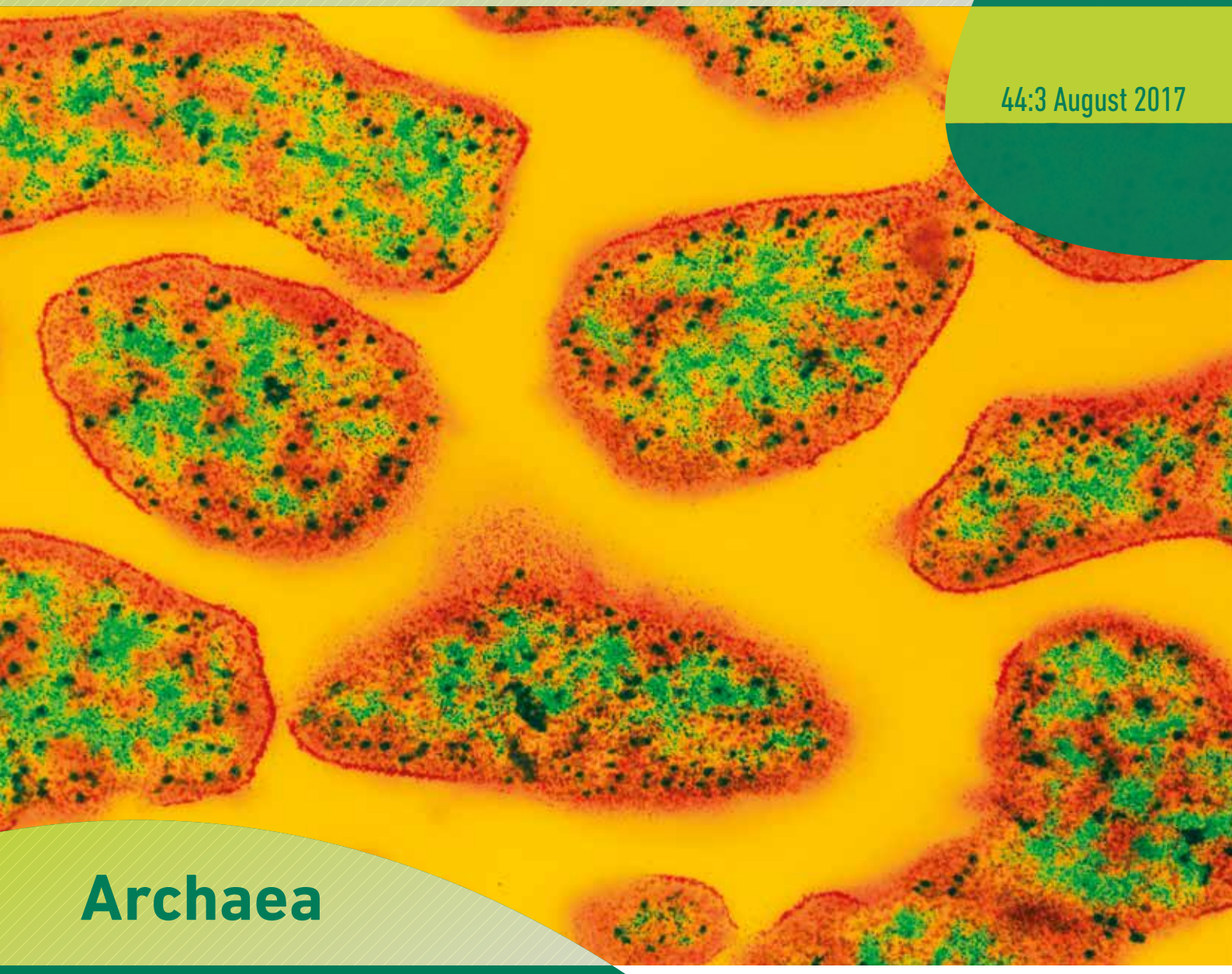
Microbiology TODAY

44:3 August 2017



Archaea

Archaea and the nitrogen cycle
Archaea in activated sludge systems
Genome segregation in heat-loving archaea
The symbiosis that changed the world
Archaea and CRISPR biology

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.

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Editorial

Welcome to the August edition of *Microbiology Today*, and one in which we consider the role of archaea and their impact on microbiology since their reclassification in the 1970s. The Archaea are a fascinating set of microbes that can thrive in unusual environments, including some of the most extreme places on the planet. They can survive in extremes of temperature, pH and pressure, and are found in many places including the deep sea, volcanoes and within the guts of animals and humans.

Whole Picture

Archaea have historically been given a back seat in terms of research and publicity, perhaps because of the generally accepted premise that there are no archaeal pathogens, and so much of the research has focused on their involvement in methane and ammonia cycling. There are also difficulties associated in culturing these microbes in the lab, and as culture-independent techniques improve, research evolves and more information about these microbes emerges. Archaea have significant roles in aspects of global ecology, and the collection of articles in this edition highlights how widespread and successful these organisms are.

Our first piece, written by Graeme Nicol, gives an insight into the role of archaea in the nitrogen cycle. The presence of large numbers of ammonia-oxidising archaea in oceans and soils has shifted global understanding of how nitrification works. Graeme discusses how the application of fertiliser during the 20th century has led to an accelerated nitrogen cycle, causing damage to the environment. He then outlines how ammonia-oxidising archaea could be utilised to alleviate some of these pollution problems.

The second article has been contributed by Marta Filipa Simões and André Antunes, and provides details of the role of archaea in the activated sludge process. This essential treatment of wastewater is relatively affordable and produces high-quality effluent. The activated sludge is known to contain a majority of bacteria, and the role of archaea, integral within the process, is still incompletely understood. There is evidence that methanogens and ammonia-oxidising archaea contribute to the activated sludge in a fundamental way, and there is a growing recognition that more work is needed to understand the diversity and function of archaea within activated sludge.

In our third piece, Daniela Barillà explains the importance of genome segregation in archaea that thrive in temperatures of over 80 °C. Building on work from archaeal pioneer Wolfram Zillig, researchers are now discovering new information on the roles of both chromosome segregation and three-component plasmid segregation machinery, relevant to all life on Earth.

Laura Eme and Thijs Ettema pose the question of archaeal involvement in eukaryotic evolution. Did chloroplasts and mitochondria arise from endosymbiosis between plants, cyanobacteria and alphaproteobacteria? Or did fusion between an archaeon and an alphaproteobacterium lead to eukaryotic cells? The availability of sequence data has revealed a surprising deep-sea link to eukaryotic origins.

CRISPR-Cas adaptive immune systems have been the focus of much scientific and media attention recently. In this article, Qunxin She and Wenyuan Han explain how these systems are unevenly distributed amongst bacteria, possibly due to the presence and pressure from archaeal viruses driving the selection of one or more CRISPR-Cas within archaea. They also discuss how Cas accessory proteins might modulate the functionality within CRISPR-Cas systems.

James Chong writes the Comment piece, highlighting the hazards (including explosions) that can be associated with working with archaea. He ponders why there are no archaeal pathogens, and the answer suggests there may be many complexities at play. Evidence proposes that archaea could be functioning as opportunistic pathogens in a range of health conditions. As in so many microbiological studies, the analytical methods employed may have, until recently, given a skewed picture. Improved techniques could lead to new questions about the status of these microbes.

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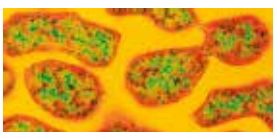

FSC Logo

Cover: Cold-loving archaea. Coloured transmission electron micrograph of a section through the archaeon *Methanococcoides burtonii*. The cell walls appear red, while the granular cell contents include scattered genetic material. These psychrophilic (cold-loving) archaea were discovered in 1992 in Ace Lake, Antarctica, and can survive in temperatures as low as –2.5 °C. As methanogenic microbes, they are able to form methane from carbon dioxide and hydrogen. Dr M. Rohde, GBF/Science Photo Library

MICROBIOLOGY SOCIETY

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From the President

The age of the earliest origins of (microbial) life on Earth extend to at least four billion years ago. There is renewed debate on exactly how and when the three major extant groups of life forms on Earth (bacteria, archaea and eukaryotes) evolved and diverged.

But, whatever the consensus emerges, it is clear that all of life is microbiological in origin and all plants and animals depend on microbial collaborations and endosymbiosis for their existence. This issue celebrates the Archaea – one of the three basic cell types on Earth, and one perhaps that few members of the general public will have ever heard of.

The late Carl Woese, a pioneer of 16S ribosomal DNA sequencing, was first to recognise the distinction between the Archaea and other prokaryotes, publishing the seminal paper on this topic in 1977. Therefore, Woese revealed a new view of the world showing that the basic arrangement and evolution of life forms on Earth comes from three basic microbial prototypes. This refined and extended the previous paradigm published in 1962 by Roger Stanier and C. B. van Niel who first established the division of prokaryotes and eukaryotes based in part on whether they had a membrane-bound nucleus. Although we have only known of their very existence for less than 40 years, it is clear that the Archaea are an ancient and fascinating independent group of organisms (see in this issue the article on p. 118 by Laura Eme and Thijs Ettema).

This issue rightly celebrates the Archaea as the least well known of the major divisions of life. We used to think of these organisms as being restricted to the more extreme environments and ecosystems. While it is true that these organisms include notable thermophilic and halotolerant species (see the review on thermophilic archaea by Daniela Barillà), it has turned out that archaea are very much more widely distributed than first thought. The importance of these organisms in many guises is set out in this issue. See, for example, the articles by Graeme Nicol describing the contributions that archaea make to soil nitrification and other aspects of the nitrogen cycle, and to the biodegradation of sewage (article by Marta Filipa Simões and André Antunes). There is also an interesting account of how the CRISPR-Cas system is linked to archaea (article by Qunxin She and Wenyuan Han). Please also read the commentary by James Chong on the apparent absence of pathogenic archaeal species.

I wonder if you read the recent article in *Cell Reports* by Asuncion Delgado from Jose Sanchez-Ruiz's lab, who showed that a 'fossil' bacterial protein (thioredoxin) could be expressed in a contemporary bacterium (*Escherichia coli*) and modify its properties. Bacteriophages need to recruit this redox protein for their replication, and what was interesting was that expression of these ancient thioredoxin proteins could, to a greater or lesser extent, render modern *E. coli* phage-immune. The reason for mentioning this is that the study of ancient microbes, and the understanding of how they evolved into modern ones, might provide novel insights and opportunities to develop desirable properties, such as virus resistance in plants and animals. Archaea are one such group of microbes that have not been fully explored in terms of their ecology and utility.

Elsewhere in this issue you can catch up on Microbiology Society news, with an overview by Laura Crick on conferences and meetings and information about the new Membership Directory from Paul Easton. The Early Career Microbiologists' Forum is now gearing up and has quickly become integrated into the central machination of the Microbiology Society (see article by Rebecca Hall). There are other Society updates from Benjamin Thompson, and also Hannah Forrest with information on schools activities and the Antibiotics Unearthed project.

Neil Gow
President
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From the Chief Executive

It has been a great privilege to attend a number of meetings in Ireland over the past few months, where I have seen some of the fascinating work being carried out by Microbiology Society members there. In Belfast, Dublin, Wexford, Cork and Kildare, there has been some amazing microbiology on display, and it has been shared in a community that gets the best out of its members by being supportive and friendly.

In May, it was a real pleasure to visit Johnstown Castle in County Wexford, one of the homes of Teagasc – the Agriculture and Food Development Authority. Society member Fiona Brennan organised a stimulating workshop on harnessing the power of plant and soil microbiomes. As well as scientists, the event was attended by policy-makers and funders from Science Foundation Ireland, the Department of Agriculture and the Environment Protection Agency. It was great to be able to present the emerging findings from the Microbiology Society's policy report on microbiomes, ahead of the main report's publication in the autumn.

Then, in June, I had enormous fun at University College Dublin, where PhD students in the School of Biology and Environmental Science presented their work at the annual Seminar Day. The postgraduate representatives – Tamsin, Sam and Laura – kindly asked me to be one of the judges. The winner of the Carmel Humphries Memorial Medal was Maeve Long, whose work on the endomembrane system referred to *Shigella* toxin and was both fascinating and impressive.

Later in the month, the first of the Society's Focused Meetings for 2017 was held in Belfast, on Microbial Resources for Agricultural and Food Security. It was organised by a long-time member of the Society, John McGrath, together with Katrina Macintosh, Jason Chin, John Quinn and Vincent O'Flaherty, who is Chair of the Society's Irish Division. There was a great range of offered papers from Ireland and further afield, and it was wonderful to learn more about the diverse roles played by microbes in agricultural systems.

The 33rd International Specialised Symposium on Yeast (ISSY33) was organised under the auspices of the International Commission on Yeasts, with the support of the Microbiology Society. It was held in June at University College Cork, the home of its driving force – John Morrissey – who is Chair of the Society's Eukaryotic Division. It explored the ways in which yeasts can be used for industrial applications, and included a keynote lecture from Steve Oliver, a member of the Society's Council, on how yeasts can be used as a model of human diseases.

And very soon, I will be back in Ireland for another of the Society's Focused Meetings at Maynooth in County Kildare, on Antimicrobial Resistance and One Health. Organised by Fiona Walsh and Thuy Thi Do, it has a lot to live up to after the success of all the other meetings!

One of the things that always strikes me when I visit members in Ireland is the sense of community. The Society's Irish Division has a long history of organising meetings that are not just scientifically stimulating, but which also make an effort to support early career members. Members in Ireland routinely attend meetings on subjects that are a long way from their own research interests, because they feel part of a vibrant and supportive community.

We are a Society of communities, and those communities can be taxonomically defined – like the Virology, Prokaryotic and Eukaryotic Divisions – or defined by career stage like the Early Career Microbiologists' Forum, or by other interests, like the Policy Committee. The Irish Division is the only geographically based group of members the Society has. But when we consulted you recently as Council prepares a new five-year strategy, there was a strong sense from the members that you want us to do more at a local level.

I am very keen to hear from you about what this means to you, and how the Society can connect and empower your local community in the way the Irish Division does so effectively.

Peter Cotgreave
Chief Executive
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News

Policy briefing: Antimicrobial Resistance

The latest in the Society's series of short policy briefings focuses on the topic of Antimicrobial Resistance (AMR). The briefing was sent to policy-makers in the UK and Ireland, and sets out the key issues around AMR and the actions needed to mitigate it. You can download it here: **www.microbiologysociety.org/briefings**

Focused Meetings 2017

Thank you to those who attended, presented and spoke at our two Focused Meetings that took place in June this year – ISSY33 and Microbial Resources for Agricultural and Food Security. These two successful meetings brought together like-minded researchers, and were only the first of a busy Focused Meetings programme for 2017. Find out more about what's still to come on page 128.

Society Champion activities

Our Champions have been busy organising events in their local areas – find out more about what they've been up to at **www.microbiologysociety.org/champions**

Annual Conference 2018

Our full exhibition and sponsorship packages for Annual Conference 2018 can now be found online. We have a number of opportunities with a range of prices to suit all budgets, but stand space is limited so contact us as soon as possible to reserve your preferred area.

Remember to note in your diaries that Annual Conference 2018 will differ from previous years and takes place from **Tuesday 10 April** to **Friday 13 April** – don't forget when booking travel and accommodation.

Read more about Annual Conference 2018 on page 126.


ICC Birmingham

Support for your invited speaker costs

Our Society-Supported Conference Grants can cover speaker costs at your microbiological event for up to £2,000. This grant can be used towards the cost of accommodation and travel. Round 1 of our 2018 awards closes on 15 December 2017. Details can be found online: **www.microbiologysociety.org/SSconferencegrants**

Deaths

It is with great sadness that the Society announces the passing of one of our members, **Professor Martin Allday**, who was internationally renowned for his work on the biology of the Epstein–Barr virus. Professor Allday joined the Society in 1982.

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.

Grant deadlines

Date	Grant
1 September 2017	Travel Grants – for eligible members wishing to present at conferences or attend training events on or after 1 October.
	Careers Conference Grant – to support Undergraduate Student Members wishing to attend the Royal Society of Biology Biosciences Careers Festival.
30 September 2017	ECM Forum Event Fund – for ECM members requiring sponsorship for local events.
1 October 2017	Education and Outreach Grants – for eligible members requiring support for projects to communicate or teach microbiology.
	Research Visit Grants – for eligible members wishing to make a research visit to a collaborator.
	International Development Fund – for eligible members wishing to contribute to the development of microbiology in low- and lower-middle-income countries.

Volunteers for Glasgow Antibiotics Unearthed pop-up event

The Antibiotics Unearthed team will be at the Glasgow Botanic Gardens on Thursday 7 September 2017 with our interactive pop-up stand, and we are looking for volunteers to help out.

The stand will include a variety of hands-on activities for visitors to engage with the issue of antimicrobial resistance and drug discovery. Members of the public are encouraged to collect a soil sample and prepare it for scientific analysis at the pop-up.

If you are interested in volunteering, please contact the Antibiotics Unearthed team at **antibioticsunearthed@microbiologysociety.org**

Antibiotics Unearthed events in 2015 and 2016.

Annual Conference 2019 session proposals

If you have an idea of a topic for an Annual Conference 2019 session, please complete a proposal form online (**www.microbiologysociety.org/proposals**) and submit for consideration by **15 December 2017**. Our Scientific Conferences Committee will be discussing all session proposals in January 2018.

Promote your microbiology events

The Society's full events listings let you promote your meetings, big or small, through our website.

Simply fill in the online form with your event's details at **www.microbiologysociety.org/submitevent**. All meetings that may be relevant to our website visitors will be added to our listings free of charge.

Contributions and feedback

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

Benjamin Thompson
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Archaea and the nitrogen cycle

The ability of some archaea to contribute to nitrogen cycling processes has been known for many decades (albeit some of these organisms were not initially recognised as archaea). These included both assimilatory (e.g. fixation of atmospheric nitrogen) and dissimilatory (e.g. denitrification) processes. However, these reactions were associated with extremophilic archaea typically found in 'exotic' habitats such as hot springs or salt-saturated lakes, rather than major terrestrial or aquatic environments, and were perhaps not considered ecologically important in a global context.

Graeme Nicol

Picking vegetables from the soil. Martin Poole/DigitalVision/Thinkstock

In little over a decade, microbiologists have not only discovered that archaea perform nitrogen transformation in more 'common or garden' habitats, but also that these contributions are vast with respect to global fluxes, and have solved several long-established mysteries with regard to nitrogen cycling in the world's oceans and soils.

The discovery of ammonia-oxidising archaea (AOA)

Nitrification is a central component of the global nitrogen cycle and involves the oxidation of ammonia to nitrate (via nitrite) by two groups of organisms: ammonia- and nitrite-oxidisers (although *Nitrospira* sp. performing complete ammonia oxidation to nitrate [comammox] have recently been discovered). Since the cultivation of ammonia-oxidising microbes in the 1890s by researchers including Percy Frankland, Grace Frankland, Robert Warington and Sergei Winogradsky, it was assumed that this biologically mediated process was dominated by the activity of specialised autotropic ammonia-oxidising bacteria (AOB). However, the discovery of ammonia-oxidising archaea (AOA) required a major re-evaluation of this process, and within a decade AOA were recognised as not only major contributors to this process, but are primarily responsible for ammonia oxidation in many environments.

From their discovery in the late 1970s by Carl Woese and George Fox, Archaea (then termed Archaebacteria) were generally considered as rather enigmatic curiosities – unique cell structures and physiologies certainly, but perhaps not contributing greatly to the major biogeochemical cycles of the planet, with the exception of methane generation in anoxic habitats. However, the use of molecular methodologies in microbial ecology in the 1990s not only led to the discovery of an unexpectedly vast diversity of novel bacterial phyla, but also resulted in the discovery of archaea in 'non-extreme' environments. The discovery of AOA arose from studies that aimed to understand the diversity and ecological function of one such lineage of uncultivated archaea, one that appeared to be related, albeit distantly, to cultivated sulfur-dependent hyperthermophilic *Crenarchaeota*. These 'nonthermophilic *Crenarchaeota*' were found to represent between 1 and 3% of all prokaryotic cells in soil, and rather astonishingly, approximately 20% of all prokaryotes in the ocean. A number of cultivation-independent studies provided tantalising evidence that these archaea used inorganic carbon, and metagenomics studies subsequently revealed that their genomes contained genes that were homologous to those encoding for ammonia monooxygenease found in bacteria. However, it was the cultivation of the archaeon *Nitrosopumilus maritimus*, isolated from a tropical marine aquarium in Seattle, that demonstrated that this lineage of nonthermophilic *Crenarchaeota* was apparently physiologically similar to AOB, growing autotrophically and oxidising ammonia as a sole energy source. Genome analyses subsequently revealed that these AOA were very different from the *Crenarchaeota* and belonged to a separate phylum, the *Thaumarchaeota*, and many representatives have now been cultivated from other environments including soil, the open ocean and terrestrial hot springs.

Archaea and the soil nitrogen cycle

AOA generally outnumber their bacterial counterparts in most soils. This was

initially surprising as there were often no major discrepancies during comparisons of AOB growth rates in culture and modelled AOB growth and nitrification kinetics measured in soil. Many initial studies focused on quantifying AOA and AOB abundance in soil using the relative number of marker genes (a proxy for cell abundance) as an indicator of relative contribution to ammonia oxidation. However, this required assumptions that all AOA and AOB populations have similar substrate affinities, growth rates, cell specific yields and utilise the same sources of ammonia. In these respects, we now understand that there are major differences, both within and between AOA and AOB.

With an increasing global population, there has been a concomitant rise in fertiliser application rates since the mid-20th century. This has resulted in a grossly accelerated nitrogen cycle where more nitrogen is now added to the world's soils in the form of inorganic nitrogen fertiliser than occurs 'naturally' through the activity of nitrogen-fixing bacteria. This has severe deleterious environmental consequences. Nitrate is leached much more readily than ammonium from soil, resulting in pollution of ground- and coastal waters, and provides the substrate for denitrification processes, a consequence being increases in emissions of the greenhouse gas nitrous oxide. Recent studies indicate that AOA may have two distinct ecological and physiological characteristics in comparison to AOB, which could be considered advantageous in attempts to mitigate nitrification-associated pollution. Firstly, while they can use added inorganic ammonium, AOA in many soils appear to preferentially use ammonium derived from mineralised

In little over a decade, microbiologists have not only discovered that archaea perform nitrogen transformation in more 'common or garden' habitats, but also that these contributions are vast with respect to global fluxes, and have solved several long-established mysteries with regard to nitrogen cycling in the world's oceans and soils.

Tropical fish on a coral reef. dangrytsku/iStock/Thinkstock

organic matter, with AOB rapidly oxidising inorganic ammonium fertiliser applied at high concentrations. Secondly, while all ammonia oxidisers generate the greenhouse gas nitrous oxide as a by-product of ammonia oxidation, the yield per ammonia oxidised is approximately half with AOA. Therefore, using fertilisation strategies that favour AOA growth and activity (e.g. use of organic fertiliser) has the potential to dramatically reduce nitrification-associated pollution.

Solving previously unexplained N-cycling processes in soils and oceans

The open ocean has extremely low concentrations of dissolved ammonium. Measurements revealed substantial discrepancies between ammonia oxidation rates observed *in situ* and those of cultivated AOB, with the half-saturation constant for activity in the open ocean orders of magnitude lower. However, the cultivation of marine AOA possessing extremely high specific affinities for ammonia, together with molecular surveys revealing a numerical dominance of *N. maritimus*-like archaea, demonstrated that AOA are primarily responsible for ammonia oxidation in the open ocean.

The discovery of AOA also provided a possible explanation for the long-standing paradox of why high rates of nitrification are often observed in acidic soils without apparent acidophilic ammonia oxidisers. All cultivated obligately aerobic ammonia oxidisers isolated during the 20th century grow at neutral or near-neutral pH when grown in standard laboratory culture. Ammonia oxidisers, as described by their name, cannot use the protonated form ammonium as a substrate, and ammonia availability is largely determined by the pH of the surrounding environment. In many acidic environments, the equilibrium between these two forms is shifted so greatly towards ammonium that they could be considered, from a microbial perspective, essentially 'ammonia-free', and intuitively a rather unpleasant environment for any ammonia oxidiser. Nevertheless, high rates of nitrification are often measured in acidic soils, where ammonium is supplied through the mineralisation of organic matter. With the discovery of archaeal ammonia oxidisers and media enabling their cultivation, the obligately acidophilic archaeon *Nitrosotalea devanaterra* was isolated from a pH 4.5 soil at the University of Aberdeen in 2011, and provided the most parsimonious explanation of why nitrification can occur in acidic soils. The subsequent cultivation of other *Nitrosotalea* strains, together with surveys of acidic soils globally, indicates that *Nitrosotalea* are major players contributing to this process. Despite growing only in acidic conditions, physiological and genomic evidence indicates that these organisms oxidise ammonia and not ammonium, and may grow by transporting ammonium intracellularly before subsequent conversion to ammonia and oxidation.

Acknowledgements

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Archaea in activated sludge systems

Marta Filipa Simões and André Antunes

Biological wastewater treatment plants were originally used mainly for removing organic matter and suspended soils, but later advances increased their goals to eliminate toxic metals, odours, nutrients and pathogens.

Aerial view of a sewage treatment plant.
Peter Chadwick/Science Photo Library

The activated sludge process (ASP) is the preferred choice in biological wastewater treatment plants, providing a major contribution to environmental protection. This process was developed in England in 1914 and owes its name to the production of activated microbial mass capable of aerobically stabilising the organic content of wastewater. It is the most versatile biological treatment process, and is able to produce high-quality effluents at reasonable costs, although it can be responsible for the release of greenhouse gases.

How does the ASP work?

In the ASP, several micro-organisms feed on organic contaminants present in wastewater. They cluster together and gradually build up to larger solids, forming the activated sludge (AS, and also known as floc). Flocs are allowed to settle to the bottom of tanks, leaving a relatively clear wastewater free of organic material and suspended solids.

Flocs must be kept in suspension during contact with the wastewater being treated, and a small percentage of AS is recirculated into the aeration tank, where it is mixed with the primary effluent. This recirculation is vital, as the recycled microbes are already well acclimated and readily metabolise organic material in the primary effluent.

The ASP mode of operation and structure can vary, but the balance of organisms present in the AS will indicate the overall health and ability of the activated system.

Microbial constitution of AS

Bacteria constitute a major percentage of the biological composition present in AS and play a key role in structural and functional activity of flocs. The predominant type of bacteria is determined by the nature of the organic substances in wastewater, mode of operation of the plant and the environmental conditions.

Archaea in AS

Most studies focusing on the microbiology of AS have centred on bacteria, while archaea have been largely neglected. Molecular-based investigations consistently detect members of the Archaea in AS, consisting of methanogens and putative ammonia-oxidising archaea (AOA) and belonging, respectively, to the phyla *Euryarchaeota* and *Thaumarchaeota*. Despite wide divergence in values, archaea seem to constitute a small fraction of the total microbial community, and play minor roles in nitrogen- and carbon-removal. Indeed, previous studies point to a range from 0 to 10% of the total microbiota, although several have likely underestimated their numbers.

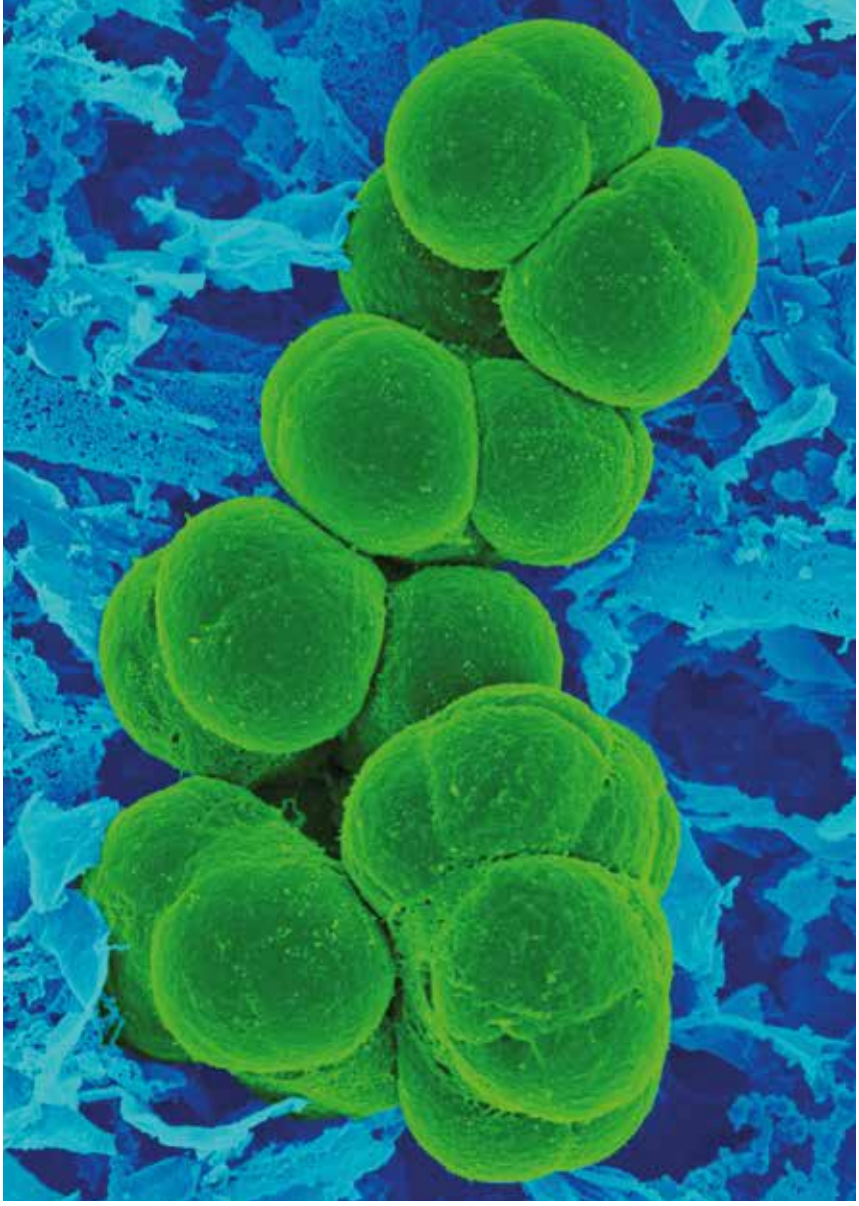
Ammonia oxidisers

AOA have been alternatively reported as completely absent, providing a minimal or equal contribution to their bacterial counterparts (AOB), or even as dominant. Relative dominance seems to be linked mostly to ammonia concentration, with

AOA being able to grow under ammonia-limiting concentrations. Other factors that condition AOA abundance are their higher sensitivity to drought, lysis, temperature and changes in pH.

The activity of AOA is still controversial, with disagreement between authors, and there are some suggestions that the detected archaeal *amoA* (the marker gene for ammonium oxidation) might be present in archaea that encode the gene but are not actively oxidising ammonia.

When detected, archaeal-based removal of nitrogen involves the phylum *Thaumarchaeota*. Previous environmental studies have highlighted their significant role in the biogeochemical cycle of nitrogen (and carbon), placing them as the main ammonia-oxidisers in, for example, oceans and geothermal habitats. Given that ammonia is the main nitrogen species in urban wastewaters, their relatively low numbers in AS are unexpected.



Coloured scanning electron micrograph of *Methanosarcina barkeri*. Dennis Kunkel Microscopy/ Science Photo Library

Methanogens

Methanogens are the most abundant archaea in AS, and are generally represented by species of *Methanosarcinales*, *Methanobacteriales* and *Methanomicrobiales*. Typical abundant genera include *Methanosaeta* and *Methanosarcina*.

The high O_2 content of AS makes it a less than welcoming environment for methanogens as they are known to be strictly anaerobic. *Methanomicrobiales* and *Methanobacteriales* form methane by CO_2 reduction, with H_2, formate or alcohols as electron donors. Some members of the latter group can also oxidise CO or reduce methanol (instead of CO_2). Members of the *Methanosarcinales* traditionally grow by dismutation of methyl compounds (methanol, methyl amines or methyl sulfides) or by splitting acetate (acetoclastic). Some can also form methane by reduction of CO_2 or methyl compounds, by using H_2 as an electron donor. Methanogens form therefore a highly specialised physiological group, unable to catabolise carbohydrates, proteins or organic compounds other than methanol, some secondary alcohols, formate or CO.

These higher loads of methanogens can be a reflection of the composition of the original wastewater. *Methanobacterium*, *Methanosaeta* and *Methanosarcina* are the prevalent archaeal genera in diverse types of industrial wastewaters (such as in breweries, wineries or dairies). Also,

Recent advances in molecular-based methodologies have significantly increased our knowledge on the phylogenetic and functional diversity of wastewater treatment systems.

many methanogens likely enter the sludge with a stream of recycled water from an anaerobic reactor. The anaerobic conditions in the reactor would allow them to thrive and develop much better.

Aerated conditions of AS do not fully exclude methanogens, however. Anoxic micro-environments can exist in deeper parts of the flocs where oxygen won't reach. Furthermore, several methanogens are now known not to be as sensitive to oxygen as originally estimated. Indeed, several reports show that they can maintain viability and activity even in the presence of high levels of oxygen. Fittingly, studies targeting metabolically active archaea in AS detected methanogens, with highest numbers within the orders *Methanonomicrobiales* and *Methanosarcinales* and in the genera *Methanocella* and *Methanosarcina*.

Despite the aforementioned evidence for a limited role and diversity of archaea in AS, some studies suggest that they might have other functions or affect the properties of AS (such as contributing to floc structure or being in symbiotic relationship with bacteria). Their contribution to floc structure is particularly important as poor flocculation and settling of AS leads to reduced effluent quality and can cause severe environmental issues.

Conclusions

Recent advances in molecular-based methodologies have significantly increased our knowledge on the phylogenetic and functional diversity of wastewater treatment systems. Most of the information is still derived from the most abundant members of the community (i.e. bacteria). We now know that archaea constitute a minor but constant and integral part of activated sludge. Differences can be observed depending on the wastewater treatment plant, mode of operation of the treatment process, time of the year, physical and chemical characteristics of the AS, or even on the methodologies used for analysis.

Even with their apparently less pronounced role and abundance, they have been linked to important functions in AS, and seem to condition the overall efficiency and quality of the process. Additional studies, preferably using polyphasic and complementing technologies, are necessary to fully understand their community's diversity, distribution and functionality in these environments.

Coloured scanning electron micrograph of *Methanosarcina mazei*. Eye of Science/Science Photo Library

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Daniela Barillà

Aerial view of the Grand Prismatic Spring, Midway Geyser Basin, Yellowstone National Park. *Sulfolobus* species have been isolated from acidic hot springs in Yellowstone. NPS photo by Jim Paeco

Genome segregation in heat-loving archaea

Archaea are remarkable objects of investigation due to their exquisitely distinctive biological properties and macromolecules. Since their discovery four decades ago, there has been an escalation in knowledge, genome sequences and publications on this domain of life. However, the fundamental process of genome segregation remains a terra still vastly incognita in this branch on the sprawling tree of life.

Archaea are single-cell organisms that populate planet Earth and which together with bacteria and eukaryotes form the three domains of life. Archaea appear similar to bacteria, but belong to a different branch of the tree of life. Both bacteria and archaea are prokaryotes, i.e. their genetic material is not wrapped by a membrane into a separate compartment, called a nucleus, which instead is a hallmark of eukaryotes such as baker's yeast, fungi, plants and animals, including humans to mention some.

Archaea are ubiquitous and constitute a considerable fraction of the global biosphere. Some live ordinary lives in mundane environments, such as lakes, seas and insect intestinal tracts, whereas others live extraordinary lives pushed to extremes in incredibly harsh habitats, such as hot springs, deep- sea hydrothermal vents, volcanic mud and salt lakes. Archaea have been instrumental in evolutionary studies on the origin of life and have revealed to us that the boundaries of life as we know it can be pushed much further than previously anticipated.

Thermophilic or heat-loving archaea

Thermophilic archaea are super microbes that thrive at 80 °C and higher temperatures in hot springs, volcanoes and deep-sea vents. These archaea exhibit fascinating properties, which make them valuable for the development of novel biotechnological applications, but also extremely interesting for basic studies on life pushed to extremes. Thermophilic archaea contain heat-stable cellular building blocks such as proteins and lipid chains in the cell membrane that represent adaptations to the habitats in which these superbugs thrive. The ability of these archaea to grow in extreme environments where no other terrestrial organism can survive has also rekindled hopes of discovering extraterrestrial life on similarly inhospitable planets of our solar system as well as in more far-flung reaches of the universe.

Genome segregation

Genome segregation is a crucial stage of the life cycle of every cell: the DNA is first duplicated, then separated and equally distributed into the two daughter cells. Despite the significant progress made in decoding molecular mechanisms in archaea in the last four decades, a paucity of information is available to date on the fundamental process of DNA segregation in these micro-organisms. The subject remains a black box awaiting investigation. Nevertheless, recent insights into this process have emerged from investigations on species of the heat-loving archaeon genus *Sulfolobus* that have been isolated from acidic hot springs and solfatara fields across the planet.

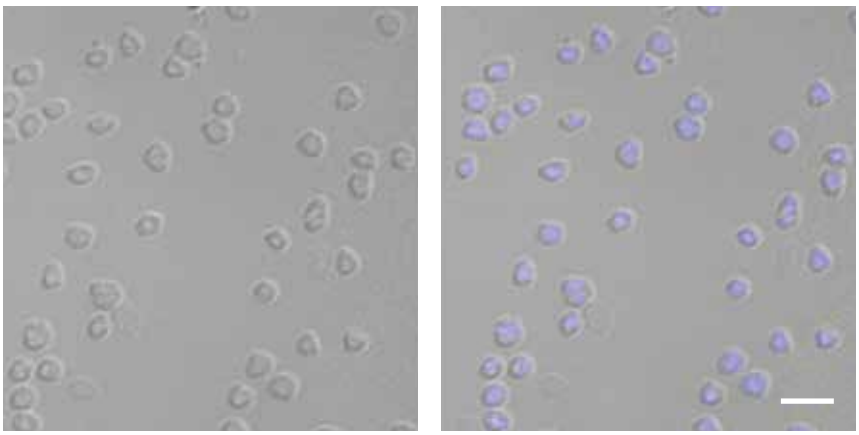
Sulfolobus solfataricus and the SegAB toolkit for chromosome segregation

The late German scientist Wolfram Zillig was an archaea pioneer. Zillig travelled from Germany to Naples in 1978 to accomplish a mission: re-isolating a thermophilic archaeon from the Earth's viscera in an area west of Naples known as Campi Flegrei or 'Burning Fields'. Campi Flegrei is a large volcanic region harbouring a caldera that is basically at ground level. It is possible to walk on the caldera terrain, which is dotted with fumaroles that emit sulfurous steam and with many pools of boiling mud. It is a truly infernal landscape. From this site, Zillig isolated an archaeal species that he called *Sulfolobus solfataricus*. This archaeon is a strict aerobe that grows at 80 °C and a highly acidic pH.

The genome sequence of *S. solfataricus* was determined in 2001. The sequence revealed two genes potentially involved in chromosome segregation, i.e. the separation and delivery of the newly replicated sister chromosomes to daughter cells at the stage of division. The genes were later designated as *segA* and *segB* for chromosome segregation. The SegA protein is a cousin of bacterial factors called ParA, which are adenosine triphosphate (ATP)-binding and -hydrolysing enzymes encoded by low-copy-number plasmids and chromosomes, and whose function is

crucial for accurate genome segregation. The SegB protein is an archaea-specific factor that does not show sequence similarity to any eukaryotic or bacterial protein.

Recent investigations have shown that SegA is indeed an ATP-hydrolysing protein that assembles into higher-order structures *in vitro* upon ATP binding, whereas SegB is a site-specific DNA-binding protein that recognises DNA sequences located upstream of the *segAB* genes. The two proteins assemble into a complex. Furthermore, SegB plays a role in dictating the accretion of SegA multi-subunit structures. The fact that SegB is attracted to specific DNA sequences and becomes glued to them is important, as the entire complex is recruited to those chromosomal locations. These sites are believed to be key to the separation of the chromosomes. When the number of subunits of SegA and SegB proteins in *S. solfataricus* cells is increased by using some genetic trickery, chromosome segregation is disrupted as shown by microscopy investigations, which reveal cells without chromosomes, others with the chromosomal DNA squeezed into one-half of the cell volume and some others with guillotined chromosomes. These defects indicate that the SegA-SegB complex plays a vital role in chromosome segregation. The SegA-SegB proteins are believed to separate and drive apart sister chromosomes, although the mechanism underpinning this process remains to be elucidated. The way one can picture this system is as a highly precise DNA molecule sorting machine.



Microscopy images of *Sulfolobus solfataricus* cells, bright field (left) and overlay with DAPI-stain (blue chromosome) (right). Bar, 4.5 µm. Brett McLeod

The Phlegraean Fields near Naples, painting by Michael Wutky (1780s). Web Gallery of Art

Borrowing building blocks from Bacteria and Eukarya: a three-component plasmid segregation machine in Archaea

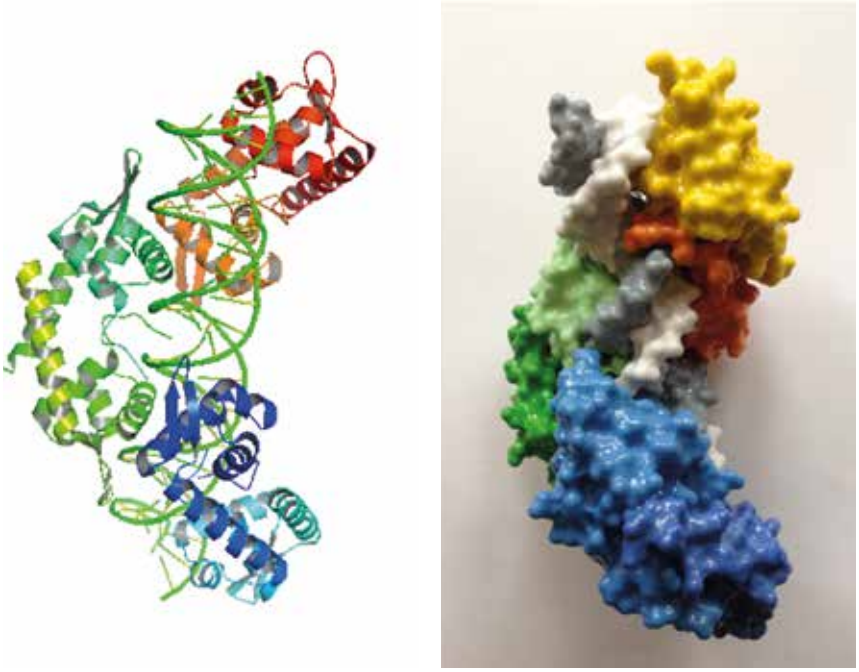
Another story dates back to the 1990s and begins with a further mission of Wolfram Zillig and coworkers, who travelled to the island of Hokkaido, Japan. From acidic hot springs at Noboribetsu in Hokkaido, Zillig isolated a *Sulfolobus* strain containing a plasmid,

> **Studies on archaea are providing new and intriguing perspectives on genome segregation that are pertinent to all life on planet Earth.**

pNOB8, that harbours three genes encoding an atypical DNA segregation system.

One of the segregation proteins encoded by pNOB8, AspA, is a site-specific DNA-binding protein. AspA recognises an inverted repeat sequence on pNOB8 and then associates to adjacent regions, thereby spreading on the DNA on which the protein forms a left-handed helix. ParA and ParB are the other two proteins of this plasmid-sorting machine. ParB is an adaptor that sits between AspA and ParA within the complex. Adaptors need to be pliable, and ParB is indeed flexible: the protein consists of two domains connected by an extended flexible linker. One of the ParB domains has a bacterial flavour; whereas the other resembles CenpA, which is a eukaryotic histone that replaces the canonical histone H3 at centromeres and is crucial for assembly of the kinetochore complex that drives chromosome pairs apart in eukaryotic cells. Structural investigations have shown that the AspA helix functions as a docking platform onto which ParB molecules assemble into a second superhelix that fits into the AspA-DNA structure in a lock-and-key fashion. In a nutshell, ParB subunits form a 'roller coaster' that is anchored on the AspA spiral, a truly remarkable assembly. ParA is then recruited into the complex via interaction with ParB and potentially mediates plasmid anchoring to the chromosome through its nonspecific DNA-binding activity. The mechanism that underpins pNOB8 partition remains under investigation.

The AspA-ParB-ParA multi-protein complex in archaea merges bacterial and eukaryotic features suggesting the possible conservation of DNA segregation principles across the three domains of life. Therefore, studies on archaea are providing new and intriguing perspectives on genome segregation that are pertinent to all life on planet Earth.



Structure (left) and 3-D printed model (right) of pNOB8 AspA-DNA complex showing three dimers (orange, green and blue) associated with DNA (white and grey). D. Barillà

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The symbiosis that changed the world

Laura Eme & Thijs J. G. Ettema

All cellular life on Earth can be classified into one of the three domains: bacteria, archaea or eukaryotes. Whereas cells of bacteria and archaea are small and simple, those of eukaryotes are generally bigger and complex, containing a nucleus that encompasses DNA, and other subcellular compartments, referred to as organelles.

There is evidence that eukaryotic cells arose during evolution from a merger of less complex cells, through a process called endosymbiosis. Recent findings have provided exciting insights into the main players in this enigmatic symbiosis that was responsible for the emergence of all complex life forms on our planet.

A eukaryotic potpourri

Bacteria and archaea are known collectively as 'prokaryotes' (from the Greek: *pro* = before, *karyon* = nucleus), as their genetic material is not enclosed by a nuclear membrane. In addition, prokaryotic cells are generally 'simple': they are small, single-celled organisms (typically between 0.5 and 5 microns in diameter) with a cell wall and a small circular chromosome. Eukaryotic cells (from the Greek: *eu* = true, *karyon* = nucleus) on the other hand are a potpourri: they can be much bigger (generally between 10 and 500 microns), and contain a diversity of specialised compartments, of which the nucleus houses the genomic DNA and is the hallmark. Other compartments include, for example, the mitochondria (best known as the 'power-house' of the cell, where energy production occurs), and a sophisticated endomembrane system (Fig. 1). Among evolutionary biologists, the question of how these eukaryotic cells and their complex features evolved has been the subject of heated debate for decades.

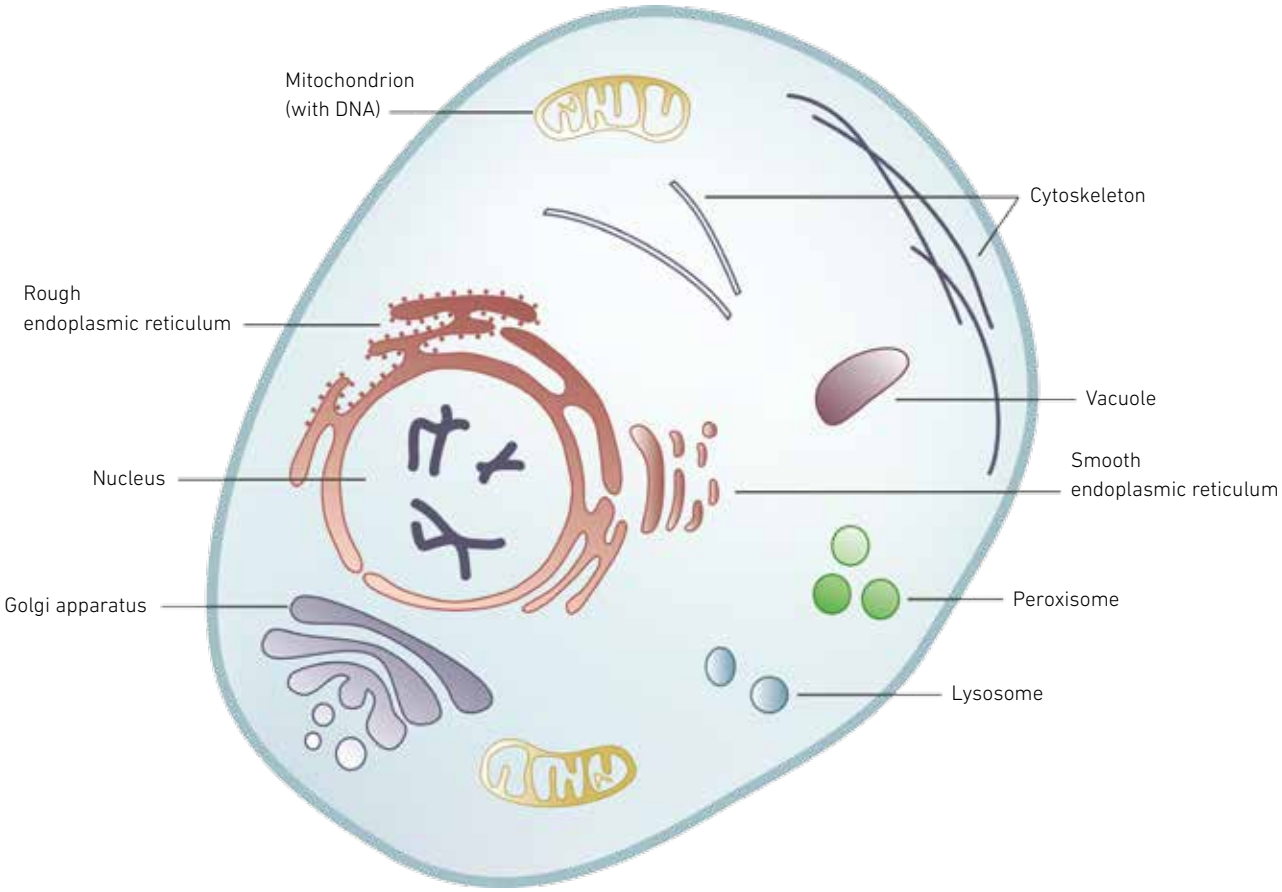
A symbiotic origin of eukaryotes?

The observation that eukaryotic cells are compartmentalised was made a long time ago. Konstantin Mereschkowski (1855–1921) noticed certain structural similarities between plant chloroplasts (the organelles in which photosynthesis occurs) and unicellular cyanobacteria, a group of photosynthetic bacteria. In 1910, he proposed that the former evolved from the latter, as the result of endosymbiosis. This refers to a process by which a cell lives inside another after being engulfed and establishes a long-term association with its host. In the 1960s, the idea that endosymbiosis might have played a pivotal role in eukaryotic evolution was re-popularised by Lynn Margulis. She proposed that, apart from chloroplasts, mitochondria also evolved from trapped free-living bacteria. The scientific community initially dismissed Margulis' ideas. But when it was discovered that mitochondria and chloroplasts contained their own genetic material that turned out to be related to that of bacteria, support for the endosymbiosis theory finally gained momentum. In particular, mitochondria were found to descend from a bacterial group known as the *Alphaproteobacteria*. These bacteria are usually free-living, but some can engage in symbioses with eukaryotic organisms. Symbiotic interactions are common practice in the microbial world, but alphaproteobacteria seem to be particularly good at this. In light of this, it is perhaps not too surprising that mitochondria have an alphaproteobacterial ancestry.

Engulfed by speculation

Whereas the alphaproteobacterial identity of the mitochondrial ancestor has been known since the 1980s, the nature of the cell that engulfed them (the host cell) has remained elusive. Ever since Carl Woese and co-workers discovered the archaea in the 1970s,

Fig. 1. **A typical eukaryotic cell and its complex subcellular organisation.** L. Eme



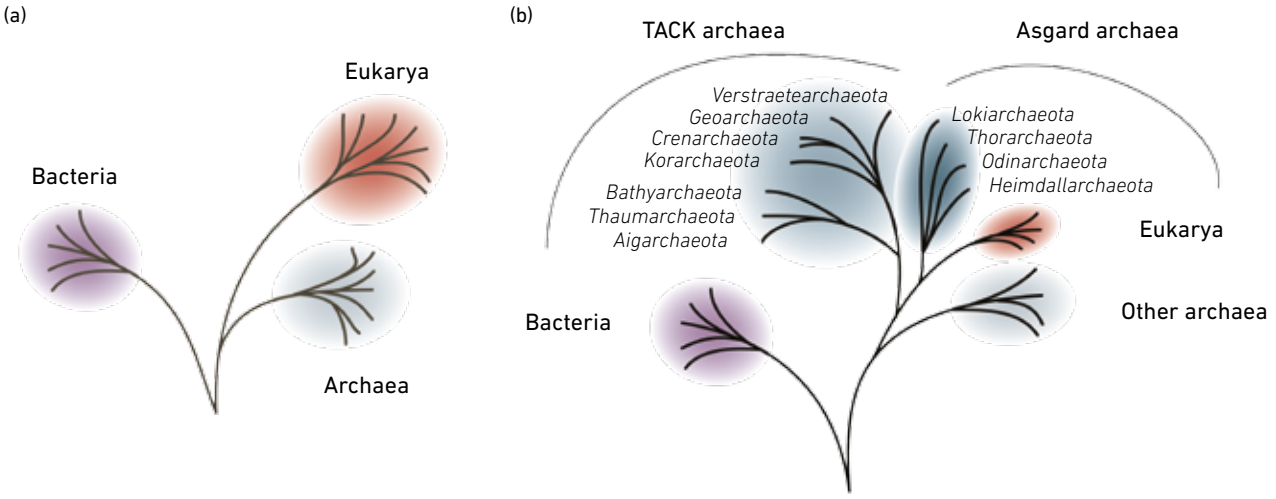
it was clear that the host cell was somehow related to these organisms – but how exactly was unclear. According to the view that was prevailing up to the 2000s, archaea and eukaryotes represented sister, but separate, groups in the tree of life (Fig. 2a). This view is most compatible with scenarios in which many of the cellular features that define eukaryotes evolved prior to the mitochondrial endosymbiosis. The host cell, in these scenarios, was thus a complex 'proto-eukaryote' that most likely engulfed the mitochondrial endosymbiont using phagocytosis – an energy-demanding ingestion process only known to exist in eukaryotic organisms.

For a long time, hypotheses for the origin of eukaryotes were mostly based on cytological observations, and, in the 1980–90s, on limited amounts of available molecular (sequence) data. This all started to change in the genomic era, when newly developed genome sequencing technologies made it possible to perform genome-wide studies to investigate eukaryotic origins.

Who's your (archaeal) daddy?

In contrast, other scenarios have suggested the fusion of a 'normal' archaeon with an alphaproteobacterium. In fact, they proposed that the mitochondrial endosymbiosis was the first event at the origin of eukaryotic cells: the burst of energy provided by mitochondria then allowed the elaboration of the complex features that are characteristic of eukaryotes, including phagocytosis. These models posed that the archaeal partner and the mitochondrial progenitor engaged in a syntrophic interaction – a symbiosis based on exchange of nutrients that is mutually beneficial. In time, this syntrophy became more intimate, culminating in the engulfment of the mitochondrial progenitor by the archaeal host cell. Yet, these so-called symbiogenic models for the origin of eukaryotes presented several problems. First, they implied that eukaryotes evolved from a bona fide archaeon, and not as a sister group of all archaea, which was at odds with the generally accepted topology of the tree of life. In addition, how did the endosymbiont end up inside the archaeal host cell if the process of phagocytosis evolved later? Finally, a third problem concerns cell membranes: eukaryotic membranes are radically different from archaeal ones, and in fact resemble bacterial membranes. Whereas the membranes of archaeal cells are comprised of isoprene-based lipids, eukaryotic membranes are similar to those of bacteria, which are made up of lipids with fatty acid chains. Hence, if

Fig. 2. **Two main competing hypotheses regarding the origin of eukaryotes. (a) Eukaryotes and Archaea were long believed to be independent sister groups. (b) Eukaryotes are now thought to descend from an archaeon. Their closest known relatives are Asgard archaea (*Lokiarchaeota*-related archaea).** L. Eme



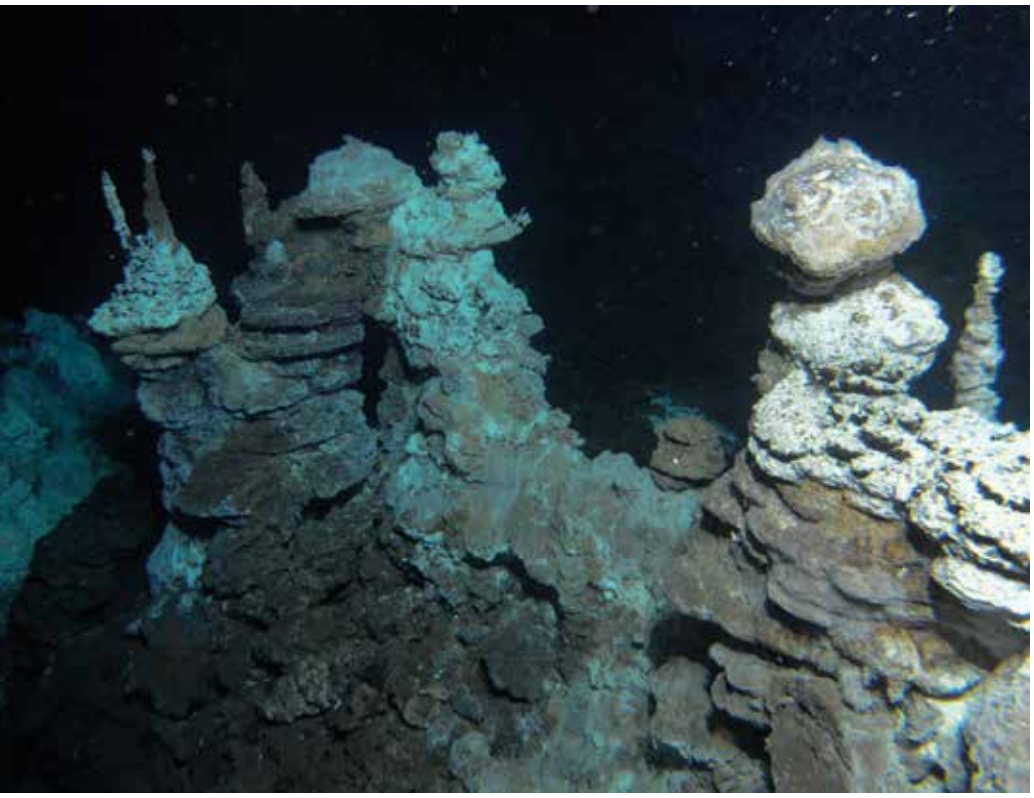


Fig. 3. **Image of a hydrothermal vent field along the Arctic Mid-Ocean Ridge, close to where 'Loki' was found in marine sediments. The hydrothermal vent system was discovered by researchers from the Centre for Geobiology at the University of Bergen, Norway.** R.B. Pedersen, Centre for Geobiology, University of Bergen (Norway)

eukaryotes evolved from an archaeon, how can their membranes contain bacterial-type lipids?

A paradigm gets shifty

For a long time, hypotheses for the origin of eukaryotes were mostly based on cytological observations, and, in the 1980–90s, on limited amounts of available molecular (sequence) data. This all started to change in the genomic era, when newly developed genome sequencing technologies made it possible to perform genome-wide studies to investigate eukaryotic origins. Intriguingly, such studies brought about a paradigm shift: efforts to reconstruct the tree of life started to reveal a picture in which eukaryotes emerged from *within* the archaeal domain (Fig. 2b). In particular, eukaryotes were found to group together with the 'TACK' archaea, a group of diverse archaeal species, which seemingly contain a number of genes that they uniquely share with eukaryotes. These observations were in support of some symbiogenic models for the origin of eukaryotes, which invoked a TACK-related archaeal host cell and an alphaproteobacterial endosymbiont. However, among the TACK archaea, scientists were not able to pinpoint a specific lineage as being more closely related to eukaryotes than the others.

Our microbial ancestry finally revealed

Recently, this story got an unexpected twist. In 2015, a new group of archaea was discovered in deep-sea floor sediments of the Mid-Atlantic Ridge, close to a hydrothermal vent system known as Loki's Castle (Fig.3). By sequencing DNA that was isolated directly from these sediments, we obtained genomic data for a new archaeal group, which we named '*Lokiarchaeota*' – or 'Loki' for short. Fascinatingly, not only did Loki appear to be the closest relative of eukaryotes in the tree of life, but its genome contained a multitude of genes that were only known to exist in eukaryotes. Among these genes were those that play an important role in eukaryotic cell biology – genes that, in a way, make the essence of a eukaryote. Yet, apart from these eukaryotic-like genes, Loki seems to be a typical archaeon. In fact, the role of these genes in Loki is still a mystery. Even more recently, we discovered additional Loki-related archaea and named them after other Norse gods (Thor, Heimdall and Odin); they all contain a large number of 'eukaryotic' genes. These discoveries reinforce the idea that eukaryotes have an archaeal ancestry, and that these ancestors were perhaps 'primed' to become complex. Future studies focusing on elucidating the cell biology and physiology of our closest prokaryotic relatives will likely reveal important clues about how, billions of years ago, complex eukaryotic cells evolved from the much simpler archaeal cells.

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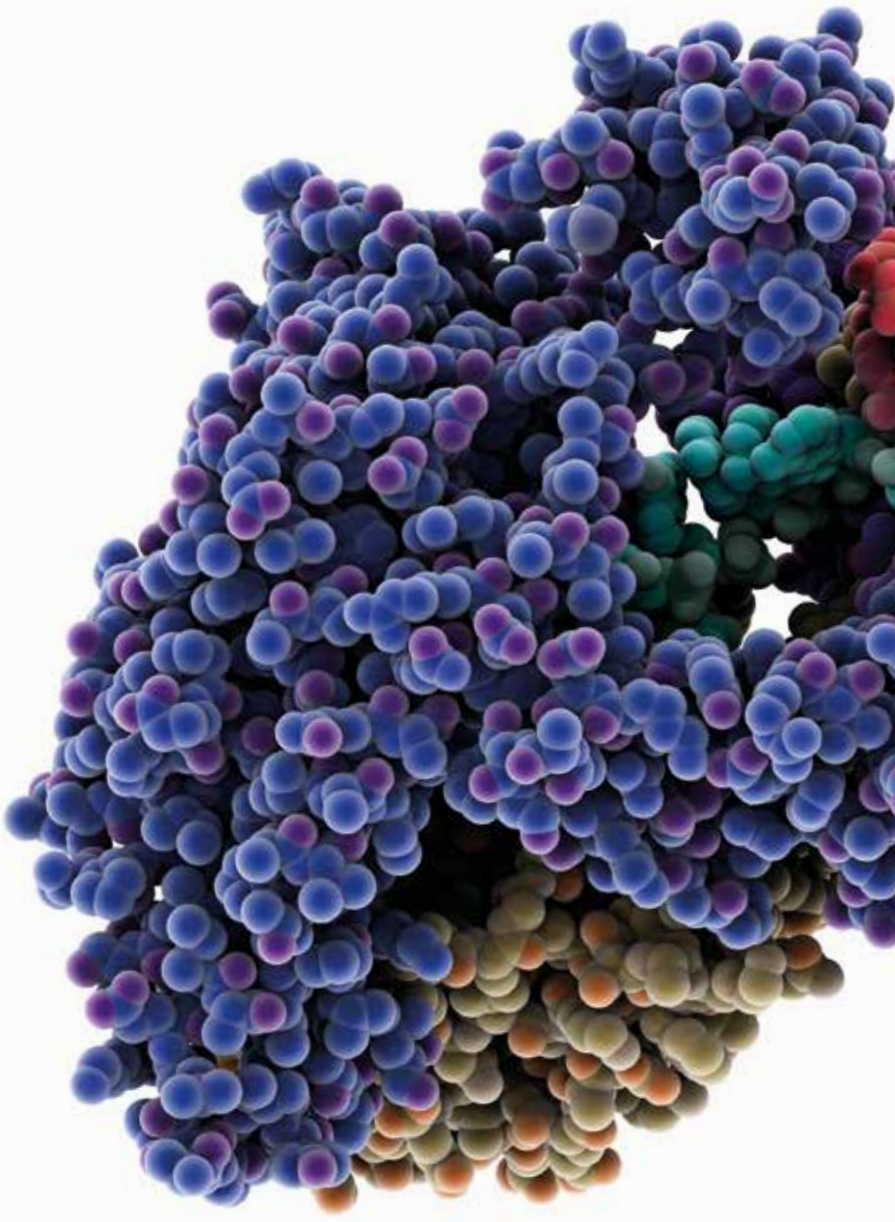
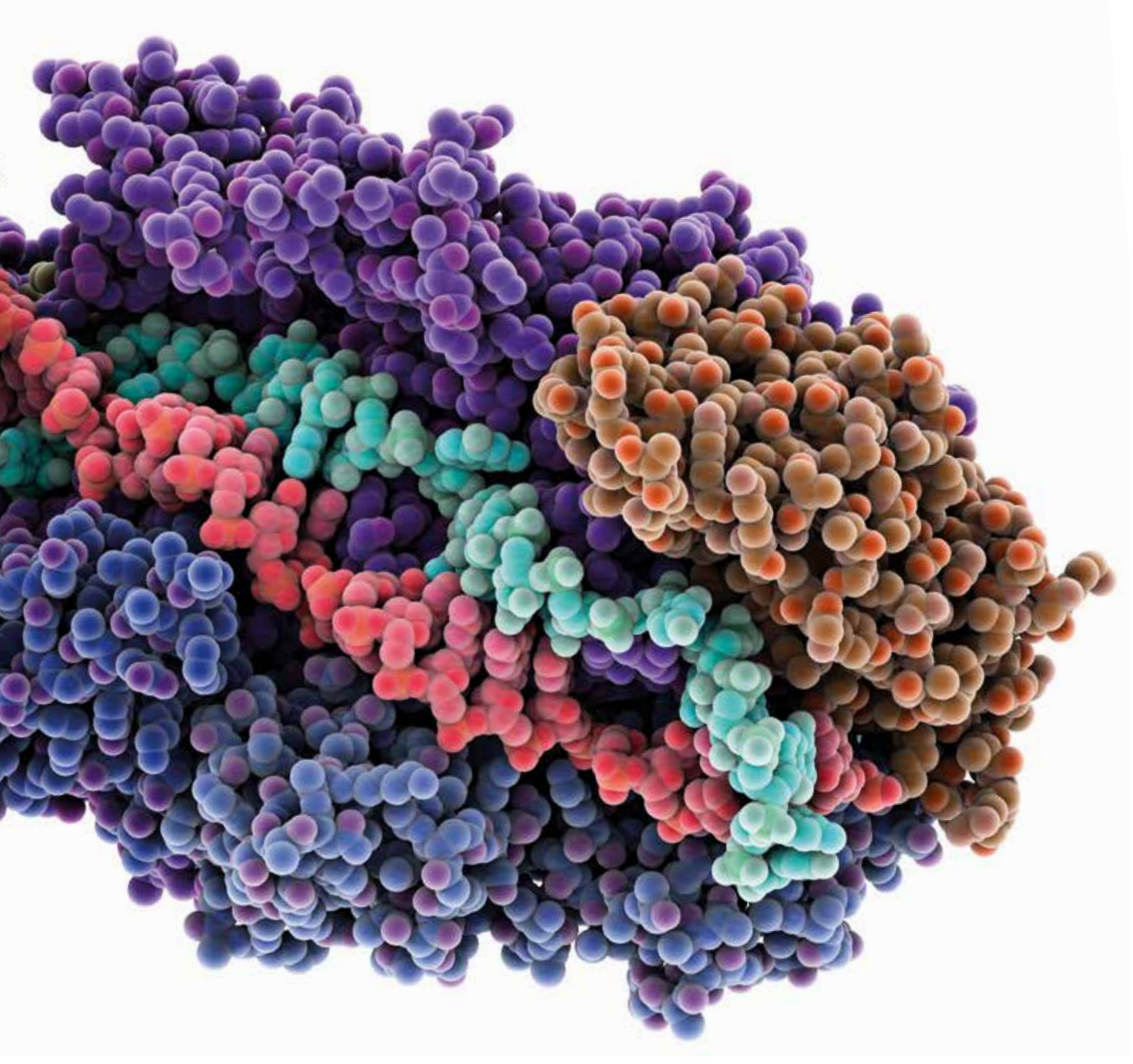


Archaea and CRISPR biology

Qunxin She & Wenyuan Han

The CRISPR-Cas system is an adaptive immune system encoded in prokaryotes to defend against invasion of foreign genetic elements. Current research data indicate that these immune systems are prevalent in Archaea, the third domain of life. Nevertheless, the prevalence probably reflects the fact that many of the current archaeal model organisms co-exist with a wide variety of viruses and are therefore enriched for the antiviral immunity. Furthermore, an additional layer of complexity of CRISPR mechanisms has recently been discovered, such that CRISPR functionality is further modulated by a widespread class of proteins named Cas accessory proteins. For this reason, these archaeal organisms provide unique resources for investigations to uncover the diversity and complexity of the immune system.



Computer model showing the CRISPR-Cas silencing Cmr subunits bound to RNA (cyan) and DNA (red). A number of Cmr atoms have been removed in order to show RNA and DNA. Laguna Design/Science Photo Library

CRISPR-Cas as an anti-viral weapon in prokaryotes

Clustered regularly interspaced short palindromic repeats (CRISPR) and the CRISPR-associated (Cas) system codes for an adaptive immunity in prokaryotes to defend against invasive genetic elements, including viruses and plasmids. The system is composed of CRISPR loci and *cas* gene cassettes. The former contain repetitive sequences that are interrupted by unique DNA sequences (spacers) derived from genetic elements, representing a memory of infection history of invasive genetic elements; the latter code for proteins of RNA-binding, helicase and nuclease domains. The immune system functions in three distinct stages (Fig. 1): first, DNA segments in foreign genetic elements are acquired as new spacers in CRISPR loci (Adaptation); then, CRISPR loci are transcribed, yielding precursor CRISPR RNAs (pre-crRNAs) that are processed to produce mature crRNAs (Biogenesis); and finally, crRNAs guide Cas proteins to specifically target nucleic acids for destruction (Interference).

Antiviral immunity was first demonstrated for *Streptococcus thermophilus*, a lactic acid bacterium, in 2007. Upon the first exposure to a new bacteriophage, most bacterial cells are killed. However, a small portion of cells survive the bacteriophage infection and, commonly, one or more DNA fragments are gained from the bacteriophage genome and inserted into the chromosomal CRISPR loci of the host. Upon the re-occurrence of the phage infection the bacterium is then immune from the infection, and the immunity

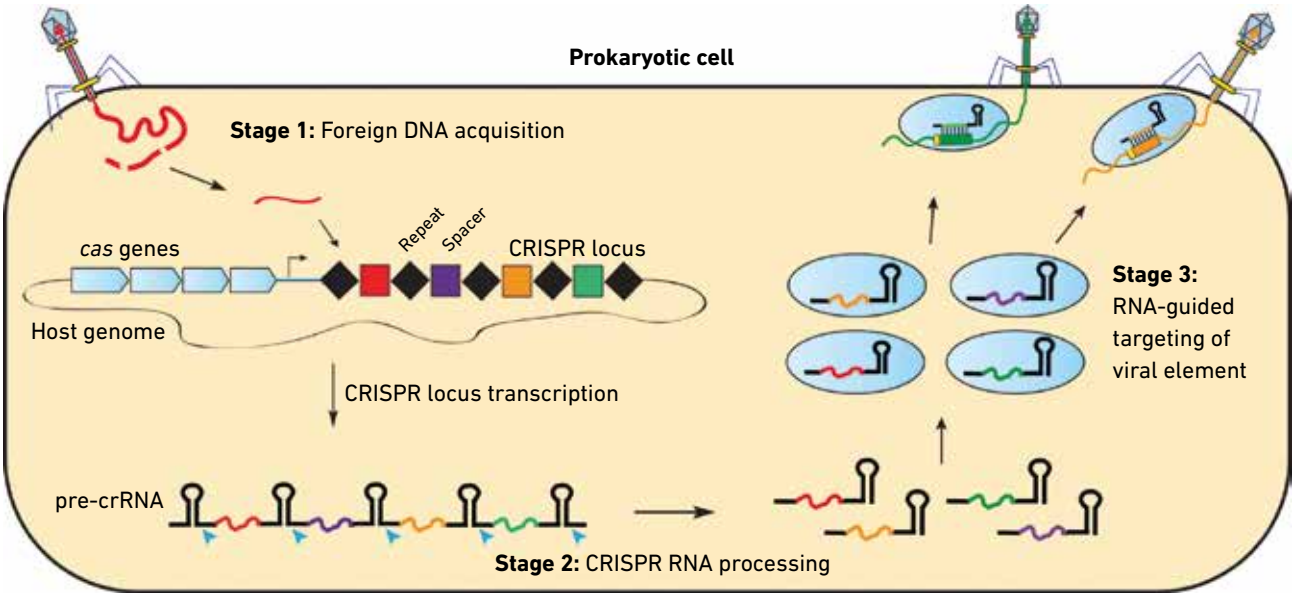


Fig. 1. **Basic mechanisms of the three-step antiviral pathway by CRISPR-Cas systems.** Jennifer Doudna, HHMI/UC Berkeley

relies on the integrity of the CRISPR-Cas system. Investigation of many other CRISPR-Cas systems in archaea and bacteria has revealed that all systems studied function under the same principle. Further studies on CRISPR-Cas effector complexes containing crRNAs and Cas proteins have led to the illustration of molecular mechanisms of target DNA destruction for each type of CRISPR-Cas system.

Striking diversity of CRISPR-Cas systems

The prevalence of the CRISPR-Cas system in prokaryotes allowed the identification of >45 families of Cas proteins in 2005, two years before the demonstration of CRISPR immunity. Most Cas proteins are not well conserved in amino acid sequence, but they form superfamilies of Cas proteins that are structurally and functionally related. Nevertheless, type-specific Cas proteins have been identified. In 2015, a major effort was made in the CRISPR community to classify CRISPR-Cas systems based on conservation of Cas proteins and the molecular mechanisms involved. This has yielded six main types of CRISPR-Cas systems, belonging to two main classes: those of Class 1 require multiple Cas proteins for interference whereas those of Class 2 use a single Cas protein for antiviral immunity. Each type of CRISPR-Cas system has a signature Cas protein, which is type-specific. For example, signature Cas proteins for the three classic types of CRISPR-Cas – Types I, II and III – are Cas3, Cas9 and Cas10, respectively. Furthermore, CRISPR-Cas systems are further divided into subtypes within each type. It is estimated that about 80% of archaea and about 40% of bacteria contain at least one CRISPR-Cas system. Since only a very small fraction of these prokaryotes are known, the diversity of CRISPR-Cas systems is much beyond our imagination. Indeed, a recent investigation by a metagenomic approach has led to the identification of several novel CRISPR-Cas systems.

In addition, some small archaeal plasmids carry a minimal CRISPR locus where no *cas* genes are identified. Nevertheless, spacers in the plasmid minimal CRISPR arrays match some viruses, suggesting that these plasmids could have developed a strategy to hijack the host CRISPR-Cas systems to silence virus infection.

The essence of uneven distribution of CRISPR-Cas systems in Archaea and Bacteria

The huge diversity of CRISPR-Cas systems raises a question as to how the systems evolve. In a CRISPR classification study, it was found that CRISPR-Cas systems show a biased distribution in Archaea and Bacteria. Whereas Type I CRISPR-Cas systems are abundant in both prokaryotic

Focused research in CRISPR biology and biotechnology will greatly increase our understanding of these unique, prokaryotic adaptive immune systems.

domains, all known Class 2 CRISPR-Cas systems are from bacteria, although some uncommon Class 2 systems are predicted in archaea, including a Type V system from the euryarchaeon '*Candidatus* Methanomethylophilus alvus' and two Type II systems from uncultivated nanoarchaea. On the other hand, archaea possess many more Type III systems than bacteria. Due to historical reasons, most known archaea belong to the so-called extremophiles in which CRISPR-Cas systems are prevalent. In particular, all known extremely thermophilic archaea carry more than one CRISPR-Cas system. The same is basically true for thermophilic bacteria. This suggests that CRISPR-Cas systems may have some additional functions that are important for certain physiological groups of organisms such as thermophiles. Interestingly, CRISPR-Cas systems are absent from *Thaumarchaea* and several bacterial taxa, further arguing for co-evolution between CRISPR-Cas systems and their archaeal and bacterial hosts. To this end, the apparent prevalence of CRISPR-Cas systems in archaea may reflect the fact that known archaea are dominated by those containing CRISPR-Cas systems. Possibly, more CRISPR-lacking phyla remain to be identified in Archaea.

Nevertheless, another possible reason accounting for the archaeal prevalence of CRISPR-Cas systems is the occurrence of highly diverse archaeal viruses that infect the archaeal model organisms. Therefore, the arms race between archaea and their diverse viruses may account for the presence of multiple diverse CRISPR-Cas systems in a single cell. In this respect, archaea and their CRISPR-Cas systems provide excellent resources for further studying CRISPR-Cas systems and their biological functions.

Cas accessory proteins as modulators of CRISPR functionality

The complexity of CRISPR biology has been further increased by the identification of a new class of CRISPR-related proteins termed 'Cas accessory proteins'. Their encoding genes are often clustered together with *cas* genes but they also appear in other genomic environments. Some of them are implicated in Adaptation while others, in Interference. They are probably not essential for the process of the three-step CRISPR immunity, but may modulate the functionality of the CRISPR-Cas system. Many of these proteins contain a CARF (CRISPR-associated Rossmann fold) domain, and they constitute the most abundant superfamily proteins associated with the CRISPR system. Cas accessory proteins belonging to the Csx1/Csm6 superfamily are probably among the most interesting ones. They are CARF domain ribonucleases, usually related to archaeal and bacterial Type III CRISPR-Cas systems that mediate transcription-dependent DNA interference. Since these systems require a cognate target RNA to activate the DNA interference, the CARF ribonuclease may modulate the CRISPR immunity by degrading viral transcripts. The mechanisms involved are one of the main focuses in CRISPR biology research, for which several archaea provide good models for investigation.

Development of CRISPR biotechnology

In 2012, Cas9-crRNA complexes were tested as a programmed endonuclease for genome editing, and the principle was soon applied in genome editing of human cell lines and mouse models. This method was termed as CRISPR technology simply because it was developed based on the CRISPR immune principle. To date, the technology has been further developed to extend the application to transcription regulation, genome imaging and epigenetic regulation. The application can also be on a genome-wide scale to assay gene functions. Focused research in CRISPR biology and biotechnology will greatly increase our understanding of these unique, prokaryotic adaptive immune systems, and facilitate CRISPR applications for years to come.

Qunxin She & Wenyuan Han

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qunxin@bio.ku.dk
wenyuan.han@bio.ku.dk

Further reading

Burstein, D. & others (2017). New CRISPR-Cas systems from uncultivated microbes. *Nature* **542**, 237–241.

Makarova, K. S. & others (2015). An updated evolutionary classification of CRISPR-Cas systems. *Nat Rev Microbiol* **13**, 722–736.

Mohanraju, P. & others (2016). Diverse evolutionary roots and mechanistic variations of the CRISPR-Cas systems. *Science* **353**, aad5147.

Tamulaitis, G. & others (2017). Type III CRISPR-Cas Immunity: Major Differences Brushed Aside. *Trends Microbiol* **25**, 49–61.

Annual Conference 2018 #Microbio18

Tuesday 10 April – Friday 13 April 2018
ICC, Birmingham, UK

Annual Conference 2018 will provide another superb programme of microbiology and networking spread over four days, and will include Prize Lectures, symposia, workshops and forums. The schedule is shaping up nicely as we begin to confirm our line-up of speakers and topics, and we are delighted to be returning to the ICC in Birmingham, where we were in 2015.

Abstract submission is open and will close on 11 December 2017. Due to a strict timeframe there will be no extension to this date, so please ensure you submit on time to be in with a chance of presenting your work through an offered talk or poster.

Registration is already open online and, due to the demand in 2017, registrations will be capped every day to avoid overcrowding. Registration will close on 12 March 2018 or sooner if sold out, whichever comes first. Please ensure you have registered before booking any accommodation and travel to avoid disappointment.

Visit our website (**www.microbiologysociety.org/annualconference**) to view all of the information on Annual Conference and follow the hashtag **#Microbio18** for regular updates.

Destination Birmingham

Birmingham has one of the youngest populations in Europe and is a dynamic, creative city that is constantly evolving. It is a natural meeting place in the UK due to its locality and transport links, and is also a crossroads for culture with diverse influences that are easy to spot everywhere in the city.

Boasting something for everyone, whether you're a culture vulture, shopaholic, food enthusiast, party animal or sports fanatic, Birmingham is a destination of limitless opportunity, offering visitors an eclectic mix of things to do. With a compelling and varied arts and social scene, Birmingham is home to inspirational organisations and venues right across the cultural spectrum. Birmingham also has a growing reputation as a foodie haven, is a critically acclaimed host of independent festivals and has a year-round calendar of world-class sporting events. Visit **www.visitbirmingham.com** to find out more about our 2018 location.

Accommodation

The ICC Birmingham is a fantastic destination as it is easily accessible from around the UK and abroad, plus there are many hotels within walking distance, and plenty of restaurants and attractions nearby.

To aid you with securing your accommodation for Annual Conference 2018, you can visit our website where we have provided a link to our booking service, Reservation Highway. Reservation Highway has negotiated rates at local hotels to suit a range of budgets and will be able to accommodate single occupancies, double rooms, group bookings and family rooms. Please ensure you register for Annual Conference before arranging your accommodation.

Travel arrangements

By car

The ICC is located centrally in Birmingham city centre and is easily accessible by road from across the UK. Visitors can travel in to Birmingham using many different routes connected to the following motorways: M1, M5, M6, M6 Toll, M40 and M42.

Car parking

There is a secure multi-storey car park located within the sister venue, the Barclaycard Arena, which is just a short walk away from the ICC. Both the ICC and Barclaycard Arena are signposted on motorways and major roads, and are marked on most road maps. The North car park is closest, or alternatively simply follow the road around on to St Vincent Street for the West car park, or carry on further around to Sheepcote Street for the South car park.

Current charges are from £2.50 for up to two hours to £15.00 for 24 hours. Payment can be made at the Pay and Display machines or online. Full cark park charge details can be found on


ICC Birmingham

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

the Barclaycard Arena website (**www.barclaycardarena.co.uk**).

Alternative parking is located at Brindleyplace or Paradise Circus.

By air

Birmingham Airport (**www.birminghamairport.co.uk**) is well connected and has over 50 airlines operating scheduled and charter services to more than 100 destinations including Europe, North America, the Middle East and the Indian sub-continent. The airport is just eight miles from the city centre and is directly linked to Birmingham International railway station via an Airlink Shuttle.

The smaller East Midlands Airport (**www.eastmidlandsairport.com**) is 42 miles away. The closest London airport is London Luton Airport (**www.london-luton.co.uk**), which is 92 miles away, and London Heathrow Airport (**www.heathrow.com**) is 107 miles.

By rail

The ICC is served by the UK's largest interchange rail station, Birmingham New Street, and the smaller Five Ways station (**www.nationalrail.co.uk**). Both stations are a short walk from the ICC, and taxi ranks are situated close by. Birmingham New Street has direct and regular services to Birmingham International railway station, which directly links to Birmingham Airport and the NEC. It also has many direct services to London Euston, including a service that takes about 80 minutes and runs every 20 minutes.

Birmingham's two other city centre train stations, Moor Street and Snow Hill, are also within quick and easy access of the ICC and directly connected to London Marylebone or London Paddington via an hourly service.

Virgin Trains (**www.virgintrains.co.uk**) offer discounted group travel for groups of between three and nine passengers travelling together. This currently stands at a 20% discount off Advance Fares booked through their website – for more information visit the group page of their website.

By coach

For information about travel by coach please visit the National Express website (**www.nationalexpress.com**).

Programme 2018

Below is a list of the session topics for our 2018 Annual Conference. Visit our website for speaker information and scheduling:

Main symposia*:

- Biological insights from studying new eukaryotic models
- Cool tools for microbial imaging
- The battle for the ribosome – how viruses manipulate host translation
- Bacterial zoonoses: ecology, epidemiology and evolution
- Breaking bad: factors affecting the commensal to pathogen
- Community interactions and the living host
- DNA repair
- Emerging model systems
- *Escherichia coli*: the model microbe
- Microbial diversity and interactions in the environment
- Microbial metal homeostasis: impacts on pathogenicity
- Models for understanding host–pathogen interactions
- Synthetic ecology: from understanding ecological interactions to designing functional microbial communities
- The games microbes play: competition, conflict and cooperation in microbiology
- The global virome
- The magic of mushrooms in nature and industry

Virus workshops:

- Clinical virology
- DNA viruses
- Negative strand RNA viruses
- Phylogeny
- Plant viruses
- Positive strand RNA viruses
- Retroviruses

Prokaryotic and eukaryotic forums:

- Environmental and applied microbiology
- Genetics and genomics
- Microbial infection
- Microbial physiology, metabolism and molecular

**Titles subject to change*

Focused Meetings and Events update

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

#AgriFoodSec17

Focused Meeting: Microbial Resources for Agricultural and Food Security

The first in our series of Focused Meetings this year took place in June at the Metropolitan Arts Centre, Belfast.

Invited speakers from local and international institutes presented their research in Microbial Resources for Agricultural and Food Security. The All Island Phosphorus Sustainability Workshop hosted the water utilities across Ireland, along with regulators and agri-food companies.

The three-day meeting included plenty of networking opportunities as well as poster presentations and offered papers during the programmed talks.

#ISSY33

International Meeting: ISSY33 Exploring and Engineering Yeasts for Industrial Application

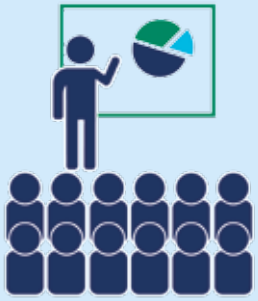
At the end of June, the Society hosted the 33rd meeting of the International Specialised Symposium on Yeast (ISSY33) at University College Cork in Ireland. We welcomed over 250 attendees from around the world, including Brazil, Japan and South Africa. We were delighted to receive over 200 abstract submissions, all of which formed an invaluable programme of talks and posters. As well as the impressive scientific programme, delegates had several fantastic networking opportunities, including evening receptions and a conference dinner held at the beautiful Ballymaloe Grainstore venue.

James Woods, School Of Microbiology, UCC

Applications welcome

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 speaker costs. Applications are welcome for any meetings taking place in 2018, and the next closing date is 15 December 2017.

Further information and application guidelines can be found at **www.microbiologysociety.org/SSconferencegrants**, and you can view the events we have sponsored in 2017 within our events listings online.



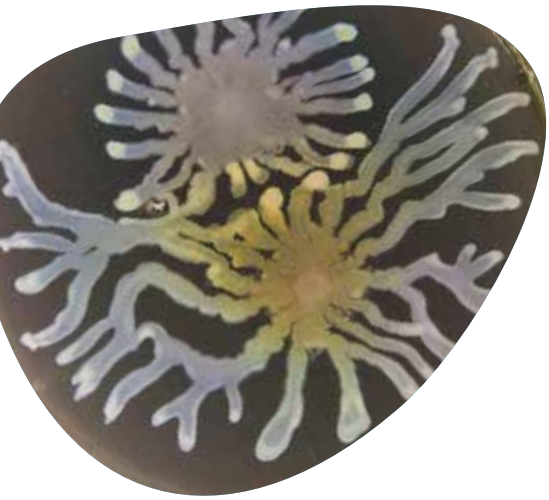
MICROBIOLOGY SOCIETY

UPCOMING Society Events

Focused Meeting

Antimicrobial Resistance and One Health

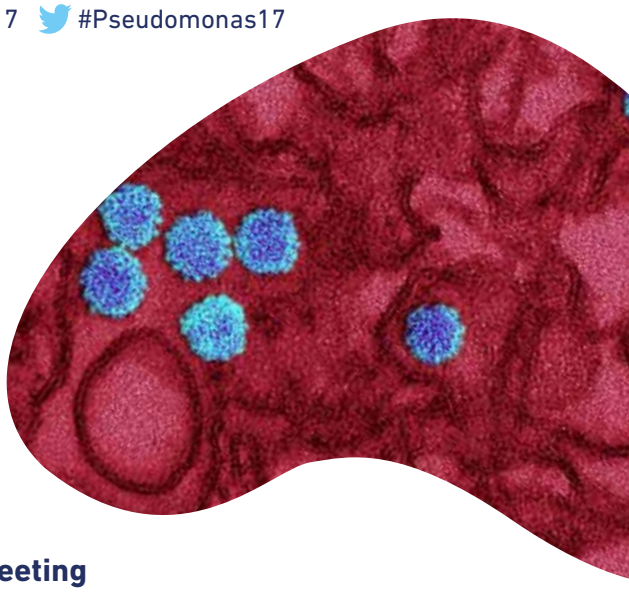
29–30 August 2017
Maynooth University, Co. Kildare, Ireland
http://microb.io/AMROneHealth17 #AMROneHealth17



Focused Meeting

16th International Conference on Pseudomonas

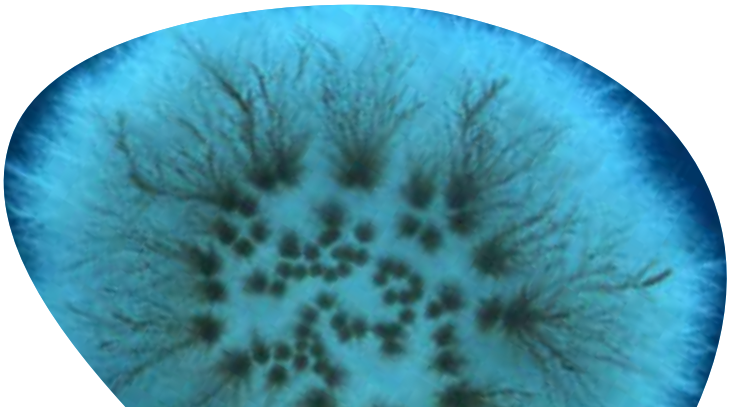
5–9 September 2017
St George's Hall, Liverpool, UK
http://microb.io/pseudomonas17 #Pseudomonas17



Focused Meeting

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

7–8 September 2017
University of Glasgow, UK
http://microb.io/IMAV2017 #IMAV17



Focused Meeting

British Yeast Group – The Versatility of Yeasts

11–13 September 2017
University of Kent, UK
http://microb.io/BYGVOY17 #BYGVOY17

Microbiology matters more than ever, and we want to make sure that the Society is well placed to serve you, our members, and the wider research community.

We're putting a few things in place to help us achieve this. Firstly, we will be launching a new five-year strategy for the Society that is putting members at the heart of everything we do. This strategy will come into effect from 2018, and will help empower you to build communities and achieve your aims. We want to give you all the opportunity to shine and make your voices heard.

We're also responding to the feedback you've given us as part of the Member Engagement Project, or when you've met staff at our conferences and events. Some of what we're doing is behind the scenes – you won't see any major changes to the way we look, but you will see some differences in the way we operate.

For example, we're streamlining the registration process for our events to save you time. We'll be improving our communications, so you'll get information that's relevant to you, in the way that you want to receive it. We're also adjusting our membership categories to ensure that they work for you, wherever your career takes you.

One of the first things you'll see is the return of the Member Directory, which will help you connect with other members of the Society. We hope that the Directory will assist you in developing networks and collaborations to further your research and career. Members will be encouraged to create and update their listings/ profiles when the Directory launches later in the year.

We think these changes are important and will help us provide a Society experience that is better suited to you. Microbiology has come a long way since the Society was founded in 1945. We want to help you take it even further.

Sarah Buckman

Director of Strategy and Members' Programmes

Membership

Good news: the Member Directory is coming

A recurring theme of the recent membership research work, undertaken over the past 12 months, has been the request for more information about other members – who they are, where they are based, what are their specialisms? The list was long and clearly indicated a wish for members to be able to engage more with others to share, learn and network.

Longer-standing members may remember we used to produce a Directory. The good news is, we are bringing it back. But this time it will be online and sit on our website, accessible to members only, by password only. The aim of it is to provide those members with opportunities to engage more with others and to have a platform and a presence within our community. There will also be the facility to make contact via email too, although individual email addresses will not be visible to others.

However, for the Directory to be useful, it requires the widest possible participation of the membership from day one. A Directory with only a few entries is not a Directory. It's a disappointment! That's why it's important to have as many of you as possible listed within it as quickly as possible. If we waited for members to list themselves, we would be waiting a long time for the Directory to achieve the critical mass needed to make it immediately useful.

That's why we intend to take the following actions to populate the Directory to get it up and running.

The first will see the automatic inclusion of every member's basic information, to include the following (where available):

Member name
Member title
Organisation name
Membership grade
Microbial group
Microbial interest
Town
Country

Most of this is available in the public domain already, but the Directory will help by bringing it all together into one place.

The second will see members being encouraged to update their entry with additional information, or to list themselves if they haven't yet done so.

The Directory will become a useful tool for finding other members in and around your place of work or study; for finding members with interests in similar fields; and by providing a platform from which you can communicate with others. In future you will be able to add additional content including a biography and photo (should you wish) by logging directly into the members' only area of the website.

We would strongly encourage you to become a part of the Directory and enjoy the benefits it will potentially bring to you and help create for others too.

However, if you would prefer not to be listed you need to let us know. You can do this by emailing **members@microbiologysociety.org** or writing to us at:

Membership Office
Microbiology Society
Charles Darwin House
12 Roger Street
London
WC1N 2JU

Please let us know by Friday 8 September 2017 if you do not wish to be listed in the Directory. If you are happy to appear in the Directory, you need take no further action.

If you have any questions in relation to the Directory, please get in touch.

Paul Easton
Head of Membership Services
p.easton@microbiologysociety.org

Publishing

CRISPR-Cas Article Collection in *Microbiology*

Microbiology is celebrating 70 years of publication this year and we are excited to have launched such an important collection, showcasing the high-quality research on CRISPR-Cas in the journal. As the flagship journal of the Microbiology Society, it is important to feature areas of research that are having a wider impact and highlight the research that has been reported in Society publications.

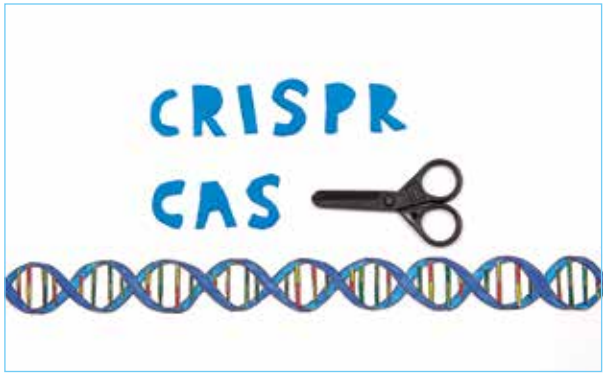
All papers in the collection have been submitted to *Microbiology* over the years and have been collated by *Microbiology* Senior Editor Victor Cid form the Complutense University of Madrid. To read this freely available CRISPR-Cas collection visit: **http://microb.io/2m7DUvU**.

Francisco J. M. Mojica at the University of Alicante, an author for *Microbiology*, summarises the introduction of CRISPR and its growing importance within the microbiology community and society:

'The search for knowledge for its own sake might not need any defence: curiosity is inherent to the human condition. However, contribution of scientific discovery to the progress of humankind may be a matter of dispute.

Basic researchers set out on adventures, with indefinite boundaries, aimed at understanding aspects of the subject under study. Once this goal is achieved, producing benefits beyond wisdom is only a question of time.

Thirty years ago, curious DNA repeats, currently referred to as CRISPR, were found in the genome of a bacterium. Soon after, similar regularly spaced repeats were also discovered in distantly related prokaryotes, evidencing that they might be biologically relevant. Even though experiments reported in the mid-1990s supported their functionality, the specific role played by the repeat locus remained puzzling for more than a decade.



In 2005, the mystery was unveiled: CRISPR cassettes witness genetic intrusions. This surprising revelation caught the attention of researchers in diverse fields within life sciences, notably microbiologists who, during the following few years, confirmed CRISPR-based adaptive immunity and deciphered the underlying mechanism. Multiple uses emerged from this basic study on the biology of prokaryotes. Initially, applications [were] framed within microbiology and biotechnology.

Subsequently, extraordinary DNA-manipulation tools were implemented with components of this immune system and CRISPR spread into other fields, from agriculture to medicine, triggering an unprecedented revolution in science. Indeed, prokaryotes can undertake a sort of rudimentary learning, based on previous experiences. We should also learn from this lesson what the value of basic research is."

If you would like to submit a paper to *Microbiology* on CRISPR-Cas or within another subject category, use our online submission service: **www.editorialmanager.com/mic**

To read more about *Microbiology* and the scope of the journal, visit the journal website: **http://mic.microbiologyresearch.org**

What's new?

JMM Case Reports and *Microbial Genomics* are now indexed in PubMed Central (PMC), and all articles published in the journals can now be found on PMC. PMC is a free full-text archive of biomedical and life sciences journal literature at the US National Institutes of Health's National Library of Medicine (NIH/NLM).

Microbial Genomics is now indexed in Medline, making all work published widely visible and easy to discover to anyone using PubMed.

Did you know that as a member of the Microbiology Society you are entitled to discounts for open access publication, or a discount on subscription fees to Microbiology Society journals (print and online)? As a not-for-profit organisation we work to bring our profits back into the Society for the benefit of our members. Members who are corresponding authors can receive up to 15% discount on Open Microbiology fees when publishing in any of the Microbiology Society journals. There is also a discount for subscriptions to the journals. For more information contact **journalsales@microbiologysociety.org**

Check out our latest Microbe Profiles (**http://microb.io/2mcFeR6**) and ICTV Profiles **(http://microb.io/2s0Z9p3**). These are series of concise, review-type articles, freely available on **www.microbiologyresearch.org**. The profiles are written by leading experts in the field, providing overviews of the classification, structure and properties of the featured taxa, and are an excellent educational resource.

Here's to 70 more years of *Microbiology*:

Dr Tanya Parish, Editor-in-Chief

Ever wondered what an Editor-in-Chief does? Well, at the *Microbiology* Editors annual meeting during the Microbiology Society's Annual Conference, we discussed current events in publishing and microbiology – making plans for the year ahead.

So, what's been happening in *Microbiology* this year so far?

In January we launched a new article type: 'Short Communications' where authors can publish smaller pieces of completed work that warrant attention but might not be as long as a full paper.

In February we published our first Microbe Profile, on the notorious pathogen *Escherichia coli* O157:H7 (**http://microb.io/2mcFeR6**). These short articles provide a digestible introduction to key organisms relevant to our readers. We also launched the CRISPR-Cas article collection (**http://microb.io/2m7DUvU**) which offers easy access to related papers of interest in one place.

Finally, we now have a direct link with bioRxiv, allowing authors to submit directly to *Microbiology*, providing an even easier route to getting your work published!

As Editor-in-Chief, it's great to see the journal continue to grow and develop, while still providing a home for high-quality research. We've been around for 70 years, and we hope that we continue being your home for microbiology for the next 70.

Microbiology Society journals now accepting direct submissions from bioRxiv

The Microbiology Society is delighted to announce that authors who post their manuscripts on bioRxiv will now be able to submit their papers directly to the Microbiology Society's suite of journals!

bioRxiv is an online archive and distribution service for preprints in the life sciences. It is operated by Cold Spring Harbor Laboratory, a not-for-profit research and educational institution. The Society has always supported posting to preprint servers, and this new collaboration will save authors time when submitting papers, by transmitting their manuscript files and metadata directly from bioRxiv.

Outreach

Antibiotics Unearthed

After a successful series of pop-up events in the summer of 2015 and 2016, the Antibiotics Unearthed Team were out again at Thetford Forest in May, crowdsourcing for new antibiotics.

Antibiotics Unearthed gives the general public, students and educators in the UK and Ireland the opportunity to work with scientists as part of a global initiative to discover new antibiotics from soil bacteria. The pop-up events encourage members of the public to get engaged with the topic of antibiotic resistance and be involved in research looking for new drugs.

In May, people visiting Thetford Forest could take a sampling kit around the forest with them, collect a soil sample and prepare a spread plate of their sample when they returned to see the bacteria present in the soil. These samples were then deposited in our soil bank, and sent to the University of East Anglia for analysis.

Visitors to the stand were welcomed by a team of expert volunteers (you can read about their work further on the website – **www.microbiologysociety.org/antibioticsunearthed**) and were informed about searching for new antibiotics in the soil, the methods used to look for new medicines and the threat of antibiotic resistance.

Samples were submitted by visitors to the forest, who are being kept updated with the analysis of the samples at the University of East Anglia via email and social media.

If you would like to know further about the project, contact the Antibiotics Unearthed Team (**antibioticsunearthed@microbiologysociety.org**).

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

Children at an Antibiotics Unearthed event.

The Antibiotics Unearthed team will be at the Glasgow Botanic Gardens on **Thursday 7 September 2017**.

TeaTime Science

Microbiology Society members Amy Easey and Michael Norman have set up their own outreach and communication social media platforms to make science and microbiology more engaging to the public. Below details their experiences and how they came to set up TeaTime Science.

Amy

I studied for my undergraduate degree in Biomedical Science at the University of Hertfordshire. Afterwards, I went on to become a trainee bar manager for a little while before returning to science as a DNA analyst at LGC forensics. After seeing an advert for a PhD I liked the look of, I have now ended up at the University of East Anglia! I'm in the third year of my PhD, researching ways to make ligases work better. Ligases are involved in DNA and RNA repair pathways and are valued tools in microbiology; the better they work, the better we can work!

Mike

I did my undergraduate degree in Microbiology at the University of East Anglia and then went straight on to doing my PhD where I research extracellular electron transport in the rock-breathing bacteria *Shewanella*. By understanding this process better, we hope to improve their use in microbial fuel cells to generate more energy.

Michael Norman and Amy Easey. TeaTime Science

Hands on demonstration. TeaTime Science

Having both come from small rural towns and being the first in our families to go to university, we're very interested in getting more people interested in science. While doing our PhDs we decided to start up a social media account dedicated to talking about science and showing the normality of life in science. This was the start of **@TeaTimeSci** on Twitter and Instagram! We post interesting science stories, publicise outreach events, explain our lab work and show the funny side – especially when things go a bit wrong! We have been to schools to talk to students about our research and how we got into science. This was a great experience and we got people who had never considered doing science before thinking about it seriously. As TeaTime Science we also hosted an online Q&A session for university undergraduate students to help answer any questions they had about careers after graduation. We took in questions, many about specific careers, and then got in contact with people who had gone on into those careers after they had graduated, to help answer these questions. We then tweeted out the questions and the answers and got a discussion going about different opinions and experiences.

We were part of a small team who organised three nights of science talks and demonstrations in a pub for Pint of Science 2017. Our theme was tech and we had a range of talks covering everything from microbial biotechnology through to AI, and how big data is used in healthcare. To help further explain the science in the talks, we had activities for people to do, including virtual reality experiences, 3D printers and grow your own protein crystals.

Last year a new branch of the British Science Association was set up in Norwich so we decided to get involved in that too! We're now co-publicity officers for the branch and together with six other members (many are fellow PhD students) we organise and run events to promote science to the public. We put on a science treasure hunt around Norwich city as part of British Science Week (**#NorwichSciHunt**) and had six stalls, run by volunteers, each focused on different science topics. People were given maps with clues leading them to the stalls where they could then take part in an activity or demonstration explaining some science. The event went down really well, with around 1,000 people taking part. We've had stalls at many other events throughout the year, each with specific themes, from the scale of our solar system to superhero bacteria! Coming up soon, we're putting on a forensics-themed activity during Norwich Science Festival in October so keep an eye on **@BritSciNorwich** to see how that goes!

It's so easy to do outreach and there're loads of opportunities! We would recommend everyone try it because you can make such a difference. If you're unsure of how/where to look please drop us a message and we will happily point you in the right direction.

Amy Easey and Michael Norman
University of East Anglia
@TeaTimeSci

Infection diagnosis in the UK

UK Standards for Microbiology Investigations are a valuable resource for microbiologists working in diagnostics labs, the clinic and in research.

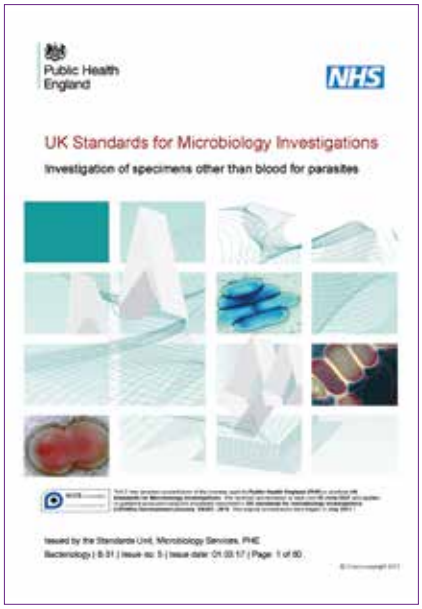
When a specimen is collected by a GP or hospital doctor for microbiological analysis, it is sent to a diagnostic laboratory. As these laboratories are increasingly outsourced to the commercial sector, what tests and procedures are considered 'standard' and should be performed? The UK Standards for Microbiology Investigations (UK SMI) develops these guidelines and welcomes consultation and feedback from the microbiology community. UK SMIs are used by practicing laboratory professionals, clinicians and commissioners of healthcare services. All of the standards are also openly available online, providing a great resource for any microbiologist wanting to know how infections caused by the pathogens they work on are diagnosed.

The Microbiology Society is one of 24 professional and learned societies and UK Government public health agencies that work together to develop and update UK SMIs, and the process is administered by Public Health England. The Microbiology Society is represented on the UK SMI Steering Committee, and you might have noticed that SMI documents that are under consultation or that have been recently released are advertised in the Society's monthly newsletter.

There are over 100 SMI documents. Some cover particular types of specimens or procedures, and they include background clinical and diagnostic considerations, specimen taking and transport, processing, culture, identification, susceptibility testing, reporting and notification procedures. Other UK SMI documents go into further details of how species are identified in the laboratory, how specific diagnostic tests are performed, or provide guidance for clinicians about which tests should be requested.

Every few years each document is updated, ensuring that they are evidence-based, eligible for NICE-accreditation and are appropriate benchmarks for recognition by the NHS. During updating, each UK SMI document is re-drafted by a committee of experts and then released for public consultation. Any microbiologist can submit comments on a document during consultation, and feedback from the microbiology community is encouraged and welcome. Comments are considered, and a finalised document is approved and issued.

As microbiologists, we don't all have access to diagnostic laboratories or are able to keep up with changes in diagnostic practice. The UK SMI documents are therefore a valuable resource to broaden our understanding of the clinical and diagnostic challenges regarding our favourite pathogens. They are also a fascinating teaching resource for our students. Ultimately, the UK SMIs are produced to ensure that the quality of diagnostic services remains high in the UK, and the health of the public is protected.



A UK Standards for Microbiology Investigations document. Public Health England

UK SMI documents and further information can be found at **https://www.gov.uk/government/collections/standards-for-microbiology-investigations-smi**. Interested members can also contact the Society's Policy Team (**policy@microbiologysociety.org**) or SMI Steering Committee representative Professor Jodi Lindsay (**jlindsay@sgul.ac.uk**).

Jodi Lindsay
Professor of Microbial Pathogenesis, St George's, University of London
j.lindsay@sgul.ac.uk

A flash poster session at the 2017 Annual Conference in Edinburgh.

Early Career Microbiologists' Forum Update: Conference highlights and prize winners

Now that the dust has settled from April's Annual Conference, I thought this would be a great opportunity to reflect on the fantastic contribution made by early career microbiologists to the whole week.

The early career networking event that kicked off the Annual Conference received lots of positive feedback, with attendees feeling that they got more out of the session than in previous years. The 'networking bingo' provided a simple but effective way to encourage people to move around groups and interact with more people than they would have otherwise. The evening then continued to the pub for some more informal socialising, organised by the ECM Forum Committee, which seemed to go down well too!

The quality of talks given by ECM Forum members was really impressive; subjects including autophagy in flu viruses, the use of antimicrobial peptides against MRSA and the characterisation of small colony variants were my personal highlights. It was great to see so many offered orals knitting seamlessly into the sessions. The Forum also supplied several co-chairs, something that we are hoping to see more of at the next Annual Conference.

The flash poster talks, several given by ECM Forum members, were excellent; it is a real skill to condense your work down into a couple of minutes. The lunchtime flash posters were well attended, and hopefully presenters will have found the experience to be useful as well increasing footfall to their posters.

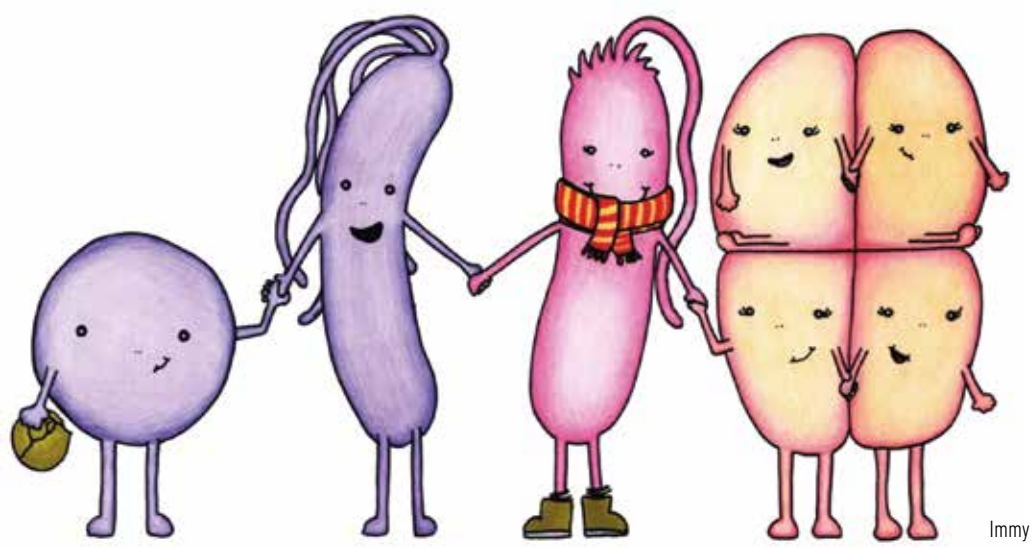
We were delighted to announce Michael Norman, University of East Anglia, and Ana da Silva, University of Nottingham, as the winners of the inaugural ECM Forum poster prize. We couldn't decide between them! Ana said, "Thanks to everyone for all their helpful insights. It is apparently a good idea to include an experiment with unexpected results to trigger interesting discussions!" Michael, who also received an Editors' Choice prize for his poster, was delighted to be chosen: "I felt really happy but also surprised, especially when I found out I'd won two prizes! It was great to talk to people about my research in a relaxed setting. People seemed genuinely interested, and I'm glad it was well received." The quality of the posters was very high with many deserving candidates and it prompted a lot of discussion amongst the Committee to decide on the eventual winners.

The Committee followed up the Annual Conference with the first in a series of annual Summer Roadshows exclusively for ECM Forum members. For 2017 these took place in Birmingham, Leeds and Glasgow. We hope that ECMs agree that they provided a platform for forming new connections with other early career researchers but, above all, they were really enjoyable too!

If the Conference has inspired you to get involved with the Society then you can sign up to the ECM Forum via the website. This will give you access to grants and a range of other benefits, including attending the Roadshows and participating in the co-chair scheme. As always, feel free to drop us an email if you have any ideas or questions.

Rebecca Hall
Communications Representative,
ECM Forum Executive Committee

Schoolzone



Immy Smith

Meet the Microbes

Society member, Naomi Chant, has written an e-Book to introduce the public to the world of microbiology and the microbes that surround us. Below, in her words, she tells us about the book and how she came to develop such an interesting resource.

Meet the Microbes is an e-Book aimed towards young readers (Key Stage 3), giving them an introduction to the weird and wonderful world of microbiology. Starting with Louis Pasteur and his discovery of germs, *Meet the Microbes* takes readers on the journey of learning about the good and the bad microbes that we live with everyday.

The book is an outcome of *I'm a Scientist, get me out of here!*, a science outreach event where students interact with scientists, voting for their favourite to win a cash prize to communicate their science to the public. Over two weeks, students aged 12–18 could ask any question they wanted in live chat rooms. It was a fantastic form of interaction as the students were more candid than in the classroom, and, as a result, I got insight into their knowledge gap when it came to microbiology and what they wanted to know about microbes.

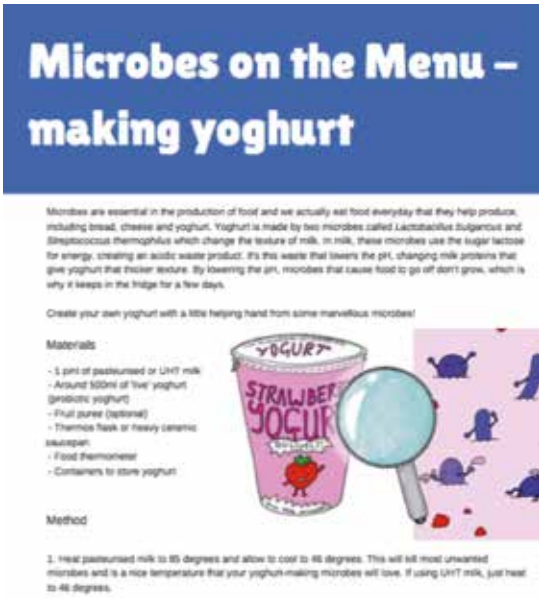
The questions the students asked, such as "How big are bacteria?" and "What do they look like?", inspired me to produce a resource that would provide the answers in an accessible format that could be used by people at home and in the classroom. I decided to make an e-Book available online that featured microbial characters and covered important microbiological topics using colourful illustrations with the thanks of the talented artist Immy Smith.

The microbes that feature in the book have names that are easier to remember than their scientific names, and I wanted them to be distinct based on what they look like (such as their colour representing their Gram stain), where they live or what they do, rather than a generic nasty-looking bug that you sometimes see. Characters in the book include menacing and mischievous microbes that cause infections, such as Mike O'Bacterium (*Mycobacterium tuberculosis*), as well as the marvelous and magnificent ones, such as Luke Onostock (*Leuconostoc mesenteroides*), that do helpful things such as making food and cleaning up hazardous waste.

Using colourful illustrations, important concepts such as taxonomy,

antibiotic resistance and infection control are covered, incorporating techniques such as mnemonics to aid remembering classification of microbes, something that I learnt in school and still find useful now. Readers can also become microbiologists themselves by carrying out experiments throughout the book. From growing their own microbes to identifying the source of an epidemic, the experiments in the book give a taste of jobs that microbiologists do in the real world and can be used as tools to promote microbiology in the classroom, using just a few simple materials.

Two of the microbial characters from the book, Mike O'Bacterium (*M. tuberculosis*) and Emma Essay (meticillin-resistant *Staphylococcus aureus*, MRSA). Immy Smith



Microbes on the Menu – Making Yoghurt, one of the experiments in *Meet the Microbes*. Immy Smith

Despite a large number of the characters in the book being bad microbes, they make up a tiny fraction of the micro-organisms that surround us all the time and it is the majority that keep us healthy, help our ecosystem and make some of the foods that we eat – this is the take-home message from *Meet the Microbes*, and I hope that the more people that read the book will become enthused about the wonderful world of microbes.

The e-Book can be downloaded from **www.meetthemicrobes.com**. Printable experiment handouts can also be found in the teacher resources section of the website.

Naomi Chant
Meet the Microbes
@naomi_chant

Membership Q&A

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

A. Mitra

Where are you currently based?

Adamas University, West Bengal, India.

What is your area of specialism?

Bacterial pathogenesis, biofilms and vaccines.

And more specifically?

Understanding the regulation of virulence in bacterial pathogens, and the role and mechanism of bacterial biofilms from clinical, food and environmental sources. I also develop vaccines for veterinary and human use.

Tell us about your education to date.

I obtained my bachelors in Pharmacy and my masters in Biotechnology from Jadavpur University, India. I then received a PhD in Microbiology from the University of Maryland, USA. This was followed by postdoctoral research at Arizona State University, USA. I have also received a Diploma in Business Management from the Institute of Management Technology, Ghaziabad, India.

Where did your interest in microbiology come from?

I was a Rotaract member (youth wing of Rotary International) during my college days. At Rotaract, we organised a free polio vaccination camp for infants as part of the community outreach activities. This was my first experience of working with vaccines and microbiology. I didn't know that one day I would be developing vaccines myself!

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

A major challenge is the development of research laboratories in university settings to perform quality research work. To address this, I have previously set up research laboratories in two universities, and also at my current university, Adamas University. Staying up-to-date with new methods of teaching and research are essential for imparting quality education too. A broader challenge is making the students and public aware of the role of science in society, and why it is crucial to fund research on infectious diseases and the development of therapeutic strategies. Being a Microbiology Society Champion has helped support this. As a Champion, I organised a workshop in my university with students focusing on the role of vaccines in combating infectious diseases, such as smallpox and polio.

What is the best part about 'doing science'?

Science is a dynamic process. Learning from results based on the careful design and execution of experiments can be very stimulating. It is equally exciting to learn from peers and leaders about cutting edge science in seminars and at conferences. Reaching out to the public through outreach activities is equally important as well. Also, making one's work known through peer-reviewed publications is essential for the progress of science. This is where open access publishing plays a very important role in bringing science to the public without barriers.

Who is your role model?

Mentors during my masters, doctoral and postdoctoral work have definitely broadened my approach towards science. I was also fortunate to meet many devoted, humble scientists at conferences and seminars. Each of those scientists inspired me through their speeches, discussions and willingness to make a difference in society.

What do you do to relax?

I find listening to music and playing my guitar can relieve stress. In addition, outdoor activities, such as hiking and rock climbing, as well sports, such as cricket, table tennis and badminton, are also refreshing. Once, I had an amazing experience of tandem skydiving from 13,000 feet!

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

It is not easy to choose a single record but it would be REM's *Automatic for the People*. With regards to the luxury item, I would take my guitar (and, if possible, a jet pack to travel around the island!).

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

Possibly, they may not know what kind of music I listen to.

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

I considered physics, engineering, pharmacy and management as career options, but microbiology and exploring the exciting field of microbes interests me the most. Possibly science public engagement would have kept me busy.

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**

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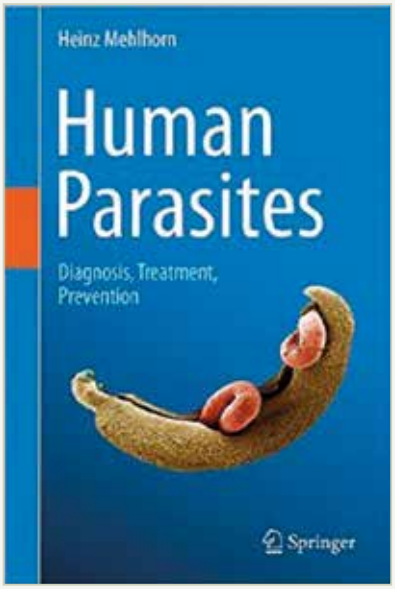
Reviews

Human Parasites: Diagnosis, Treatment, Prevention

Written by H. Mehlhorn
Springer International Publishing (2016)
£48.99
ISBN 978-3319328010

The author has very concisely covered parasitology in a handy-sized book, although there are some grammatical errors due to it being transcribed from German.

Its sections are clearly laid out with each parasite being broken down into smaller parts, making it easier for the reader to refer to. I particularly enjoyed the option of being able to find studies from recent papers in the further reading section after each parasite. However, the book lacks pictures; there is a lot of text for which a picture could have been used to keep the reader interested and to give an example. This is especially the case for malaria, where each microscopic stage could have been captured to give the book a balance of text and pictures where appropriate.



There was a lack of detail for laboratory diagnosis, which was disappointing as, in a concise book such as this, it would have made an interesting read and quick referral. Overall, I enjoyed the layout of the book and shall use it to refer back to when I need to.

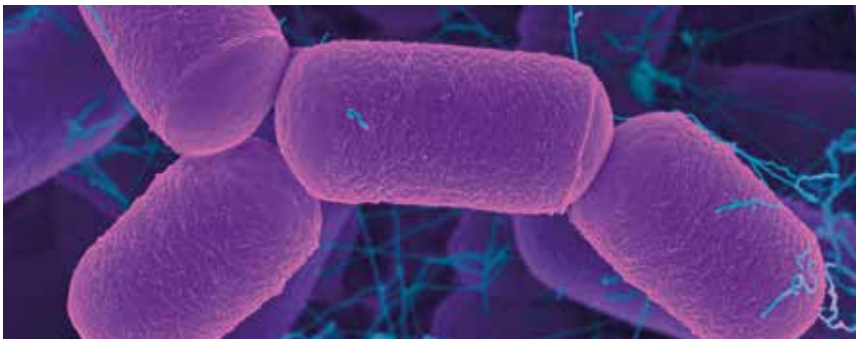
Rashmita Bodhani
Hospital for Tropical Diseases and HSL Analytics LLP

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

Comment

Archaea: closet pathogens?

James Chong



Coloured scanning electron micrograph of an archaeal human intestine prokaryote (*Methanobrevibacter smithii*).
Dennis Kunkel Microscopy/Science Photo Library

There are lots of hazards associated with growing archaea, that group of prokaryotes best known for their extreme lifestyles. A momentary lapse of concentration when dealing with a hyperthermophile growing above 80 °C can easily result in a nasty burn.

My own lab, which focuses on the growth of strict anaerobes (requiring media with less than 10 parts per million oxygen), has been the site of a couple of minor, fortunately injury-free, explosions. One was due to our underestimation of the rate at which a (new to the lab) *Thermococcus kodakarensis* strain produced hydrogen. With insufficient headspace in a closed 1 litre bottle for an overnight culture, we returned the next day to discover that the bottle had exploded, throwing the metal lid off the 85 °C waterbath which had housed the bottle and littering the lab floor with broken glass. The second incident was due to an equipment failure that resulted in escaped hydrogen (normally used to feed methanogens) finding a spark and blowing the door of an under-bench cupboard off its hinges. Luckily for the postdoc involved, the door missed him on its way across the lab.

There is an inherent risk when working with organisms that either produce or use hydrogen. I'm sure that if my Departmental Health and Safety Officer is reading this article, he'll agree that we work hard to ensure that these risks are minimised. Which is why, despite feeding methanogenic archaea a diet of 80% hydrogen (explosive) to produce methane (highly flammable) – sometimes with a dash of (highly toxic AND explosive) hydrogen sulfide – I have only two incidents to relate from almost 20 years of working with these very strict anaerobes. I should emphasise to my Health and Safety Officer that the stories I relate concerning postdocs being blown across the laboratory by exploding anaerobic glove boxes, or accidently injecting themselves with (oxygen-free) gases, are ones that I have heard only second-hand from overseas colleagues. I have never witnessed such incidents (thankfully the parties concerned also emerged relatively unscathed), and we have all reasonable measures in place to absolutely minimise such hazards when we grow archaea in York...

While the growth requirements of many archaea can be hazardous, the organisms themselves are not. A silver lining for my risk assessments perhaps, but an aspect I've always considered to be a distinct disadvantage when it comes to writing applications for funding. Why would anyone want to fund research on microbes that don't kill anyone or anything? Are there *really* no archaeal pathogens? And if not, why not?

For a microbe, pathogenesis is a fundamentally bad idea. From an anthropomorphic point of view, why would you kill the host that is providing you with food and board at no cost? Is this not a poorly thought-through error of judgement? Surely a much better approach to propagation of one's progeny is to hide in a corner and hope you're not noticed? By minimising the burden on your host – or, better yet, offering them some service – they are more likely to tolerate, or even encourage, your presence. This approach is taken by many bacteria – providing increased metabolic capacity (the ability to digest, convert or produce molecules of interest) for a host makes a prokaryotic guest a more attractive proposition. Therefore, bacterial disease must occur mainly through opportunity and competition: bacteria enter their host through a compromised barrier and then (inappropriately) employ mechanisms to compete for resources (production of siderophores to sequester iron, release of toxic molecules) or cause physical damage to host cells by proliferating in tissues.

To date, the predominant archaea detected in humans (and other animals) are methanogens. Human-indigenous methanogenic species have been hard to detect, requiring specific protocols to disrupt their cell walls for DNA extraction. Do they offer their hosts a metabolic advantage? Hydrogenotrophic methanogens, which reduce carbon dioxide with hydrogen to produce methane, compete with faster-growing, sulfate-reducing bacteria for hydrogen. The presence of methane rather than highly reactive, DNA-damaging hydrogen sulfide in the gut is likely indirectly protective against intestinal disorders such as ulcerative colitis and colorectal cancer. The recently described *Methanomassiliicoccales* potentially detoxify methanol produced by other gut residents via hydrogen reduction to methane. Acetoclastic methanogens may reduce obesity through the consumption of acetate that would otherwise be used by their hosts. So, archaea may be welcome guests, but do they ever exhibit antisocial behaviour?

The evidence is growing that archaea may indulge in opportunistic pathogenesis: *Methanobrevibacter smithii*, apparently the most abundant methanogen in human guts, has been reported to be found more often in stool samples from patients with diverticulosis than healthy individuals. The non-acetoclastic *M. smithii* has also been reported to increase obesity in germ-free mouse models when grown syntrophically with *Bacteroides thetaiotaomicron*. *Methanobrevibacter oralis* is found in and around the gums of about 5% of healthy subjects but up to 10 times more frequently in patients exhibiting periodontitis symptoms. Recently, this same organism was found in 40% of human brain abscesses but only 10% of controls. Injection of a million *M. oralis* cells into the brains of 22 mice resulted in 77% mortality after seven days, compared to no deaths in the 14 buffer-injected controls. Of course, the injection of a million live cells of almost any microbial species into a mouse's brain seems likely to cause problems, but methanogens appear to be no different. While these studies have been relatively small scale and none of them have the 100% statistics we would like to satisfy Koch's postulates, bacteria are often in the same position. Meningitis can be caused by both viruses and bacteria – even bacterial meningitis is caused by different organisms. In the USA, bacterial meningitis cases can generally be attributed as about 45% *Haemophilus influenzae*, and roughly 16% each *Neisseria meningitidis* and *Streptococcus pneumoniae* (with proportions of the latter two species varying by season). This leaves nearly 20% of cases that could be caused by different organisms. No one questions that any of these organisms are pathogenic.

Why has it been so difficult to convincingly demonstrate archaeal pathogenesis? Our ability to detect archaea has certainly been an obstacle. Improved DNA extraction methods have demonstrated that methanogens are more common in the human gut than previously suspected. The recent description of new, uncultivated, archaeal lineages assigned to the Asgard clade has also been facilitated by advances in high-throughput sequencing and bioinformatics methods to analyse these data. Another possibility is that we have not recognised the symptoms of archaeal diseases. The similarity of some archaea, such as *Lokiarchaeota* to eukaryotes, could compound this problem. I have previously speculated (to myself) that proteins from archaea with high similarity to proteins in their eukaryotic hosts could be the trigger for some conditions that have been labelled as 'autoimmune'. Leeuwenhoek first described bacteria in 1674, archaea were only recognised as a separate group of prokaryotes by Carl Woese in 1977. Perhaps we simply have not yet had enough time to identify the effects of these closet pathogens.

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@insanity_one

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NC 3Rs

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