are only too delighted to hear from those who wish to contribute this knowledge and insight.

Neil Gow
President
president@microbiologysociety.org

From the Chief Executive

As always, the Annual Conference in Edinburgh in April was one of the highlights of my year. It was fantastic to see so many members coming together and networking, both to share scientific results, insights and challenges, and also to learn from one another, develop collaborations, solve research problems, discuss fresh ideas, admire elegantly-conducted experiments, forge new friendships and renew old ones. Bringing together the whole microbiology community is the core function of the Society, and it was heartening this year to see a record number of abstracts submitted – double the number of a few years ago.

The Annual Conference goes from strength to strength because the Society continues to put the needs and wants of its members first. This year, we took on board feedback that previous meetings were so full of great sessions that sometimes there was not enough time to study the posters properly. That matters because the poster sessions at a big meeting are often where you get a glimpse of novel, early-stage research being carried out by up-and-coming stars of the future. The Divisions that organise the Society's scientific programme work incredibly hard to make sure that the sessions at our conferences will be stimulating for any microbiologist, whatever your particular field. And that applies not just to the Annual Conference, but also to the programme for the rest of the year, which offers something for everyone, whatever kind of microbe you study, wherever you work, and whatever your particular interests.

The Focused Meetings will cover a wide range of areas from a number of different angles. Some focus on particular taxa of microbes, such as the 16th International Conference on Pseudomonas and the British Yeast Group meeting on 'The Versatility of Yeasts'. Others will involve a range of different microbes with themes such as 'Microbial Resources for Agricultural and Food Security' and 'Antimicrobial Resistance and One Health'. Others will focus on particular sets of interactions, such as 'Arboviruses and their Vectors'.

A particular highlight this year is the 33rd International Specialised Symposium on Yeast, or ISSY33, which is organised under the auspices of the International Commission on Yeasts, with support from the Microbiology Society. It will be held at University College Cork and the theme is 'Exploring and Engineering Yeasts for Industrial Application'.

And for members particularly interested in clinical microbiology, there is the Federation of Infection Societies (FIS) meeting in Birmingham in November, which is organised each year by a range of like-minded partners, with the Microbiology Society playing an important part.

If you really can't find anything among all of these meetings to suit your interests, take a look at the list of Society-Supported Conferences – meetings that are organised by members with some financial backing from the Microbiology Society. There are meetings later in the year on RNA granules in human disease, anaerobic protists, *Staphylococcus*, microbiomes, hepatitis C, the molecular mechanisms of host–pathogen interactions, and one covering a broad range of fungal research.

And if after that, you still think there is nothing in your field, you can do something about it by making an application for a Focused Meeting, or for funds to run your own Society-Supported Conference, or you can propose a session for a future Annual Conference or FIS meeting.

I try to get out and about and speak to as many members as possible each week, and I ask you what the Society does well and what more you want from us. As Council finalises the strategy for the next five years, one thing that is clear is how much you value the conference programme. It is a success because you propose great ideas, because the Divisions and Scientific Conferences Committee work hard to shape those ideas into a diverse and engaging programme, and because the staff team are constantly on the lookout for innovations and developments.

I look forward to seeing some of you at Focused Meetings, Society-Supported Conferences and FIS later in the year.

Peter Cotgreave
Chief Executive
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News

Annual Conference

Thank you to all those who attended, presented and helped organise our 2017 Annual Conference in Edinburgh – the turn-out was fantastic and exceeded expectations once again. You can watch our summary video of the event by visiting our YouTube channel (**http://microb.io/2oYhdhn**).

Our Conferences team is already part-way through organising Annual Conference 2018, taking place 10–13 April at the ICC Birmingham. Find out more about the upcoming programme on page 79.

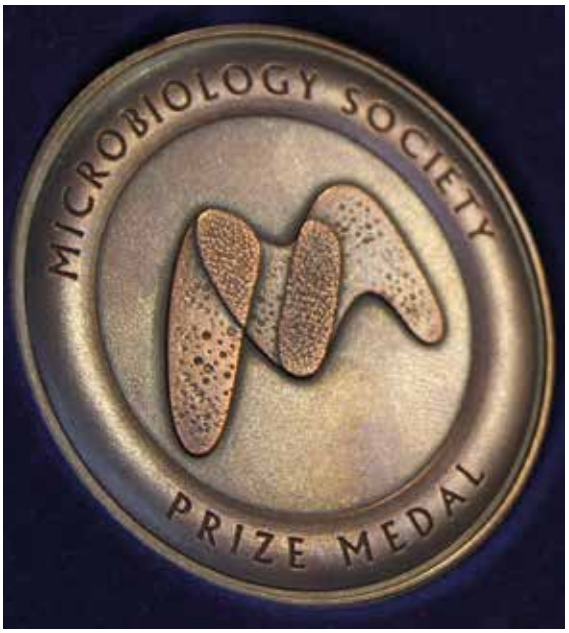
Microbiology Society journals

This month, the Microbiology Society is celebrating 70 years of our journal, *Microbiology*. Society publishing is looking to the next 70 years, launching redesigned articles, implementing continuous publication, introducing journal-sponsored poster prizes, and publishing the first ICTV Virus Taxonomy Profiles. See pp. 82–83 for more information.

ECM Forum summer roadshow

The ECM Executive Committee is touring the country over the summer to meet Forum members and share their plans for the next few months. This will be a great opportunity for early career researchers to meet members in their local area. To find out more, please see our website (**www.microbiologysociety.org/ECM**).

Prize Lecture nominations



Nominations are still open for the Society's Prize Lectures. Our Prizes recognise significant contributions to the field of microbiology by any researcher, regardless of background or location. Find full details and nominate an outstanding microbiologist before 7 June: **www.microbiologysociety.org/prizelectures.**

Society-Supported Conference Grants

Running your own event? Why not apply for a Society-Supported Conference Grant to cover some costs of your invited speakers? Our second round of submissions closes on 12 June 2017. Read more on page 84.

Focused Meetings 2018 proposals

The deadline date for Focused Meeting proposals for our 2018 series is 12 June 2017. Find out more on page 80.

Policy consultation responses

Over recent months, the Society has responded to several UK Parliamentary and Government science policy consultations. Jointly with the Society for Applied Microbiology, we responded to the House of Commons Science and Technology Committee's Genomics and Genome-editing inquiry. The Society also contributed to the Royal Society of Biology's responses to the Science and Technology Committee's Closing the STEM skills gap inquiry (**http://microb.io/2mHNf1s**) and the UK Government's Building our Industrial Strategy consultation. Information about our responses and opportunities to inform them is available on our website (**www.microbiologysociety.org/policy**), in the monthly newsletter, or by contacting our Policy Officer (**policy@microbiologysociety.org**).

Updated educational resources

Alongside a refresh of our education website, Microbiology Online, the Society has updated some educational resources to provide students and teachers with the most up-to-date and relevant information. Fact files on tuberculosis, cholera, H1N1 influenza, HIV & AIDS, antibiotic resistance, and influenza have all been updated to cover the latest research developments in these areas. Also refreshed are some of our comics, which cover topics such as handwashing, brushing teeth, the discovery of yeast and antibiotic resistance.

Our range of resources, aimed at primary to post-16 students, is carefully targeted to meet curriculum requirements and fit in with the specifications for science. Single copies of non-chargeable resources are free to anyone involved with teaching microbiology in the UK and Ireland. Classroom sets of these resources, along with single copies of chargeable resources, are available if you have a School Membership of the Society.

Download the new resources now from **www.microbiologyonline.org** or contact **education@microbiologysociety.org**.

Grant deadlines

Date	Grant
1 June 2017	Travel Grants – for eligible members wishing to present at a conference or attend a short course between 1 July and 30 September.
1 September 2017	Travel Grants – for eligible members wishing to present at a conference or attend a short course between 1 October and 31 December.
30 September 2017	ECM Forum Event Fund – for ECM members wishing to host a local event from 1 May onwards.
1 October 2017	Research Visit Grants – for eligible members wishing to visit a collaborator from 1 December onwards.
	International Development Fund – for eligible members wishing to contribute to microbiology development activities in low-income economy countries from 1 December onwards.
	Education and Outreach Grants – for members wishing to conduct a microbiology teaching, outreach or public engagement activity from 1 December onwards.

Deaths

It is with regret that the Society announces the passing of **Mr John S. Page *FCA***, who joined the Society in 1982 as an Honorary Member.

Please contact **mtoday@microbiologysociety.org** if you wish to notify the Society of the death of a member whose details can be included in this section.

Contributions and feedback

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

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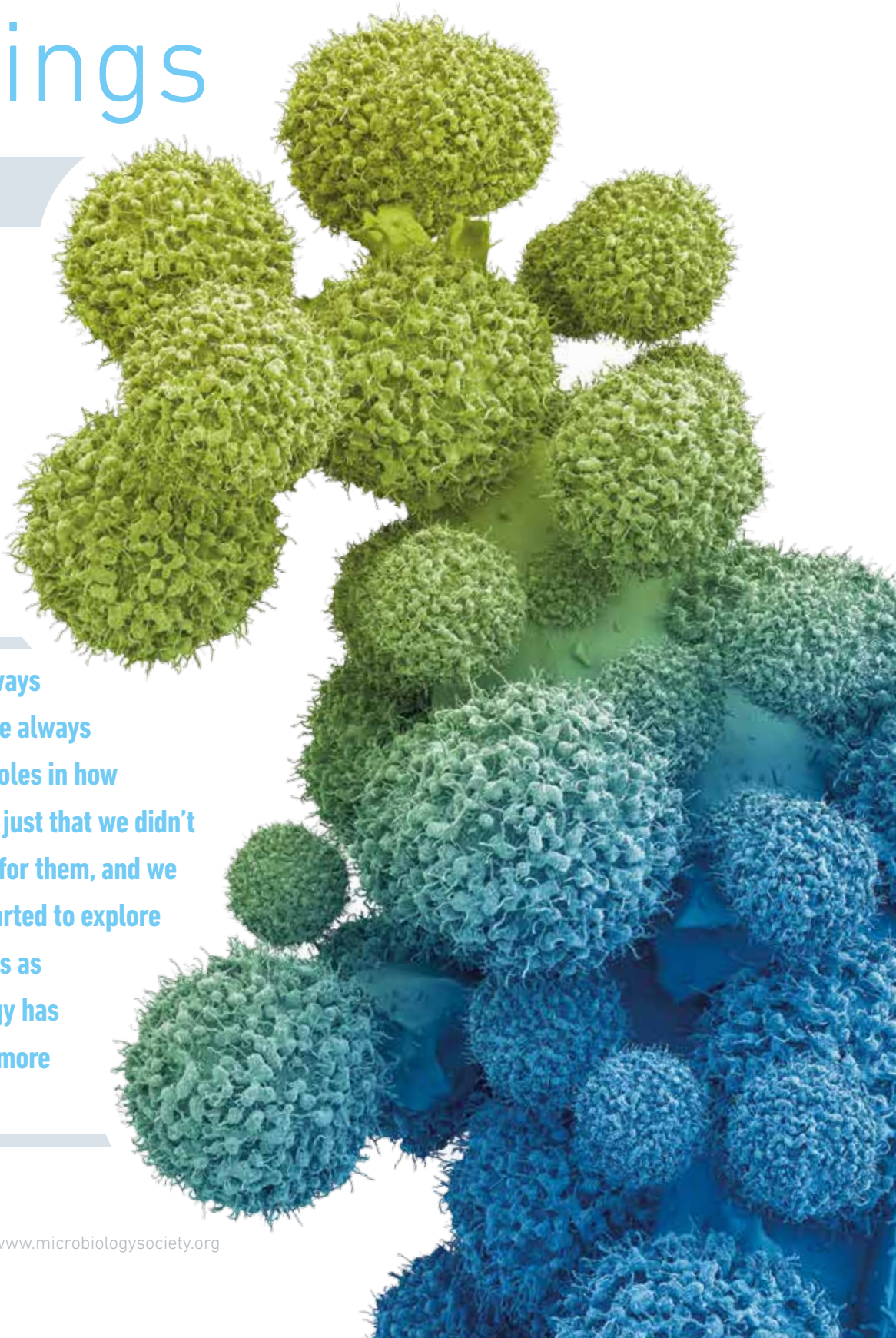
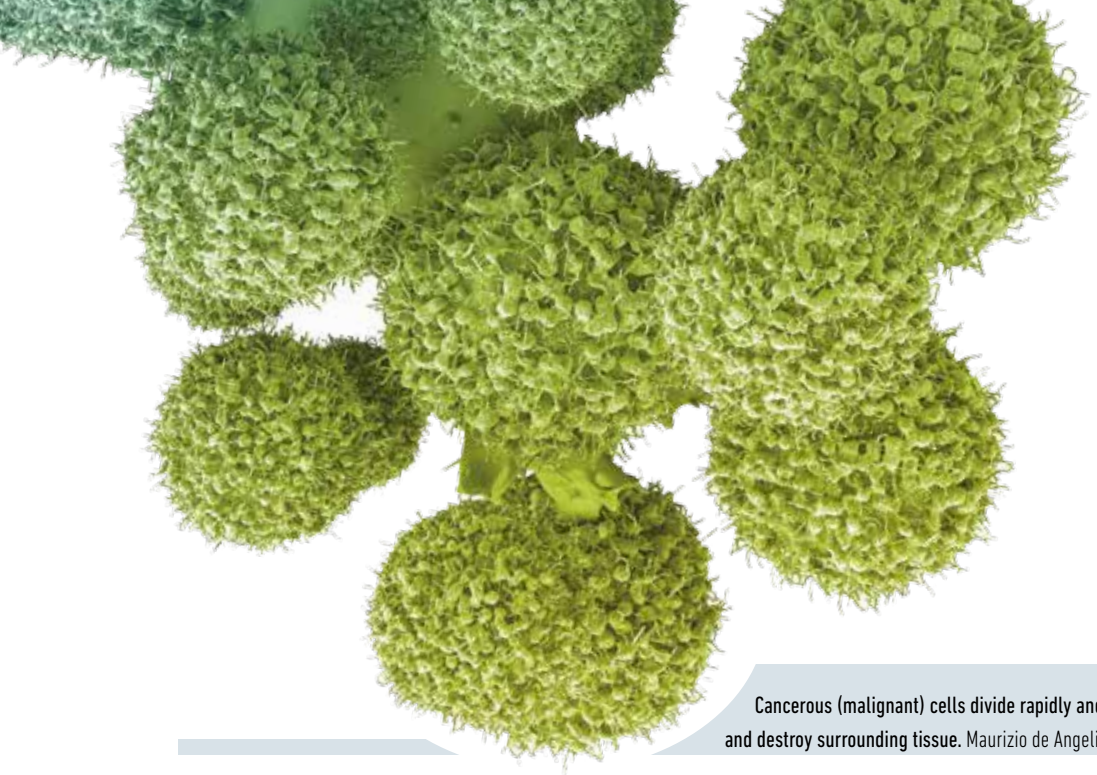
The microbiomes of things

Julian R. Marchesi



Microbiomes have always been with us, and have always played fundamental roles in how systems function. It's just that we didn't have a specific name for them, and we have only recently started to explore them in large numbers as sequencing technology has become cheaper and more high throughput.



Cancerous (malignant) cells divide rapidly and uncontrollably and are able to invade and destroy surrounding tissue. Maurizio de Angelis/Science Photo Library

One of the first mentions in the literature of microbiomes was in the 1988 book, *Fungi in Biological Control Systems*, edited by Michael Burge, in which John M. Whipps, Karen Lewis and Roderic C. Cooke reviewed mycoparasitism and included a section heading titled 'Microbiomes, delivery systems and disease control' in which they explored both aerial and soil microbiomes. Later in 1992, John Whipps, in a review of biological disease control in horticulture, mentions in his abstract, "Strategies for selection and direct application of microbial antagonists are reviewed for aerial, root and growing media/soil microbiomes." However, it seems that Joshua Lederberg has been attributed with creating this neologism when one searches Google, but Jonathan Eisen, on his microBEnet site, has a nice potted history of the etymology of this word which clarifies the situation. The next mentions come 10 years later in a review by Fergus Shanahan and a conference communication from David Relman, and after that the usage starts to increase dramatically (Fig. 1).

One current working definition of a microbiome is "the entire community of micro-organisms (bacteria, archaea, lower and higher eukaryotes and viruses) within a habitat and the surrounding environmental conditions." This definition is derived from a recent discussion document that Jacques Ravel and I published in the journal *Microbiome*, with the aim to start a

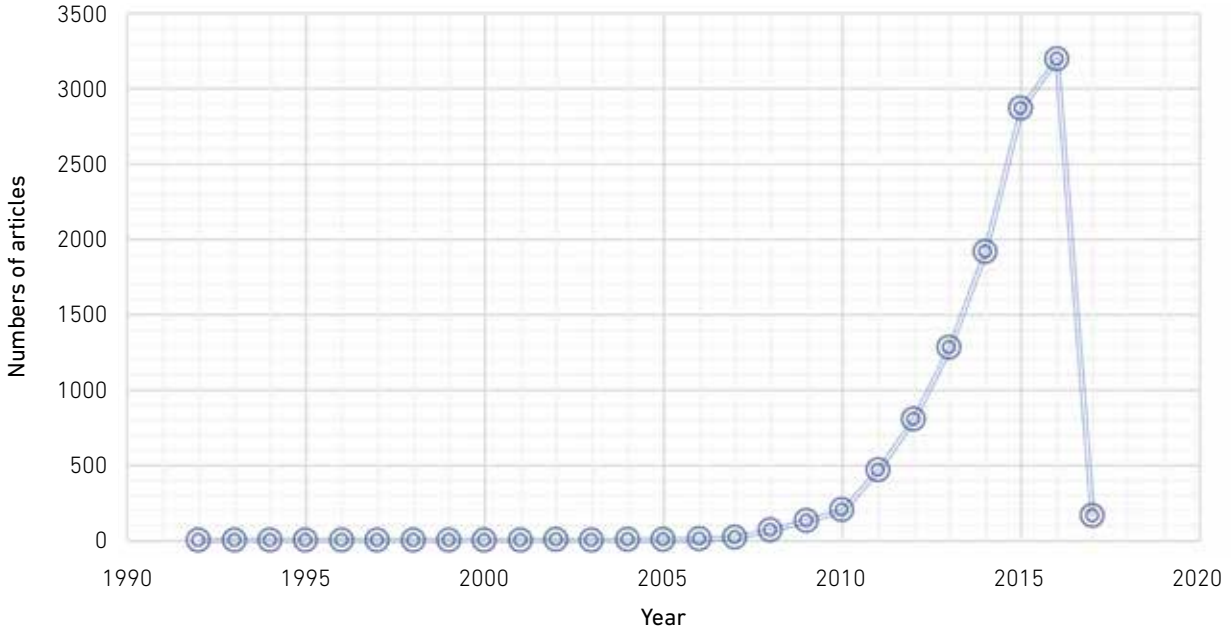
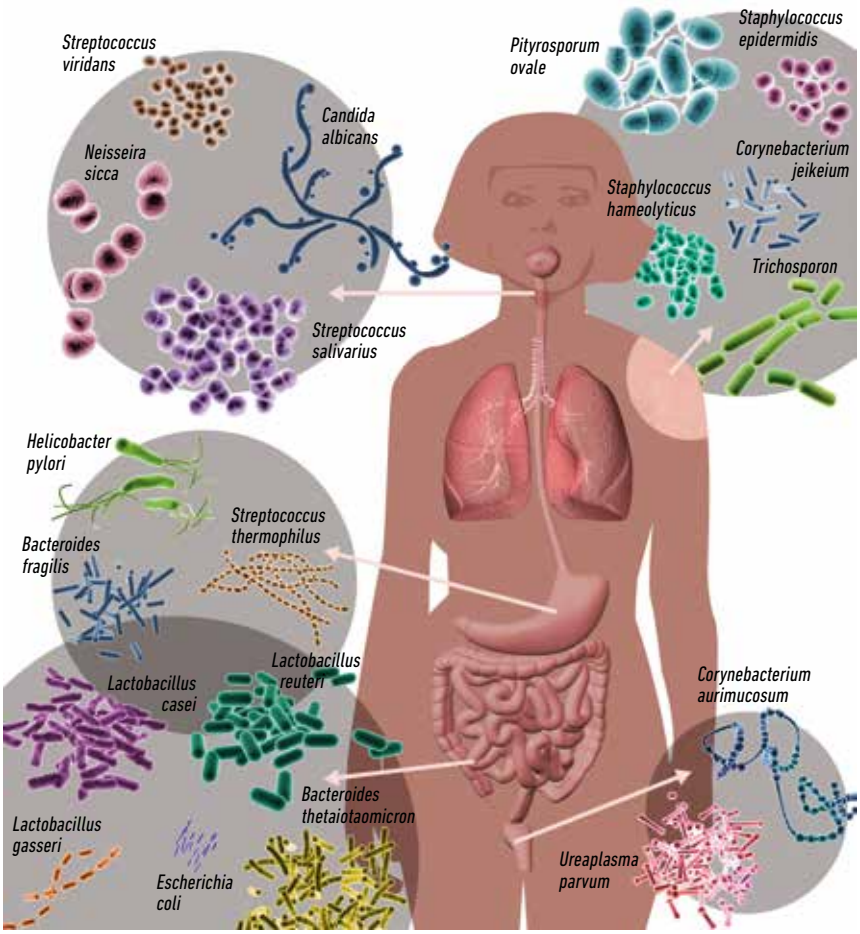


Fig. 1. Numbers of articles which contain the word microbiome or microbiomes found on Scopus.

debate in the wider community on the terminology, as there is some confusion in the literature.

But how come we are now suddenly so excited by research into microbiomes and what they do? One of the simplest explanations is that we now have the tools to allow us to capture, at different omic levels, e.g. genomes, transciptomes and metabonomes, a whole microbiome and its microbiota and metagenome. We can look into a system across time and across multiple samples, and for the first time determine who's there and what they are potentially doing, and what we have found is astounding. We are now able to take a holistic rather than reductionist approach to try and explain how different microbiomes are involved in ecosystem and biosystem function. One of the features of microbiome research is that it is based on a multi-disciplinary research model, unlike traditional microbiology, where a scientist can make a career looking at a single species. In microbiome research, due to the large and complex datasets, the microbiologist needs, for example, biological chemists to create the data for metabolite profiles, and physicists to help make sense of it and answer the research question set in the first place. For the first time we can start to try and map the interactions between different microbes and the surrounding system, and this approach is throwing up some challenging notions – for example, what is mammalian biology? Previously we would have considered it to be the interaction between the host's genome and the environment, but now we need to include the metagenome of the microbiota with which we have co-evolved.

Of course, just like in microbiology, research into microbiomes has focused



Computer illustration of the human microbiome showing the various different types of bacteria commonly found on human skin and the linings of organs. Gunilla Elam/Science Photo Library

on the role of the microbiota in maintaining the healthy human status and how they are involved in diseases. Because of 'The Human Condition', we are very focused on any new situation that potentially can lead to improving the quality and longevity of life. To meet this need, the majority of microbiome research in the last 10–15 years has focused on understanding the role of the microbiota in human biology. Notable examples of this include the now-completed Human Microbiome Project and the MetaHIT project (**www.metahit.eu**), both of which made significant contributions to our knowledge of how extensive the human microbiome is. One of the areas that most interests me is the role of the host microbiota in cancer, which has been referred to as the cancer microbiome or oncobiome. The microbiota in the gut microbiome have been implicated in playing a role not only in the initiation of colorectal cancer – by producing carcinogens or genotoxins which caused the 'first hit' in the oncogenes – but also in interacting with the developing adenoma as it evolves into a carcinoma. Recently, the gut microbiota has been hypothesised to be responsible for host response

to cancer treatments such as the new immunotherapies being trialled.

However, while we all have a personal interest in understanding human microbiomes and how they influence health and disease, in the wider arena, environmental microbiomes are fundamental to global ecosystem functions, services and life. All of the major global geochemical cycles, for example the nitrogen cycle, would fail if specific microbiomes, which are responsible for keystone steps within the cycle, were perturbed in such a manner that they failed to fulfil their evolved roles. Using a microbiome-led approach will help us understand where we need to invest our efforts to ensure that these environmental cycles continue to support an ecosystem conducive to life.

We currently stand on the verge of an exciting new era in microbiology in which we have the potential to fully define the importance of microbes in supporting microbiome function, and how we can modulate it in order to maintain the services and improve them when we have destroyed them.

While we all have a personal interest in understanding human microbiomes and how they influence health and disease, in the wider arena, environmental microbiomes are fundamental to global ecosystem functions, services and life.

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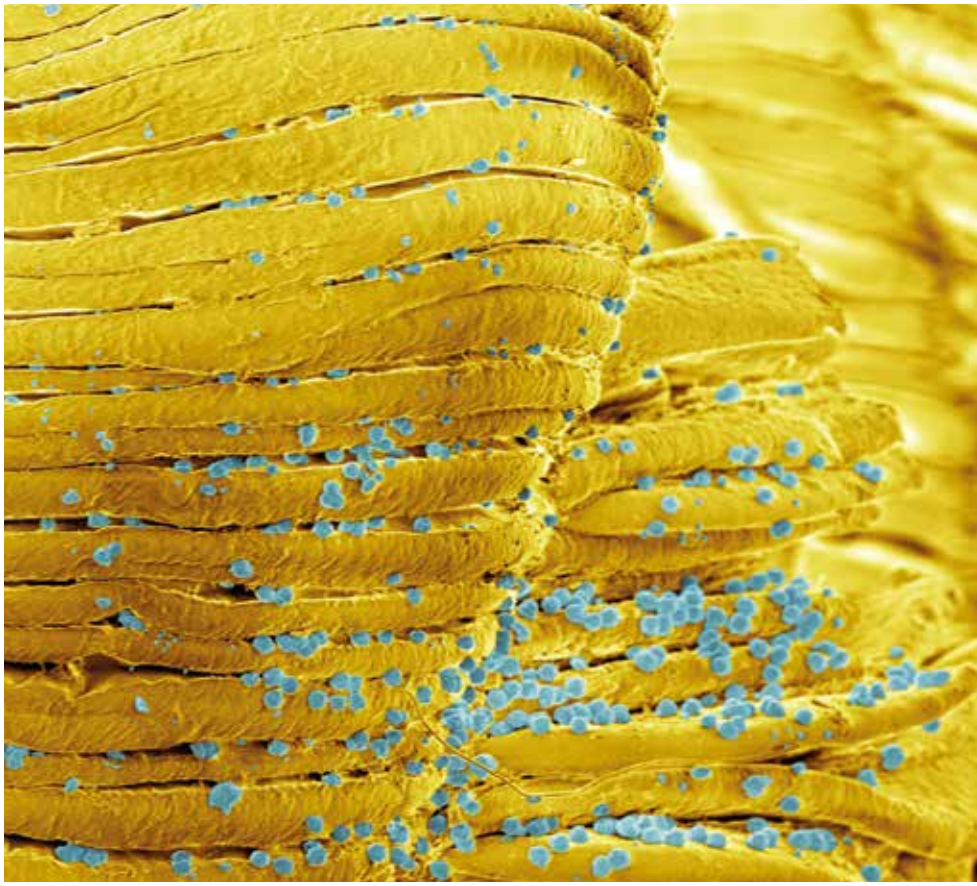
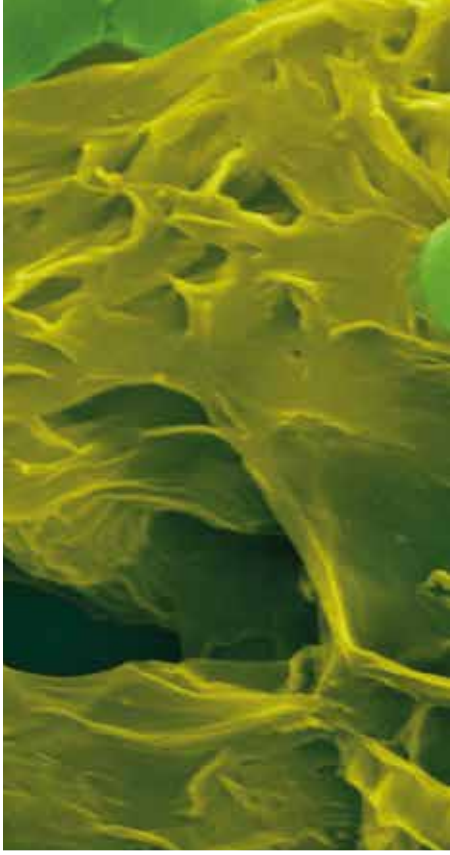
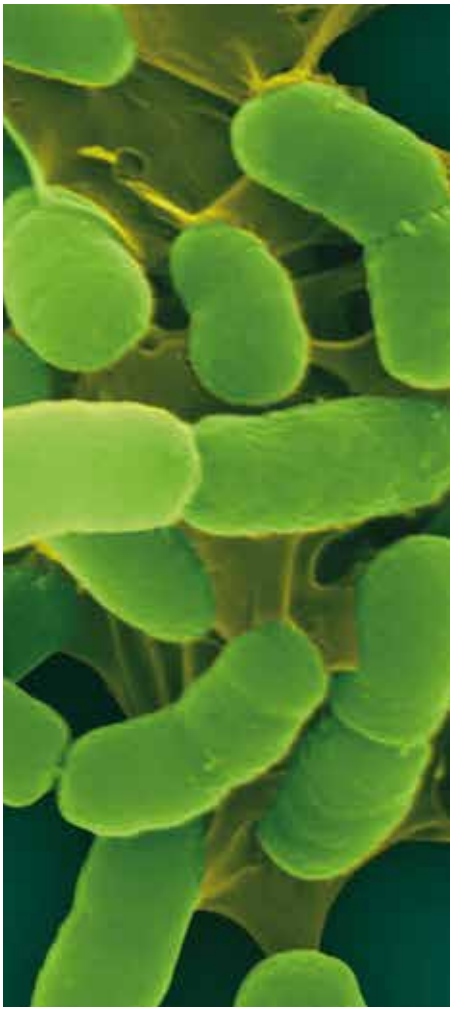


Deep sea bacteria (blue) on the surface (yellow) of annelid worms (*Alvinella* sp.).
Thierry Berrod, Mona Lisa Production/Science Photo Library

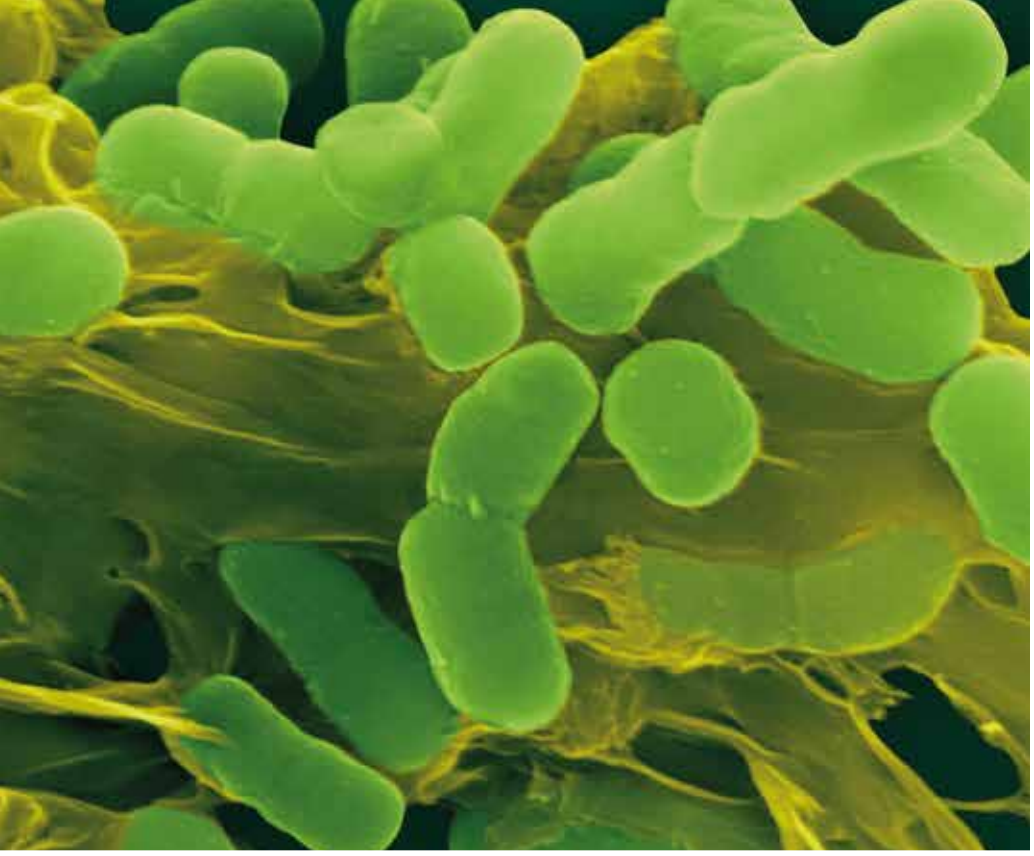


Microbiomes and nutrient cycling

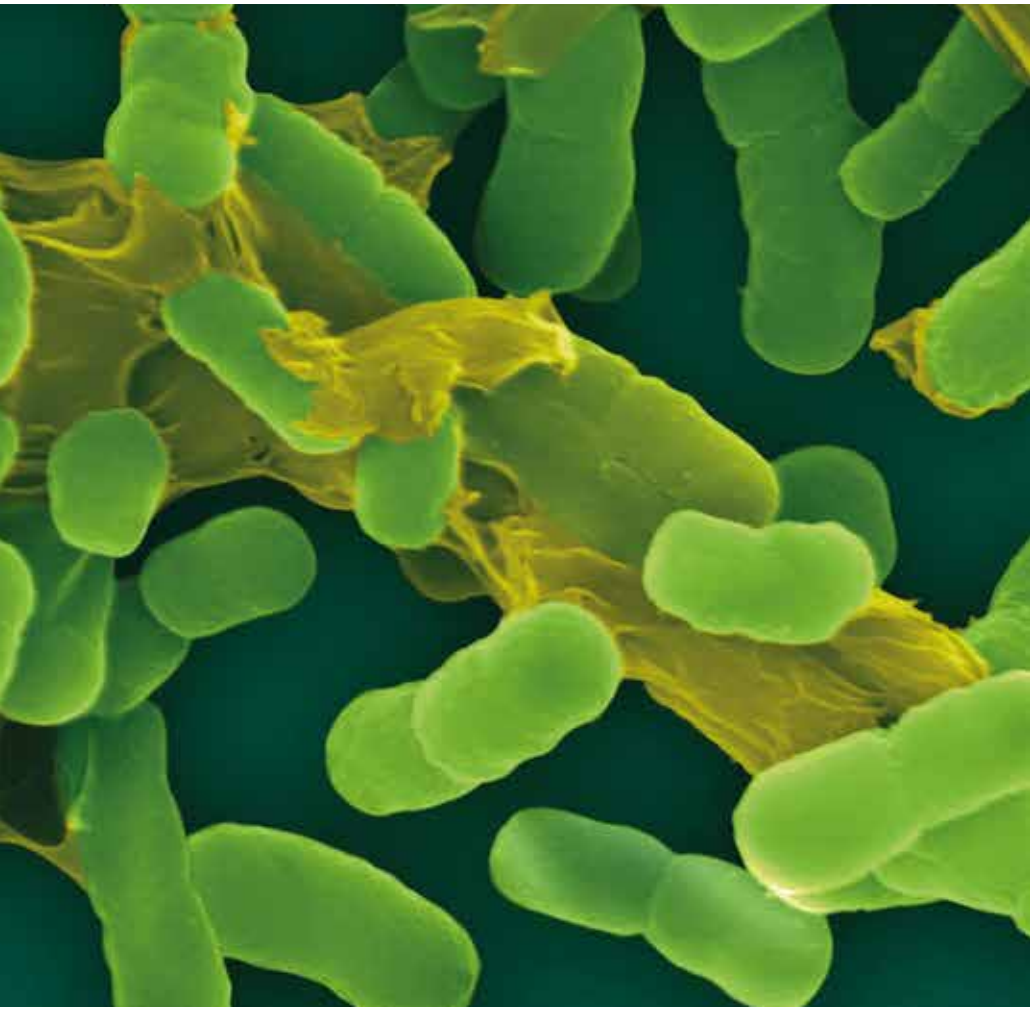
Thorunn Helgason



Any gardener will tell you that the key to a productive and healthy crop is a 'good' soil. It is well understood that the sand, silt and clay content of a soil determines its nutrient cycling and water retaining properties. This reflects centuries of development in agricultural practices. Crop rotation, especially with legumes and their nitrogen-fixing bacterial symbionts, became a cornerstone of the agricultural revolution in Europe from the 18th century onwards and created significant increases in crop yields throughout the 19th century. The 'nitrogen hypothesis' proposes that this directly enabled the growth of the European population and, hence, the Industrial Revolution.



Coloured scanning electron micrograph of multidrug-resistant *Acinetobacter baumannii*.
Dennis Kunkel Microscopy/Science Photo Library



In the early 20th century, development of the Haber–Bosch process (for which Fritz Haber and Carl Bosch were awarded the 1918 Nobel Prize for chemistry) made synthetic fertilisers widely available for the first time. Combined with the Green Revolution during the second half of the century, millions of people were brought out of food poverty.

Agricultural production has, so far, been able to feed the world's expanding population, but this may not last. Soils are being lost – to erosion, drought, flooding, salination and urbanisation – faster than they can be replaced by geological weathering. The steady increase in crop yields based on plant breeding technology is slowing down and cannot keep pace with population growth. Now, attention is turning to the soils: understanding their structure and function will give us ways of managing agricultural land that will maintain crop yields in the increasingly smaller spaces we have for farming.

Soil microbes and healthy soil

The aim, then, is to create agricultural soils that are "good" and "healthy" in the way gardeners understand. But what is a "healthy" soil? There has been much debate recently about this among farmers, researchers and government. What we all agree on is that the soil microbiome – the living component of the soil including bacteria, fungi, protists and other single-celled organisms – is key. It plays many roles in soils, but as yet we understand rather little about them.

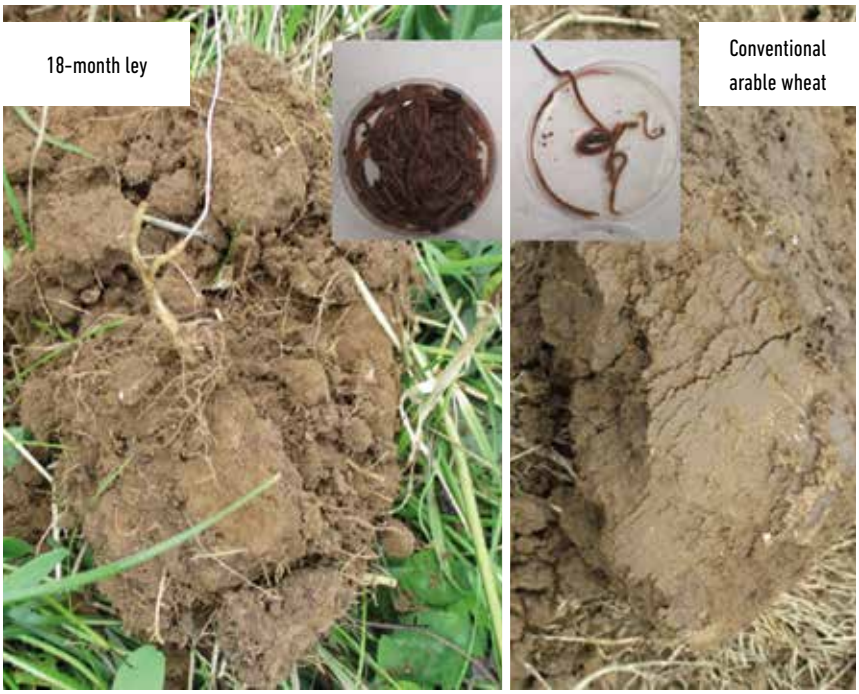
We do know that organic matter in soils, derived from microbes, is essential. Microbes capture and bind together organic matter and mineral soil particles to create the structure on

which soil fertility so strongly depends. Most importantly, it appears that a soil with a diverse microbial community will have more large soil particles, called macroaggregates. Macroaggregates are water-stable particles larger than 250μm in diameter, which improve how water and nutrients are maintained within the soil.

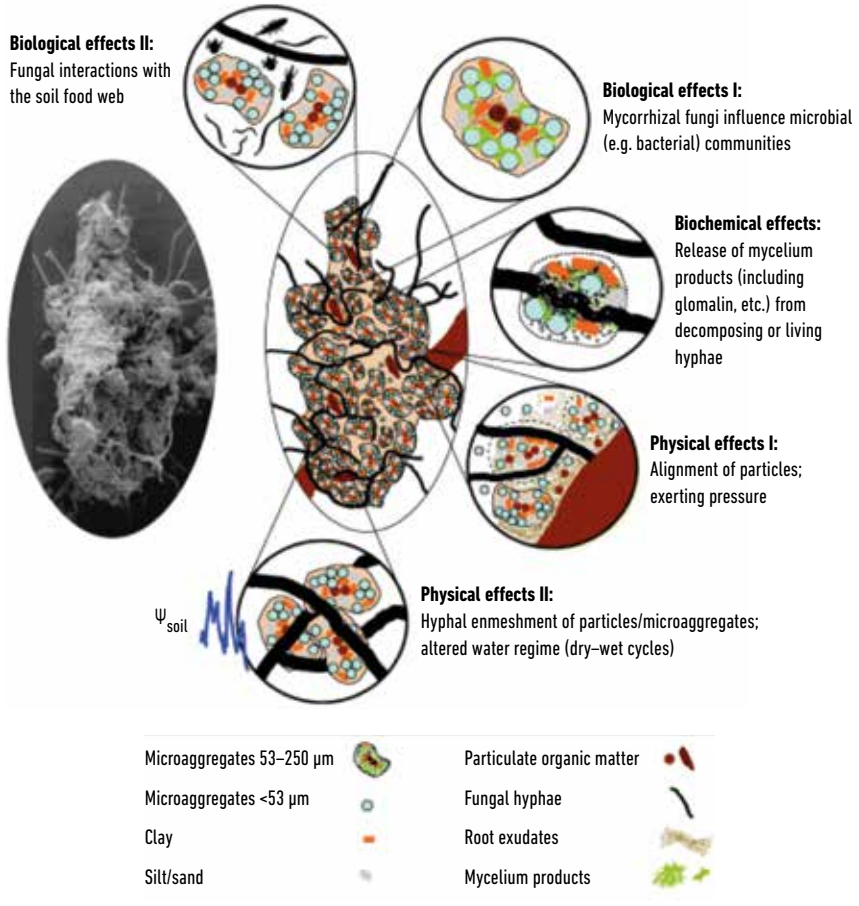
A very sandy soil is rather like a bowl full of peas: all the particles are the same size and shape, and they pack together neatly resulting in a very low water holding capacity. By contrast, a sandy soil with a substantial proportion of larger organic macroaggregates, or a bowl of peas and grapes, is unevenly packed, with more airspaces of varying sizes, allowing more water to fit in the bowl.

Like the bowl of peas and grapes, soils with thriving microbial communities and plenty of macroaggregates, i.e. soils that have better structure, hold more water. This benefits both crops and the surrounding environment: if rainfall is taken up into the soil, then there will be less surface runoff and thus less flooding in other areas. And fertilisers spread on crops are available to the crops for longer, increasing efficiency, and reducing downstream pollution.

Evidence suggests that microbes are essential for the development and maintenance of macroaggregates. Particles of sand and clay are bound by bacteria, and fungal hyphae further tie these together into particles of increasing size. Soil microfauna, protists and earthworms are attracted to these rich sources of nutrients, increasing the biological activity around them. These microscopic biological factories effectively bind nutrients within soils where plant roots can access them – without them, the nutrients simply wash



Soils dug from a ley strip (left) and conventional arable field (right). Note the difference in texture of the soils. Inset: the number of earthworms extracted from each of the soil samples. T. Helgason



Mycorrhizas and soil structure.
Reproduced with permission from *New Phytologist* **171**, 41–53; doi:10.1111/j.1469-8137.2006.01750.x

> **Better structured soils are more fertile and less vulnerable to loss from drought or flood, and our food security depends on being able to reduce the threat to soil.**

away. Unfortunately, typical agricultural soils have fewer macroaggregates, and this may be limiting crop yield.

White Rose Sustainable Agriculture Consortium, and the farm-scale experiments

In 2011, researchers from the Universities of Leeds, Sheffield and York came together to develop the University of Leeds farm as a platform where large scale experiments to understand the soil microbiome could be integrated into a working mixed arable farm. One of the management strategies being investigated is the use of grass/clover leys (or fallow) to recover soil structure and function.

Grass/clover leys

Planting a mixture of grass and clover has been a traditional ley/fallow rotation all over Europe since the 19th century, but cheap synthetic fertilisers have encouraged farmers to leave less land fallow. We are investigating how quickly leys improve soil structure and fertility, and early data suggests it can happen surprisingly quickly. Soil from a ley strip has a visibly 'crumbly' texture after 18 months that is absent from the ploughed strip alongside and, even without the statistical analysis, we can tell the number of earthworms has increased.

We are currently looking for the microbes that build the structure. We expect to find bacteria that secrete sticky polysaccharides, and other molecules that attract particles together. Of particular interest are the arbuscular mycorrhizal (AM) fungi – beneficial symbionts that colonise plant roots. They grow extensive hyphal networks into the soil that again bind large particles together and from which the hyphae capture mineral nutrients that are moved to the host plant in exchange for carbon.

Agricultural practices such as ploughing and extended periods of bare ground in fields, reduce the diversity and quantity of AM fungi. We know that productivity tends to increase when AM fungi are present, most likely because they act as a link between the plant and the rest of the soil microbiome, enabling the plant to access nutrients and water in a way it cannot do without them. We can demonstrate these effects in simple experiments, but the challenge now is to show this at the farm scale, to understand the mechanism that drives this, and to find out what the other microbial groups, such as nitrogen fixers and fungal pathogens, are doing. New DNA sequencing technologies that enable fast, cheap and data-rich genome sequencing have transformed microbiology, and the study of soil microbiomes is no exception. These technologies allow us to identify these microbes, and observe any change in diversity and function as the ley develops so that we can understand who is doing what, where and why.

The 21st century and beyond

We urgently need to find ways to improve soil structure. Climate change models predict that extreme weather events will become more frequent, increasing soil damage and erosion. Better structured soils are more fertile and less vulnerable to loss from drought or flood, and our food security depends on being able to reduce the threat to soil. The microbiome is the living community that binds the soil together and gives them their most useful properties. There is a case for saying the industrial revolution, and by extension the world we live in now, was created because of symbiotic nitrogen fixers. Imagine what could be done if we only understood what *all* of the microbes are doing?

Acknowledgements

Thorunn Helgason's work on soil microbiomes is funded by the NERC Soil Security Programme and BBSRC GFS-Sarisa **https://www.soilsecurity.org**.

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Microbiome –

Melissa Dsouza & Jack A. Gilbert

In recent years, vast improvements in the cost efficiency of high-throughput sequencing technologies and the sophistication of statistical bioinformatics have transformed our ability to investigate microbial communities in a wide range of environments across the globe.

These improvements have led to the emergence of several, large-scale initiatives such as the Human Microbiome Project, the *Tara* Oceans Project, and the Earth Microbiome Project, as well as large citizen science surveys such as the American Gut Project. Consequently, we have observed a tremendous increase in our knowledge of microbial diversity and microbial community dynamics across diverse biomes, including humans, animals, plants, air, soil, rock, marine, freshwater, sediment, and even built environments, among many others. Likewise, microbiome research has enabled the development of surveillance programs that hold the promise of protection, restoration and remediation of ecosystems impacted by anthropogenic pollution and climate change. In this article, we highlight major breakthroughs in microbiome research that extend beyond the human microbiome, and briefly consider the challenges and opportunities awaiting this exciting field, which is still very much in its infancy.

Working together on the *Tara* Oceans Project and the Earth Microbiome Project

Over the last decade, we have experienced a resurgence of natural history surveys of microbial ecosystems. Empowered by technological advances, programs of research such as *Tara* Oceans and the Earth Microbiome Project are an embodiment of true, collaborative success and the unrestrained ambition of multidisciplinary teams of scientists tasked with the complex goal of constructing a catalogue of the uncultured microbial diversity of this planet. The *Tara* Oceans researchers,

beyond the gut

Coral reefs are extensive and diverse marine ecosystems. Scubazoo/Science Photo Library

who spent more than three years collecting over 30,000 samples of water, sediment and plankton, revealed their findings in five reports in the May 2015 issue of *Science*. Collectively, their work represents a significant leap in our knowledge and understanding of the numerous, previously uncharacterised, planktonic organisms, including bacteria, protists and viruses that form vital components of marine food webs, and that provide half of the oxygen generated each year on Earth. Likewise, the success of the Earth Microbiome Project (EMP) is captured by two recent studies that make notable contributions to the fields of microbiome evolution, symbioses, and functional network-based modelling. First, Thomas & others generated extensive data through the EMP on microbial symbiont communities associated with 81 species of marine sponges collected through an extensive collaboration of scientists from 20 countries. Their observations of the sponge core–microbiome evolution and of host–microbe symbiotic interactions represent a valuable resource enabling further research and access to biotechnologically important, symbiont-derived natural products. Similarly, an EMP-sponsored survey of the soil microbiome associated with patches of remnant prairie grass across the Midwest of the United States provided a clear indication of the importance of certain bacterial taxa and functions associated with this vast ecosystem, and resulted in the discovery of a new bacterial species, '*Candidatus* Udaeobacter copiosus', that appears to be ubiquitously distributed across the world's grasslands. Importantly, large-scale studies of environmental microbiomes have led to an improved understanding of what structures communities of microbes, which lay the foundation for predicting how they will be influenced by climate change. For example, examining the bacteria, archaea, fungi and eukaryotic microbes associated with forest soils across China provided Ma & others with the power to understand the role of climate regions in shaping the interactions between these kingdoms. They employed co-occurrence network patterns at a continental scale to reveal complex associations that can be used to predict spatial organisation, and how changes in precipitation may impact soil health, stability and management. These survey projects, like the Human Microbiome Project, have paved the way for more specific hypothesis testing to elucidate specific mechanisms of action that underpin the observed ecological characteristics. They provide the scientific community with large, publicly available datasets that

are an incredible resource for the study of microbial ecology and the evolution of life.

Microbiomes to the rescue

The expansion of microbiome research has created novel opportunities to develop surveillance strategies to better monitor and protect pristine environments such as the soil and aquatic ecosystems in the Antarctic. Similarly, a better understanding of microbial biochemistry and ecology is helping us to devise new approaches to restore and remediate sites impacted by changing climate, such as the Great Barrier Reef with warming and acidifying oceans, and the Gulf of Mexico following the recent Deepwater Horizon oil spill. Coral reefs are home to at least 25% of all marine species making these biomes the most biodiverse marine ecosystem on the planet. Rising levels of environmental pressure due to nutrient enrichment, increased sedimentation, and climate change-induced ocean acidification and warming have deleterious effects on coral reef health and biological diversity. At research institutions such as Woods Hole Oceanographic Institute and the Australian Institute of Marine Science, microbiome researchers are actively exploring the adaptive capacity of many reef organisms and their microbial symbionts to the cumulative pressures of climate change and degraded water quality. Their work is particularly critical for the restoration and conservation of coral reefs around the world, and to improve our understanding of how microbiomes can contribute to host adaptation in the face of climate change. In 2010, the tragic explosion of the Deepwater Horizon oil platform killed 11 workers and released 700 million litres

Coloured scanning electron micrograph of the purple non-sulfur bacterium *Rhodobacter ferrooxidans*.
Dennis Kunkel Microscopy/Science Photo Library

Despite the technological advances, there still remain many challenges that need to be addressed to gain a deeper understanding of the role of microbiomes and their interactions within the environments and hosts they inhabit.

of oil over a few months into the Gulf of Mexico, producing drastic changes to the ecology of the sediment and water. Subsequently, multidisciplinary teams of scientists worked tirelessly to deepen our understanding of microbial hydrocarbon degradation, its regulation, and capacity in marine environments. Their research was the first to utilise multi-'omic-based approaches to comprehensively investigate the diversity and physiology of the microbes that responded to this hydrocarbon infusion, to characterise the several microbial hydrocarbon degradation pathways, and to determine the impacts of dispersant application on resident microbial communities and their activities.

Microbiome studies have also made meaningful contributions to a number of different research areas, including those investigating the effects of urbanisation on microbial distribution patterns and microbe-driven biogeochemical cycles in lakes, rivers, and soils; those determining the impact of microbes associated with controlled environments such as aquaria on the health and well-being of animals in captivity; those studying the occurrence and prevalence of multidrug resistance genes in terrestrial, marine, and freshwater environments; and others exploring novel means for preventing microbial surface attachment and biofilm formation on membrane filters designed for water purification and wastewater treatment.

Challenges facing microbiome research

Despite the technological advances, there still remain many challenges that need to be addressed to gain a deeper understanding of the role of microbiomes and their interactions within the environments and hosts they inhabit.

One of the major obstacles facing microbiome research is the computational and bioinformatics bottleneck. Some examples of these include determining cellular functions of the uncharacterised proteins in current annotation databases; the development of biome-specific annotation platforms to improve interpretation; and the development of algorithms enabling integration of multi-'omic data. Another major obstacle is the lack of a global initiative to process and integrate all microbiome data. It is crucial that we develop a long-term strategy that will support the storage, utilisation, and exploration of the large quantities of data generated worldwide by high-throughput sequencing technologies. Ongoing development of data science-related tools such as Qiita (**http://qiita.microbio.me**) and the Joint Genome Institute's Genomes Online Database can facilitate the systematic review and meta-analysis of data produced, thus greatly advancing our understanding microbes and their environments.

Where do we go from here?

Challenges aside, microbiome researchers are ready to usher in new projects and collaborative ventures following the announcement of the National Microbiome Initiative by the White House Office of Science and Technology Policy (OSTP). We are poised to enter a new golden age of microbiome research wherein we achieve a holistic understanding of microbial life; develop novel diagnostic and therapeutic strategies to treat diseases; mitigate risks associated with microbial multidrug resistance; identify sustainable solutions for restoring, remediating and protecting the environment; and eventually realise and harness the power of Earth's microbial ecosystems.

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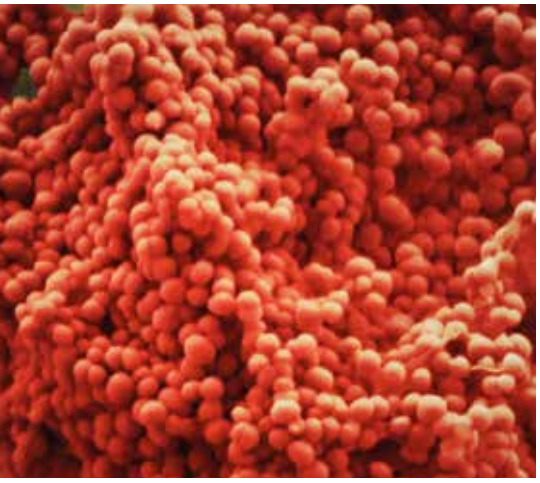
Microbial communities within the chronic wound



Wound infection currently costs the NHS more than £4 billion per annum, with over 100,000 chronic wounds diagnosed each year. It is understood that all types of wounds are readily colonised by micro-organisms of either endogenous or exogenous origin.

Sarah E. Maddocks

Acute wounds, such as surgical site incisions, cuts, abrasions or traumatic skin damage, often become infected but resolve quickly, usually without the aid of antimicrobial intervention. Conversely, chronic wounds are characterised by their failure to heal in a timely, predictable manner, and instead remain stuck in a non-healing state for many months or even years. When the microbial load of a chronic wound exceeds $1x10^6$ colony forming units per gram of tissue, it is regarded as being clinically infected.

Traditional cultivation-dependent methods of microbial isolation and identification have largely biased the recovery of certain bacterial and fungal species from chronic wounds, namely those that thrive in isolation under laboratory conditions such as *Staphylococcus aureus* and *Pseudomonas*

Coloured scanning electron micrograph of meticillin-resistant *Staphylococcus aureus* (MRSA, red) on the microscopic fibres of a wound dressing. Science Photo Library

aeruginosa. Next-generation molecular techniques and metabolic analysis of chronic wound microbial populations have begun to reveal the true complexity of the chronic wound microbiome, with an estimated 300–400 different species identified from a variety of chronic wounds to date. Despite this advance in identification, inconsistent findings between wounds at different anatomical sites, of different sizes and depth, highlight the need to establish a better understanding of the chronic wound microbiome.

Co-occurence of micro-organisms

The skin is primarily colonised by bacteria of four major genera: *Acinetobacteria*, *Bacteroidetes*, *Firmicutes* and *Proteobacteria*. These comprise a mixture of aerobic and anaerobic bacteria whose predominance is determined by location. For example, anaerobes are more prevalent in the groin, under the arms and between the toes. In addition to this, there are several endogenous fungi including genera such as *Candida*, *Malasezzia*, *Debaromyces* and *Penicillium* to name a few. Members of these bacterial and fungal genera typically also constitute the chronic wound microbiota, most likely because of their proximity to

the original site of epithelial damage. Commonly encountered, chronic wound bacteria include *Staphylococcus aureus, Pseudomonas aeruginosa, Enterococcus faecalis,* coagulase negative staphylococci, *Proteus* spp., *Streptococcus* spp., *Citrobacter* spp., *Morganella* spp., *Propionibacterium* spp. and *Corynebacterium* spp. Common fungi include *Candida albicans, Candida parapsilosis, Malasezzia restricta* and *Curvularia lunata*.

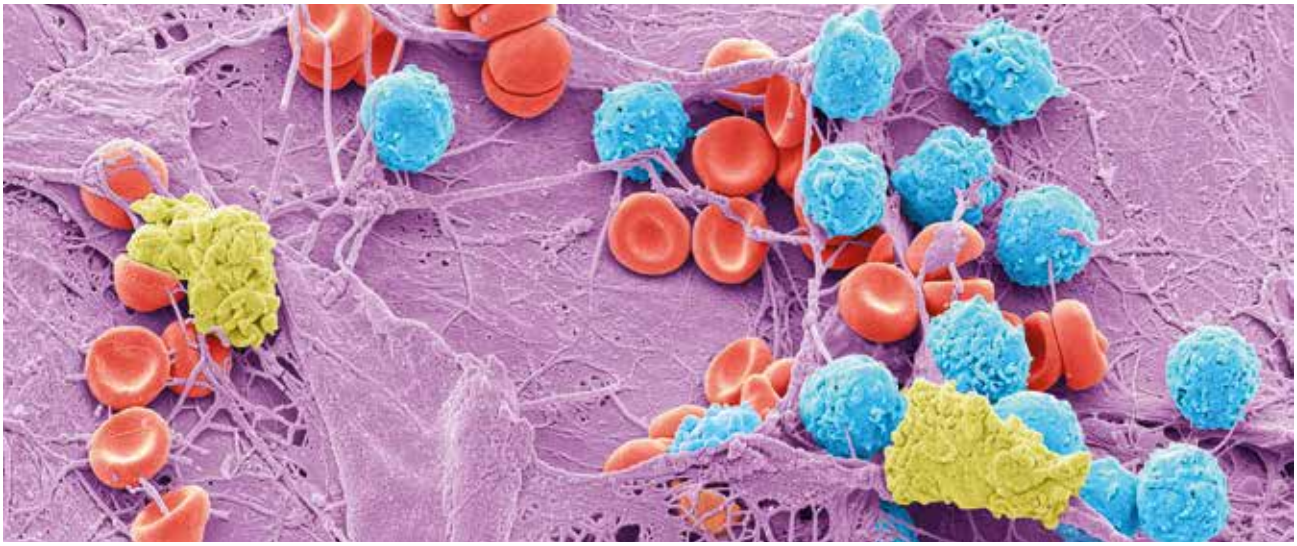
The co-occurence of micro-organisms is characterised by the presence of biofilm, which is associated with 60% of chronic, infected wounds. Significantly, polymicrobial biofilm within the wound bed has been shown to impair healing by disrupting the finely tuned, sequential events necessary for wound closure to occur. This is concurrent with a dampening of the pro-inflammatory immune response which is critical for innate immune clearance, and consequently maintains low-grade production of cytokines which perpetuates the tissue damage that favours colonisation. Currently, the specific types of micro-organism that mediate impaired healing remain to be defined, but a combination of multiple bacterial species and the nature of the biofilm lifestyle appears to be critical.

The complexity of the chronic wound microbiota has given rise to the proposition that chronic wound infection cannot be reduced to a single bacterial species.

A definitive shift from colonisation to infection in the chronic wound has long been thought of as solely the consequence of microbial load. However, it has become progressively apparent that other elements are at play, including species diversity and pathogenicity. As wound chronicity progresses, an eventual diminution of microbial species occurs until a small number of dominant, pathogenic micro-organisms remain and this reduction in microbial diversity has been correlated with a worsening prognosis. Furthermore, community symbiosis, because of specific or non-specific microbial interaction, is linked to increased pathogenicity and documented for many chronic infectious diseases such as lung infection in sufferers of cystic fibrosis or chronic obstructive pulmonary disorder, or periodontal disease in the oral cavity.

The chronic wound microbiome

Little is known about the temporal and spatial development of the chronic wound microbiome. A combination of cooperation and competition for space and nutrients invariably drives niche partitioning, where those best adapted to the local environmental conditions will thrive at the expense of those less well adapted. For example, bacteria with a lower oxygen requirement are likely to predominate in the deeper tissues. Population analysis using both



Coloured scanning electron micrograph of a skin wound. A fibrin mesh supports a variety of blood cells at the site of an early wound, red and white blood cells (blue) as well as platelet clots (yellow) are visible. Steve Gschmeissner/Science Photo Library

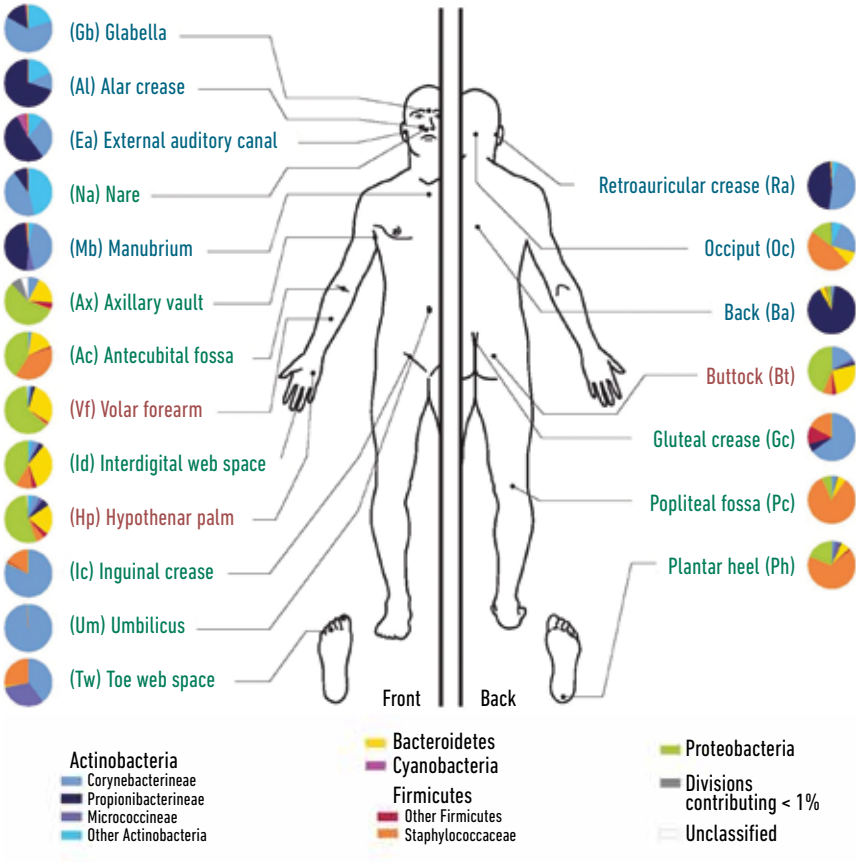


Diagram showing the distribution of micro-organisms over the skin of the human body.
Darryl Leja, Nhgri/Science Photo Library

phenotypic and molecular methodology has so far indicated a high degree of species segregation amongst the chronic wound microbial populace, with commonly co-isolated pathogens such as *S. aureus* and *P. aeruginosa* found at distinct regions within wound biopsies, indicating that despite sharing the same environment, they are unlikely to interact *in vivo*. Despite the current scarcity of evidence thoroughly describing interactions between members of the chronic wound microbiota, evidence has highlighted specific interactions between *S. aureus* and the opportunistic fungi *Candida albicans*. For example, *S. aureus* has been observed attached to the hyphae of *C. albicans* and this interaction is thought to promote invasion of an ordinarily non-motile bacterium into the deeper skin tissues.

Regardless of the large body of evidence describing the composition of the microbial community of chronic infected wounds, a robust mechanistic understanding of community development and microbial interaction remains to be established. Attempts have been made to utilise knowledge of the oral microbiota and plaque development as a means of informing models of chronic wound colonisation and progression to clinical infection. Currently, these have culminated in the concept of genetically distinct, co-occurring bacteria behaving as functional equivalent pathogroups resulting in so-called pathogenic biofilms — much like members of the oral microbiota. Drawing on knowledge of oral microbial communities, it is not unreasonable to suggest that chronic wound colonisation occurs in a similar manner, with initial colonisation by skin microbiota followed by secondary colonisation by pathogens. By applying many of the techniques traditionally employed in the study of oral biofilms, such as temporal analysis of microbial interactions, it might in future be possible to establish a sequential model for the development of chronic wound biofilm.

The complexity of the chronic wound microbiota has given rise to the proposition that chronic wound infection cannot be reduced to a single bacterial species. This notion challenges Koch's postulates and, with regards to the diagnosis and management of chronic infected wounds, confers several problems. Not least because diagnosis of infection has traditionally relied upon the isolation of specific micro-organisms subsequently targeted for treatment selected by analysis of pure culture. Therefore, a comprehensive theoretical model of the chronic wound microbiome, taking into consideration temporal development, spatial distribution and synergistic bacterial interactions, has the potential to provide an invaluable clinical tool to inform appropriate, timely intervention to manage chronic wound infection.

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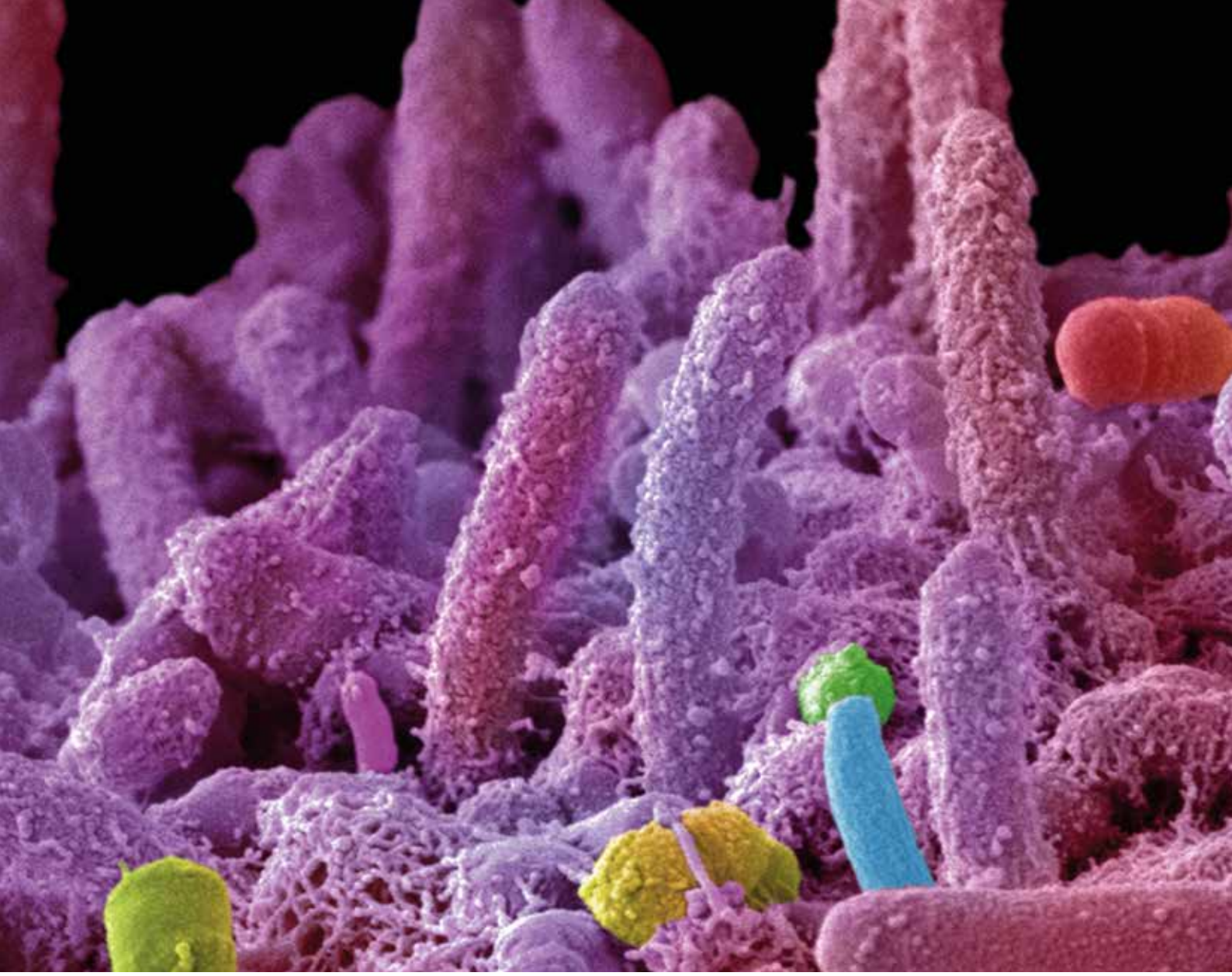
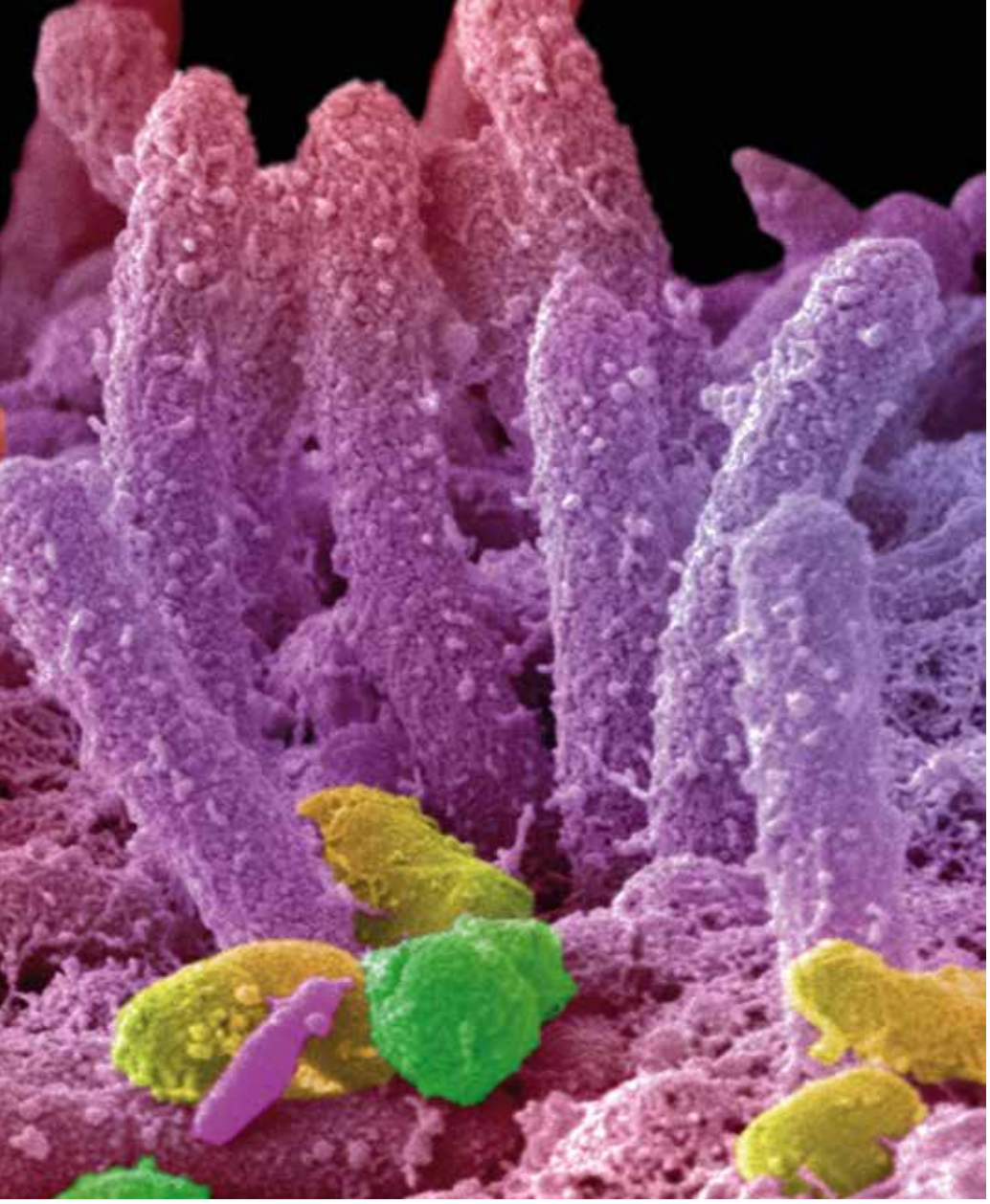


Paul W. O'Toole

Microbiome–health associations: status and perspectives



Coloured scanning electron micrograph of mixed oral bacteria. Steve Gschmeissner/Science Photo Library

Over the last decade, there have been many exciting advances in the understanding of the microbiome – the community of organisms present in a particular location, often a sample from an animal, plant or the environment. Although research on the human microbiome grabs most of the headlines, many of the key methodologies were taken or adapted from environmental microbiologists who are used to dealing with very complex microbial communities that are very difficult to grow in the laboratory.

How we got here

We have known for a long time that humans and animals harbour a resident community of microbes on and in their bodies, but these micro-organisms are nutritionally fastidious and often strictly anaerobic, making their culture in the laboratory, identification and characterisation very challenging. The development of high-throughput DNA sequencing methods made it possible to apply culture-independent methods to construct inventories of organisms from any sample with sufficient numbers of cells to generate DNA for amplification by the polymerase chain reaction. Sequencing these pooled amplicons tells the investigator what bacteria are present. If there are even more cells to work with, the total pool of microbial DNA can be extracted and sequenced en masse (so-called 'shotgun sequencing'), revealing not only what organisms are present, but also what genes they carry and what metabolism they are predicted to be capable of. Although the latter approach is much more expensive than simply profiling the sample, knowing their coding potential is usually much more biologically informative. Technical variations of this approach are used to identify mammalian viruses, bacterial viruses (bacteriophage), fungi, yeast and protozoa, but knowledge of these microbial communities in mammals is less developed than that of the bacterial microbiome.

Studies of the human gut are currently more common than studies of other body sites, but the microbiome of skin, lung, oral cavity and liver, for example, are receiving increasing attention. A common denominator to many studies is the search for links between an altered microbiome composition and a disease or disease

risk (Fig. 1). The list of such diseases linked to the intestinal microbiome includes obesity, inflammatory bowel disease, irritable bowel syndrome, type 2 diabetes and colorectal cancer, but associations of microbiome alterations with extra-intestinal conditions such as cardiovascular disease, and depression/behaviour are also being investigated. Because there are known ways or plausible new mechanisms whereby gut bacteria can influence inflammation, microbiome links to diverse conditions such as asthma, arthritis and frailty in older people are being investigated.

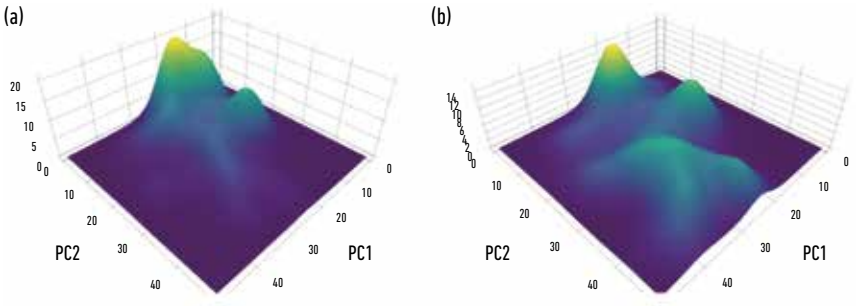


Fig. 1. **Altered microbiome in health and disease. Principal coordinates analysis with density weighting of the microbiome composition in colonic mucosal biopsies of (a) healthy controls and (b) subjects with colorectal cancer.** B. Flemer & P. W. O'Toole. Studying the microbiome: "Omics" made accessible. *Semin Liver Dis* **36(4)**, 306–311

The complexity of microbiome–host interactions

It has proven difficult to establish mechanistic links between microbiome alterations and disease, with one of the first conditions studied – obesity – proving most controversial of all. Rather than being able to fulfil Koch's Postulates as one would for a bacterial pathogen, by finding the responsible organism and using a pure culture to replicate diseases symptoms in a model, it has not been possible to identify single organisms or definitive microbiome configurations that translate reproducibly from human to model systems and that cause obesity. This is probably due to a multiplicity of mechanisms by which the microbiome can influence metabolic health, involving diverse human processes such as calorie harvest from the diet, fat synthesis in the liver, inflammation, satiety, and levels and kinds of bile salts made in the liver to process fatty foods. Explaining how variations in a microbiome (composed of several hundred species, each with several thousand genes) interact with a multifactorial human pathophysiology was never going to be easy. Another high profile condition with microbiome links, inflammatory bowel disease (IBD), is apparently not characterised by a unifying set of depleted or over-represented micro-organisms across all patients and studies. Studies in twins suggest that up to half of the risk factors for IBD are environmental, so notwithstanding the accepted role of host genetic factors, it is highly likely that micro-organisms contribute to the disease in a manner as yet unclear.

A characteristic of many diseases that feature microbiome alterations such as IBD, obesity, type 2 diabetes, and frailty in the elderly is loss of microbiota diversity, sometimes reflected in lower overall bacterial gene count.

Translating microbiome knowledge

The clearest role for the gut microbiome in disease is arguably *Clostridium difficile*-associated diarrhoea. Depletion of the gut microbiome by repeated antibiotic treatment allows a bloom of this organism (sometimes called C-diff) which can become recurrent and cause colitis and diarrhoea. A normal microbiome can be restored by faecal microbiota transplantation (FMT) in which the patient receives an enema or colonoscopic injection of a slurry prepared with the faeces of a healthy donor. The material is donated by a person selected by the recipient or their physician, or in some cases is acquired from a stool bank. FMT leads to 80%–90% cure rates in uncomplicated cases. The broadly accepted mechanism was simply the microbiome restoration, coupled with conversion by the incoming bacteria of primary bile acids to secondary and tertiary bile acids that inhibit *C. difficile* spore outgrowth. However, a recent small pilot study showed that sterile bacteriophage filtrates (not bacterial cells) also led to clinical remission, so even in this apparently 'simple' disease, the microbiome involvement may be more nuanced.

A characteristic of many diseases that feature microbiome alterations such as IBD, obesity, type 2 diabetes, and frailty in the elderly is loss of microbiota diversity, sometimes reflected in lower overall bacterial gene count. This is referred to by some authors as 'dysbiosis' but because two healthy people can have very different microbiota, dysbiosis is hard to reliably define. This makes routine microbiome profiling of healthy subjects of debatable value. Although identifying mechanisms linking microbiome alterations to health effects is still a work in progress, there is emerging evidence for the value of using microbiome markers to manage weight gain in obesity, predict post-prandial glucose in pre-diabetics, to stratify subjects with irritable bowel syndrome, and to detect colorectal cancer (see our recent review for details). Even more striking is the recent discovery that whether or not cancer patients derive clinical benefit from immunotherapy with checkpoint inhibitors (monoclonal antibodies that prevent inhibition of T-cell activation) is dependent on their baseline microbiota, which also determines whether or not they suffer from severe side effects that may require therapy withdrawal. These findings make profiling the gut microbiome not only clinically valuable (perhaps even sensible routine practice), but they also raise the prospect of rationally manipulating the microbiome to promote response to therapeutics in people who would otherwise be non-responders. A handful of drugs are already known to interact with the microbiome in ways that modulate their efficacy or side-effects, so this topic warrants considerably more attention.

Fig. 2. **Some aspects of the microbiome can be modelled by inoculating fermenter vessels with faecal samples, single isolated cultures or artificial consortia, and applying a range of analyses including transcriptomics and metabolomics to measure interactions and products.** M. Perez & P. W. O'Toole

Where to now?

When all the initial excitement of microbiome research dies down, we will realise that inventories of organisms and gene annotations are starting points, not end-points. There is a lot of microbiology research that needs to be done on microbial genes, enzymes, metabolites, cell models, pre-clinical models, and human subjects. Fastidious organisms will need to be cultured and grown as single cultures or as defined consortia, for example in artificial colon models (Fig. 2). Microbiologists will work intensively in their own labs, but also alongside bioinformaticians, metabolic modellers, cell biologists, physicians and epidemiologists, to unravel how the microbiome modifies risk for health and disease.

Acknowledgements

Microbiome work in PWOT's laboratory is supported by Science Foundation Ireland through a Centre award to the APC Microbiome Institute (SFI/12/RC/2273), and a Department of Agriculture, Food and the Marine (DAFM) award (11/F/053) for the ELDERFOOD project.

Dedicated to the memory of the late Professor George T. Macfarlane whose pioneering work on gut microbial ecology and biochemistry helped to lay the foundations.

Paul W. O'Toole

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Further reading

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Annual Conference 2017

3–6 April 2017, EICC, Edinburgh, UK

At the start of April, we were delighted to welcome over 1,800 of you to the EICC in Edinburgh to once again enjoy some amazing science and socialising opportunities over the course of four days.

Delegates attended our Conference from all over the globe to hear breakthrough research, and to network and build new connections. Our 2017 Conference programme included:

- 29 scientific sessions
- over 600 posters
- over 250 offered talks
- talks from over 200 invited speakers

And for the first time:

- We ran two sessions dedicated to professional development.
- We provided a fun platform over the lunch period with flash poster presentations.
- We awarded four poster prizes, including an Early Career Microbiologists' Forum prize, a people's choice award, prizes from our journal Editors, and a prize selected by principal investigators.

To see for yourself what we got up to at Conference, why not check out our YouTube channel to view our videos from the event and see if you can spot someone you know!

I. Atherton


ICC Birmingham

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

Annual Conference 2018

10–13 April 2018, ICC Birmingham #Microbio18

Preparations are underway for Annual Conference 2018 and the programme is looking spectacular. Session topics have now been confirmed and key speakers are being identified to ensure that once again our Conference provide delegates access to hot topics, new developments and leading researchers. Keep your eyes peeled for abstract opening and updates on our website later this year.

Main symposia*:

- Biological insights from studying new eukaryotic models
- CLIMB workshop (Genome bioinformatics)
- Cool tools for imaging
- DNA repair to cover control of mutation leading to evolution, recombination, MutS/MutL, phase variation and radioactive tolerant organisms
- Drivers and consequences of virus diversity
- *E. coli* to cover environmental isolates, UTI, cell biology and strains from animals and plants
- Immunity session and immune models
- Microbial diversity: Community interactions in live hosts to cover microbiome, signalling
- Microbial diversity: Community interactions in the environment
- Microbial mayhem – breaking bad to cover switch of commensal to pathogen including in immunocompromised host
- Microbial metal homeostasis: impacts on pathogenicity
- Synthetic ecology: from understanding ecological interactions to designing functional microbial communities
- The games microbes play
- The magic of mushrooms in nature and in industry
- Viruses and translation
- Zoonosis to cover food security and companion animals

Virus workshops:

- Clinical Virology
- DNA Viruses
- Negative Strand RNA Viruses
- Phylogeny
- Plant Viruses
- Retroviruses

Prokaryotic and Eukaryotic forums:

- Environmental and Applied Microbiology
- Genetics and Genomics
- Microbial Infection
- Microbial Physiology, Metabolism and Molecular

**Session titles to be confirmed*

Sign up to our newsletter to ensure you are receiving regular updates about Conference and other Society news, and visit **www.microbiologysociety.org/events** for further information.

Society-Supported Conferences

The Microbiology Society is pleased to announce that nine meetings have been awarded funding in the first round of Society-Supported Conference Grants. The supported conferences include national and international events that are expected to attract over 1,000 delegates.

Seventh Advanced Lecture Course on Human Fungal Pathogens: Molecular Mechanisms of Host–Pathogen Interactions and Virulence
13–19 May 2017, La Colle sur Loup, France

15th UK Meeting on the Biology and Pathology of hepatitis C virus
19–21 May 2017, Cumbria, UK

24th International HIV Dynamics and Evolution Workshop
23–26 May 2017, Isle of Skye, UK

London Microbiome Meeting
7 June 2017, London, UK

The Annual Irish Fungal Society Conference 2017
15–16 June 2017, Limerick, Ireland

Young Microbiologists' Conference (YMC) 2017 Beyond Petri dishes: Capacity Building for Applied Research
27–28 June 2017, Ilishan Remo, Nigeria

EMBO Conference – Anaerobic protists: Integrating parasitology with mucosal microbiota and immunology
31 Aug–3 Sep 2017, Newcastle upon Tyne, UK

The 2nd International Symposium on Stress-Associated RNA Granules in Human Disease and Viral Infection
10–12 Sep 2017, Heidelberg, Germany

Staphylococcus Great Britain and Ireland 2017
14–15 Sep 2017, Swansea, UK

Call for Round 2 applications

Round 2 of our Society-Supported Conference Grant application is now open! The next closing date is **Monday 12 June 2017**. If you are organising a conference in any field of microbiology and meet the eligibility requirements, don't miss out on the opportunity to receive up to £2,000 to cover invited speakers' costs.

Further information and application guidelines can be found on the Microbiology Society's website: **www.microbiologysociety.org/proposals**

Focused Meetings 2017

Focused Meetings are a central part of the Microbiology Society's events programme, with each meeting on a specific microbiological theme. They offer the opportunity of a smaller scale meeting, allowing for informal networking and dedicated time on one subject.

Dr Microbe/ iStock/Thinkstock

Microbial Resources for Agricultural and Food Security

#AgriFoodSec17

21–23 June 2017 – Metropolitan Arts Centre, Belfast, UK

The meeting will run over three days, with the All Island Phosphorus Sustainability Workshop on day one, followed by the conference on days two and three.

Key workshop topics:
- Industrial perspectives on phosphorus recycling
- Policy, research and future directions for phosphorus sustainability
- Regulatory perspectives on phosphorus management

Key conference topics:
- Harnessing microbial processes within the agri-food sector
- Nutrients in the environment with a focus on agricultural systems
- Microbial ecosystems and nutrient cycling

Abstracts have closed for this meeting but registration is open.

Find out more online – **http://microb.io/agrifoodsec17**

Tomás Tyner, UCC, Ireland

International Meeting 2017: ISSY33 – Exploring and Engineering Yeasts for Industrial Application

#ISSY33

25–29 June 2017 – University College Cork, Ireland

Four days of science, fascinating speakers, networking, posters and the magical city of Cork.

Key topics:
- Analysing and engineering regulatory networks in yeast
- Cell factory product pitches
- Engineering novel (to yeast) product pathways
- Evolutionary approaches for yeast strain improvement
- Exploration of yeast biodiversity for industrially relevant traits
- Hybrid genomes of industrial yeasts: analysis and engineering
- Metabolomics and proteomics of industrial yeasts
- New synthetic pathways in yeast
- New tools for yeast genome engineering

Registration is open.

Find out more online – **http://microb.io/ISSY33**

JK1991/ iStock/Thinkstock

Antimicrobial Resistance and One Health

#AMROneHealth17

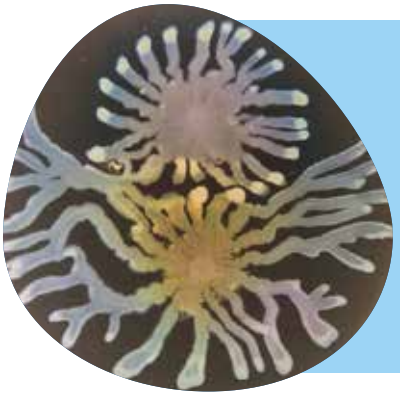
29–30 August 2017 – Maynooth University, Co. Kildare, Ireland

Key topics:
- Antimicrobial resistance in animals
- Antimicrobial resistance evolution in science and politics
- Antimicrobial resistance in human health
- Antimicrobial resistance in the environment

Abstract submission and registration is open.

Find out more online – **http://microb.io/AMROneHealth17**

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



Edgar Lissel & Steve Diggle

16th International Conference on *Pseudomonas*

#Pseudomonas17

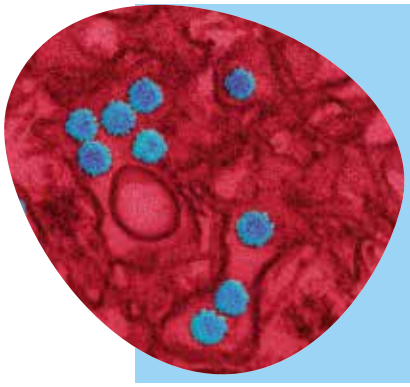
5–9 September 2017 – St George's Hall, Liverpool, UK

Key topics include:

- Antibiotics and biofilms
- Genomics
- Mechanisms: signalling, systems and synthetic
- Ecology, evolution and environment
- Infections and host–pathogen interactions

Abstract submission and registration is open.

Find out more online – **http://microb.io/pseudomonas17**



AMI Images / Science Photo Library

2nd International Meeting on Arboviruses and their Vectors (IMAV)

#IMAV17

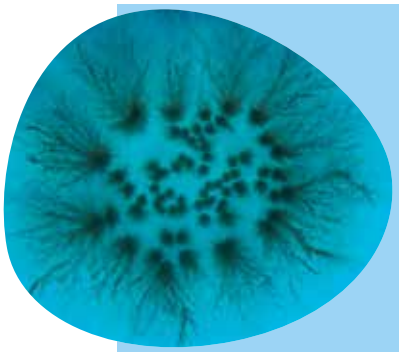
7–8 September 2017 – University of Glasgow, UK

The meeting will run over two days. The key topics will be:

- Antivirals/vaccines
- Vector biology & ecology
- Virus–host interactions and evolution
- Emergence from A to Zika
- Virus discovery

Abstract submission and registration is open.

Find out more online – **http://microb.io/IMAV2017**



Kent Fungal Group University of Kent

British Yeast Group (BYG) – The Versatility of Yeasts

#BYGVOY17

11–13 September 2017 – University of Kent, UK

The key topics will be:

- Chromosome structure and function
- Protein folding and quality control
- The cytoskeleton
- Molecular biology of pathogenic yeasts
- Synthetic and evolutionary genomics
- Yeast metabolism

Abstract submission and registration is open.

Find out more online – **http://microb.io/BYGVOY17**

Call for 2018 Focused Meeting proposals

All Microbiology Society Focused Meetings are the result of accepted proposals from our members, and it is our members who provide the expertise in the wide range of fields that shape the Focused Meetings series. We deeply value the relationships we have and the partnerships we make when working together with our members to deliver such fantastic events.

We encourage our members to submit their ideas and proposals for our Focused Meetings series in 2018 and applications are now open. It is a great opportunity to put your name to a meeting and work alongside the Microbiology Society to turn your vision into reality.

The deadline for 2018 applications is 12 June 2017. All forms will be reviewed by our Scientific Conferences Committee, who oversee our scientific programme.

Please send your 2018 proposals to **conferences@microbiologysociety.org** by the deadline.

The application form and the terms and conditions can be found on the Microbiology Society website – **www.microbiologysociety.org/events**.

Publishing

70 years of *Microbiology*

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This year represents 70 years of publication for *Microbiology*, the Society's oldest journal. The journal started publication as the *Journal of General Microbiology*, renamed *Microbiology* in 1994. The current Editor-in-Chief is Dr Tanya Parish (Infectious Disease Research Institute, USA), who has been a long-standing member of the Editorial Board.

Recent journal developments include the launch of Microbe Profiles – mini reviews focusing on specific microbes from leading names in the industry – and Short Communications, a shorter body of completed research. Currently published Microbe Profiles are '*Escherichia coli* O157: H7 – notorious relative of the microbiologist's workhorse' (**http://microb.io/2mcFeR6)** and '*Oenococcus oeni*: Queen of the cellar, nightmare of geneticists' (**http://microb.io/2nRmVkr)**.

Of the journal, Tanya says: "We have published many articles aimed at understanding the basic biology of micro-organisms. There are other changes happening in the publishing arena right now, including increased visibility and recognition for reviewers; the development of online preprint servers; and increasing use of social media to discuss research topics. At *Microbiology* we look forward to incorporating many of these ideas to take us into the next 70 years."

For more information about the journal please see *Microbiology*'s homepage (**http://mic.microbiologyresearch.org**). To submit to the journal please use our online submission system (**www.editorialmanager.com/mic**).

Article redesign and continuous publication

Microbiology Society journals have launched a new article redesign that better align with our journal branding. Alongside our article redesign, we have moved to continuous publication.

Previously, the Society's hybrid journals (*Microbiology*, *Journal of General Virology*, *Journal of Medical Microbiology* and *International Journal of Systematic and Evolutionary Microbiology*) were published monthly. With continuous publication, as soon as an author has approved their copy-edited and typeset proof, the Society's production team will do a final check and then publish the article online.

Each month, these will be grouped together into an online issue, which will also be printed and dispatched to subscribers. The change means that readers will see the best version of the article as soon as possible, and will lead to significant improvement of the Society's article publication times.

The first ICTV Virus Taxonomy Profiles are now online

Last year, the Microbiology Society announced that *Journal of General Virology* would be publishing ICTV Virus Taxonomy Profiles – a freely available series of concise, review-type articles that provide overviews of the classification, structure and properties of individual virus orders, families and genera.

We are pleased to say that the first Profiles are now online and include summaries on *Flaviviridae, Ascoviridae, Geminiviridae* and *Ourmiavirus* (**http://jgv.microbiologyresearch.org**).

ICTV Virus Taxonomy Profiles are written by International Committee on Taxonomy of Viruses (ICTV) study groups, comprised of leading experts in the field. The profiles summarise the individual chapters from the ICTV's online *10th Report on Virus Taxonomy*, and will become the go-to place for researchers looking for up-to-date taxonomic information on viruses.

Prizes sponsored by Microbiology Society journals

Microbiology Society journals offer sponsorship for poster prizes and oral communication prizes for early career researchers. Past winners have received a certificate, a small cash prize and a year's complimentary membership to the Microbiology Society.

To see what some of our 2016 winners have been up to since they received their prizes, read the news story on our website (**http://microb.io/2hW6QqG**).

We continue to award prizes and some of our 2017 winners so far include:

- Dara Niketic, University of Utah – *Microbiology* winner at BLAST XIV Meeting.
- Keenan Lacey, Trinity College Dublin – *Microbiology* winner at Dublin Academy of Pathogenomics and Infection Biology Meeting.
- Dearbhla Lenehan, University College Dublin – *Journal of Medical Microbiology* winner at Dublin Academy of Pathogenomics and Infection Biology Meeting.

Dearbhla Lenehan (left) and Dara Niketic (right) receiving their prizes.
DAPI (Dublin Academy of Pathogenomics and Infection Biology)

Research Visit Grants: supporting international collaboration

The Society's Research Visit Grant scheme supports early career members to build collaborations, whether that's on a local scale or internationally. With funded projects, including those bolstering existing collaborations and those establishing new ones, the grant scheme supports the growth of networks of microbiologists throughout the world. Read about the experience of some of our recent grant recipients below.

Agata Lisik, from NUI Galway, visited Dr Hélène Agogué at the University of La Rochelle, France, to compare the nitrate reduction and biogeography of nitrate reducers in intertidal sediments from the French and Irish Atlantic coast – accessing samples from France to compare to those collected in Ireland. During her visit, Agata was able to learn and apply two new research techniques, and the results of the work will contribute to a joint publication by the two groups.

Agata says, "Working at the University of La Rochelle added an international aspect to my research that has benefited and improved my laboratory skills together with communication, troubleshooting and lab management practice. This research visit has broadened my future career perspectives, improved my scientific skills and will benefit me in upcoming job searches on the Irish and international job market."

Matthew Moore, from the University of Liverpool, visited Dr Roger Levesque at the Integrative and Systems Biology Institute (IBIS) at Université Laval in Québec, Canada, in late 2016. Matthew wanted to visit the Levesque group to access a large genome sequence dataset of 2,000 isolates of *Pseudomonas aeruginosa* from around the world – the dataset is particularly detailed as it has associated detailed genotypic, phenotypic and patient data. As it was not possible to arrange to analyse the data in Liverpool, the research visit allowed Matthew to try to assess adaptation of *P. aeruginosa* to the cystic fibrosis lung, and compare this to environmental isolate genomes.

Matthew says, "Through this collaboration I gained skills and experience in managing these large datasets, efficient use of computing to complete the project in the time that I was in Quebec, and was able to discuss in depth the merits of various methodological approaches and alternative hypotheses to the established understanding of these infections currently."

The next round of Research Visit Grant funding opens on 1 July with a deadline of 1 October – visits should take place from 1 December onwards. To find out more see our website **www.microbiologysociety.org/grants**.

Maria Fernandes
Professional Development Manager

Early Career Microbiologists' Forum Update: Summer schools, socials and new roles

It has now been a month since the Society's Annual Conference in Edinburgh! We hope you found the pre-Conference networking event to be a useful activity and that you made use of the 'networking checklist'. These apply to any situation where you find yourself in a group of unfamiliar people, so keep practising!

Your ECM Forum Executive Committee met back at the end of January with a focus on developing the Forum and providing more opportunities for its members. This was our first meeting with the new Undergraduate Representative, Amiee Allen, who is exploring ways to increase the integration of undergraduates into the Society. As a result, we are investigating how to achieve this. Amy Richards, your Conferences Representative, is in the process of designing ECM-focused meetings to facilitate better networking between all ECM Forum members, whilst sharing our collective wealth of knowledge. We aim to roll the first event out in the summer of 2018 so keep an eye out for more information! We also discussed an annual Summer Social – a more informal event held in a few areas across the UK to enable all Forum members to get together once a year.

We are also developing a way to involve ECMs in a co-chairing scheme at the Annual Conference, with them working alongside session organisers. This is a great way to push yourself out of your comfort zone, meet new people and gain experience in how sessions at conferences are run. If this sounds like something that might interest you, drop us an email and we can give you some more information about what it involves and how to apply.

There will soon be nominations open for several positions on the Executive Committee. Amiee's term lasts for one year and so we will be looking for an Undergraduate Representative to replace her. If you have a keen interest in microbiology and want to network with people further down the line in their career then this is the role for you! The Programmes Representative role is being split to allow the Executive Committee to have one member on each committee within the Society's structure. This means that Andrew Day will become the Policy Representative and we will be holding elections for a new Publishing Representative, as well as for a Chair-Elect. If you think you might like to put yourself forward for any of these roles then the current committee is more than happy to chat with you about it. Nominations for these will open in the summer so keep your eyes peeled.

As always, if you have any questions or comments then do get in touch via email on **ECM@microbiologysociety.org**.

Rebecca Hall
Communications Representative,
ECM Forum Executive Committee

Education and Outreach and the microbiome

Antimicrobial resistance and the microbiome

Dr David Cleary's research and work focuses on antimicrobial resistance and the microbiome. Using a grant, David and colleagues are continuing their outreach work from last year by delivering activities based around microbiology and infectious disease to Jersey-based A-Level students attending a Biomedical Sciences Summer School.

As a Research Fellow working in microbial genomics, David's research concerns how bacteria in the airways cause acute respiratory infections or exacerbations in chronic conditions such as COPD or asthma. This involves examining the dynamics of the microbiomes of the upper respiratory tract, the focus being on how the microbiome and, in particular, the epidemiology of *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis* change in response to the introduction of new vaccines.

In 2016, David, along with Dr Michael Head and Dr Rebecca Brown, went to Jersey College for Girls to run an outreach activity. Three areas of microbiology research stood out as being particularly topical: antimicrobial resistance (AMR), microbiomes, and the continued need for vaccines and vaccine-related research. The group decided to give three talks throughout the day to introduce the topics and highlight the importance of each in the context of infectious disease research.

The talks were designed to pique the students' interests and underpin the learning of what, to the group, was the most important element: getting students into the

Participants in the Summer School at Jersey College for Girls. Dr Michael Head

laboratory to give them hands-on experience of microbiology-related activities. Throughout the day, the group ran a laboratory session that focused on concepts that were highlighted in the AMR talk. The practical itself was straightforward: the group gave the students a choice of common household cleaning products (disinfectants, hand gels) as well as more natural products such as onion, garlic and various spices. The students then had to apply their expectations as to what would be the most effective antimicrobial against *Escherichia coli*.

The outreach award from the Microbiology Society will help the team improve the practical session. They plan to combine the general overview topics from the first event with a practical drawn from the current research that will introduce the students to the use of genomics to identify AMR genes in bacterial pathogens. The general methodologies that they are adopting will also provide the opportunity to characterise the microbiome of the student's nasopharynx (the bit at the back of the nose). Their approach will be to give students hands-on experience using some of the latest DNA sequencing technologies to generate their own data, either on common bacterial species resident in the respiratory tract or from their own microbiome. The team aim to then publish their output – and hope that the students seeing their microflora 'in lights' will inspire them to continue a career in research.

Dr David Cleary

Good Germs, Bad Germs

Dr Jamie Lorimer and colleagues from the University of Oxford are running a project called 'Good Germs, Bad Germs' to engage the public with the growing field of microbiome research, and investigate people's attitudes towards cleanliness.

The project is led by social scientists and looks at hygiene – how people think about and practise it. Investigations are centred on the domestic kitchen microbiome and participants were asked to swab various areas of their household kitchen before and after some kind of hygiene intervention. The difference with this project compared to other citizen science projects is that the participants were involved in the formation of the research questions, known as a 'participatory approach' to science.

The group has run a series of focus groups in Oxford with 14 households who meet every few months to design the next experiments, and for the team to assess the participants' perceptions of microbes. These perceptions include what they think microbes are, where they come from, and what constitutes a 'clean' kitchen.

Several experiments have been carried out so far. In one experiment the effectiveness of various cleaning products, and what happened to the microbiome of surfaces before and after products were used, has been investigated. The results of this experiment showed that the product used made little difference to the types of bacteria present on the surface, but it was the cloth that was most important in re-seeding the surface after it was cleaned. Other experiments include: each household swabbing the same five surfaces in their kitchen and an additional surface of their choosing; using a brand new chopping board and recording what it had been used for while swabbing at various intervals over a two-week period; swabbing participants' fridges to look at the make-up of the microbiome, and the effect temperature has on the microbiome. In addition to these experiments, participants were allowed to decide on their own experiments individually. Most households chose to incorporate their pet's microbiomes in some way and to look at where their pet's microbiome signature shows up in their kitchen.

It is hoped that the results of this project (**www.goodgerms.org**) will reveal how households' attitudes towards hygiene have changed during the study. By introducing microbes and the concept of the microbiome to people, this will help to inform people about what good hygiene is and debunk the idea that all micro-organisms are bad.

Dr Jamie Lorimer

To find out about Education and Outreach activities, visit **www.microbiologysociety.org/education-outreach**

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Public Engagement Officer
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Connecting microbiome research stakeholders

Participants at the Society's Microbiome Research Stakeholder Workshops discussed opportunities and challenges for microbiome research and innovation.

Microbiomes aren't just receiving attention from microbiologists. Internationally, governments, funders, regulators and other science policy stakeholders are also increasingly interested in the potential impacts, implications and innovations arising from microbiome research.

Responding to the need for accessible expert information on this rapidly growing area, the Society's Microbiome Expert Working Group is producing a science policy report on microbiome research and its relevance to health, agriculture and food, biotechnology and the environment.

Stakeholder workshops

To inform the policy report and to facilitate interdisciplinary networking and knowledge exchange, the Society organised five workshops in the UK and Ireland.

Collectively, these multidisciplinary workshops involved around 160 participants, including researchers and representatives from government, research funders, industry, regulators and science communicators.

Discussions highlighted cross-cutting opportunities and challenges for microbiome research relevant to health, agriculture and food, biotechnology and the environment.

Opportunities

Participants identified wide-ranging current and future opportunities for science, society and the bioeconomy from our growing knowledge of microbiomes, and the development and application of novel tools and biotechnologies to characterise, manage and exploit them. Opportunities included precision microbiome-based diagnostics and biotherapeutics, bioprospecting microbiomes for natural products, and novel tools and technologies for increased agricultural productivity and sustainability or for bioenergy and bioremediation.

The relevance and opportunities of research investigating linkages between different host and environmental microbiomes for a One Health agenda and tackling antimicrobial resistance was also emphasised.

However, participants were clear about the early-stage nature of much microbiome research and challenges that need to be addressed to deliver on these opportunities.

Hype and engagement

Hype around microbiomes is a key challenge, but also an opportunity to engage policy-makers and the public about the importance of microbiome research and microbiology generally. Misinformation, poorly-evidenced products and applications, and perceived overselling of research could risk public confidence and safety, and affect future investment in the field. Building the evidence base, clearly communicating research, and public engagement are vital.

Public and stakeholder engagement was also highlighted as important in relation to social and bioethical considerations, for example, around synthetic biology and implications of research for behaviour, lifestyle and health (e.g. diet, childbirth).

Research and knowledge gaps

The early-stage nature of microbiome research also means that there are knowledge gaps and challenges common to host and environmental research. Participants highlighted the inherent complexity and diversity of microbiomes as a broad challenge for the field, for example, making establishing baselines

and biomarkers for 'healthy' versus 'disturbed' microbiomes challenging. Support for big data and longitudinal studies will be key.

While studies characterising microbiome diversity are important, the need for more focus on and support for mechanistic and functional research was emphasised, for example, to move from correlation to causation in microbiome disease studies, and facilitate development of robust interventions.

The importance of increasing focus on the non-bacterial members of microbiomes such as viruses and fungi, as well as undetected microbes, was also highlighted.

Lack of fundamental and long-term understanding about the consequences of manipulating host and environmental microbiomes was also a concern.

Knowledge integration and capacity building

Increasing interdisciplinary working was a key theme. Microbiome research is inherently multidisciplinary, requiring improved collaboration and integration of skills and expertise across informatics, microbiology, biochemistry, systems biology and other disciplines, and communication between researchers working on different microbiomes. Better collaboration between academia, industry, regulators and end-users is also needed to facilitate translation.

Skills and expertise gaps in bioinformatics and microbiology, and the need for more integrated training of these and other skills, were also repeatedly raised as issues.

Improving the reproducibility and comparability of studies, and access to samples and datasets was also seen as key. Development and adoption of standards and best practice for sampling, analysis and data will be important; the inadequacy of metadata (e.g. clinical, environmental information), for example, was a commonly cited issue. Development of infrastructures, including microbiome biobanks, accessible and interoperable databases and cloud-computing platforms are also needed.

Making progress

Importantly, participants suggested community-led activities and support from funders, learned societies and other stakeholders that could help, or are already helping, to progress microbiome research and translation. Ideas and examples broadly included improving informatics and technology platforms; targeted funding and training to meet needs; and interdisciplinary networks, meetings and initiatives to strengthen collaborations and focus efforts.

Outputs and next steps

Feedback from participants was very positive, with many valuing the opportunity for interdisciplinary knowledge exchange and discussion. Information and perspectives gathered have been used to inform the Society's microbiome policy report, consultation responses and subsequent meetings with policy stakeholders.

The Society will launch the policy report later this year when Expert Working Group members will present findings to policy-makers and other stakeholders. The Society will also focus on other activities to disseminate the report and facilitate engagement to help progress and inform about microbiome research and microbiology.

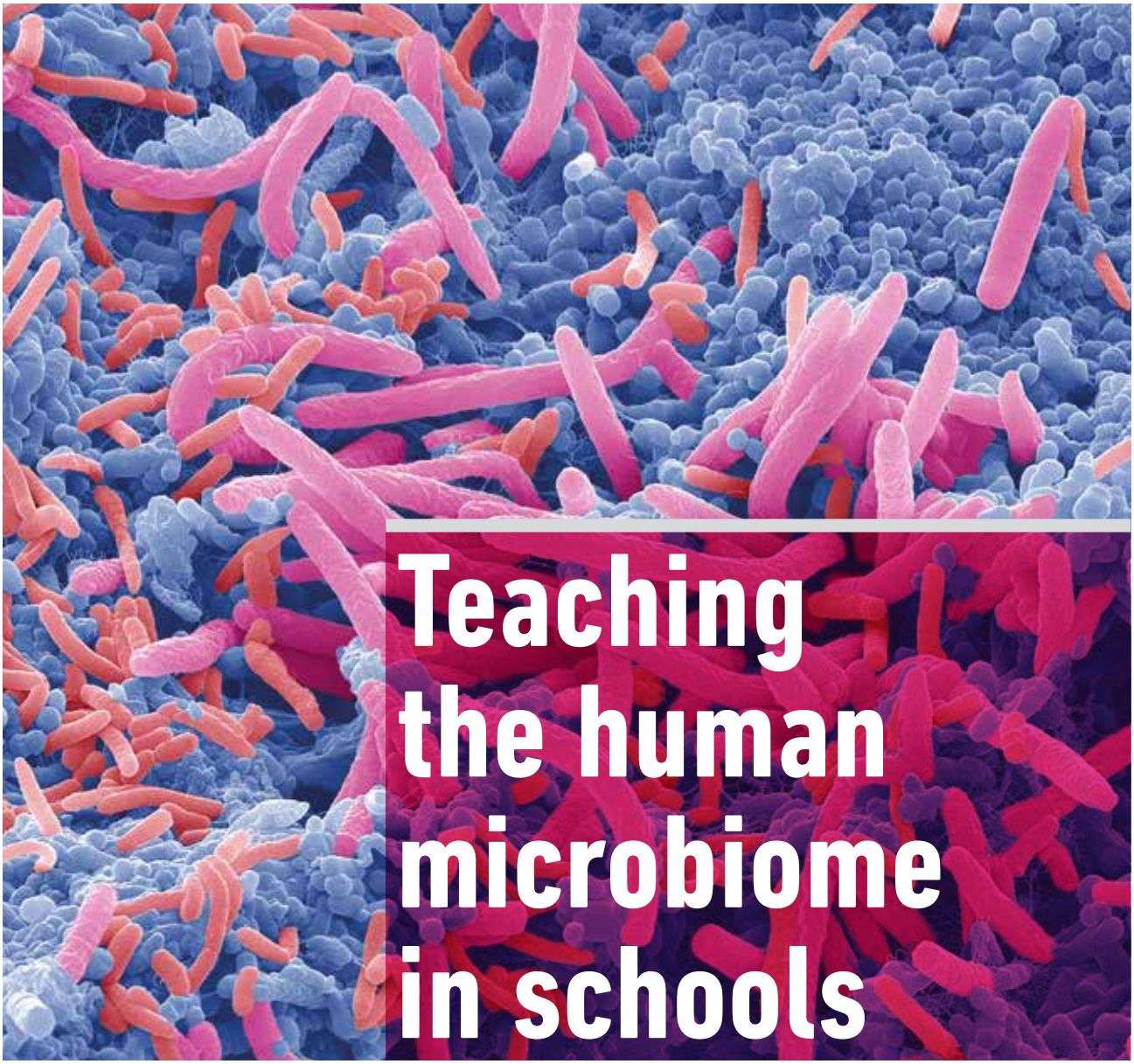
For more information about the stakeholder workshops and our Microbiome Policy Project visit **www.microbiologysociety.org/microbiome** or contact the Policy team (**policy@microbiologysociety.org**).

Participants attending a Microbiome Research Stakeholder Workshop.

Paul Richards
Policy Officer

Isabel Spence
Head of Public Affairs

Schoolzone



Teaching the human microbiome in schools

Coloured scanning electron micrograph of bacteria on the surface of a human tongue.
Steve Gschmeissner/Science Photo Library

Every surface of the human body, inside and out, is covered in billions of different species of micro-organisms. These micro-organisms are mainly bacteria, but also include viruses and fungi, and are collectively known as the 'human microbiome'. The bacteria that make up the human microbiome live together in a close relationship with us and some even help the body perform vital functions.

These bacteria exist in unique communities on each person and live in every part of our body, from our mouths to our intestines, which are known as the oral or gut microbiomes, respectively. Some bacteria in the microbiome do not have any effect on the human host, while others can be beneficial and some might cause disease. The balance between health and disease relies on the interaction and balance of these bacteria in their particular environment.

Our microbiomes are influenced by our environment and the micro-organisms that we interact with at various stages of our life. This includes any animals we touch, the food we eat and the antibiotics we take. When teaching about the microbiome, encourage students to think about their own microbiome and what will have influenced theirs in the past month.

Classroom research activity

As briefly described above, there are a number of environments that have unique compositions of micro-organisms and microbiomes. Working in small groups, pick one of the following environments to investigate further:

- mouth
- nose
- gut
- skin

There are many aspects of these specific environments for the students to investigate, such as:

- The make-up of the organisms surviving in that specific area. These include bacteria, viruses, fungi and eukaryotes.
- The physical characteristics of the environment and how this might influence what can inhabit this environment.
- The functionality of each of the micro-organisms on the host and each other.
- What happens if there are disruptions to the balance of these micro-organisms? And what causes these imbalances (i.e. drugs that may kill off a type of micro-organism)?

When the students have completed their research, ask them to present their findings to the rest of the class as a poster that could include an infographic to show a visual representation of the possible number and range of organisms, and the factors affecting their microbiome.

Drawing the microbiome

It is estimated that there are somewhere between three and 10 micro-organism cells to every one human cell in the human body. These micro-organisms vary in their shape and size so trying to visualise the microbiome can be difficult.

Get your students to think about how their gut microbiomes differ from their classmates'. Ask them what they think influences the bacteria that are within their gut.

After brainstorming what might be in their gut, get the students to draw a magnified image of the inside of their gut, depicting the different micro-organisms that reside there. Think about the specific types of bacteria that are commonly found in the human gut and possible foreign microbes that may be present, i.e. from recently eaten food. This is their chance to get creative with micro-organisms! Tweet your pictures to the Society's Twitter account (**@MicrobioSoc**) or send a picture of them to **education@microbiologysociety.org** and we will share our favourites.

Hannah Forrest
Public Engagement Officer
h.forrest@microbiologysociety.org

Membership Q&A

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

D. Morse

Where are you currently based?

School of Dentistry, Cardiff University, Wales, UK.

What is your area of specialism?

Oral biofilms and infections.

And more specifically?

Microbial interactions within denture-associated biofilms; the effects of bacteria on candidal virulence and pathogenicity; 3D tissue model development; and biofilm infection and subsequent host cell responses.

Tell us about your education to date.

I obtained my Biomedical Sciences undergraduate degree from the University of the West of England. I was then recruited by a probiotic and antimicrobial biotechnology company in Cardiff as a laboratory technician, and promoted to R&D Scientist leading the R&D projects for both probiotics and antimicrobial product development. I applied for a PhD studentship at Cardiff University in 2013, and started in October. I have since worked on developing polymicrobial biofilms with a particular interest in oral acrylic biofilms (denture-associated infections), and how bacteria influence candidal virulence and pathogenicity *in vitro* and within a 3D tissue model to mimic infections.

Where did your interest in microbiology come from?

After choosing my first microbiology module as an undergraduate, it was like love at first sight! I was fascinated by the world of micro-organisms – the vast variety, how they exist and interact, and what they can do. During my undergraduate degree, I chose further microbiology modules to deepen my knowledge in the field. Microbiology continues to amaze me, even now.

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

My current work involves metataxonomic profiling of micro-organisms within sites in the oral cavity through next-generation sequencing, looking at the microbiome. This results in an incredibly large data set, which needs a lot of analysis, interpretation and careful consideration of the results. On a 'bigger picture' scale, I think the immediate future for science is going to be a challenge – the potential reduction in funding and the changes in the worldwide view of scientific research. Additionally, as an early stage researcher (final stage PhD student), career options are of course on the horizon – whether I can secure a postdoctoral research position, fellowship, eventual lectureship and supervision of my own students to keep on doing what I am doing.

What is the best part about 'doing science'?

It's amazing and so much fun. Sure, there are days where you can bang your head against a wall again and again, but the satisfaction of knowing you are working towards making a difference to scientific knowledge and getting hands-on in research is an incredible feeling. It's very humbling to be able to say, "I'm a research scientist".

Who is your role model?

Let's set the bar high: Sir Alexander Fleming, Louis Pasteur, Robert Koch and of course my PhD supervisor, Professor David Williams. If I can be a fraction of what they are and what they've achieved, I'll be very happy!

What do you do to relax?

I have a young family, so I love to spend time with my wife and two boys – they are my world. I also play guitar in a rock band, so music is an eternal love, and I like to run.

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

Blink 182 – *Take Off Your Pants and Jacket* (my absolute favourite album of all time). It reminds me of my school days, and my school friends, and just growing up and having the best time. Luxury item... probably my guitar, to keep me sane.

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

During my school days, I was quite the geek – I would spend hours playing video games, and represented Wales (as part of a team). I also used to be an online radio presenter for a gaming radio station (cringe)!

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

I can't imagine doing anything else. I would love to have been an A&E doctor... Or a musician or professional gamer.

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**

Podcast – *Microbe Talk*

How do yeast help to give beer its taste? We took a trip to the Institute of Food Research and had a pint with the scientists behind the National Collection of Yeast Cultures (**http://microb.io/2hrjX2X**).

We also visited the bottom of the ocean, to learn about the microbes that thrive there (**http://microb.io/2kJSqMG**), and took a trip back in time to the era of the Byzantine Empire to hear about the phylogeny of ancient diseases (**http://microb.io/2lPZB5D**).

YouTube channel

Vaccines are one of the miracles of public health, but how do they work? We went to the London School of Hygiene & Tropical Medicine to speak with Dr Adam Kucharski, who told us about vaccination strategies, and how herd immunity protects people who can't be immunised (**https://youtu.be/cEn1PKyBUNc**).

Also on our channel is the latest in our 'How to' videos, this one covering the skills you need to help you effectively network at a conference (**http://microb.io/2mNtW3v**).

The latest from the Microbiology Society

Find out what you may have missed from the Microbiology Society. This is a roundup on some of the latest from each of our channels, with details of where you can find them.

Blog – *Microbe Post*

Spider silk is certainly one of the world's most awesome materials, but can it be used to deliver antibiotics? We spoke to Professor Neil Thomas from the University of Nottingham, who is looking at ways to embed antibiotics within spider silk for use as potential wound coverings (**http://microb.io/2igrG5L**).

In our continuing series about emerging diseases, we learnt about Oropouche, a virus estimated to have caused over 500,000 infections since its discovery in 1955 (**http://microb.io/2jhpSlu**).

Facebook

Back in February, we recorded the second of our Facebook Live videos – this time from Orbital Comics in London's Soho area. In the stream, we talked with Sara Kenney and Dr Adam Roberts about *Surgeon X*, a comic book series set against the backdrop of an antibiotic apocalypse in near-future London.

Also on our Facebook page are the latest videos from our recent Annual Conference, which highlight some of the research presented at the event.

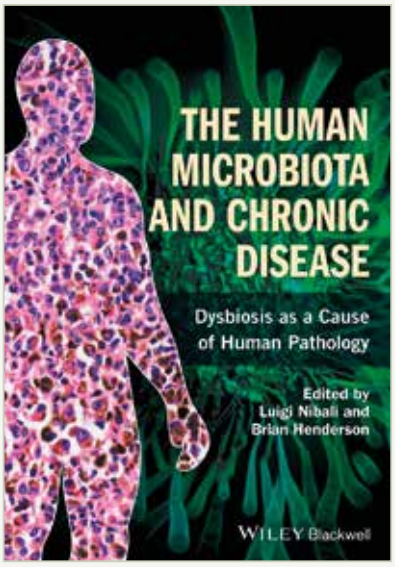
The Microbiology Society is producing more content than ever before – don't miss out!

Reviews

The Human Microbiota and Chronic Diseases: Dysbiosis as a Cause of Human Pathology

Edited by L. Nibali & B. Henderson
Wiley-Blackwell (2016)
£120 ISBN 978-1118982877

A highly popular topic, this book provides extensive coverage of human microbiota at different anatomic sites with a clear illustration of proportions of various micro-organisms in each site. The historical evolution of human microbiota, its relevance to environmental factors and dysbiosis have been discussed. The effect of microbiota on human gene expression has been reviewed although, at one occasion, microbiota has been considered as 'pathogenic', 'indigenous' and 'probiotic' while microbiota is always indigenous (page 185). The possible relationship between dysbiosis and diseases at different body sites – including cancer; chronic and metabolic diseases such as rheumatoid arthritis; inflammatory bowel diseases; and diabetes – has been explored. The book concludes with a chapter on probiotics and prebiotics and their application in medicine, and 'microbial therapy' for cystic fibrosis.



A comprehensive book on a popular subject with up-to-date reviews. It is clearly written and enhanced by clear illustrations. I would recommend it for researchers and students.

Azra Pachenari
Middlesex University

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

Comment

Advances in the study of the microbiome

James I. Prosser

Computer artwork of a protein microarray. Alfred Pasieka/Science Photo Library

Microbiomics, the study of microbial communities in the context of their environmental characteristics, is effectively microbial ecology and the suffix 'ome' nicely combines the concept of 'biomes' with modern developments in 'omics' approaches.

The explosion in use of the term 'microbiome' and the less explosive, but still dramatic, increase in community studies result largely from development of molecular techniques to characterise microbial communities. Until the early 1990s, we typically studied natural communities by incubating solid growth medium, inoculated with environmental samples, and then isolating pure cultures, which were identified by measuring many physiological characteristics. These physiological data allowed us to explore relationships between isolated organisms and environmental characteristics, providing a basis for development, and experimental testing, of ideas, explanations and ecological concepts.

Molecular techniques provided a major advance by liberating us from reliance on laboratory cultivation. 16S rRNA genes, amplified from extracted DNA, enabled identification by comparison of sequences with those in burgeoning databases, assessment of diversity and comparison of communities. Findings were remarkable. We discovered considerable diversity,

even in familiar cultivated microbial groups, and abundant microbes in high-level taxonomic groups with no cultivated representatives. This approach was extended to functional genes and was greatly facilitated by decreasing sequencing costs. It is worth remembering that no technique is perfect and molecular community analysis has bias and limitations. Some cells lyse more easily than others, some genes are easier to amplify, etc., but this tremendous technical advance generated many surveys and sequence lists. This is now the standard approach to community analysis but in some senses it represented a backward step. Ironically, this is partly because genome sequencing of cultivated microbes demonstrated considerable lateral transfer of genes, particularly those of ecological importance. We therefore have only limited information on relationships between (16S rRNA-based) phylogeny and function, which is the basis of evolutionary and ecological theory, and the valuable link between environmental and physiological characteristics was broken.

Microbial ecologists attempted technical solutions to this problem. Sequencing of transcripts and proteomics, respectively, indicate which genes are stimulated and translated following environmental change. Increases in gene abundance tell us which organisms are growing. Stable isotope probing indicates which organisms assimilate a particular substrate. Sequencing all genes (metagenomics) indicates potential function, but relies on the (dangerous) assumption that gene presence is linked to activity and ecosystem function. It is easy to be seduced by these techniques but they are only as good as their ability to answer scientific questions and test hypotheses.

This introduces what I believe to be a major limitation to advances in microbiomics. Many of the promises made for microbiomics and 'omics' techniques are reminiscent of those made for early molecular techniques 25 years ago. Our limited ability to deliver on these promises results from an apparent reluctance to ask important, critical scientific questions or to propose ideas, hypotheses and explanations for unexplained natural phenomena. Most studies are not question- or hypothesis-driven, and microbiomics is dominated by descriptive and correlation-based studies. Correlation-based studies attempt to gain information on links between phylogeny and function by looking for correlations between 16S rRNA gene sequences and environmental characteristics. It is relatively easy to obtain such data but the environmental characteristics measured are usually those that are cheap and easy to measure, rather than those of ecological relevance. These studies also assume, implicitly, a relationship between phylogeny, physiology and environmental characteristics. As a consequence, they are usually descriptive and situation-specific and are rarely based on important scientific questions. They can be used to generate hypotheses and explanations, but these are rarely tested.

Hypothesis-based studies also lead to discoveries. Our first molecular studies of soil ammonia oxidisers tested the hypothesis that soil pH selects different groups of these organisms. Sequence data answered this question but we could not avoid discovering extremely high sequence diversity or groups with no cultivated representatives. These discoveries were unexpected and raised new ecological questions, but this study exemplifies the point that discoveries do not require unstructured surveys. It can even be argued that important discoveries are more likely to arise from question- and hypothesis-driven research.

The field of microbiomics is enormously exciting and provides intellectually interesting and stimulating scientific challenges that are important within and beyond microbial ecology. We have never before had such powerful techniques to study microbial communities, but we must think carefully if they are to be fully exploited. We will only make significant advances in scientific understanding of the links between communities and their environments if we begin by identifying interesting phenomena and questions, and suggest explanations and potential answers that can be tested experimentally, thinking carefully about which techniques are required. Important scientific questions are unlikely to be answered by hoping that explanations will 'fall out of the data' and microbiomics will advance faster, and deliver its promise, only when we can match technical ingenuity with intellectual effort, creativity and the confidence to develop and test original ideas and concepts.

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NC 3Rs

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