

Microbiology TODAY

43:2 May 2016

What is life?

Are viruses alive?

Astrobiology

Synthia: playing God in a sandbox

Changing views on the tree of life

Archaea and the meaning of life

CHLORAMPHENICOL

CAPSULES

PIP: 106-5796

AAH: CHL600B

ALLIANCE: 065995

MOVIANTO: CHL25060

Widely distributed throughout the body, including CSF¹

Oral levels comparable to i.v. levels²

Rarely implicated with *C.difficile*^{3,4}

Effective against serious infections including:

- *H. influenzae*^{1,5}
- Typhoid^{1,5}
- MRSA²
- VRSA⁶
- *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.

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ESSENTIAL GENERICS

For further information, please contact: Essential Generics, 7 Egham Business Village, Crabtree Road, Egham, Surrey TW20 8RB, UK

Editorial

Grappling with the question 'What is life?' is not for the fainthearted. Reaching a consensus, even within the scientific community, is both a challenge and an aspiration. However, as a community of scientists, it is apparent that microbiologists are extremely well placed to influence the debate.



As technological and scientific advances push forward our knowledge boundaries, the answer to 'What is life?' is becoming tantalisingly closer. As I have learnt during my tenure at the Norwich Medical School, scientists are not the only voices grappling with this question.

Ethicists, the legal community and different religious communities to name a few continue to debate this issue as scientists continue to advance the meaning of life and living as technology and scientific advances continue to progress. Very recently, researchers working with Craig Venter published a report in *Science* describing a bacterium, Syn 3.0, that has been engineered to have the smallest genome of any freely living organism. Its genome has been pared down to the bare essentials; just 473 genes are needed to survive and reproduce. The evidence that is coming through seems to suggest that it is becoming more and more unlikely that 'The answer to the ultimate question of life, the universe and everything is going to be 42'. So far the evidence is pointing to 473.

The first article asks the question 'Are viruses alive?' Clearly, viruses have shaped history. Viruses by their very nature challenge our understanding

of what it means to be alive, and this question has been at the heart of an ongoing debate that has been around for more than a century. Different sides of the argument are presented by David Bhella and Nigel Brown.

John Ward writes our next article. He describes how astromicrobiology is perfectly placed to ask (and answer) whether there is life on Mars. Looking at microbial life forms that can survive and thrive in extreme environments on Earth is providing scientists with clues about the possibility and viability of life on our neighbouring planet.

The role of scientists in the 'What is life?' debate is evolving too. Sarah Richardson and Nicola Patron have co-authored an article that describes how synthetic biology is opening up new opportunities to manipulate, transplant and create new organisms. They also describe why scientific advances cannot take place in a vacuum but require a complete package of intellectual property assessment, ethical debate and philosophical review.

Next, Martin Embley and Tom Williams describe how new models based on molecular sequencing and metagenomics analysis using environmental DNA samples challenge the traditional three-domain tree of

life. The new model supports two domains instead of three, with eukaryotes originating from a common prokaryotic ancestor shared with Archaea. To coincide with the Molecular Biology of Archaea Focused Meeting to be held in London later this year, Hannah Marriott and Thorsten Allers pick up the Archaea story. They describe how this brand new domain of life contains more than an exotic group of extremophiles. In fact this 'newest' domain of life is one of the most ancient and ubiquitous. Our previous conceptions of archaeal life continue to be challenged as scientists continue to find new lineages.

Finally, Adam Staines from the BBSRC has written the Comment article. It focuses on one of the most important issues to occupy scientists' minds after the meaning of life question: what are the policies that underpin funding for research?

As our knowledge about the microbial world continues to expand, my money is on microbiologists finding the answer to the question 'What is life?' and also where did it begin?

Laura Bowater

Editor

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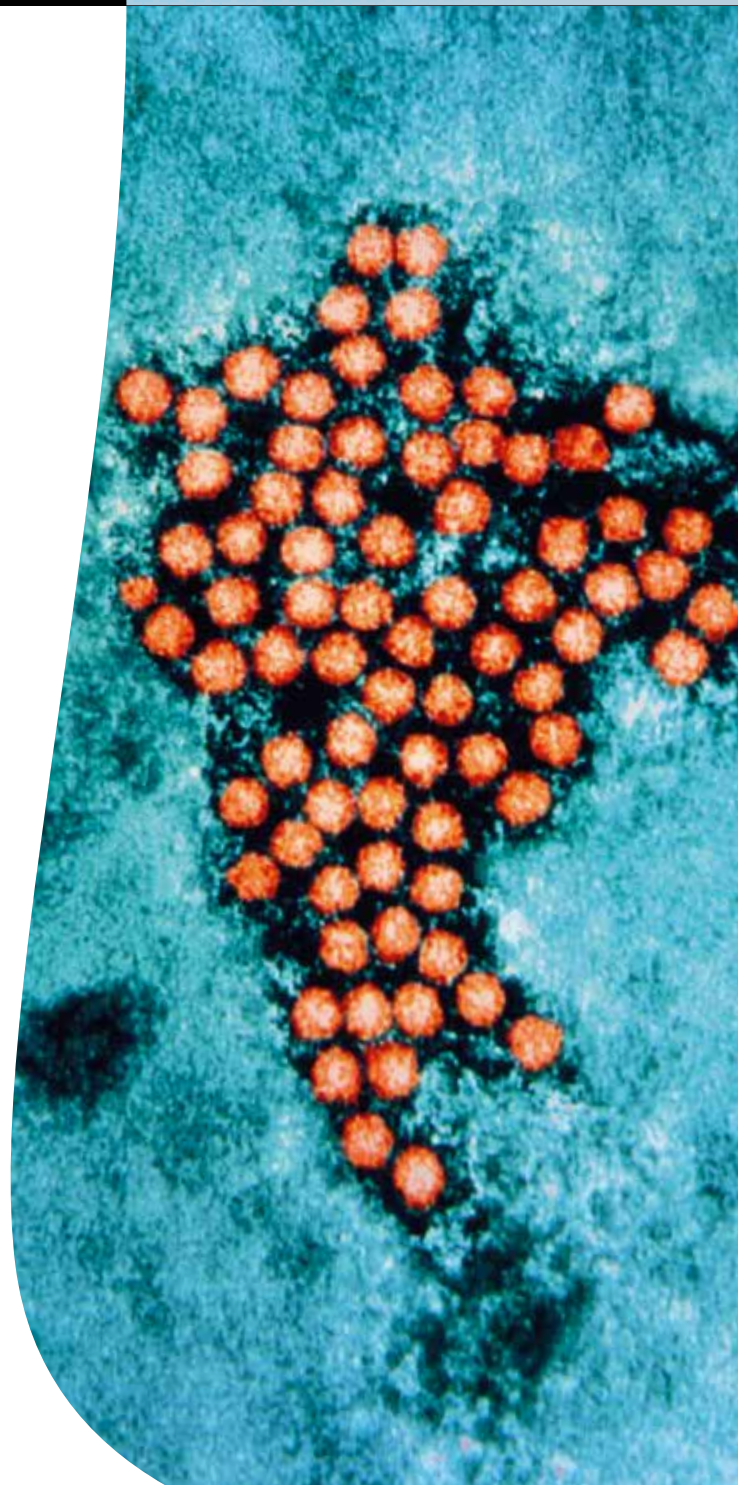
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Design **Ian Atherton, Corbicula Design (www.corbiculadesign.co.uk)**

Printed by **Charlesworth Press, Wakefield**

© 2016 Microbiology Society

ISSN 1464-0570

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Coloured scanning electron micrograph of strands of *Actinomyces viscosus*. Science Photo Library

Council 2016

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From the President

We are looking for your involvement in a number of issues in the coming months. The Society is about to enter a thorough review of our membership and is setting up a Membership Research Project Working Group.



The aim of the project is to gather data from members, non-members and lapsed members through structured questionnaires, focus groups and one-to-one interviews, to enable us to understand and meet the needs of a changing membership in a sustainable manner. Our objective is to ensure that the benefits we offer meet the needs of today's members but are also 'fit for purpose' for future members.

The ballot for elections to Council, Committees and Divisions will open Monday 23 May and I urge all eligible member categories to utilise their right to vote. It is important to the governance of the Society that we remain open and transparent, and that the membership is truly represented on the bodies whom we trust to drive forward our strategy. The ballot will be received electronically, or via post from the Electoral Reform Services, who are administering the process, so check your email spam filters if you have not received it by Tuesday 24 May. Why not also think about whether you personally should be standing for election for one of our posts in the Society? If you want to widen your influence and contribute to the field of microbiology then there are some interesting and important opportunities coming your way. Next January (2017) we will need applicants to put

themselves forward for vacancies on Council and on some of our Committees. In addition, we are looking for younger members to become part of our newly established Early Career Microbiologists' Forum. It is important to me and the Society that we have the widest possible representation on our Committees, so please consider getting involved.

At the time of writing I am looking forward to our annual meeting in Liverpool, but there is also an exciting Focused Meeting being planned, titled Molecular Biology of Archaea 5, taking place 1–3 August. For information about registration, visit the website (<http://microb.io/archaea5>).

We always aim to cover the length and breadth of microbiology in *Microbiology Today*, and this issue may claim to extend the boundaries of biology, science and science fiction more than any previous one. We have notable articles that span the entire tree of life on Earth, as well as an article on astrobiological 'life off Earth' and that found in extreme climates, written by John Ward. These are complemented by a review of the archaea (by Hannah Marriott and Thorsten Allers) that represent the third branch of life on Earth along with the bacteria and eukaryotes. If you've seen the movie *The Martian* with Matt Damon you

may, as a microbiologist, have questions about whether he was the only living thing left on the Red Planet and have been primed to think more about where microbial life exists outside the Blue Planet. Also have a look at the articles by Sarah M. Richardson and Nicola J. Patron on synthetic bacteria and the debate between two of our microbiology heavyweights – David Bhella and Nigel Brown – on whether viruses can be considered to be 'alive'. We are therefore covering life, the universe and everything in one magazine and considering the nature of life itself, as well as how we can make new 'designer' life forms. Beat that!

This issue also includes important information about our education and outreach activities and more information about the Early Career Microbiologists' Forum. You can follow us, and get regular updates on our activities in a wide variety of other ways. I am told for example that we now have more than 10,000 Twitter followers, so I know we are connecting through multiple traditional and social media formats.

Neil Gow

President

president@microbiologysociety.org

From the Chief Executive

When the Divisions met to begin discussing next year's Annual Conference, it was easy to see the importance of microbiology just by looking at the day's newspapers – three front pages were about the fight against malaria, the Zika virus, and the human microbiome. This brought home to me how crucial it is for our community's expert microbiological knowledge to feed effectively into public and political discussions about how we react to a whole range of major challenges.



One of the four pillars of the Microbiology Society's strategy is 'engagement and knowledge transfer'. That means we work hard to support members and share your unique, deep and broad specialist understanding with a wide range of people. One of those audiences is the policy world – MPs and Lords in the UK, TDs in Ireland, civil servants, government ministers, European officials and parliamentarians, and politicians and administrators in Holyrood, Cardiff and Stormont.

These groups have different working practices and timescales from researchers, so communicating with them can be challenging, especially when you are busy with your daily lives. The Society fosters communities and channels of communication to empower your voices to be heard in policy debates.

Following workshops with members around the country, Council agreed a policy roadmap that starts from the overarching grand challenge of climate change and sustainability, and then focuses on two major challenges where microbiology has a big role – food security and infectious disease. Using this framework, and with a very small, highly focused team of staff, we can have a real impact by concentrating your knowledge and the valuable time you are able to devote to policy work.

One way we do this is by responding

to governments' and parliaments' agendas, such as the response we made (jointly with the Society for Applied Microbiology) to a UK parliamentary inquiry into the lessons learned from last year's Ebola outbreak. This topic was the subject of a debate at our Annual Conference and a number of fascinating papers in the *Journal of General Virology*. Our response, which drew on the expertise of members including Ed Wright and Ian Goodfellow, was quoted repeatedly in the Parliamentary Committee's final report.

It is important to respond to such opportunities, but it is also crucial that the scientific community sets the agenda, drawing attention to issues that have not yet reached the notice of key decision makers and influencers. During 2015, the Society published briefings and position statements on energy from food waste, emerging zoonotic diseases, microbiology and climate change, food security from the soil microbiome, animal research and open access. Again, they were based on the expertise of members including Robin Sen, Penny Hirsh and Thorunn Helgason. They prompted questions in the Irish and UK Parliaments, quotations in debates in the House of Lords, face-to-face meetings with members of the policy community, and a sheaf of letters and requests for more information from members of the parliaments and assemblies in London,

Dublin, Belfast, Edinburgh and Cardiff.

These activities are only a fraction of what the Society does in the policy world on your behalf, overseen by a Policy Committee. They are augmented by a whole variety of events and partnerships that offer members the chance to influence policy and to learn more about the policy process. These include sitting on external committees, attending Parliamentary events, blogging, and helping to draft briefings, position statements, responses to consultations and other documents. These are things that it is often hard for active research scientists to get involved with, and the Microbiology Society's structures make it possible for more of you to participate. One recent example was the Voice of the Future event, at which members Rebecca McHugh, Benjamin Johns, Andrew Day and Rachel Edgar were able to quiz MPs and ministers directly on important issues.

Please get in touch if you want to know more about what the Society does in this area, or how to use your microbiological expertise to help strengthen local, national and international policies.

Peter Cotgreave

Chief Executive

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News

Focused Meetings 2016

Focused Meeting 2016, Irish Division: Host-Pathogen Interactions

30 June–1 July
Trinity College, Dublin, Ireland

Focused Meeting 2016: Molecular Biology of Archaea 5

1–3 August 2016
London School of Hygiene and Tropical Medicine, UK

Focused Meeting 2016, Irish Division: Exploring the Microbe-Immune System Interface

1–2 September
Rochestown Park Hotel, Cork, Ireland

Focused Meeting 2016: The Dynamic Fungus

5–7 September
Mercure Exeter Rougemont Hotel, Exeter, UK

Focused Meeting 2016: Molecular Biology and Pathogenesis of Avian Viruses

27–29 September
Charles Darwin House, London, UK

Deaths

It is with regret the Society notes the deaths of the following members.

Professor Craig Pringle, who joined the Society in 1961.

Mr Peter J. James, who joined the Society in 1965.

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.

New subject category for *Microbiology*

The Society's journal *Microbiology* has recently introduced a new biotechnology subject category and article submissions are now invited in this area. The journal has appointed two new Editors to cover the topic: Dr Louise Horsfall and Professor Saul Purton. To find out more about the journal and how to submit your paper, go to <http://mic.microbiologyresearch.org>.

Small World Initiative – Research Councils help to search for new antibiotics



In Autumn 2015, Professor Melanie Welham, Executive Director of Science at the Biotechnology and Biological Sciences Research Council (BBSRC), and Dr Simon Kerley, Head of Terrestrial Sciences at the Natural Environment Research Council (NERC), joined in the Society's search for new antibiotics as part of the Small World Initiative. They kindly collected a soil sample from the grounds of Polaris House in Swindon, home to the seven UK Research Councils including the BBSRC and NERC, which was sent to the University of East Anglia for analysis. It joined samples from our Citizen Science pop-up events from last summer, a sample from 10 Downing Street and a sample from the Arena and Convention Centre Liverpool, collected by the Lord Mayor of Liverpool to celebrate the Society's 2016 Annual Conference in March.

Professor Melanie Welham and Dr Simon Kerley at Polaris House. Nancy Mendoza



Athena SWAN Biosciences Best Practice event

In December last year, the Society led the organisation of the first Athena SWAN Biosciences Best Practice workshop, in partnership with the Royal Society of Biology, Biochemical Society, British Ecological Society and Society for Experimental Biology.

The workshop, held at the headquarters for all the named societies, Charles Darwin House in London, brought together staff from university bioscience departments that have received, or are applying for, Athena SWAN Awards. The Awards recognise commitment to tackle gender inequality in higher education. Delegates listened to inspiring talks from Dr Rachel Simmonds (University of Surrey) and Professor Jane Hill (University of York), who shared advice from their own departments' successful applications for awards. Sarah Fink from the Equality Challenge Unit, which runs the Athena SWAN scheme, ran workshop sessions on how to collect and present data to support applications. The workshop was chaired by Professor Hilary Lappin-Scott, former President of the Microbiology Society and current Equality and Diversity External Advisor.

This event came about as part of the work the Microbiology Society has been carrying out to embed equality and diversity across all of its activities. Alongside monitoring and collecting of data, the Society now has an Equality and Diversity Ambassador on Council and on each of its committees, who come together to share best practice and review collected data.

Useful best practice information from the Athena SWAN workshop, including speaker interviews, slides and other resources, and further information about our equality and diversity activities, can be accessed here: <http://microb.io/1nVEoER>. For more information, please contact the Society's Policy team (policy@microbiologysociety.org).



First Athena SWAN Biosciences Best Practice workshop at Charles Darwin House.

Nominations for Prize Lectures has re-opened

Following our diversity check, the Society has re-opened the nominations process to encourage broader representation of the microbiology community. The Society is supportive of Equality and Diversity issues and encourages members to consider the widest talent pool available when submitting nominations.

We are accepting nominations for the 2017 Peter Wildy Prize, Marjory Stephenson Prize, Colworth Prize and Fleming Prize, and for the 2018 Microbiology Society Prize Medal.

The deadline for nominations is now **Friday 29 July**. Full information can be found on the Society website: www.microbiologysociety.org/nominations.

Society quoted in parliamentary report on Ebola

In January, the UK House of Commons Science and Technology Committee published the findings from their inquiry *Science in emergencies: UK lessons from Ebola*. The report criticised systematic delays in the UK's response to the epidemic and lack of 'research readiness', and made recommendations to improve UK preparedness for future disease emergencies at home and abroad. The report quoted issues and recommendations made in written evidence that was submitted by the Microbiology Society and the Society for Applied Microbiology, which was drafted in consultation with members involved in the Ebola response and infectious disease research.

Human Fungal Diseases policy briefing

The Society's latest policy briefing *Human Fungal Diseases* was published in March. The briefing, which was informed by experts working in medical mycology, highlights the overlooked burden of these diseases and issues relating to diagnostics, antifungal drugs, research and public health surveillance. The briefing has been sent to UK and Irish parliamentarians and policy-makers, but is also useful as an education resource. The fungal diseases briefing, and our past briefings, can be downloaded here: www.microbiologysociety.org/briefings. Contact our Policy Officer, Paul Richards (policy@microbiologysociety.org) for further information about the Society's briefings and how to help with our policy work.

Voice of the Future 2016

Voice of the Future 2016 took place at the Houses of Parliament in March. Science and engineering students and early career researchers took the seats of a Parliamentary Committee and grilled prominent witnesses about science policy, including the Government Chief Scientific Advisor Sir Mark Walport and MPs from the House of Commons Science and Technology Select Committee. The Microbiology Society was represented by members Andy Day, Rachel Edgar, Benjamin Johns and Rebecca McHugh. Andy and Rebecca asked questions about science funding and government preparedness for disease emergencies to Jo Johnson MP, the Minister for Universities and Science, and Labour's Shadow Science Minister, Yvonne Fovargue MP, respectively. The event was organised by the Royal Society of Biology and hosted by the Science and Technology Committee. You can read about Rachel's experience on the Society blog, *Microbe Post*.

Voice of the Future 2016 meeting.
Royal Society of Biology



Grant deadlines

Date	Grant	Notes
1 June 2016	Travel Grants	For conferences and courses from 1 July onwards*
6 June 2016	Society Conference Grants Inclusion Grant Undergraduate Student Conference Grant	For support to attend the Focused Meetings on Molecular Biology of Archaea 5, and Host-Pathogen Interactions
4 July 2016	Society Conference Grants Inclusion Grant Undergraduate Student Conference Grant	For support to attend the Irish Division Meeting on the Human Microbiome
1 August 2016	Society Conference Grants Inclusion Grant Undergraduate Student Conference Grant	For support to attend the Focused Meeting on Molecular Biology and Pathogenesis of Avian Viruses

Rolling application

Local Microbiology Event Sponsorship

All members can apply for funds to support microbiology-related events, e.g. sponsored talks.

**Please note, you do not need to have received confirmation of abstract acceptance to apply for these grants as conditional offers will be made. In this case, evidence of acceptance is required to claim your grant.*

Elections for Council, Committees and Divisions

The Society elections for Council, Committee and Division members will launch later this month. If you are an Honorary, Full, Full Concessionary or Postgraduate Student Member then you have a right to vote on who represents the membership on these bodies.

Candidate information and the electronic ballot will open on 23 May. You will receive an email to your registered

member email address from Electoral Reform Services, who will administer the process.

Contributions and feedback

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

Benjamin Thompson

Head of Communications

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Are viruses alive?

What does it mean to be 'alive'? At a basic level, viruses are proteins and genetic material that survive and replicate within their environment, inside another life form. In the absence of their host, viruses are unable to replicate and many are unable to survive for long in the extracellular environment. Therefore, if they cannot survive independently, can they be defined as being 'alive'?

Taking opposing views, two microbiologists discuss how viruses fit with the concept of being 'alive' and how they should be defined.

Nigel Brown & David Bhella



Coloured transmission electron micrograph of a group of foot-and-mouth disease viruses.
Power and Syred / Science Photo Library

No, viruses are not alive

Nigel Brown

In many ways whether viruses are living or non-living entities is a moot philosophical point. There can be few organisms other than humans that have caused such devastation of human, animal and plant life. Smallpox, polio, rinderpest and foot-and-mouth viruses are all well-known for their disastrous effect on humans and animals. Less well known is the huge number of plant viruses that can cause total failure of staple crops.

In teaching about simple viruses, I use the flippant definition of a virus as 'gift-wrapped nucleic acid', whether that is DNA or RNA and whether it is double- or single-stranded. The gift-wrapping is virtually always a virus-encoded protein capsid and may or may not also include a lipid coat from the host. The viral nucleic acid is replicated and the viral proteins synthesised using the host cell's processes. In many cases the virus also encodes some of the enzymes required for its replication, a well-known example being reverse transcriptase in RNA viruses.

Over the last 15 years or so, giant viruses found in amoebae have complicated our picture of viruses as simple non-living structures. Mimiviruses and megaviruses can contain more genes than a simple bacterium and may encode genes for information storage and processing. Genes common to the domains Archaea, Bacteria and Eukarya can be found in different giant viruses, and some researchers argue on this basis that they constitute a fourth domain of life.

However, a crucial point is that viruses are not capable of independent replication. They have to replicate within a host cell and they use or usurp the host cell machinery for this. They do not contain the full range of required metabolic processes and are dependent on their host to provide many of the requirements for their replication. To my mind there is a crucial difference between viruses and other obligate intracellular parasites, such as bacteria; namely, viruses have to utilise the host metabolic and replication machinery. Intracellular bacteria may merely use the host as the environment in which they can supplement their limited metabolic capacity and they usually have their own replication machinery. Organisms such as *Chlamydia* spp. have not yet been grown outside cell culture

but they carry their own transcriptional and translational machinery and fall into the evolutionary kingdom of Bacteria. Like many other 'difficult' pathogenic bacteria, we may eventually be able to grow them in cell-free systems.

Caetano-Anollés and colleagues examined the phylogenomic relationships of viruses to living organisms through analysis of viral proteomes and assigned protein fold superfamilies. The authors concluded that viruses originated in 'proto-virocells' that were cellular in nature and they implied that viruses and modern bacteria evolved from common ancestors. They further claim that this means that viruses are indeed living organisms.

This is not an argument I am comfortable with. If a virus is alive, should we not also consider a DNA molecule to be alive? Plasmids can transfer as conjugative molecules, or be passively transferred, between cells, and they may carry genes obtained from the host. They are simply DNA molecules, although they may be essential for the host's survival in certain environments. What about prions? The argument *reductio ad absurdum* is that any biologically produced mineral that can act as a crystallisation seed for further mineralisation (hence meeting the criterion of reproducibility) might also be classified as living!

The explicit sexism apart contained in the wording, I can do no better than to quote Dr Kenneth Smith in the Preface to his classic book *Viruses* (Cambridge University Press, 1962): "As to the question asked most frequently of all, 'Are viruses living organisms?', that must be left to the questioner himself to answer". This questioner currently considers viruses to be non-living.

The argument *reductio ad absurdum* is that any biologically produced mineral that can act as a crystallisation seed for further mineralisation (hence meeting the criterion of reproducibility) might also be classified as living!

Yes, viruses are alive

David Bhella

The question of whether viruses can be considered to be alive, of course, hinges on one's definition of life. Where we draw the line between chemistry and life can seem a philosophical, or even theological argument. Most creation stories involve a deity that imbues inanimate matter with the 'spark of life'. From a scientific perspective, attempting to find a working definition for 'life' seems to me to have little practical value, but it is fun to think about.

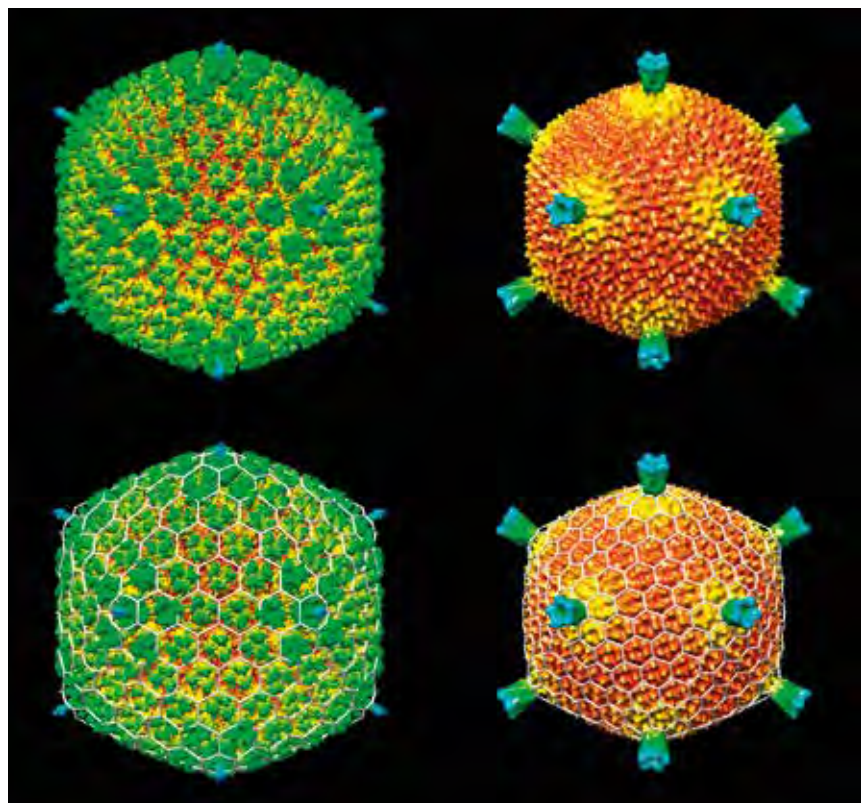
Arguments over the life/not life status of viruses are often rooted in evolutionary biology and theories of the origins of life. All cellular organisms can claim a direct lineage to a primordial cell or cells, a continuous chain of cell divisions along which the 'spark' has been passed. Are viruses able to claim a similar ancestry?

The contention that viruses have no place in the tree of life is often supported by the assertion that viruses do not have a comparable history – viruses are polyphyletic. Viruses are at a terrible disadvantage in this comparison, however. We are aware of only a tiny fraction of the total genetic diversity of viruses. Moreover, their genomes evolve far more rapidly than cellular organisms. So, from the small islands of sequence data we have, it is hard to argue that a coherent phylogeny does or does not exist. Interestingly, conservation of folds in viral proteins has begun to highlight possible common ancestries that could never be inferred

from genome sequence data. A striking example is domain duplication of the beta jelly roll motif which gives rise to the pseudo-sixfold symmetry of trimeric hexon capsomeres in adenovirus. This is also found in viruses that infect insects, Gram-positive and Gram-negative bacteria and extremophile archaea.

Viruses assemble their capsids from surprisingly few distinct protein folds, such that convergent evolution seems highly implausible.

A recent study has investigated viral origins by analysis of the evolution and conservation of protein folds in the structural classification of proteins (SCOP) database. This work identified a subset of proteins that are unique to viruses. The authors conclude that viruses most likely originated from early RNA-containing cells. If viruses made an evolutionary leap away from the cellular form, casting off its weighty metabolic



Human adenovirus type 5 (left – EM databank 1579) and sulfobolus turreted icosahedral virus 2 (right – EM databank 1679) assemble their capsids from trimeric capsomeres in which each protomer comprises a domain duplication of the beta jelly roll fold. This allows each trimer to pack with pseudo-sixfold symmetry – the geometric cage indicates the positions of local six-fold symmetry in the icosahedral capsid structure. This highly conserved feature has led to the proposal of a common viral lineage for these viruses that infect eukaryotes and archaea, respectively. David Bhella

shackles to opt for a more streamlined existence, did they cease to be life? Have they reverted to mere chemistry?

Viruses are genetically simple organisms; the smallest viral genomes are only 2–3 kbp while the largest are ~1.2 Mbp – comparable in size to the genome of *Rickettsia*. They all have surprisingly complex replication (life) cycles, however; they are exquisitely adapted to deliver their genomes to the site of replication and have precisely regulated cascades of gene expression. Viruses also engineer their environment, constructing organelles within which they may safely replicate, a feature they share with other intracellular parasites.

While a virion is biologically inert and may be considered 'dead' in the same way that a bacterial spore or a seed is, once delivered to the appropriate environment, I believe that viruses are very much alive.

Fundamental to the argument that viruses are not alive is the suggestion that metabolism and self-sustaining replication are key definitions of life. Viruses are not able to replicate without the metabolic machinery of the cell. No organism is entirely self-supporting, however – life is absolutely interdependent. There are many examples of obligate intracellular organisms, prokaryote and eukaryote that are critically dependent on the metabolic activities of their host cells. Humans likewise depend on the metabolic activity of nitrogen-fixing bacteria and photosynthetic plants along with that of our microbiota. There are very few (if any) forms of life on Earth that could survive in a world in which all chemical requirements were present but no other life.

So, what does define life? Some have argued that the possession of

ribosomes is a key ingredient. Perhaps the most satisfying definition, that explicitly excludes viruses, emerges from the 'metabolism first' model and concerns the presence of membrane-associated metabolic activity – a tangible 'spark' of life. This draws a neat distinction between viruses and obligate intracellular parasites such as *Chlamydia* and *Rickettsia*. This definition also confers the status of life on mitochondria and plastids, however. The endosymbiosis that led to mitochondria is thought to have given rise to eukaryotic life. Mitochondria have metabolic activity on which we depend, they have machinery to manufacture proteins and they have genomes. Most would accept that mitochondria are part of a life form, but they are not independent life.

I would argue that the only satisfactory definition of life therefore lies in the most critical property of genetic heredity: independent evolution. Life is the manifestation of a coherent collection of genes that are competent to replicate within the niche in which they evolve(d). Viruses fulfil this definition.

It is estimated that there are 10^{31} virus particles in the oceans – they vastly outnumber all other organisms on the planet. Alive or not, viruses are doing rather well!

All cellular organisms can claim a direct lineage to a primordial cell or cells, a continuous chain of cell divisions along which the 'spark' has been passed. Are viruses able to claim a similar ancestry?

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Astrobiology

I had just finished my first degree and was about to start a PhD when, in 1976, we were all gripped by the excitement of finding evidence of life on another planet. The Viking mission to Mars by NASA had experiments on board the lander that were designed to show whether there were any living organisms in the surface soil of Mars. The labelled release experiment showed a huge release of radiolabelled CO₂ when ¹⁴C labelled nutrients were mixed with a sample of Martian soil.

The Gusev Crater, Mars. JPL-Caltech / Cornell / NMMNH / NASA / Science Photo Library

John Ward



We know now that this was probably due to the highly reactive oxidised compounds in the soil created by solar UV radiation on the Martian surface. Mars has such a thin atmosphere and no ozone layer so UV from the Sun would not be absorbed before reaching the ground. The UV reacts to form highly oxidised chemicals that would break down the nutrients added in the Viking experiments releasing CO₂.

Life on Mars?

Years later I would return to thinking about life on Mars and other planets in our Solar System when starting to do research in Astrobiology. Astrobiology is the study of life in the universe and also its origins here on Earth. It also

investigates life in extreme environments on Earth such as extremely cold, dry habitats like the Antarctic dry valleys, hot, dry desert environments such as the Namib or Atacama Deserts and volcanic-associated vents on land and in the deep ocean. Microbes are the organisms that astrobiologists are primarily interested in and it was in these extreme environments that the Archaea were first found. It's a salutary lesson to us as microbiologists that it was only recently in 2002 that we discovered the most abundant free-living organism on Earth. This is the bacterium *Pelagibacter ubique* SAR11 and there are estimated to be 2.4×10^{28} SAR11 cells in the world's oceans. Often we fail to see what is there in front of us because of our fixed understanding of what we should be looking for.

Mars–Earth history

Mars is small, a little more than half the diameter of Earth. In the history of formation of the Solar System when all the planetary bodies were being formed by accretion of material around the proto-Sun, Mars being smaller than Earth would have cooled more quickly. If the conditions for life are liquid water, protection from damaging radiation, and nutrients and energy, then Mars would have had these conditions before Earth. The Earth is thought to have cooled at about 3.9 billion years (G yr) before present (BP). Mars could have cooled to have liquid water and an atmosphere as dense as the current Earth by about 4 G yr BP. The first evidence for life on Earth is about 3.8 G year BP and there is good geological evidence for large amounts of material blasted off the surface of Mars by asteroid impacts raining down on Earth in those early days of the Solar System. So there is the

possibility that microbial life, if it had evolved on Mars during those 200 million years, could have been carried from the surface of Mars by asteroid impacts and been deposited on Earth, possibly helping or kick-starting life on Earth.

The mass of Mars is about 10 times less than that of Earth and the gravity on Mars is 38% that of Earth. Mars also lost its magnetic field about 4 G yr BP and a consequence of the low gravity and lack of magnetic field is that Mars would have started to lose its atmosphere soon after it formed. The solar wind exerts a constant stripping pressure on a planet's outer atmosphere and a strong magnetic field, such as the one on Earth, prevents charged particles from the Sun stripping the outer layers of the atmosphere away. A dense atmosphere protects a planet's surface from harmful solar radiation such as hard UV. Mars, unlike Earth, does not have a magnetic field, so as Mars cooled and allowed microbial life to evolve, its protective atmosphere was gradually being stripped away. The current conditions at the surface of Mars are an atmospheric pressure of only 6 mbar (Earth's atmosphere is 1 bar, 166 times more dense than Mars) and a daytime temperature at the equator of -58°C . This is below the triple point of water so liquid water cannot exist stably at the surface.

Cosmic radiation on Mars

A second consequence of the lack of a dense atmosphere on Mars is that highly energetic charged particles from the Sun (protons) and galactic cosmic rays (mainly protons and helium nuclei) have nothing to block them until they hit the Martian surface. When these energetic particles hit Earth's atmosphere they produce showers of secondary particles which themselves



produce further energetic charged particles in a spreading cone of radiation, reaching its peak at what is called the Pfozter (or Regener) maximum, and on Earth this Pfozter maximum is 15 km, about 5 km above the normal cruising height of modern commercial jets. On Mars the Pfozter maximum is in the top few metres of the soil surface. Thus, not only is the Martian surface effectively sterilised by solar UV, the Martian soil to a depth of a few metres will be exposed to sufficient radiation to destroy biomolecules over a period of 0.4 to 6 million years at a depth of 5 metres. We looked at the radiation resistance of terrestrial cells such as *Deinococcus radiodurans* (Fig. 1) and Antarctic isolates combined with the annual radiation doses on Mars, and calculated the survival time of dormant populations of the cells. Bacteria can be radiation-resistant because, when active, they successfully repair the DNA breaks caused by ionising radiation. However,

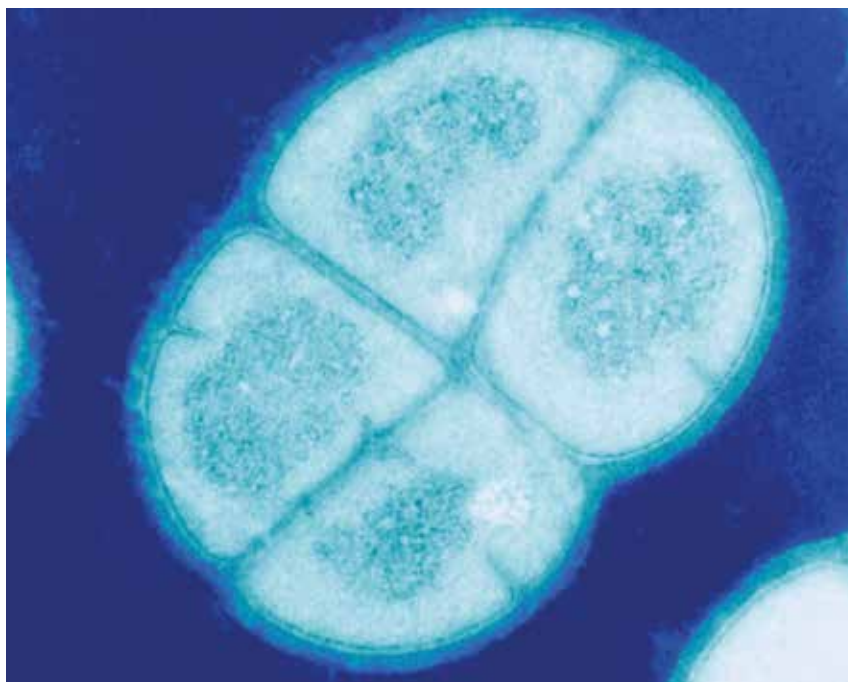


Fig. 1. Coloured scanning electron micrograph of four *Deinococcus radiodurans* bacteria forming a tetrad. Michael J. Daly / Science Photo Library

Given that phages are very tough and many can withstand conditions that their hosts cannot, I would advise looking for phages on Mars.



Fig. 2. Miers Valley, Antarctica. Samantha Whiting

when cells are dormant, such as frozen in the subsurface of Mars, they are preserved but unable to repair radiation damage, which accumulates to the point where the cell becomes permanently inactivated.

At a 2-metre depth a radioresistant organism would have had to be reanimated to repair its DNA within the last 450,000 years to still be viable. Given that the temperature is too low for living processes at the surface we should look for evidence of life, e.g. biomolecules and microbes, at a depth below 5 metres.

Mars analogues on Earth

Astrobiologists like to hunt for bacteria and archaea on Earth in places that could be thought to be similar to at least some of the conditions on Mars. The Antarctic dry valleys at McMurdo Sound (Fig. 2)

are amongst the driest and coldest places on Earth, and microbiologists have sampled these valleys to determine whether micro-organisms can survive there. There are in fact quite extensive microbial communities in the soils there and even lichens (an algae or cyanobacteria mutualism with fungi) in the surface of rocks. Plating studies of Dry Valley micro-organisms (Fig. 3) and more recently 16S ribosomal DNA metagenomics show a large range of bacteria, with *Firmicutes*, *Proteobacteria* and *Actinobacteria* being the main phyla in all depths of soil down to 20 cm, and the *Acidobacteria*, *Actinobacteria*, *Bacteroidetes* and *Gammaproteobacteria* more abundant in the interface with the permafrost.

What should we look for on Mars?

If the conditions were compatible for life to evolve on Mars in those few hundred million years before conditions became too tough and possibly drove it

underground, then we should be looking for bacteria or their biosignatures.

We now understand that on Earth, bacteriophages, or phages (Fig. 4) – viruses that infect bacteria – outnumber bacteria by about 10 to 1. Given that phages are very tough and many can withstand conditions that their hosts cannot, I would advise looking for phages on Mars. Of course we can't use plaque formation in soft agar to see whether phages are present because we would need a live host for each phage type – a real chicken-and-egg conundrum. But filtering a sample of Martian regolith from about 2 to 5 metres underneath the surface and using an electron microscope to search for phages might not be a bad idea.

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Fig. 3. Miers Valley bacteria after 12 weeks' growth. Samantha Whiting

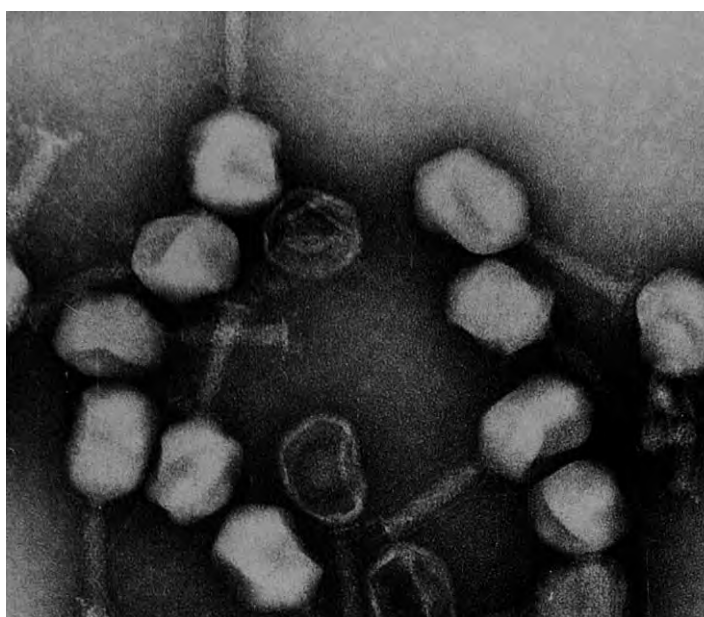
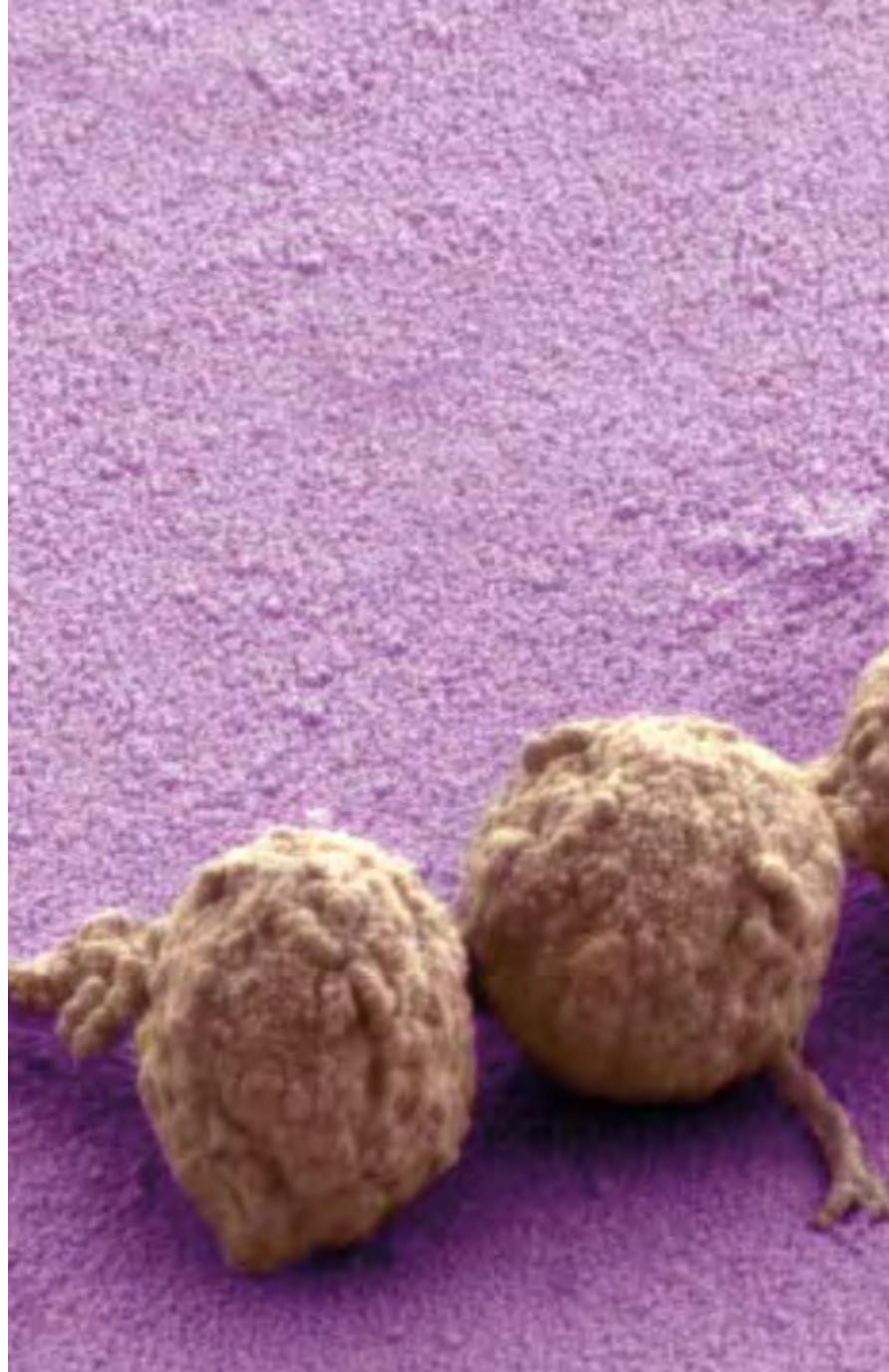


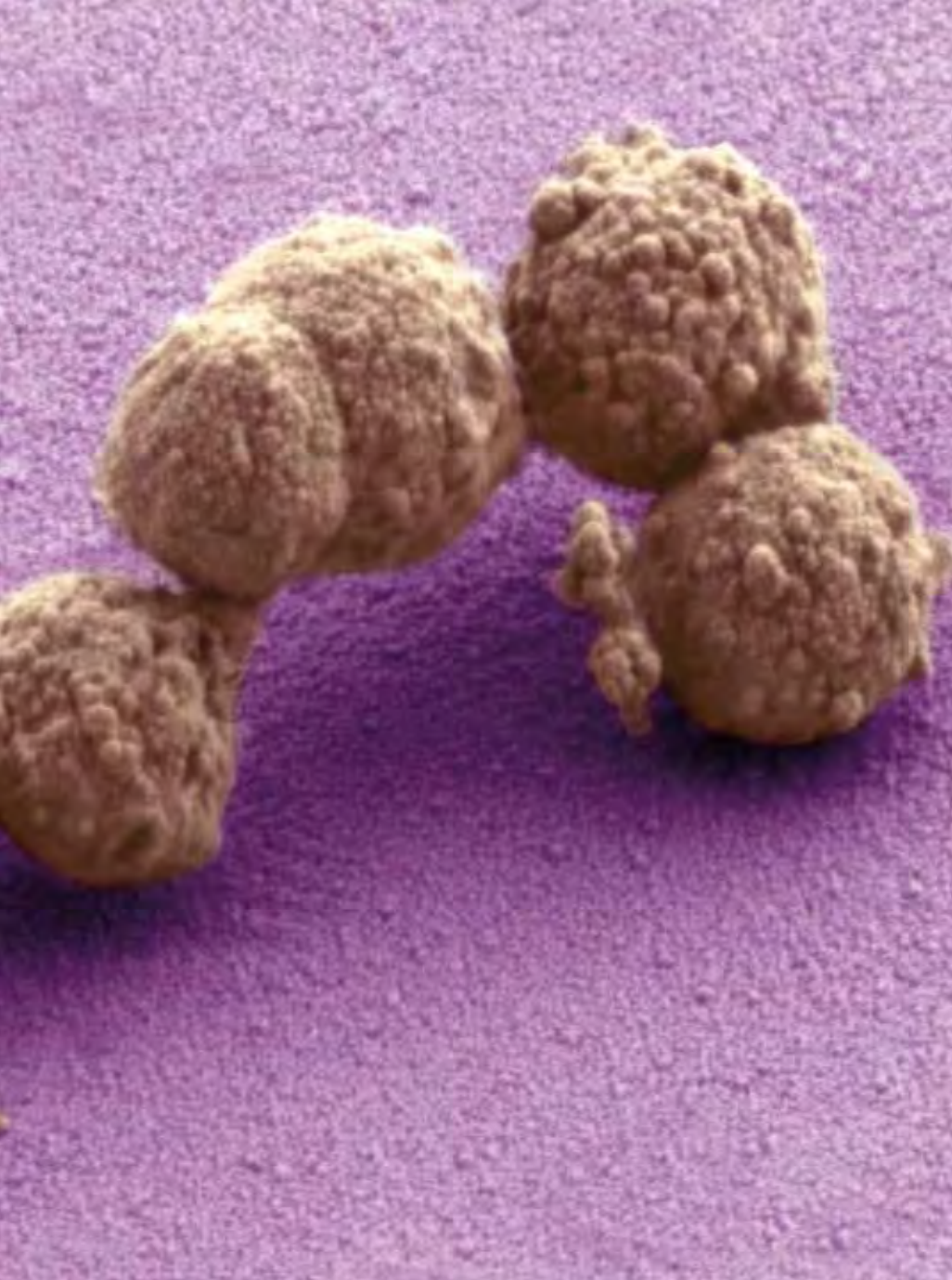
Fig. 4. T4 phage. Linda Wallace

Synthia: playing God in a sandbox



Sarah M. Richardson & Nicola J. Patron

In 2010 researchers at the J. Craig Venter Institute (JCVI) added a recombinant *Mycoplasma mycoides* genome into *Mycoplasma capricolum* cells and grew them until they shed their original genomes. It took 15 years of hard and steady work to develop and refine the technologies required to ‘transplant’ their chemically synthesised genome.



Coloured scanning electron micrograph of 'synthetic' bacteria. Thomas Deerinck, NCMIR / Science Photo Library

This project relied heavily on large-scale purchasing of DNA from commercial vendors, followed by assembly and sequencing. The researchers bought 1,078 carefully designed and sequence-verified 1 kb DNA fragments that they assembled in 109 separate reactions into 10 kb fragments by passage through yeast cells and then *Escherichia coli* bacteria. The 10 kb fragments were sequence verified and then joined into 100 kb fragments by a second passage through

yeast cells. These 11 huge pieces were carefully separated from the yeast and then reintroduced to assemble into a final 1,000 kb molecule. This was harvested from the yeast and introduced to competent, immune-compromised *Mycoplasma capricolum*. At this stage, the genome had been passaged through so many living cells that 'chemically synthesised' hardly seems applicable, especially in light of a transposon (a DNA sequence that can change its own position) hitchhiker picked up from

E. coli. 'Designer' doesn't seem right, either, because *M. mycoides* JCVI-syn1.0, (in showman's terms, *Mycoplasma laboratorium* or even 'Synthia') was not so much designed as copied. The genome is almost entirely the same as the previously sequenced genome of *M. mycoides* subspecies *capri* GM12. The final, synthetic genome differed only by the intentional inclusion of four non-functional 'watermarks' and one selectable marker, as well as 29 unintentional variations: 27 DNA single base pair (bp) changes, one 85 bp duplication, and the aforementioned *E. coli* transposon. The laudable work was the assembly itself – but while Synthia has the biggest piece of DNA ever crafted by humans to run a cell, she doesn't say anything new with it.

Synthia is synthetic biology showing off – flexing muscle without doing any lifting. A goat pathogen would not usually be considered a prime candidate for synthetic biology; JCVI picked *Mycoplasma* for their tiny genomes, and *M. capricolum* specifically for its relatively rapid growth rate.

New *in vivo* technologies, such as those adapted

from the recently famed CRISPR/Cas system make rebuilding a whole genome look as appealing as buying monochrome cathode ray tube monitors.

Then and today, the same final genome sequence could be achieved without assembly and far more rapidly using established technologies for mutating DNA and inserting new sequences into bacterial genomes. New *in vivo* technologies, such as those adapted from the recently famed CRISPR/Cas system make rebuilding a whole genome look as appealing as buying monochrome cathode ray tube monitors. Although synthetic biologists are now betting that industrial production will make the shift from chemical synthesis to biosynthesis, nobody is betting on complete genome synthesis; biosynthesising organisms are generally too large, too recalcitrant and too complex.

Nevertheless, there is another player in the synthetic genome game: an academic team peopled mainly by undergraduate students. In 2014, they reported the redesign and production of a fully functional chromosome from the baker's yeast *Saccharomyces cerevisiae*. Their eventual goal is a completely 'synthetic' yeast genome, but they do not intend to create a mere copy. They began with the publically available sequence and altered, removed, and added many different features. Their 'Sc2.0' genome will be 12 times as big as Synthia and will result in an organism that is arguably functionally very different from its forbear. The yeast project may have avoided some of the criticism garnered by Synthia because it was published second and will take another 5 to 10 years to fully assemble, but also because *S. cerevisiae* has classically been regarded as non-pathogenic. The project also exemplified the values of the nascent academic synthetic

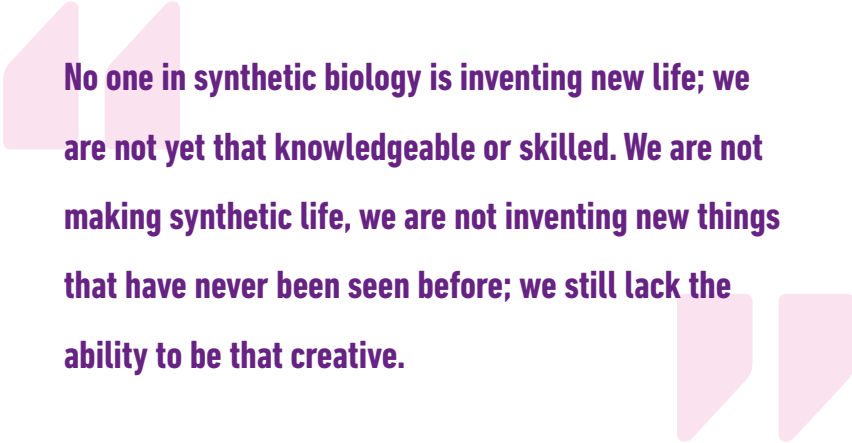
biology community through the establishment of an international consortium to do the work and address biosafety and ethical concerns: Sc2.0 members must pledge that their science will be done only in service to 'peaceful purposes' and that any potential harm will be minimised. Further, no intellectual property rights or restrictions on data and materials sharing are to be exercised on the clones used to generate novel strains, intermediary strains, or the final 'synthetic' strain. These self-imposed guidelines satisfy the scientific community but, just as with other emerging areas of science, the

technology is often ahead of ethical, policy and regulatory frameworks.

In response to the arrival of Synthia, the US Presidential Commission for the Study of Bioethical Issues published a report on synthetic biology. The Commission found that synthetic biology offers extraordinary promise to create new products for clean energy, pollution control and medicine; to revolutionise chemical production and manufacturing, and to create new economic opportunities. Despite the noise around Synthia, it found no reason to endorse additional regulations or a moratorium on work in this field at this time. They



The synthetic biology sandbox: sifting the environment for tools and pieces that will be useful in the laboratory. Sangeeta Nath



No one in synthetic biology is inventing new life; we are not yet that knowledgeable or skilled. We are not making synthetic life, we are not inventing new things that have never been seen before; we still lack the ability to be that creative.

acknowledged our duty to attend carefully to potential risks, be responsible stewards, and consider thoughtfully the implications for humans, other species, nature and the environment. Such discussions may be the most productive thing to come from the announcement of Synthia.

In the last six years the synthetic biology community has blossomed: iGEM, an international student competition in synthetic biology, has grown from 37 teams in 2006 to 280 teams in 2015; investment in new synthetic biology companies has surpassed a half billion dollars and a number of companies are now focused on engineering specific microbes for specific purposes. Oxford (UK)-based Green Biologics uses *Clostridium* to produce biofuels and other industrial chemicals from sustainable feedstocks; Boston (USA)-based Ginkgo Bioworks design microbes that produce cultured ingredients such as fragrances, flavours and sweeteners while companies like Synthace and Zymergen are focused on improving the technologies for automating the selection of new strains with machine learning.

All of this activity has been supported by a precipitous fall in the price for chemically synthesised DNA, new technologies that improve the ease with which synthesised fragments can be assembled and the development of easy-to-program molecular tools for editing the sequences of existing genomes. But no one in synthetic biology is inventing new life; we are not yet that knowledgeable or skilled. We are not making synthetic life, we are not inventing new things that have never been seen before; we still lack the ability to be that creative. We are recombining, sifting through the environment for tools and pieces, and using chemical DNA synthesis to move them from the environment to the laboratory. More than synthetic genomes, we need an even better understanding of what else we haven't observed yet. The accurate copying of a genome in the laboratory was an excellent demonstration that the technologies needed to support a DNA-dependent biosynthesis economy have come of age – but now the field is headed in a different direction.

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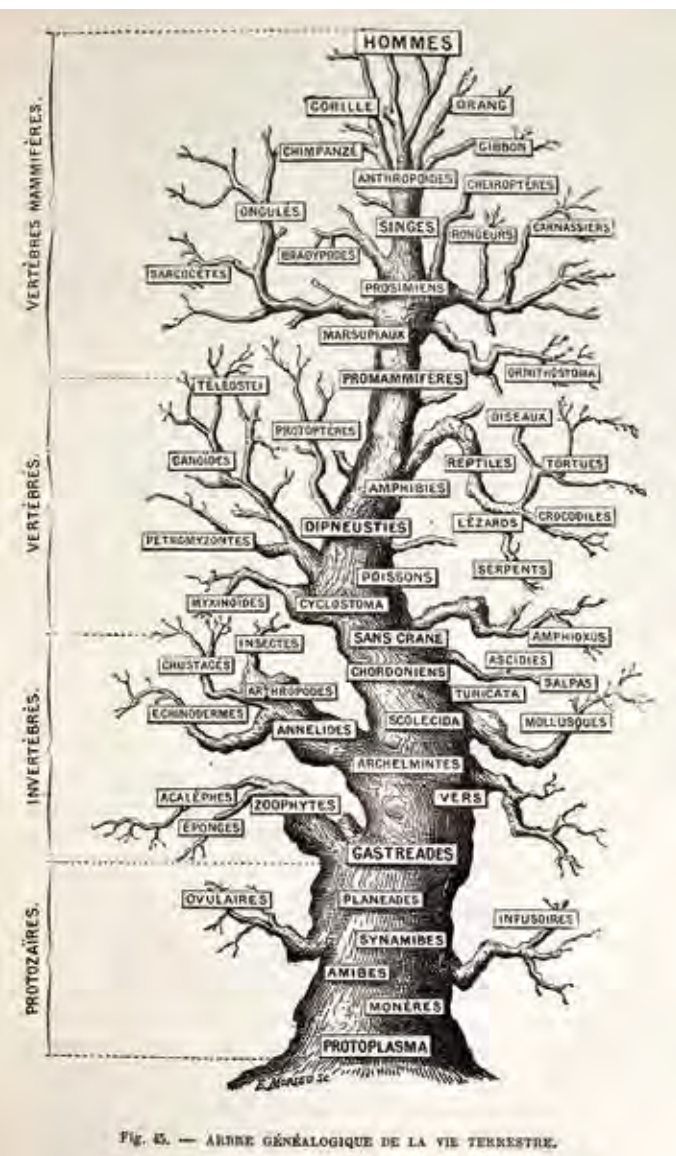
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Only two domains, not three: changing views on the tree of life

The Human family Tree from Haeckel's *Anthropogenie* (1874) (French copy from 1886). Paul D. Stewart/Science Photo Library

T. Martin Embley and Tom A. Williams

In 1857, Charles Darwin sent a letter to Thomas Huxley in which he wrote: "The time will come I believe, though I shall not live to see it, when we shall have very fairly true genealogical trees of each great kingdom of nature."

A tree for all of life – the three-domains tree

Genealogical or evolutionary trees show the relationships between organisms based upon common ancestry, like the family trees that we use to investigate our own parentage. For many biologists, Darwin's dream was realised on the grandest scale when, in 1990, Carl Woese and colleagues proposed that all cellular life could be placed into one of three separate fundamental groups or 'domains' – the Bacteria, the Archaea and the Eukarya, based upon sequence comparisons of small subunit (SSU) ribosomal (r) RNA sequences. According to the 'three-domains tree', the Eukarya and Archaea are more closely related to each other than they are to the Bacteria (Fig. 1). Hence, in this tree our closest cousins are the Archaea, a group of micro-organisms once thought to be restricted to anaerobic and other hostile habitats like hot springs and thermal vents in the deep ocean. However, although the three-domains tree of life

has dominated debate about how to organise life's diversity at the highest level for the past 20 years or so, there is now increasing evidence that it is not the best-supported hypothesis for the evolutionary relationship between eukaryotes and Archaea.

Data and evolutionary models – how are trees made?

Although morphology has long been used to classify animals and plants, Archaea and Bacteria – which between them comprise much of Earth's genetic and biochemical diversity – lack the wealth of morphological characters needed to reconstruct their relationships to each other or to eukaryotes. In 1965, double Nobel prize winner Linus Pauling and his collaborator Emile Zuckerkandl proposed that the sequences of the DNA, RNA and proteins found in all cells were "documents of evolutionary history" and hence were the best source of data for making global evolutionary trees. The basic procedure is to collect sequences from different species and

to use a mathematical model of how we think sequences evolve to infer the evolutionary relationships between them, typically expressed in a tree diagram. Because of their central importance in the process of making trees, it is important to appreciate that all of these mathematical models use simplifying assumptions to make the analyses computationally tractable, and that they are not accurate representations of how sequences really evolve: in the words of statistician George Box, "all models are wrong, but some are useful." In the early days of computational molecular evolution, the models used were very simple because the computers of the time were so slow. It was during this period that the three-domains tree first came to prominence, so it is interesting to ask how the tree has fared as both computers and models have improved.

Most of the models traditionally used to make the three-domains tree have assumed that the same sequences in all organisms evolve in much the

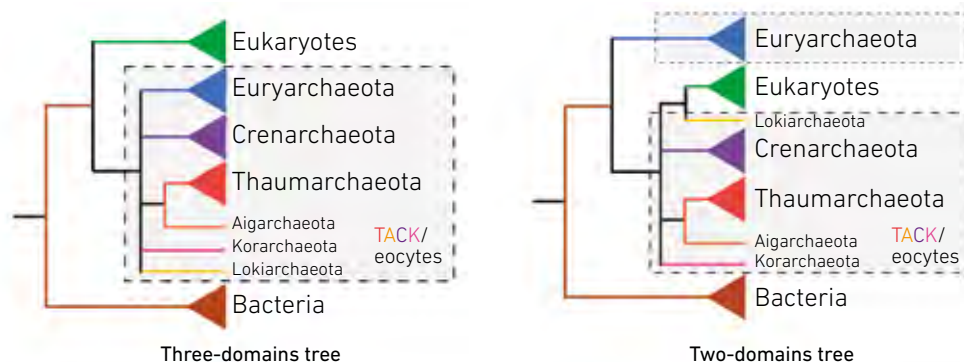


Fig. 1. The three-domains and two-domains trees – competing hypotheses for the origin of eukaryotes. The iconic three-domains tree appears in most textbooks and divides cellular life into three separate major groups or 'domains': the Bacteria, the Archaea and the Eukaryotes. In this tree the Eukaryotes are held to have originated from a common prokaryotic ancestor shared with the Archaea (enclosed in the shaded box). By contrast, the two-domains/eocyte tree recovers Eukaryotes nested inside the Archaea with the newly discovered Lokiarchaeota currently thought to be the closest archaeal relatives of the Eukaryotes. In the two-domains/eocyte tree the eukaryotic lineage had an ancestor that was already an Archaea. Studying uncultured archaeal diversity in nature thus holds the promise of finding ever-closer relatives of Eukaryotes. The genomic and cellular features of these lineages could potentially illuminate important stages in the evolution of eukaryotic cells like our own. The *Thaumarchaeota*, *Aigarchaeota*, *Crenarchaeota* and *Korarchaeota* are commonly called the TACK Archaea in the literature. Modified from Williams *et al.* (2013) *Nature* 504, 231–236.

same way, but this is not supported by real sequence data. For example, the nucleotide composition of SSU rRNA sequences, which are by far the most widely used molecules for making broad-scale evolutionary trees, varies dramatically in different species. This provides strong evidence that the ways in which SSU rRNA sequences have evolved in different species have changed over time. In tree building, using a model of sequence evolution that does not fit the data being analysed can often produce an incorrect tree with strong support. Recent work now suggests that this can explain why past analyses have recovered the 'three-domains' tree.

Two domains is better supported than three when new methods are used

Over the past few years, a number of new models have been developed by statisticians to try and better accommodate aspects of real molecular sequence evolution. For example, models are now available that recognise that the same sequences in different species can evolve differently in terms of their amino acid or nucleotide compositions, and other models have been developed that allow individual sites in molecular sequences to evolve in different ways to each other. Although it is widely recognised that even the best currently available models have important

limitations, they fit real sequence data much better than the simpler models used in the past. Interestingly, when the new models were first used to analyse the molecular sequence data commonly taken to support the three-domains tree, an alternative hypothesis for the relationship between Archaea and eukaryotes called the 'eocyte tree' was better supported. In the long-neglected eocyte tree, which was first proposed by James Lake and colleagues in 1984 based upon ribosome structure, the Bacteria and Archaea can still be considered distinct primary domains but the eukaryotes originate from *within* the domain Archaea (Fig. 1). In other words, in the 'two-domains/eocyte tree', the eukaryotic lineage has an archaeal parent.

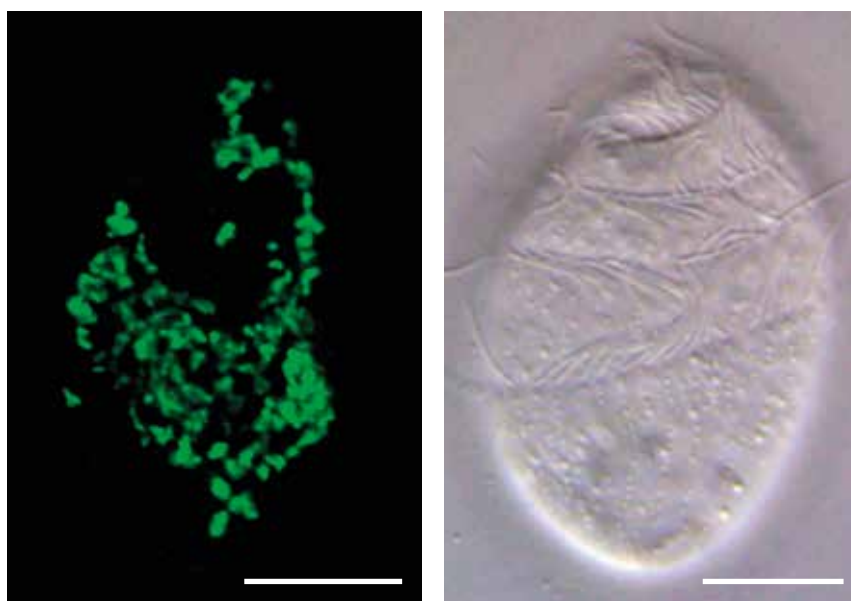


Fig. 2. Molecular methods can be used to identify environmental micro-organisms without cultivation. The figure on the right shows a light micrograph of an anaerobic ciliate protozoan called *Trimyema* that is commonly found in freshwater ponds in the UK and elsewhere. *Trimyema* is the host for a particular type of Archaea called a methanogen because it makes methane. Like many environmental Archaea the intracellular methanogens have not yet been isolated into laboratory culture but they can nevertheless be identified as a single new species of *Methanocorpusculum* based upon their SSU rRNA sequences, which can be isolated and read using modern DNA technology. On the left a fluorescent DNA probe (green) was used to confirm that all of the many methanogens living inside *Trimyema* have the same SSU rRNA sequence. Similar probes can facilitate isolation experiments because they can be used to identify samples enriched in the target species and also to confirm when a target species has been successfully cultured. Bars, 10 μ m. Kindly provided by Mr Will Lewis (University of Newcastle)

Adding new groups of Archaea increases confidence in the new tree

Microbiologists have long suspected that the micro-organisms that have been studied in the laboratory are only a tiny fraction of natural microbial diversity. The original eocyte Archaea included species like *Sulfolobus* (later called the Crenarchaeota in 1990 by Woese and colleagues) that live in hot acidic springs, so they were seen as rather unusual and exotic micro-organisms. In the past few years, sampling of the natural microbial world has greatly increased, driven by the availability of new molecular methods to investigate uncultured microbial diversity (Fig. 2). Recently discovered Archaea related to the eocytes include a variety of new lineages that have been informally grouped together as the 'TACK' Archaea. Some of the TACK Archaea have major roles in the soil and marine nitrogen cycle, suggesting that their discovery and further study is not just important because of their potential relationship to eukaryotes, but also for understanding



Fig. 3. Part of the Soria Moria hydrothermal vent field along the Arctic Mid-Ocean Ridge. The picture was taken close to the Loki's Castle sampling site from which the DNA samples used to recover the genome of *Lokiarchaeota* were isolated. The detailed methods used to reconstruct the *Lokiarchaeota* genome are described by Spang *et al.* (2015) *Nature* **521**, 173–179. Kindly provided by Dr Rolf Birger Pedersen, Centre for Geobiology, University of Bergen, Norway

globally important nutrient cycles. Improved sampling of lineages often has a positive impact on the accuracy of tree reconstruction, particularly if the new sequences populate parts of the tree that were previously poorly sampled. Importantly, all of the recent analyses that have included a broad sample of the new TACK Archaea have supported the two-domains/eocyte tree (Fig. 1).

Can the new tree help us to better understand eukaryotic origins?

The perspective on eukaryotic evolution provided by the two-domains/eocyte tree of life has already had a profound influence on ideas about how eukaryotes first evolved from their prokaryotic ancestors. Eukaryotic cells have an internal structural complexity that is not found in prokaryotes and the origins of this complexity have long been a major evolutionary puzzle. A key prediction of the two-domains/eocyte tree is that Archaea can be discovered that are more closely related to eukaryotes than the species that we already know about, and, because of this closer common ancestry,

that their genomes will be more similar to eukaryotes in their protein repertoires. This prediction appears to have been vindicated by the discovery of a new archaeal lineage called the *Lokiarchaeota* (Fig. 3). The *Lokiarchaeota* are the closest archaeal relatives of eukaryotes in evolutionary trees and, consistent with that closer relationship (Fig. 1), their reconstructed genomes contain more genes for proteins that were previously thought to be eukaryote-specific. These include proteins that, in eukaryotes, are used for the cytoskeleton, in membrane remodelling and in phagocytosis, all features long-held to be unique to eukaryotic cells. At present, the evidence for the existence of *Lokiarchaeota* comes from metagenomes constructed from environmental DNA samples so it is now critically important to isolate viable cultures into the laboratory, to determine the cellular roles of their eukaryote-like proteins. Achieving that goal may be difficult and will require all of the classic tools of microbiology, including selective isolation, microbial physiology and cell biology, and cutting edge microscopy.

The perspective on eukaryotic evolution provided by the two-domains/eocyte tree of life has already had a profound influence on ideas about how eukaryotes first evolved from their prokaryotic ancestors.

However, the prize to be gained is potentially enormous because success will bring the study of eukaryotic origins much more firmly into the realm of experimental science.

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Further reading

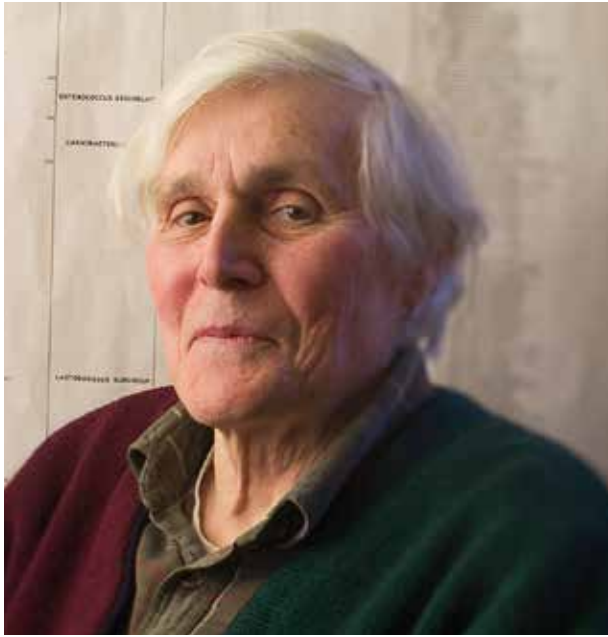
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Archaea and the meaning of life

Hannah Marriott & Thorsten Allers



Humans are inordinately fond of dividing things into two – our approach to taxonomic classification is no exception. The earliest system published by Linnaeus divided living organisms into animals and plants, and by the 1960s this was superseded by a more fundamental split between prokaryotes and eukaryotes. So it should come as no surprise that the idea of a third domain of life – Archaea – met with fierce resistance when it was proposed in the 1970s.



Above **Carl Woese**. Don Hamerman, Institute for Genomic Biology, University of Illinois at Urbana-Champaign



Geothermal areas and hot springs from Waiotapu geothermal area (Rotorua, New Zealand) and Yellowstone National Park (USA). Far left A mud pool, Waiotapu. Second from left Champagne Pool, Waiotapu. Centre A hot spring in Yellowstone National Park. Above Sulfur deposits, Waiotapu. Right Lady Knox Geyser, Waiotapu. All Ian Haidl, except centre Sonja-Verena Albers

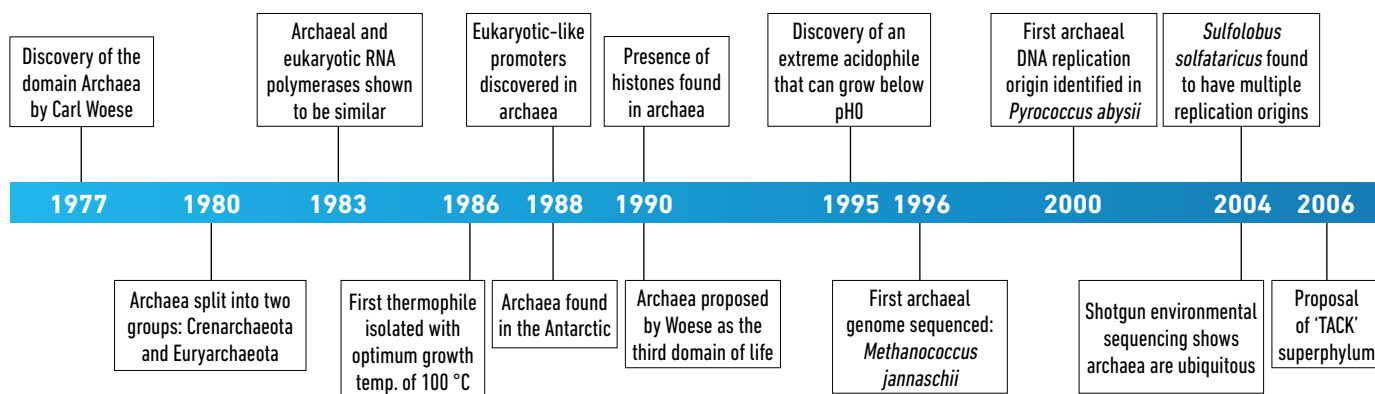
A brief history of Archaea: 1977 to present

Archaea are widespread on Earth yet relatively little is known about them, outside of the select groups of people that study these fascinating organisms. They are a mystery that is being slowly unravelled since their 'discovery' in 1977 by Carl Woese and his group, including George Fox, while working at the University of Illinois.

Methanogens (archaea that produce methane) and other groups of micro-organisms, including halobacteria (now called halophilic archaea) as well as thermophiles, had already been discovered, but they had been misclassified under the domain Bacteria. Woese found that these organisms did not just share a love for extreme environments, but also that they are phylogenetically related to each other.

However, he was surprised to find that they are fundamentally distinct to bacteria.

Woese was using small-subunit rRNA (ribosomal RNA) to build a new phylogenetic tree. Small-subunit rRNA is an essential component of all self-replicating organisms and shows remarkable sequence conservation. This made it a perfect choice for a molecular chronometer. At the time this molecular



Timeline of Archaea from their discovery to present day. Ian Haidl, Sonja Albers, Thorsten Allers

approach to phylogeny was novel – previous methods relied instead on visible characteristics such as cell shape or growth conditions. Woese found that the prokaryotes are not one coherent domain, but are made up of two distinct groups: Bacteria and Archaea. At the time they were named 'Eubacteria' and 'Archaebacteria', respectively, but these two groups of prokaryotes were found to be no more similar to each other than they were to eukaryotes. Woese proposed that the tree of life has three equal branches – Archaea, Bacteria and Eukarya – and that the term 'prokaryote' should be abandoned because it has no taxonomic meaning. Unsurprisingly, his ideas were not universally popular.

As with any new discovery there are sceptics, but biochemical data from Wolfram Zillig supported the 16S rRNA data collected by Woese. Over time, the new domain of Archaea was accepted by the scientific community. Interest in archaea increased further after whole genome sequencing took off in the 1990s, and researchers increasingly switched from bacteria or eukaryotes to working on these exotic micro-organisms. But contrary to popular belief, not all archaea are extremophiles. They have also been found in 'normal'

environments such as soil and the ocean, and in environments where they cohabit with bacteria. For example, in the human gut archaea are responsible for producing methane! However, unlike bacteria, no pathogenic archaea have ever been found.

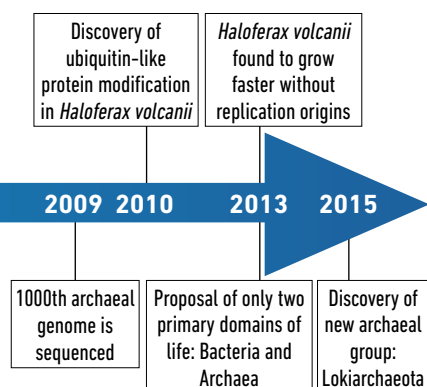
Almost 40 years have passed since their reclassification into a new domain but still many more species of archaea are being discovered. DNA sequencing has improved dramatically, meaning that archaea no longer have to be cultured to be characterised. This has led to the discovery of entirely new lineages. Based on phylogenetic data (16S rRNA and other genes) the domain Archaea was originally split into two groups; the Euryarchaeota and the Crenarchaeota. However, since 2006 three more lineages have been discovered: Thaumarchaeota, Aigarchaeota and Korarchaeota. These three new groups are often combined with the Crenarchaeota to form the 'TACK' superphylum (more on this later). Even more recently there have been reports of new lineages of 'nano' archaea, which are characterised by a small cell size with very few genes. The constant unearthing of new species and groups make the Archaea a very fluid domain, with the phylogenetic

tree changing as each new discovery is made.

The origins of life?

Archaea may look like bacteria at a first glance and there are certainly many superficial similarities, but dig deeper and archaea have more in common with eukaryotes. In fact, it is now widely accepted that archaea are the ancestors of all eukaryotes.

Archaea, like bacteria, are single-celled organisms with a circular double-stranded DNA genome, and they have neither a nuclear membrane nor organelles. This means that they are similar to bacteria in terms of cell structure, although there are differences. Archaea do not have a bacterial-style cell wall and their plasma membrane is different to that found in both bacteria and eukaryotes. But on the inside of the cell, archaea show a striking family resemblance to eukaryotes. This is especially so for the enzymic machinery that processes genetic information – DNA packaging and replication, transcription into RNA, and translation into protein. All of these processes are essentially the same in archaea and eukaryotes, and are quite distinct from bacteria.



This prompts the question: if archaea are more closely related to eukaryotes than bacteria, then how do they fit in the tree of life?

The phylogenetic tree proposed by Woese was split into three equal domains, with Archaea and Eukarya sharing a common ancestor that had already diverged from Bacteria. However, biologists working on the origins of life have recently concluded that Eukarya and Archaea are not sister groups. Instead, eukaryotes are the direct descendants of archaea, and our long-lost ancestor belongs to the 'TACK'

superphylum of Archaea. One of the most exciting new discoveries of the last year was the identification of a 'missing link' between Eukarya and Archaea. Called Lokiarchaeota, they were found near a hydrothermal vent at a site known as Loki's Castle in the Arctic Ocean.

Can we use our knowledge of archaea to trace the origins of complex life? Eukaryotic microfossils can be dated back to 1.8 billion years ago but biological methane has been found in rocks that are 3.4 billion years old. The only source of biological methane is methanogenic Euryarchaeota, so we know that archaea have been around since the very beginnings of life on Earth. As for life on other planets, it is tempting to speculate that archaea may have also colonised Mars – evidence is mounting that methane in the Martian atmosphere has a biological origin.

Woese's revolution

What do the recent discoveries mean for us humans? Given our desire for dichotomy, we should be relieved that the tree of life has been pruned back to just two primary branches – Bacteria

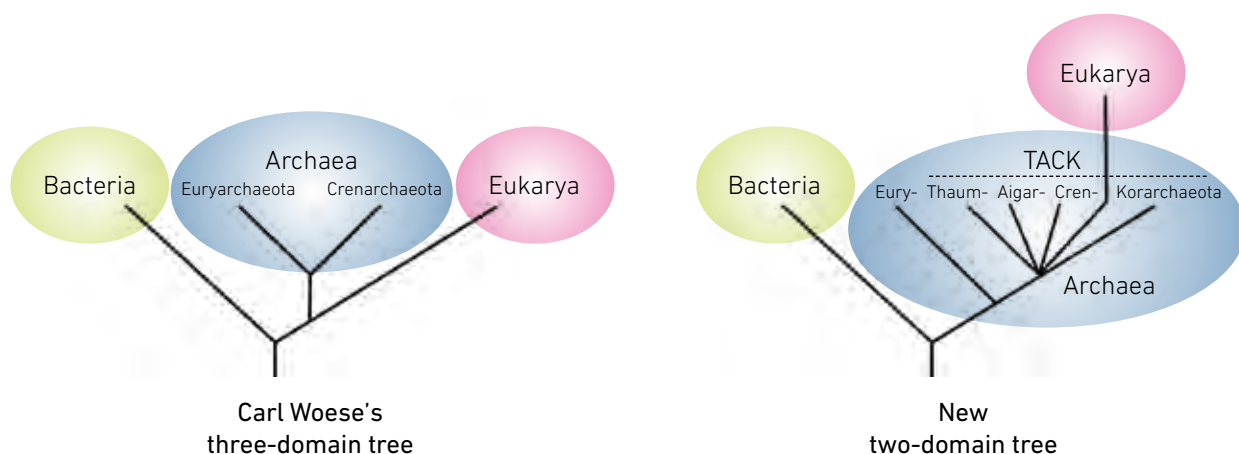
and Archaea. And more than anything else, we should give credit to Carl Woese, whose taxonomic revolution has allowed us to trace our ancestors all the way back to their humble beginnings as archaeal cells.

Hannah Marriott & Thorsten Allers

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Further reading

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Universal phylogenetic trees in rooted form, showing the three domains. Ian Haidl, Sonja Albers, Thorsten Allers

Annual Conference

Annual Conference 2016 | 21–24 March, ACC Liverpool

Thank you to all of our delegates, invited speakers and exhibitors who helped make our Annual Conference one of the Society's best yet. During March, we welcomed over 1,400 of you to the ACC in Liverpool to enjoy four days of science and socialising, which included our super talented band *The Radicals*, who brought the party atmosphere and encouraged some movers and shakers to hit the dance floor!

Delegates attended the Conference from all over the globe to hear breakthrough research, take part in panels and debates, and to network and build connections. Once again our 2016 Conference featured a packed programme of 29 sessions,

over 300 talks and 400 posters, all covering a range of microbiology, and this year we included additional lunchtime and evening events as part of the conference experience.

Particular highlights included our Prize Lectures, our Hot Topic Lecture on Zika virus, and our social programme.

As in previous years, research from our Conference received huge attention from the press, with researchers appearing in newspapers, on radio stations and on television channels across the globe.

Thank you to all those who gave us feedback; as always, we value your comments.



Ian Atherton

Society-sponsored events in 2016

Every year we provide financial support for microbiology events held by other organisations. Below are some of the events we have sponsored so far this year. The next deadline for 2016 event applications will be 17 June 2016.

11th Recently Independent Virology Researcher's Meeting, 2016 (RIVR 2016)	4–5 January	Derby
21st Glasgow Virology Workshop (GVW)	30 January	Glasgow
<i>Legionella pneumophila</i> (1976 to 2016) – From Whole Guinea Pigs to Whole Genome Sequencing: Do We Understand it Any Better After 40 Years?	31 March	London
The 7th European Spores Conference	18–20 April	London
14th UK Meeting on the Biology and Pathology of Hepatitis C virus	20–22 May	Cumbria
Protistology-UK Spring Meeting 2016	6–8 June	Bournemouth
Young Microbiologists Symposium on Microbe Signalling, Organisation and Pathogenesis	29–30 June	Dundee
British Yeast Group	29 June–1 July	Swansea
Within Host RNA Virus Persistence: Mechanisms and Consequences	24–26 August	St Andrews
8th Meeting of the European Society for Chlamydia Research	6–9 September	Oxford
Structural Aspects of Infectious Disease	September	Belfast



Edinburgh. Convention Edinburgh

Follow the Society on
Twitter to keep up-to-date:
@MicrobioSoc

Annual Conference 2017

3–6 April 2017, EICC Edinburgh

#Microbio17

The countdown has begun to Conference 2017 and in preparation our Divisions have already started to create our next programme. Session titles have now been confirmed and speakers are being identified to ensure that once again our Annual Conference provides delegates access to hot topics, new developments and leading research.

Main symposia:

- Anaerobes in infection
- Aquatic microbiology
- Cell biology of pathogen entry into host cells
- Circadian and cell rhythms
- Endemic mycoses
- Epigenetic and non-coding RNAs in eukaryotes
- Geomicrobiology
- Heterogeneity and polymicrobial interactions in biofilms
- Just passing through – virus infections of the gastrointestinal tract
- Macromolecular machines
- Microbial cell surfaces
- Microbial genomics: whole population to single cell
- Microbial mechanisms of plant pathology
- Protistology UK Annual Meeting

- Regulation of RNA expression during virus infection
- Synthetic and systems biology applications in microbiology

Virus workshops:

- Antivirals and vaccines
- Clinical virology
- Evolution and virus populations
- Gene expression and replication
- Innate immunity
- Pathogenesis
- Plant virology

Prokaryotic forums:

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

Add the date to your diary to not miss out next year. Sign up to our newsletter at www.microbiologysociety.org/newsletter to ensure you are receiving regular updates about the Conference and other Society news, and visit www.microbiologysociety.org/events for further information.



Peshkova/iStock/Thinkstock

Applications and proposals welcome

Our programme of events is developed and driven from proposals submitted by our members. In addition to the Focused Meeting proposals, we also welcome proposals for Conference sessions to take place at our annual meeting and applications for grants to support speaker expenses at external events. Further information can be found online, including terms and conditions and forms, at www.microbiologysociety.org/proposals

The next key deadlines are below:

- **Proposals for Focused Meetings 2017**
17 June 2016
- **Society-Supported Conference Grants 2016/17**
17 June 2016
- **Proposals for Annual Conference 2017**
16 December 2016

Further information can be found in our events section online:
www.microbiologysociety.org/events

Focused Meetings

Could you run a Focused Meeting with the Microbiology Society?

The Microbiology Society is now into our third year of Focused Meetings, a series of events dedicated to exploring specific topics within the field. Working with members, we have so far produced five successful meetings on subjects ranging from 'Industrial Applications of Metal-Microbe Interactions' to 'Arboviruses and their Vectors'. This article explains why you should consider submitting an application for a meeting and how the Society can help you make it a success.

Focused Meetings provide a forum for people working or studying in the same, or related, areas to network, collaborate and learn from each other. They combine talks from leading scientists with opportunities for new researchers to present their work.

There are many benefits to becoming a Focused Meeting organiser: you get to play a key role in deciding the structure of the event, see papers at an early stage of their development, and help shape the scientific programme. Organising a Focused Meeting for your

peers means that you can be a part of the future direction of your field. It's also a valuable skill to have when working in microbiology and looks great on a CV.

If you have an idea for a Focused Meeting we advise you to discuss it first with your Division. You then need to submit an application, which will be considered by the Society's Scientific Conferences Committee. If your proposal is accepted, Society staff will work with you to organise a successful event. The Conference and Events Team will take care of all venue searching,



Delegates viewing posters at the IAMMI meeting in London, UK, 9–10 November, 2015.

The IMAV 2015 meeting was my first experience of running a Focused Meeting. It turned out to be a great occasion that really fulfilled the aims of bringing the community together and showcasing great science. The experience and support of the Society team was hugely important in the smooth organisation and running of the event.

Alain Kohl, University of Glasgow, Organiser, Focused Meeting 2015: *International Meeting on Arboviruses and their Vectors*

A friendly atmosphere allowed for good conversation and discussion. I was able to make a couple of strong links that I hope to get further research opportunities from.

Delegate, Focused Meeting 2014: *Emerging Challenges and Opportunities in Soil Microbiology*



Delegates attend a session at the IAMMI meeting.



administration and logistics. The Society will support you and the other speakers to create a solid scientific programme, and will market the event effectively so you get the right people there.

To find out more about running a Focused Meeting, go to **www.microbiologysociety.org/proposals** or contact the Society's Conference and Events Team at **conferences@microbiologysociety.org**. The deadline to submit applications for Focused Meetings in 2018 is **31 December 2016**.

A full listing of Society Focused Meeting events can be found at **www.microbiology.society.org/focusedmeetings**

We found organising a Focused Meeting with the Microbiology Society a very pleasurable, hassle-free experience. We were extremely well supported by the administrative team at the Society, which allowed us to concentrate on putting an excellent scientific programme together.

Carol Munro, University of Aberdeen, Organiser, Focused Meeting 2014: *Infection Models to Investigate Microbial Disease and Antimicrobial Therapies*



Upcoming Focused Meetings – abstract submissions and registration now open

Molecular Biology of Archaea 5

1–3 August 2016, London School of Hygiene and Tropical Medicine, London, UK

Topics include:

- DNA, chromosomes and cell cycle
- RNA, CRISPR and viruses
- Molecular assemblies and protein modification
- Genomes and evolution

Early bird registration rate closes on: **Monday 27 June 2016**

Grant application deadline: **Monday 6 June 2016**



The Dynamic Fungus

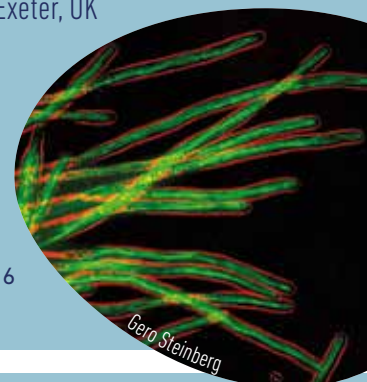
5–7 September 2016, Mercure Exeter Rougemont Hotel, Exeter, UK

Topics include:

- Dynamics of the fungal cell
- Mathematical modelling in fungal science
- Dynamics of cellular differentiation
- Dynamics in fungal pathogenicity
- Dynamic evolution and adaptation of fungi

Early bird registration rate closes on: **Monday 25 July 2016**

Grant application deadline: **Monday 27 June 2016**



Molecular Biology and Pathogenesis of Avian Viruses

27–29 September 2016, Charles Darwin House, London, UK

Topics include:

- Molecular biology and genetics of avian virus replication
- Tropism and host range restriction
- Pathogenesis of avian viruses
- Host antiviral responses and virus immunomodulation
- New and improved approaches to the control of avian viruses

Early bird registration rate closes on: **Monday 1 August 2016**

Grant application deadline: **Monday 4 July 2016**



Further information on the programme and registration can be found online: **www.microbiologysociety.org/focusedmeetings**

Focused Meetings – Irish Division

Our Irish Division has been busy organising two Focused Meetings this year, one in Dublin and one in Cork. These meetings are open to all of the microbiology community.

Host–Pathogen Interactions

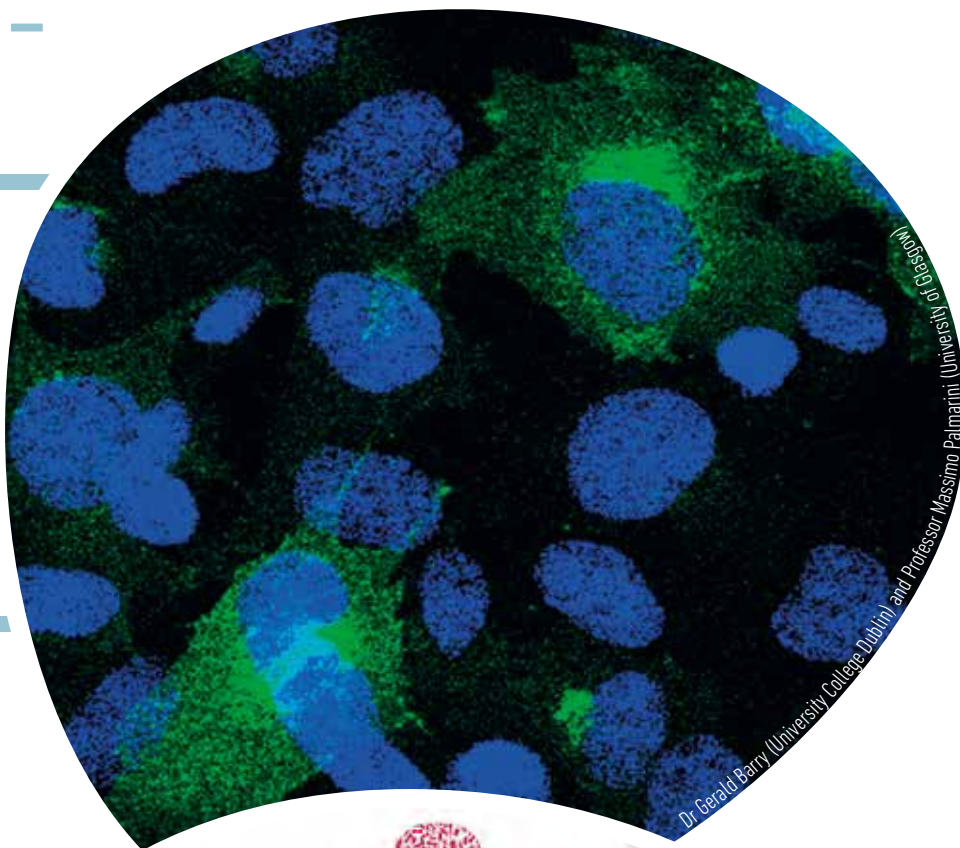
30 June–1 July 2016 (two half-days)
Trinity College Dublin, Dublin, Ireland

Exploring the Microbe– Immune System Interface

1–2 September 2016
Rochestown Park Hotel,
Rochestown, Cork, Ireland

Further information for each meeting including the full programme, confirmed speakers, registration deadlines and grants can be found online: www.microbiologysociety.org/focusedmeetings

For further information contact conferences@microbiologysociety.org



Early Career Microbiologists' Forum: the Executive Committee

The Early Career Microbiologists' (ECM) Forum is a new initiative that will bring our early career members together to play a key role in shaping the Society. This is part of a wider programme to enhance the professional development of our members, and is a fantastic chance to get involved with the Society, have your say, and improve your transferrable skills.

The Forum will provide a voice for early career researchers within our membership – enabling early career members to influence the work of the Society across all of its activities, including conference content, policy work, our journals and our professional development activities. We hope that it will play a major role in helping shape the future development and governance of the Society. Quite simply, we want to hear from you and learn what you want to see us do.

To enable the Forum to feed into the way the Society is run, it will be represented by an Executive Committee – voting for these representatives will take place later this month. Early career members of the Society have to register their interest in joining the Forum, to be able to vote for the Executive Committee. Each member of

the Executive Committee will join one of the Society's Committees or Council. This way, the Forum will have representation throughout our governance, giving it a real opportunity to bring the ECM viewpoint to all proceedings, feeding in the thoughts of the wider Forum.

The roles that will be available are:

- **The Chair** – who will work with Council and the Professional Development Committee and be a member of both Council, which governs the Society, and the Professional Development Committee.
- **The Treasurer** – who will look after the financial responsibilities of the Forum.
- **The Conferences Representative** – who will work with the Scientific Conferences Committee, which considers the scientific content of Society meetings.
- **The Programmes Representative** – who will work with both the Policy and Publishing Committees, which look after the Society's impact in the policy arena and oversee our journal outputs, respectively.

- **The Communications Representative** – who will work with the Communications Committee, which oversees *Microbiology Today*, education and outreach activities and the Society's other communications channels.

- **The International Representative** – who will work with the International Working Group, which ensures the Society is considering its international endeavours.

Each Executive Committee member will serve a term of two years, to enable as many ECMs to benefit from a term in office as possible. Of course, we want to ensure the work and structure of the Forum is set by the Forum itself, so the committee will evolve from these positions over time.

We think this will be a great opportunity for early career microbiologists within our membership. Join today to be involved in the Forum's activities and make the most of the opportunity to have a real impact on our current work and future direction.

Contact: ECM@microbiologysociety.org

Maria Fernandes

Professional Development Officer
m.fernandes@microbiologysociety.org

Life finds a way

Concepts around when life evolved, and how life is formed, can be complex for students to understand. These examples of practical activities can be done with students to demonstrate how long microbes have been in existence, and also show how cells assemble, giving both large-scale and small-scale demonstrations of where life comes from.

How do cells assemble?

Have you ever wondered how cells form? Do they just appear immediately at random as the beautifully coloured structures we see in textbooks? Of course not! Cells self-assemble due to polar forces and interactions with phospholipids. In this experiment, you can demonstrate how the cell wall can assemble in a clear and visible way.

What you need

- flask with a stopper – a jar with a lid will suffice
- cooking oil
- one egg
- small bowl
- eye dropper
- water

What to do

1. Add 100 ml of water to the jar.
2. Add 25 ml of oil.
3. Place the lid on the jar and give it a good shake for 3–5 seconds. The liquids should appear mixed at first and then start separating.

4. While the mixture is separating, crack the egg into the smaller bowl. The egg yolk contains fats, oily compounds and phospholipid compounds.
5. By now, the oil and water should have completely separated and the oil has formed a layer on top of the water. Take the eye dropper, squeeze it and stab it into the centre of the yolk. Get a sample of yolk and add a drop to the jar with the water and oil. The drop of yolk should fall through the oil but float on top of the water layer.
6. Place the lid back on the jar and shake again for 3–5 seconds, like before.
7. Watch what happens to the oil layer this time – there will be some movement!

What is happening

Water molecules are attracted to one another (hydrophilic) due to the polar forces between them. Oil molecules, on the other hand, are non-polar (hydrophobic) and are repelled from the water. This is why you see two distinct layers when oil and water are placed together. Due to oil being less dense, it forms the top layer.

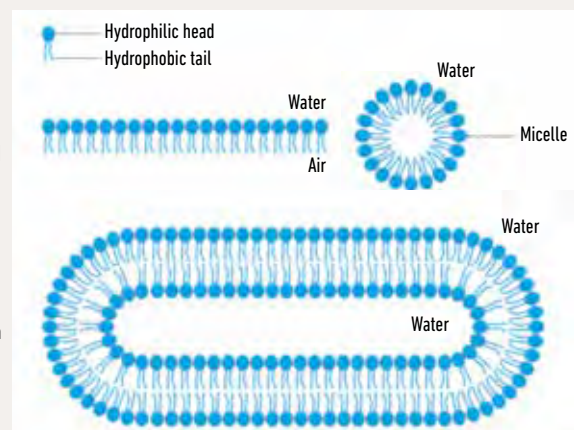
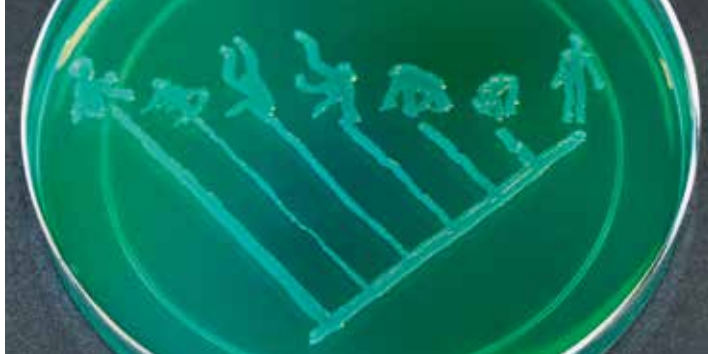


Illustration of phospholipids forming biological membranes.
Science Photo Library



Escherichia coli cultured to produce a phylogenetic tree showing the relatedness of primates. Gregory Lab/microbialart.com/Science Photo Library

How old are microbes?

The Earth is around 5 billion years old and a lot has happened since its formation. Microbes have been around for a large portion of this time. For most people it is too hard to quantify this timescale – so let's visualise it using significant events that led up to life as we know it today.

What you need

- large pieces of card, making up 5 metres in length

Molecules within the yolk are classed as phospholipids, which have a hydrophilic 'head' and a hydrophobic 'tail', as shown by the diagram. This means they can attract both polar and non-polar molecules. Phospholipids make up the majority of the cell wall, by forming a bilayer around polar molecules such as water, DNA or RNA.

Two things are happening when the yolk is added to the oil layer. Firstly, phospholipid and oil molecules will combine and float to the top of the oil layer and form a micelle. Secondly, a bilayer will be formed, similar to that pictured and encapsulate a water molecule, this will move to the lower half of the oil layer.

As the centre of the bilayer has a non-polar core, it makes it very difficult for polar molecules to freely pass through it (due to repulsive forces) and therefore the contents within these vesicles will not leak out. This is how a cell keeps all of its important contents inside!

- 20 small cards
- marker pen
- metre ruler
- tape/glue

What to do

1. Start by laying out the card so there is one long continuous length of 5 metres. This represents 5 billion years and the geological timescale you are working with. (Note – every 1 metre represents 1 billion years and every 10 centimetres represents 100 million years.) It might be an idea to make a mark at every metre to show when 1 billion years has occurred.
2. At one end of the line, mark this with 'present day' and at the other end mark with '5 billion years ago'.
3. Write each of the statements in the table below on one of the 20 cards and place them at the

corresponding length along the line from the 'present day mark'. You may need to draw arrows when it gets closer to present day as a lot of events happen in a short space of time!

4. Once all twenty cards are stuck down along the timeline you can appreciate the history of the world and the origin of life timeline.

Questions to consider

- How do you think scientists know the ages of organisms such as dinosaurs and microbes?
- What factors do you think have influenced major events in the lifetime of the Earth?
- Why do you think single-celled organisms have survived so long?
- What was the difference between the first cells and the first single-celled organisms?

Event	Where on the timeline	Event	Where on the timeline
Earth forms	4.6 m	First cells appear	3.8 m
Single-celled organisms appear	3.5 m	Viruses are present	3.0 m
Cyanobacteria appear	2.2 m	First Ice Age	2.3 m
Eukaryotes appear	2.0 m	Eukaryotes divide into three groups (plants, fungi and animals)	1.5 m
Multicellular animals appear	80 cm	Second Ice Age	7.7 cm
Marine invertebrates appear	60 cm	Earliest fish appear	50 cm
Trees appear	35 cm	Reptiles appear	30 cm
Dinosaurs appear	23.5 cm	Mammals are present	22 cm
Extinction of dinosaurs	6.5 cm	Flowering plants appear	4 cm
Humans diverge from their closest relatives	6 mm	Humans appear	0.005 mm

Hannah Forrest

Public Affairs Administrator

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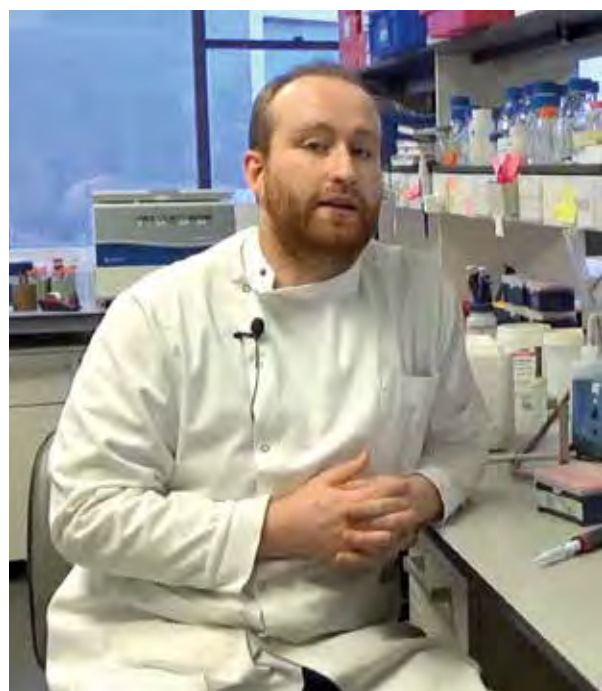
Outreach

Crowdsourcing new antibiotics

Research Associate Jake Newitt has been working hard at the University of East Anglia over the last six months on the samples from our pop-up events last August, as part of the Small World Initiative. Here, he gives his views on working on the project so far.



Participants collecting soil samples.



Jake Newitt in the lab at UEA.

The Small World Initiative is giving the general public, students and educators in the UK and Ireland the opportunity to be part of a global initiative to discover new antibiotics from soil bacteria. The samples collected by the public at the pilot pop-up events are now at the University of East Anglia and I have been looking at each to identify any potentially interesting micro-organisms that are producing antibiotics.

I feel that I am a science communicator at heart, which is why I was so enthusiastic to start my Research Associate position for the Microbiology Society. The work that I do entails a classical screening programme for natural products, with an emphasis on outreach and engagement with the general public. The pilot events were organised at Thetford Forest, Suffolk/Norfolk, and Alice Holt, Surrey, for the general public to get involved with the hunt for new antibiotics by collecting soil samples and following their analysis online (www.microbiologysociety.org/smallworld). At the University of East Anglia (where I am based) I plated out



each of these soil samples and took photographs, which were shared with the general public, who were encouraged to try to identify some of the bacteria.

Additionally, I have filmed a video series called Lab Diaries, documenting the stages of this classical screening for natural products. This is in a video blog style that aims to break down barriers between the public and scientific research, which can all be viewed on YouTube (<http://microb.io/1mv04FT>). I found this challenged me more than I thought it would, despite the fact that I was a writer and editor for a popular science magazine as an undergraduate! When it came to explaining my field of expertise I was so used to using technical jargon that I found it difficult to describe it in simple, understandable terms.

When I was isolating bacteria, I was predominantly looking for *Actinomycetes*, and, in particular, *Streptomyces*. The reason for my focus on this group of bacteria is that more than half of all known antibiotics come from *Streptomyces*. They are quite often easy

to spot – they are usually white and fluffy – and many of them also inhibit the growth of other bacteria around them. These were prime candidates for further analysis. Having isolated over 30 different bacteria (and counting), it was my mission to show that they produced compounds that had antimicrobial properties. Initial bioassays were conducted using soft nutrient agar and an indicator strain (a microbe that we are testing for activity against). This mixture was poured around a small spot of bacteria (that I had isolated from soil), the indicator was given time to grow, and then I would look for an area of inhibition around the isolate.

The future of my work will focus on the elucidation of these compounds; many will likely be rediscovered known compounds, but there is always a chance that a new compound may be found. One

thing that has really struck me about my time during this position is just how time flies. There is always more to be done. I have found that, in truth, science is a real labour. A labour of love, but a labour nonetheless. What keeps me going is the idea that I'm pushing the frontiers of the field forward. I believe that the future of natural product discovery lies with molecular engineering, modifying existing organisms in ways that unlocks silent pathways, producing compounds never before seen under laboratory conditions. Whether we can find a new antibiotic this way using the samples from this project will be known with time!

Jake Newitt

University of East Anglia, Norwich
Research Park, Norwich NR4 7TJ, UK



The interactive stand, where participants could look at *Streptomyces* strains and mixed cultures from soil samples as well as submit their soil sample.

Membership

Q&A

This is a regular column to introduce our members. In this issue, we're pleased to introduce **Suresh Mahalingam**.



S. Mahalingam

Where are you currently based?

I am currently a research professor at the Institute for Glycomics at Griffith University on the sunny Gold Coast in Queensland, Australia.

What is your area of specialism?

I am a virologist, with a particular interest in the pathogenesis and treatment of viral inflammatory diseases.

And more specifically?

In the past 10 years we have focused on understanding how viral infections cause disease in humans. We use animal models to dissect the mechanisms and we also work closely with clinicians to obtain human tissue samples so that we can bridge the gap between basic and clinical data. My work focuses on a number of viral infections in humans, particularly those that cause viral inflammatory disease, such as chikungunya virus, Ross River virus and dengue virus. We also work with respiratory viruses that affect young children, particularly respiratory syncytial virus and human metapneumovirus, for which we have very reliable animal model systems. Once we know the mechanisms that are involved, we can look at current drugs in the market that can be used against the virus. We are also developing vaccines.

Tell us about your education to date

I was raised in a small rural village in Malaysia near the east coast, with little surrounding it in any direction except the Malaysian jungle. It was a simple upbringing, without the distractions of big city life. The education system didn't

cater very well to students in remote villages, and so I was keen to finish school and head to Kuala Lumpur to follow my passion for biology. My second-year research project informed me clearly that my passion lay in biomedical research. I was fortunate to obtain a PhD scholarship at the John Curtin School of Medical Research at the Australian National University, which had a very high performing viral immunology programme, and I was inspired by the Nobel Prize-winning work of Rolf M. Zinkernagel and Peter C. Doherty that had been done there in the 1970s. This was an exciting time for me and confirmed that biomedical research was my true vocation.

Where did your interest in microbiology come from?

As a child, I was always fascinated by biology. During my undergraduate years in Kuala Lumpur, I came down with dengue fever (caused by dengue virus and transmitted by mosquitoes) and spent a very uncomfortable two weeks in hospital. The fact that there were no vaccines or specific antivirals for this virus stimulated a desire to work in the area of infectious disease, with a goal of helping people suffering from dengue and other infectious diseases. My goal remains to use my research skills to make a real difference, particularly for emerging virus diseases that affect poorer, developing countries.

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

The main challenge in research is funding,

as the grant success rate is often very low and a lot of good grants don't get funded. We have been very lucky to secure funding for our research from the Australian National Health and Medical Research Council. One other important thing is to be able to get interest from pharmaceutical companies. We are also trying to foster collaboration with biotechnology and big pharmaceutical companies, and at times this can be challenging as they may have different priorities and goals. I have found it most beneficial to meet with directors of biotechnology and pharmaceutical companies to discuss their drugs or vaccines, and apply them to my research as part of a collaboration. We're also working hard to increase our collaborations with clinicians, so that we can take our research from the bench to the bedside. The best science comes about from being surrounded by the right environment – and it is particularly important to be in a strong intellectual environment, with a critical mass of researchers with overlapping areas of interest.

What is the best part about 'doing science'?

I get enormous satisfaction from the scientific process. The thrill of conclusively proving (or disproving) a hypothesis is hard to beat, followed by the challenge of convincing the scientific community, particularly the reviewers of high impact journals! I also get considerable satisfaction from doing basic science that can influence change in clinical practice or provide a new pathway to therapeutic development.

I feel a deep sense of gratitude for the opportunities that have come my way, and I am passionate about giving back to the scientific community. I take special pleasure in nurturing the younger generation of scientists and the career development of scientists in my lab is a high priority. I am also on the national board of the Australian Institute of Policy & Science and serve this institute as a Tall Poppy Campaign Ambassador. This involves recognising Australian scientific excellence and encouraging younger Australians to follow in the footsteps of our outstanding achievers.

Who is your role model?

I greatly admire leading researchers in the field for their achievements. There are several that I look up to and aspire to follow in their footsteps.

What do you do to relax?

My wife Helen and I have two children, and these days it is family life that keeps me busy outside of the lab. One of my sons is autistic, which presents its own challenges, but he is still the sweetest and most lovable boy I know. My wife often teases me that I am married to my work, but the truth is that family life is the most important to me, and I work very hard to maximise my family time. I also enjoy watching tennis and listening to Indian classical music.

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

I would bring my drum to play and listen to classical performances of great South Indian musicians.

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

I am highly trained in Indian classical music, playing the mirthangam, a South Indian drum. My father taught me and I used to give numerous concerts in Malaysia and Australia.

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

I can't think of any job I would prefer, but perhaps a CEO of a large company, particularly one that supports the community and gives something back to the community.

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

Focused Meeting 2016:

Molecular Biology and Pathogenesis of Avian Viruses

27-29
SEPTEMBER

CHARLES DARWIN HOUSE,
LONDON, UK



Topics will include:

- Molecular biology and genetics of avian virus replication
- Tropism and host range restriction
- Pathogenesis of avian viruses
- Host antiviral responses and virus immunomodulation
- New and improved approaches to the control of avian viruses

Registration and abstract submission is now open. Early bird rates valid until 1 August 2016.
<http://microb.io/avian16>



Organisers:

Mike Skinner (Imperial College London, UK)
Venugopal Nair DBE (The Pirbright Institute, UK)



@MicrobioSoc
#Avian16
<http://microb.io/avian16>



Comstock/Stockbyte/Thinkstock

As preparation for taking part in the consultation process, we would ask you to start thinking now about some of the bigger challenges facing organisations like ours.

We operate in a very different environment now compared with the one just 10 years ago. How we received and paid for our information then looks very different to how many of us receive it now. Cheques, CDs and hard copy were still very much the currency of the day. Compare this with now. Anywhere, anytime and very often for free are today's expectations. Keeping pace with the rate of change in technology presents challenges for all of us.

But more importantly for membership organisations like ours, is our need to keep pace with what our members and prospective members expect from us. How should we position

ourselves to continue to deliver a valued service to members for the next 10, 15, 20 years?

Some may argue that in the age of the internet, learned societies have no place. After all, every one of us now has the potential to build our own networks and find sources of reliable information online. Why would we pay to join an organisation when we can get these benefits for free? It's a valid question.

So where can we add value? How can the Society ensure its relevance going forward?

Part of the answer will lie in making much more of the experiences that cannot easily be replicated online. Our events for example, offer unique opportunities for people to meet each other face-to-face, interact, and be part of a wider discussion and conversation. Many of the benefits of attending conferences and meetings can't be easily quantified. These occasions always bring the unexpected – the introduction you didn't know would lead to the samples you needed; the offer of help made by someone you weren't aware of working on the same problem; a contact about a job; a discussion about a possible funding lead. They are all examples of face-to-face interactions that add value to being part of our wider microbiological community.

And it is perhaps being part of this wider community where membership really comes into its own. Individually, of course, we pursue our own career and professional agendas, whether online or off. But only by acting collectively, through societies like ours, can we really support each other and strengthen the standing and impact of our profession. Through membership, we are able to provide opportunities and make them

available to the widest range of people. We support individual members with grants. We offer career-enhancing governance opportunities. We provide work experience opportunities. We offer peer recognition through a range of prizes and awards. We influence policy-makers. None of this would be possible without our membership.

So, in looking forward to what space we seek to occupy in the future, perhaps a challenge for all of us is to work harder to raise members' consciousness above the level of the individual and the tangible, to the wider view that speaks more about the sense of 'microbiological community' and belonging that comes with membership, and the impact we can have on the collective whole. Maybe we all need to work harder at demonstrating and communicating this.

If you have thoughts and views to share about membership, we'd love to hear them. What are the questions we should be asking? What do you get out of membership? What do we do well? What don't we do that we should be doing? If we were starting the Society from scratch today, how different would it look? How can we ensure what we offer is sustainable? Here's your opportunity to let us know your thoughts so please do!

Look out for the opportunities to contribute during the year, or if you can't wait, send your comments now to **p.easton@microbiologysociety.org**. These will feed into the review process on your behalf during 2016.

Paul Easton

Head of Membership Services

p.easton@microbiologysociety.org

Best of the blog

As the weather warms up for those of us here in the Northern Hemisphere, I thought it might be right to look at some of the temperature-related blog posts we've had over the past few months.

Firstly in this roundup, we learnt about the ancient 'Iceman', also known as Ötzi, whose body was discovered in 1991 after spending millennia buried under snow and ice in the Alps. This remarkable find gave researchers the chance to gaze far back into our past. One of these researchers is Dr Frank Maixner, who has been studying Ötzi's gut microbiota. Frank spoke to our Multimedia Producer Anand Jagatia about the work, which may help us better understand human migration thousands of years ago (<http://microb.io/1UPpY6l>).

When the weather's warm, I like to go surfing. Sadly, I am quite bad at it and spend more time in the sea than on my board. Might this lead to me increasing my risk of coming into contact with antibiotic-resistant bacteria? Anand went to Cornwall to interview Anne Leonard, a PhD student at the University of Exeter Medical School, who is running the Beach Bum Survey to assess the gut bacteria of surfers in Southwest England (<http://microb.io/1QRL2t1>).



Ötzi, the 'Iceman'. Thilo Parg / Wikimedia Commons

You know what're warm? Hand driers are warm (alright, this is getting a little tenuous now). Might the air coming out of the jet hand driers be responsible for spreading viruses in public washrooms? We spoke to Dr Patrick Kimmitt at the University of Westminster, who has been researching this issue (<http://microb.io/1pvgyRy>).

We don't tend to find many microbiology-related papers in the journal *Nature Physics*, but this is exactly the source of some new research we covered in a podcast earlier this year. We learnt from the University of Cambridge's Professor Raymond Goldstein about how the mathematical principals can be used to explore both the swimming of bacteria and the spin of electrons (<http://microb.io/21Vn99m>).

We've learnt about a lot of newly discovered microbes over the

past few months. Some of my favourites include: *Lactobacillus wasatchensis* from aged cheddar cheese (<http://microb.io/1Uajtu9>); the ultramicrobacteria *Aurantimicrobium minutum* (<http://microb.io/1SwuG8x>); and three new species of *Bifidobacterium* isolated from the faeces of baby marmosets (<http://microb.io/1Uajtu9>).

At the time of writing, we're yet to have this year's Annual Conference, but if the quality of the abstracts is anything to go by, I'm sure you'll have an amazing time. There'll be a host of Conference-related posts and podcasts on our site, so don't forget to have a read of the *Microbe Post* to see what you might have missed.

Benjamin Thompson

Head of Communications

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Reviews

Thermophilic Microorganisms

Edited by F. Li

Caister Academic Press (2015)

£159.00 ISBN 978-1910190135

Thermophilic micro-organisms are quite a diverse group of micro-organisms and have brought us fascinating scientific and biotechnological interests, such as the diversity and evolutionary history of these thermophiles, their ecological roles and adaptation mechanisms to high temperature environments, and their applications in bioprocessing and bioremediation scenes.

This book presents 10 selected topics of thermophilic micro-organisms

by the leading experts in each field. It covers subjects such as the ecology of deep-sea thermophiles and their genetic systems, the diversity of thermophiles and their roles in carbon cycling and biomass degradation, and the biochemical properties of a variety of heat-active enzymes and their current and possible applications. Each chapter is concise and readable, providing lucid explanations about the current understanding and prospective views of the fields.

This book would be an invaluable resource for any researcher interested in these exotic microbes and their applications, from senior undergraduates and postgraduates to scientists and engineers.



Takashi Itoh

RIKEN BioResource Center

Focused Meeting 2016:

Molecular Biology of Archaea 5

1-3 AUGUST

LONDON SCHOOL OF HYGIENE
& TROPICAL MEDICINE,
LONDON, UK



Topics will include:

- DNA, chromosomes and the archaeal cell cycle
- RNA, CRISPR and viruses
- Molecular assemblies and protein modification
- Genomes and evolution

Registration and abstract submission is now open. Early bird rates valid until 27 June 2016.
<http://microb.io/archaea5>



Organisers:

Thorsten Allers (University of Nottingham, UK)
Malcolm White (University of St Andrews, UK)



@MicrobioSoc
#Archaea5
<http://microb.io/archaea5>



Microbiology: A Clinical Approach (2nd Edition)

Written by A. Strelkauskas, A. Edwards, B. Fahnert, G. Pryor and J. Strelkauskas
Garland Science (2015)
£60.00 ISBN 978-0815345138

There is no shortage of textbooks that deal with general or clinical microbiology. I have nine in my own office and many other microbiology textbooks that deal with more specialist topics. It is important therefore that books introduced into this market approach the topic from a different angle. My initial thought on being sent this book was that there is little space for a new text in the market or even on my shelf, but having spent time reading this book I believe that it has succeeded in differentiating itself from other apparently similar offerings. The book is aimed mainly at nursing and allied health students and, based on my own experience, I believe that this would be a useful resource for the pharmacy students that I teach.

The topics and depth of coverage reflect a 'need-to-know' approach for the intended readership, reflecting the way that allied health disciplines are often taught. Material is presented clearly and with emphasis at the start of

each chapter on why a given topic is important. Each chapter has been colour-coded with 'fast fact' and 'keep in mind' sections that condense the main messages and provide relevant context.

To facilitate learning, chapters have sections titled: 'self-evaluation' and 'chapter-confidence', with a series of multiple choice questions; 'depth of understanding', with more discursive questions; and 'clinical corner', which reinforces the clinical relevance of chapter material.

The book is nicely illustrated throughout and well supported by a website, which incidentally is also excellent. The 'bug parade' section of the website even has embedded sound files to cover the pronunciation of bacterial names and links these to morphology, disease and to the associated chapters in the book. A large number of excellent videos are also available.

In summary, this is an excellent learning resource that is targeted at pre-nursing and allied health students but would be a useful resource for medical and microbiology students and their lecturers.

Andrew McBain

University of Manchester



• **Acidophiles: Life in Extremely Acidic Environments**
April 2016

• **Climate Change and Microbial Ecology: Current Research and Future Trends**
March 2016

• **Virus Evolution: Current Research and Future Directions**
January 2016

• **Thermophilic Microorganisms**
September 2015

• **Halophiles: Genetics and Genomes**
May 2014
"up-to-date and highly readable" (Biospektrum)

• **Bioinformatics and Data Analysis in Microbiology**
April 2014

• **Cold-Adapted Microorganisms**
September 2013
"a wealth of interesting findings" (Biospektrum)

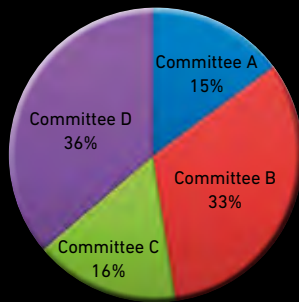
• **Extremophiles: Microbiology and Biotechnology**
January 2012
"recommended" (Microbiology Today)

• **Archaea: New Models for Prokaryotic Biology**
April 2008
"...captures the imagination of students, researchers and PIs" (Microbiology Today)



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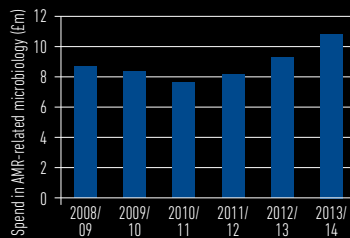
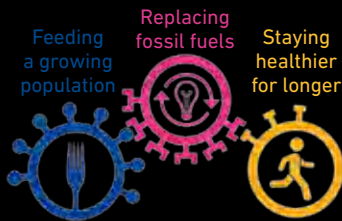
BBSRC invests
>30% of its
research budget
on microbiology



BBSRC invested
in over
2100 grants

over 95
institutions

over
950 PIs



examples of Research Councils working together such as the new AMR programme.

Though the BBSRC microbiology portfolio is very healthy there are some areas where we need to do more work in partnership with the community. Plant virology and research on animal fungal pathogens form relatively small parts of the portfolio – there is a need to encourage the next generation of researchers into these fields – and levels of funding on foodborne pathogens has been falling at a time when Defra and the Food Standards Agency funding has also reduced. BBSRC is currently discussing these issues through our various advisory structures. I would note if anyone is interested in joining a BBSRC panel or committee, our annual call for new members opens in May.

Acknowledgements

This analysis fed into an expert working group chaired by Professor Sarah Gurr, and I would like to thank all the participants for their time and consideration on this.

Adam Staines

Head of Strategy (joint): Agriculture and Food Security, BBSRC
adam.staines@bbsrc.ac.uk

For more information about BBSRC, our science and our impact see: www.bbsrc.ac.uk.

To note: 'microbiology' is defined by investments containing a substantial component investigating the microbes themselves, i.e. excluding microbes just being used as a research tool.

species, and microbes that interact with animal, human or plant systems.

So one of the myths I would like to dispel is the type of research BBSRC supports. I have heard comments that we only support basic microbiology in model systems or that we are only interested in applied microbiology. Well, in keeping with our strategic priorities, which cover both areas, the good news is we invest in the continuum of microbiology research, from fundamental discovery science, through to more translational and applied areas. This is also reflected in the sources of funding, which include ~40% funding through the Responsive Mode mechanism, and the rest is split pretty evenly between initiatives and institute programmes.

One of the strengths of the microbiology community is that their research spans all four BBSRC Responsive Mode Committees, depending on the nature of the research question. The downside of this is that any individual committee member only has visibility of a subset of the microbiology grants we fund. I think this has, in part, led to some of the misconceptions about our portfolio; one committee member who reviewed the portfolio apologised to me for being 'grumpy' about microbiology investments when he saw how

much was funded through the other committees and mechanisms.

Another myth I was pleased to dispel was around success rates. The data demonstrated that microbiology does better than the average success rates in three out of four committees, and better than average overall. I think there is an inherent frustration from applicants when grant proposals are unsuccessful, and with 20–25% success rates that is most applicants, most of the time. But I can reassure the microbiology community that they do well in our Responsive Mode system.

There were also a number of pleasing trends in the portfolio; we have been investing in an increasing level of human gut and skin microbiome research; the use of industrial schemes has doubled in the last six years too (12% of the microbiology portfolio). We also identified many new exciting impacts from the research we have invested in.

We often find ourselves discussing with the community how we handle interdisciplinary proposals. An RCUK-wide agreement ensures all Responsive Mode research proposals have a home, and where proposals have elements in other councils' remits, co-funding is often provided. There was no evidence from the portfolio of an issue in this regard; and there are lots of positive

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Professor Steven Bentley, Editor-in-Chief (Wellcome Trust Sanger Institute, UK)



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IMMUNOBIOLOGY

NINTH EDITION

Kenneth Murphy, Washington University School of Medicine, USA

Casey Weaver, University of Alabama at Birmingham, USA



Janeway's Immunobiology is a textbook for students studying immunology at the undergraduate, graduate, and medical school levels. As an introductory text, students will appreciate the book's clear writing and informative illustrations, while advanced students and working immunologists will value its comprehensive scope and depth.

The Ninth Edition has been thoroughly revised bringing the content up-to-date with significant developments in the field, especially on the topic of innate immunity, and improving the presentation of topics across chapters for better continuity.

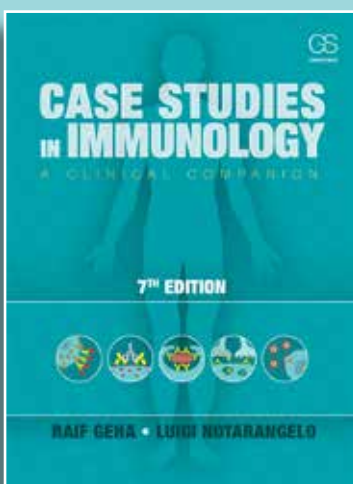
Also new to the Ninth Edition is a Question Bank available to adopting instructors, and the Garland Science Learning System which allows instructors to assign online tutorials with assessments on specific immunology topics and review the performance of the entire class, as well as individual students, via the instructor dashboard.

April 2016 • Paperback • 928pp • 624 illus

978-0-8153-4551-0 • £60.00

New Seventh Edition Case Studies in Immunology

Raif Geha and Luigi Notarangelo, both at Harvard Medical School, USA



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Each case history is preceded by essential scientific facts about the immunological mechanisms of that specific disorder. The cases themselves demonstrate how immunological problems are deconstructed in the clinic and each one is followed by a concise summary of the clinical finding and questions which can serve as discussion points.

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March 2016 • Paperback • 358pp • 255 illus

978-0-8153-4512-1 • £41.00

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GS Garland Science
Taylor & Francis Group
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