microbiologist

March 2017 : Vol 18 No 1: ISSN 1479-2699

The magazine of the
Society for Applied Microbiology

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Microbiologist

Microbiologist is published quarterly by the Society for Applied Microbiology, a registered charity. ISSN 1479-2699.

Copy Dates:

Vol. 18. No.2 June 2017
Wednesday 5 April

Vol. 18. No.3 September 2017
Wednesday 5 June

Vol. 18. No.4 December 2017
Wednesday 4 October

Vol. 19. No.1 March 2018
Wednesday 10 January

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Paul Sainsbury reviews the content of this issue

microbiologist

Living in harmony

Seeking inspiration for the March editorial, I turned to the dictionary to find the etymology of symbiosis – the theme to this edition of *Microbiologist*.

Symbiosis: late 19th century: modern Latin, from Greek *sumbiōsis* 'a living together', from *sumbioun* 'live together', from *sumbios* 'companion'.

As I write this, the political effects of a toxic combination of the most prolonged period of economic stagnation and the worst refugee crisis since the end of the Second World War are materializing across the globe. A looming Brexit, Trumpism and the rise of right-wing political parties across Europe does not a feeling of 'togetherness' engender.

Perhaps it is time we took lessons from the experts in living together. Bacteria.

Every few months more details emerge about a biological organism (or part of an organism) with its own distinct -biome and about the implications that particular symbiotic relationship has to our wider understanding of the world in which we live. An interesting example was recently published in the journal *Environmental Microbiology*, with research showing that the microbiome of flower pollen could have major implications both for allergy sufferers and for bees. Read all about it at http://bit.ly/2leWmC8.

This issue explores some other bacterial symbiotic relationships that you not may be familiar with. We take a look at the microbiomes of plants, aphids, flies and even an architect's vision of what a living building might look like. Louise Hill-King's feature on *Wohlfahrtiimonas chitiniclastica* is particularly gripping, although it does have a few stomach-churning moments… Don't Google myiasis for images – you can't 'un-see' them.

If the microbiome is of particular interest to you, we recommend you join us at our **Microbiome and Human Health** meeting on 12th April 2017. We are also pleased to announce that the Early Career Scientists Science Communications workshop at the **Annual Applied Microbiology Conference 2017** will feature Holly Squire from The Conversation and David Gregory-Kumar from the BBC. Check out the Members' Wall in this issue for further information, and book your place for all SfAM events on our website.

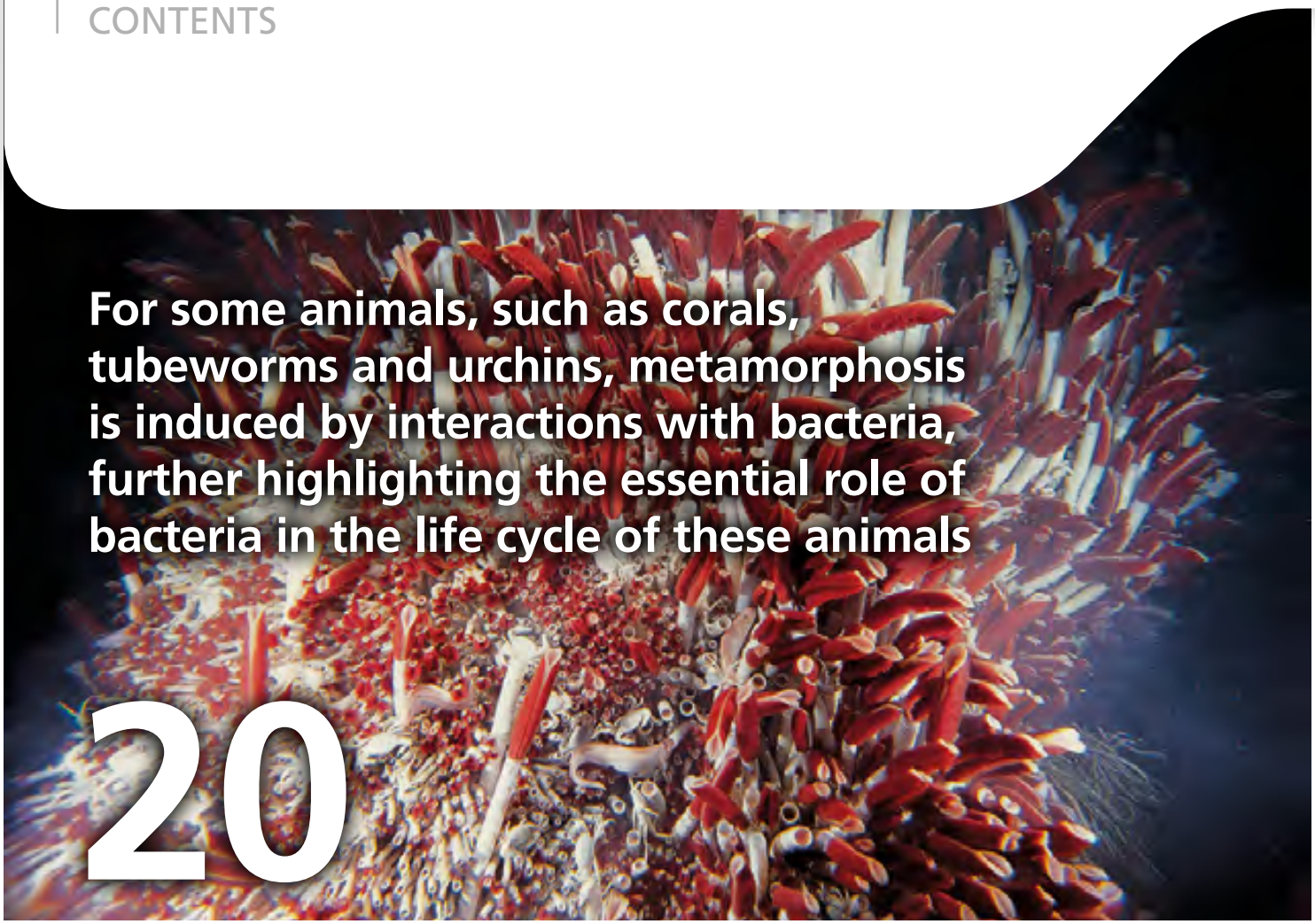
Perhaps it is time we took lessons from the experts in living together. Bacteria.

NEWS IN BRIEF

Mark Walport is to take on the most powerful job in UK science. From 2018, he will be the first head of a new central funding organization called UK Research and Innovation (UKRI), which will oversee more than £6 billion (US$7.4 billion) of research funding per year.
http://go.nature.com/2kldQfv

International rules to ensure that developing countries benefit when foreign companies make use of their biological resources could delay the supply of seasonal influenza vaccines or render those vaccines less effective, warn vaccine manufacturers and researchers.
http://go.nature.com/2lpWBdV

Paul Sainsbury, *Editor*



For some animals, such as corals, tubeworms and urchins, metamorphosis is induced by interactions with bacteria, further highlighting the essential role of bacteria in the life cycle of these animals

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MEMBERS' WALL

COMMERCIAL

President's column

The year 2017 promises to be a very busy one for the Society as we consolidate the changes from the move to Charles Darwin House and bring a number of planned initiatives into action. We do of course have a programme of meetings organized throughout the forthcoming year and I hope to see many of you at these.

The Annual Conference in July this year is on *New Insights into Food Safety* and will be held at the BALTIC Centre for Contemporary Art in Gateshead. This is an exciting programme with a range of international speakers, covering both our current understanding of the key pathogens involved in foodborne disease and new approaches for control. We have included offered paper slots again in the programme and so we encourage you to send in your abstracts as potential speakers. One of the highlights of the Annual Conference is of course the W H Pierce lecture. The W H Pierce Prize is the Society's most prestigious prize and is awarded annually to a young Society Member (under the age of 40) who is considered to have made a substantial contribution to applied microbiology. The prize was established by Oxoid, and is administered by the Society, in commemoration of Bill Pierce who was the Chief Bacteriologist of Oxoid Limited and became a prime mover behind the foundation of the Oxoid range of dehydrated culture media, with which we are all familiar. Last year the prize was awarded to Professor Jack Gilbert who is the Director of the Microbiome Center and a Professor of Surgery at the University of Chicago. Those of you who attended the conference in Edinburgh will have had the pleasure of hearing Jack's fabulous lecture on *Invisible influence: how the indoor microbiome influences health*. We had the added pleasure in Edinburgh of Bill Pierce's family being able to attend the lecture.

Nominations for this award can be made by Full and International Members of the Society and we are always pleased to receive suggestions for potential nominees.

Microbiome analysis is a fast-moving field which has developed with the advent of high-throughput genome sequencing and associated genome analysis methods which have enabled non-culture based characterization of complex microbial communities. This has allowed us to gain a much greater insight into our external and internal environments than was previously possible. One of these aspects, *The Microbiome and Human Health*, is the topic for our one-day conference in April, which will consider our developing knowledge of how microbiomes influence a range of functions from our immune system to our behaviour. Also in April is our Early Career Scientists (ECS) 6th Annual Research Symposium, this year with a workshop on Bioinformatics. There will of course be more to come over the rest of the year, but I hope this shows what an exciting year we have planned ahead.

Finally, I would like to say thank you to those long-standing Members of the Society who have written to thank me for the 50-year membership badges we sent them last year. It has been a delight to receive your letters and to know this small token has been so appreciated.

Christine Dodd
President of the Society

Harper's Postulates

Notes from the Chief Executive

Collaboration, collaboration, collaboration

As I mentioned in my previous column for *Microbiologist*, one of the many benefits of the Society's move to Charles Darwin House is that we are now in such close proximity to so many like-minded organizations. This facilitates collaboration, information and knowledge exchange, and of course the sharing of best practice.

Ever since the Society was founded in 1931, SfAM has worked collaboratively with organizations such as Med-Vet-Net, British Society for Immunology, Microbiology Society, Royal Society of Biology and Biochemical Society on activities such as public engagement, scientific meetings and policy. In fact, the basis of the Society's beginnings was a need amongst a group of dairy bacteriologists to work together, share ideas and make progress.

A great example of the collaborative activities the Society has been involved with since our move to London includes our Twitter chat on Antimicrobial Resistance (AMR) #AntibioticFuture, which was held on Antibiotic Awareness Day, 18 November 2016. We worked alongside the Biochemical Society and the Royal Society of Biology, engaging with our rapidly increasing Twitter audience.

We also continue our collaboration with six other Learned Societies through the Learned Society's Partnership on Antimicrobial Resistance (LeSPAR). This group aims to provide a single, unified voice and mobilize the UK's collective research community in order to enhance understanding and knowledge sharing between academia, industry and clinicians. The group is focused on taking action, championing best practice and raising awareness of the global challenge of antimicrobial resistance. LeSPAR are organizing an early career scientists workshop during 2017 which will focus on diagnostics in AMR and aims to foster interdisciplinary collaborations in this important policy area.

With an increased emphasis on interdisciplinary research across scientific research, the need for collaboration has never been so important. Collaboration brings a perspective which an organization would find impossible to gain when operating alone. For us it provides the Society with a strength and resilience which wouldn't have been possible otherwise. To this end, we have a number of collaborative scientific meetings in the pipeline which we feel will benefit the Society, our collaborators and delegates who will be able to foster interdisciplinary connections and collaborations themselves as a result.

In the words of Charles Darwin, the namesake of our new HQ: "*In the long history of humankind, those who have learned to collaborate and improvise most effectively have prevailed*".

In the long history of humankind, those who have learned to collaborate and improvise most effectively have prevailed

Lucy Harper
SfAM *Chief Executive*

The academic bottleneck

As life science PhD students many of you will aspire to an academic career and if so, the route is well planned. Finish your PhD, spend a few years as a postdoc and then apply for permanent jobs. Although postdoctoral research positions remain accessible for those who want them, the transition from researcher to lecturer is becoming an area of major concern.

This is partly caused by a large increase worldwide in the number of PhDs being awarded over the last couple of decades, in contrast to the number of faculty positions available at universities which has remained unchanged for the last 30 years. This has led to the number of postdocs in the US almost tripling over the same period, meaning that eventually, more than 80% of PhD students will end up leaving academia. Although these statistics are focused in the US, the trends in this country are broadly the same.

My own story was that after completing my PhD I moved to a postdoc in Oxford for three years, after which my then boss moved to Kingston University and brought me with her to establish a new research lab and to take up a lectureship. This was a very fortuitous turn of events and I certainly buck the trend as, on average, people spend at least 4–5 years in postdoc positions before they obtain a permanent position (although it is not unusual for it to be more than 10 years).

So what can you do to prevent getting stuck in the postdoc loop? The first thing to realize, and the reason I wrote this article, is that you may not end up in an academic career and so it is important to plan accordingly. If you want a career in academia you need to be as flexible as possible, especially in terms of where you live. Like in any job market staying in one place too long is counterproductive and the more flexible you are the more chances you will have for progression. It is also important to foster relationships – the more people you know, the better your chances of moving on. If you are going to move away from academia think about how you can gain the skills that are important for the type of job you might want to apply for. A good example is management skills – why not offer to take charge of an MSc or undergraduate project for your supervisor? Presentation skills are also vital, so speaking at conferences is always a bonus, but why not suggest starting a weekly journal club in your group if you don't have one already?

We are all living in a world where job markets are becoming more and more competitive. The best piece of advice I think you can get when entering it is to have an open mind.

sfam ECS EarlyCareerScientists

Ali Ryan
ECS Publications Officer

THE NAGOYA PROTOCOL: access and benefit-sharing of genetic resources in microbiology – a UK perspective

The importance of microorganisms is evident and without the work of microbiologists the world we live in would be very different. A diverse range of sectors include microorganisms in their research and development programmes. Everything from pharmaceutical, transport, food and beverage to emerging biotechnologies employ microbiologists tasked with making the next discovery in medicines, biofuels, foodstuffs and other products we take for granted.

Microbiology research relies on access to genetic resources in the form of microorganisms. There is interest in microorganisms around the world and from a diverse range of ecosystems such as forests, oceans or indeed, the gut microbiome of dispersed populations. Access to these genetic resources is critical if scientists are to continue addressing some of today's global challenges, including food security, pollution and climate change, and tackling diseases.

In 2014, *the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization* entered into force, addressing the third component of The UN's Convention on Biological Diversity (CBD). Commonly shortened to *The Nagoya Protocol on Access and Benefit Sharing (ABS)* the legislation sets out the framework by which those utilizing genetic resources in research and development programmes must first seek consent and agree terms with those providing the resources, acknowledging the sovereign right countries hold over their genetic resources. To date, 93 countries have ratified the Protocol, with the UK becoming Party in May 2016.

FURTHER READING

The CBD: The Nagoya Protocol
https://www.cbd.int/abs/

ABS Clearing House
https://absch.cbd.int

EU Commission
http://ec.europa.eu/environment/nature/**biodiversity/international/abs/index_en.htm**

Regulatory Delivery and ABS
https://www.gov.uk/guidance/abs

Benefit sharing is a key component of The Nagoya Protocol and can be applied in a variety of ways. It is not solely restricted to monetary benefits and indeed non-monetary benefits can result in significant value addition with on the ground impact. The benefits that arise from microbiological research and development have the potential to be significant and far reaching, and provider countries will have the opportunity to benefit by implementing effective legislation which simultaneously protects their sovereign rights and facilitates access to genetic resources. For many, the concept of benefit sharing is not new with both academic and research institutions as well as culture collections having all actively participated in training and exchange programmes, sharing research results and technology transfers. The Nagoya Protocol and associated legislation formalizes the process somewhat through the requirement for certain permits and contracts. In the UK, Regulatory Delivery (RD) is the Competent Authority for ABS, appointed by DEFRA and responsible for enforcing the EU ABS Regulation in the UK. A primary objective of RD is to support UK businesses and organizations to comply with ABS legislation, firstly by bringing it to their attention and supporting understanding, and in time through compliance checks of those utilizing genetic resources. Achieving this objective without the support of the sectors themselves would be an onerous task, and within the microbiology sector, RD is working with the UK Biological Resource Centre (UKBRC) Network to support awareness raising and compliance requirements within the community.

As with any new area of legislation, there are challenges ahead. However, as stipulated under the CBD, access and benefit-sharing has the potential to positively influence biodiversity and its continued application in the discovery of new products and services is for the global good.

Katie Beckett
Department for Business, Energy and Industrial Strategy

BIOFOCUS

Working with Government to ensure support for UK research

The Royal Society of Biology has been working to represent the views of its members and member organizations in our policy work, as the Government approaches the challenging Brexit negotiations ahead.

We set out our position in a policy briefing on '*Arguments in favour of public investment in UK research and innovation*', and were pleased to see the importance placed on research and development (R&D) in the Autumn Statement. The Chancellor said that the UK "*does not invest enough in research, development and innovation*" and that to amend this, the UK will build on its strength in innovation in science and technology, to ensure the next generation of technological discoveries are made and developed in the UK. The announcements of funding and regulatory support built on the new substantial investment in R&D worth £2bn per year by 2020, revealed shortly beforehand by the Prime Minister.

We welcome the Government's commitments to helping the UK maintain its leading role in R&D. The RSB is keen to continue working with and advising Government to ensure that global collaboration and the international flow of talented people is enabled and supported, and the right regulatory environment created, in order to truly benefit from the financial investment in UK R&D.

In December, representatives from the RSB took part in discussions with Robin Walker MP from the Government Department for Exiting the EU, along with other scientific and conservation charities. The discussion included topics such as funding for research and innovation, continent-wide collaborative programmes, talent recruitment in the science community and the importance of maintaining international environmental standards, as the UK leaves the EU. We look forward to ongoing discussions with the Government and others, and to building on collaborative and joint working approaches across the sector.

The provision of scientific advice is a key activity for the RSB and our members. So we were very pleased that the Cabinet Office withdrew from the proposed 'anti-lobbying clause' in their grant standards, which would have restricted publicly funded scientists and researchers from using their expertise to advise MPs and Ministers. As an early intervention in March 2016, I, along with chief executives of eight member Learned Societies, including *Sf*AM, wrote to the Cabinet Office Minister Matt Hancock to highlight community concern and seek a solution. We are relieved that Government has listened to the concerns of the community, removed uncertainty, and officially acknowledged that informing policy and public debate is an integral part of the research process.

The RSB's public engagement work brought food experts to Cardiff for a 'Come Dine with the Future' event in November. Five researchers outlined strategies including urban farming, insect eating, GM livestock and rice grown using recycled sewage, in order to create a menu of the future which could sustainably nourish our growing population. We also crowned the hedgehog the Favourite UK Mammal with a huge majority of the 5,000 votes in our public poll; which aimed to highlight population decline and conservation of diverse UK mammals, especially during the winter months.

During World Antibiotic Awareness Week, the RSB worked with the Biochemical Society and *Sf*AM to run a live tweet chat with AMR experts. The hour-long Q&A was a great success with questions pouring in on everything from farming to diagnostics, to vaccines and phage therapy. It was great to work across audiences to increase engagement and understanding of this important and complex topic.

The UK will build on its strength in innovation in science and technology, to ensure the next generation of technological discoveries are made and developed in the UK

Dr Mark Downs CBiol FRSB
Chief Executive of the Royal Society of Biology

WHAT DID YOU

Not so long ago, life in my NHS microbiology lab revolved around a modest number of bacteria. Had I asked a fellow biomedical scientist to write a list of the organisms we would typically encounter, one sheet of A4 would probably have sufficed. Perhaps a particularly enthusiastic colleague would have made it onto the back of the sheet.

All of that changed in 2011 when we launched ourselves into the brave new world of MALDI-TOF. Our horizons expanded exponentially overnight. No longer could we blithely send reports to our clinicians, cosseted in the familiarity of *Staphylococcus aureus*, *E. coli* and *Pseudomonas aeruginosa et al*. At that time, the Biotyper database of organisms (Bruker, Bremen, Germany) contained 3,995 strains representing approximately 330 genera and 2,000 species. With the current database, these numbers have risen to 6,903, 424 and 2,461, respectively.

In one sense, this new 'black box' seemed almost like magic, reducing the need for experienced scientists to apply their knowledge and understanding in order to identify the potential pathogens in patient samples. In goes a smear of an organism on a metal plate and, a few minutes later, out pops the identification. There was talk of redundancy of skills. In another sense, however, this technology paved the way for us to apply our minds to a new challenge: for each identification of an unexpected or unfamiliar species we needed to ask, '*What is the significance of that?*' The next question quickly became, '*How can we do antibiotic susceptibility testing for these organisms which do not appear in BSAC or EUCAST tables?*' We are still grappling with the answers to those questions. It will be some time before extensive research can collectively provide evidence on which to base our decisions.

To harness the wonder of new MALDI-TOF users (and convince non-users that they were stuck in the Dark Ages) the company who manufacture and sell the Microflex instruments produced a series of T-shirts, posing the question, 'What did you identify today?' Beneath these words was an image of a MALDI-TOF spectrum along with the name of a hitherto unheard-of organism. I was the proud owner of the first of these T-shirts, brandishing the name *Wohlfahrtiimonas chitiniclastica*. I had to know more!

In 1770, a German surgeon described a fly, the larvae (maggots) of which he had removed from a patient's eye. After a period of being called *Sarcophila magnifica*, the fly was renamed *Sarcophila wohlfahrti* by Portschinsky in 1875. Portschinsky is reported to have advised people to avoid sleeping outside during the hours of 10:00 and 16:00 to avoid the risk of the flies falling into open mouths – a portal of entry which could lead to subsequent infestation of oral tissue. The current name of *Wohlfahrtia magnifica* came into being when the genus *Wohlfahrtia* was created by Brauer and Bergenstamm in 1889. It is commonly known as the spotted flesh fly.

Myiasis is the term used to describe infestation of vertebrate tissues by dipterous larvae. Three major species are responsible for this affliction which is widespread across Eurasia and associated with severe losses in animal husbandry: *Cochliomyia hominivorax* (New World screwworm), *Chrysomya bezziana* (Old World screwworm) and *W. magnifica*.

The eggs hatch into legless larvae which feed voraciously on the flesh of their host

IDENTIFY TODAY?

Colonies of W. chitiniclastica growing on chocolate agar

Insects are known to carry numerous bacterial symbionts. One such example is the Gram-negative bacillus, *W. chitiniclastica*, harboured by several flies including *W. magnifica*. The clue to the bacterial contribution to the fly's life cycle is in the name: *Wohlfahrtiimonas chitiniclastica* literally means chitin-cleaving monad (unit) of Wohlfahrtia.

Adult flies lay their eggs on exposed vertebrate flesh. The eggs hatch into legless larvae which feed voraciously on the flesh of their host, able to wriggle through it with the aid of digestive enzymes. As they feed they grow, passing through three stages (instars), moulting between each stage. It is then time to migrate to a dark place to form a pupa with a hard brown chitinous shell. Within this protective shell the adult fly develops, forming legs and wings. The species name *chitiniclastica* is derived from the strong chitinase activity that the organism has been shown to display. As the chitinous shell is broken down the adult fly can emerge, soon to lay more eggs to begin the cycle again.

Despite the plethora of literature regarding myiasis and known symbiotic relationships between insects and bacteria, relatively little can be found in the medical literature about human colonization and infection with *W. chitiniclastica*. I was therefore taken aback when, in 2013, a blood culture isolate in my laboratory was identified as this organism by MALDI-TOF. Much excitement ensued and the T-shirt was dug out from the back of my wardrobe. But where had this isolate come from?

A sad story unfolded as it transpired that the patient was an 82-year-old lady who had been found collapsed in her garden, probably undiscovered for 3–4 days. She was infested with larvae, especially in her ear canals. The larvae were not of *Wohlfahrtia magnifica*, which are not commonly found in the UK; they were of the common green bottle fly, *Lucilia sericata*. The clinical significance of *W. chitiniclastica* in the blood culture of our patient was uncertain as it yielded a mixed growth of four organisms. Nevertheless, the story awakened our interest and had a happy ending; the lady responded to treatment and made a good clinical recovery.

Two previous groups had reported isolation of *W. chitiniclastica* from human samples, one in Argentina and the other in France. They both involved homeless

individuals with a history of alcoholism, one of whom died from fulminant sepsis. It can be speculated that reports of this organism are so sparse because many diagnostic laboratories do not have the capability to identify it. Two widely used traditional methods for identification of Gram-negative bacilli, Vitek-2 and api 20ne (bio Meriéux, France) have both been reported to misidentify *W. chitiniclastica* as *Acinetobacter lwoffii*. This is an organism which may even have made it onto the aforementioned sheet of A4 so the name would not have alerted anybody to the possibility of a much less common isolate. Dismissal of *A. lwoffii* as a skin contaminant is common practice.

Time will tell how significant *W. chitiniclastica* is in human clinical samples. As more and more laboratories adopt MALDI-TOF and other such techniques with high discriminatory ability, we will collectively be able to inform our response to the questions, '*What is the significance of that?*' and, '*How can we do antibiotic susceptibility testing for these organisms which do not appear in BSAC or EUCAST tables?*'

In the meantime, I must rise to the challenge of isolating the bacterium highlighted on the second T-shirt of the series: *Laribacter hongkongensis*. Maybe a trip to the Orient is on the cards?

Insects are known to carry numerous bacterial symbionts

FURTHER READING

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With thanks to James Clayton, Royal Surrey County Hospital, for clinical information.

Louise Hill-King
Frimley Park Hospital

LIFESTYLE BACTERIA in aphids

"I'm fed up with aphids on my roses. Is there a way to control them?

This is a common question that gardeners continue to ask, but for the time being, there isn't a satisfactory answer.

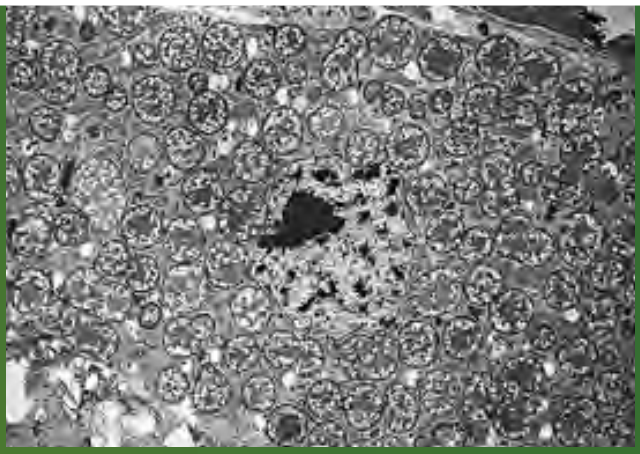
Fascinating bacterial communities live inside the aphid and understanding them could one day help us to control them and the plant viruses they transmit.

Most insects harbour symbiotic bacteria that affect their lifestyle and aphids are no exception. They are a group of species in which the interactions between the host insect and their internal bacteria are quite well understood. Broadly speaking, there are two types of symbiotic bacteria in aphids. An obligate bacterial symbiont, called *Buchnera aphidicola*, that virtually all aphids carry and a group of taxonomically diverse bacteria known as facultative or secondary symbionts. All of these bacteria are transmitted directly from the mother to the offspring.

The association with *Buchnera aphidicola* is obligate from both the aphid's and *Buchnera*'s point of view. Aphids feed on the phloem sap of plants, a very sugar-rich and nitrogen-poor diet lacking essential amino acids. *Buchnera* is able to synthesize these, especially tryptophan, and trades them with the aphids for shelter and other nutrients. The association between aphids and *Buchnera* is ancient, approximately 170 million years old, and the aphids have developed a specialized organ that houses the bacteria. There are about 4,400 aphid species, many of them serious agricultural pests. Without *Buchnera* or a similar bacterium, it is unlikely that they would have ever been able to acquire the phloem-feeding lifestyle. Many other insects with a very specialized diet have similarly established a close link with bacteria that make up for the nutritional deficiencies in their food.

Facultative symbionts are a much more diverse group of bacteria, both taxonomically as well as in the effects that they have on the host. Unlike *Buchnera*, the aphid does not require the facultative symbionts to survive but it gains other benefits from its occupants. Facultative symbionts have been described as 'lifestyle bacteria' because whether or not they help the host depends on the environmental and ecological conditions that the aphid experiences. They can, for example, protect the host from its natural enemies or extreme temperatures and there is some evidence that they also allow aphids to feed on specific plant species that would otherwise be unsuitable.

One particularly fascinating example is the relationship between aphids, their facultative symbiont *Hamiltonella defensa* (γ-Proteobacteria) and parasitoids. Parasitoids are insects with a gruesome life cycle: they lay their eggs into or onto another insect; the parasitoid eggs and larvae develop, eventually killing the host. In aphids, the larva develops in the living host until the parasitoid larva is ready to pupate. In the process, the parasitoid consumes most of the aphid's inners. The aphid usually fails to reproduce before it dies. *Hamiltonella* can rescue the aphid. It carries a phage called APSE in its genome, which encodes toxins that affect eukaryotes. It is thought that these toxins kill the developing parasitoid egg or larva and thus allow the aphid to grow and reproduce normally. Some parasitoids have evolved ways of countering this defence but the physiological mechanisms are not known. They have also developed behavioural responses, which can involve avoiding aphids that carry *Hamiltonella* altogether or laying more eggs to overcome the defence.



Buchnera aphidicola in host cell

Aphids are also attacked by other natural enemies, such as pathogenic fungi and predators. The fungi have a very similar life cycle to the parasitoids; they develop inside the living host and kill it to then sporulate and infect the next victim. Also similar to the parasitoid story, bacteria can help the aphid to survive. The mechanisms of how bacteria achieve this are unknown, but when certain bacteria are present, the aphids can survive fungal attack. There is quite a wide range of bacteria that are able to protect the host in this way: best known probably, the γ-Proteobacterium *Regiella insecticola*, but also other γ-Proteobacteria (*Rickettsiella viridis* and a species known as X-type), a *Rickettsia* sp. (α-Proteobacteria) and some isolates of *Spiroplasma* sp. (Mollicutes).

Some of the symbiont species can provide multiple benefits for the host, including the defences mentioned above, but also protection from heat shock. This should make the bacteria a more attractive partner for the host who needs to provide the resources that the symbionts need. An alternative to carrying a symbiont with multiple benefits might be to harbour more than one species and in fact many aphids have two or more symbionts. Understanding these more complex interactions is an important gap in our knowledge. What happens when two ecological threats occur simultaneously? How do bacterial symbionts in the same aphid interact with each other? For example, can a bacterium offering tolerance to heat, protect another that provides resistance to a parasitoid? We need to understand these scenarios better to be able to develop more targeted and sustainable methods to control aphids and other pests in the future. Next time you ponder how to get rid of the aphids in your garden, spare a thought for the fascinating communities within and around them. They might in the future be able to help you.

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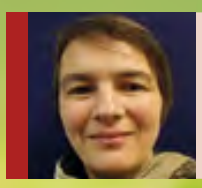

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Plant–microbe symbiosis

Plant pathologists (that is, students of plant diseases and of the microbes that cause them) have contributed greatly to the understanding of plant–microbial symbiosis. It was Heinrich Anton de Bary (a plant pathologist) who in 1879 offered a definition of symbiosis ("*the living together of unlike organisms*") which is favoured by many to this day, and not just plant pathologists. It was another plant pathologist, George McNew, who in the 1960s formalized the disease triangle, a simple but highly effective conceptual tool to explain infectious diseases as the outcome of a three-way interaction between a pathogen (that is, a disease-causing infectious agent), its host (plant or otherwise), and the environment that the pathogen and host share. Then there was Curt Leben (also a plant pathologist), who in 1965 made the case that the disease triangle felt too 'flat' and should feature a 'fourth dimension', one that represents the non-pathogenic members of what he called the plant "*microflora*". Leben argued that the size, composition and function of these plant-associated non-pathogenic microbial communities are likely to impact the abundance and activity of cohabiting pathogens and so by extension would be able to influence the manifestation of disease. This sounds like a pre-omics premonition of what we have come to accept as the essential role of host microbiomes in relation to host health. Interesting to note here is that one of the earliest definitions of the term 'microbiome' was actually coined by (you guessed it) a plant pathologist: in 1988, John Whipps used it to refer to a "*characteristic microbial community*" occupying a physico-chemically distinct habitat that serves as a "*theatre of activity*" where members of the microbiota (pathogens as well as non-pathogens) interact.

Typically, plant pathologists define themselves and each other along distinct dividing lines: for example, they may study either foliar, trunk or root diseases, they are experts on either bacterial, fungal or viral pathogens, or they specialize in tree, fruit or vegetable crops. There is no line that separates plant pathologists who study pathogens from those who study non-pathogens, because such a line would mark, in the traditional sense of plant pathology, the boundary of the discipline. However, plant pathologists have been known to cross into non-pathogen territory on occasion. A classic example is the case of 'biocontrol', which in this context is the exploitation of microbe–microbe interactions such as antagonism and competition to protect plants from harmful pathogens. Indeed, many research labs in academia and the agro-industry are heavily invested in prospecting Leben's 'fourth dimension' for bacteria, fungi and other microorganisms with traits that have practical potential for mitigation of pathogen establishment on plants. Other highly sought-after microbial traits are those that aid plants in the acquisition of essential nutrients such as phosphorus or in dealing with environmental stresses such as drought. These so-called plant-growth promoting microorganisms, together with the aforementioned biocontrol agents, can be thought of as "*probiotics for plants*", capable (in theory, greenhouse or sometimes field setting) of keeping plants healthy in the face of one or more biotic and abiotic challenges.

As plant pathologists entered the -omics era, they came into possession of tools to explore the structure and function of plant-associated microbiota in ways that would have left Leben with envy, excitement or probably both. These tools are bringing many new advances to the understanding of the role of the environment (for example, soil and air) as a source of pathogenic and non-pathogenic microorganisms that colonize surfaces and internal tissues of plants. Also, much has been learned about the types and numbers of plant genes that underlie the selection for or against associations with microbial beneficials, commensals or pathogens. The field has gained enormously from the use of model plants such as *Arabidopsis thaliana*, the lab mouse of the plant world, for which extensive resources, including a genome sequence, gene knockouts and model pathogens are available. The comparison of whole-genome sequences from pathogenic and non-pathogenic microorganisms has not only helped the search for genes and gene products that contribute to pathogenicity and virulence, but also created a greater appreciation for the types of genes that contribute to microbial survival on roots, leaves and other plant parts. These may or may not be compartment specific, for example, genes that are enriched in leaf surface colonists to deal with damage from UV exposure and the dangers of desiccation, or genes that maximize survival in the face of shared access to limited nutrient sources and that code for high-affinity uptake systems, synthesis of plant hormones to stimulate nutrient release from the host or the production of antimicrobial compounds. Lastly, these plant microbial genomes also provide first clues about the genes and gene clusters that pathogens need for survival when they are not (yet) realizing their pathogenic potential, or when plant symbionts (pathogenic or not) find themselves dissociated from their plant host.

For sure, these are exciting times for plant pathologists. Many are intrigued by or already pursuing the prospect of a fuller mastery of 'their' pathosystem through closer acquaintance with all microorganisms that cohabit 'their' plant host and may interact with 'their' plant pathogen. In doing so, they continue the tradition of making impactful contributions to the field of plant–microbial symbiosis and to our understanding of the incentives, outcomes and applications of the microbe–microbe interactions that play out in the 'theatre' known as the plant microbiome.

Johan Leveau
University of California

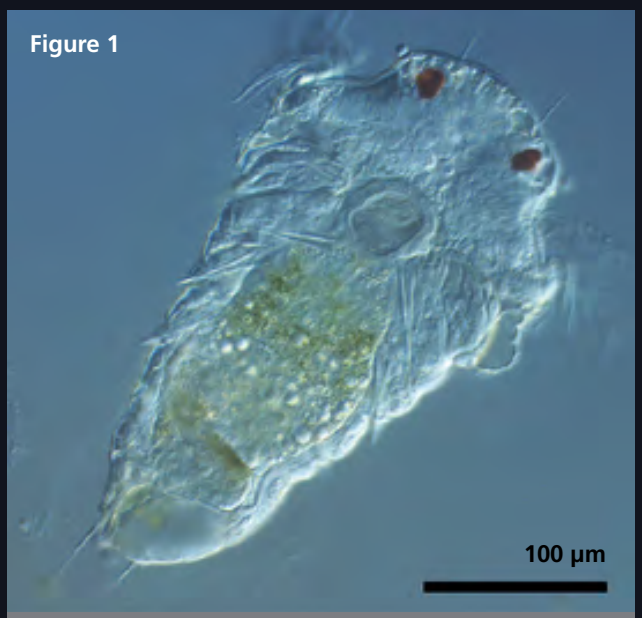
How MICROBES mediate marine animal development

Communities of microorganisms form thin coats across solid surfaces in the sea and the larvae of many benthic marine invertebrates use these biofilm components as cues to appropriate settlement sites. Understanding this symbiotic behaviour may enhance coral restoration and artificial reef recruitment attempts as well as informing efforts to inhibit the costly accumulation of organisms on the hulls of ships (i.e. biofouling).

Many of these marine invertebrates also require an environmental cue to undergo metamorphosis, a life phase shift from free-swimming larva to bottom-dwelling juvenile. For some animals, such as corals, tubeworms and urchins, metamorphosis is induced by interactions with bacteria, further highlighting the essential role of bacteria in the life cycle of these animals. However, the bacterial factors mediating this beneficial bacteria–animal interaction remain enigmatic. The marine tubeworm, *Hydroides elegans*, is an emerging model organism to investigate bacteria–animal interactions because their larvae require bacteria to undergo metamorphosis. This metamorphosis, in response to single or multiple species of bacteria, serves as a robust biological readout for animal development (Figures 1 and 2).

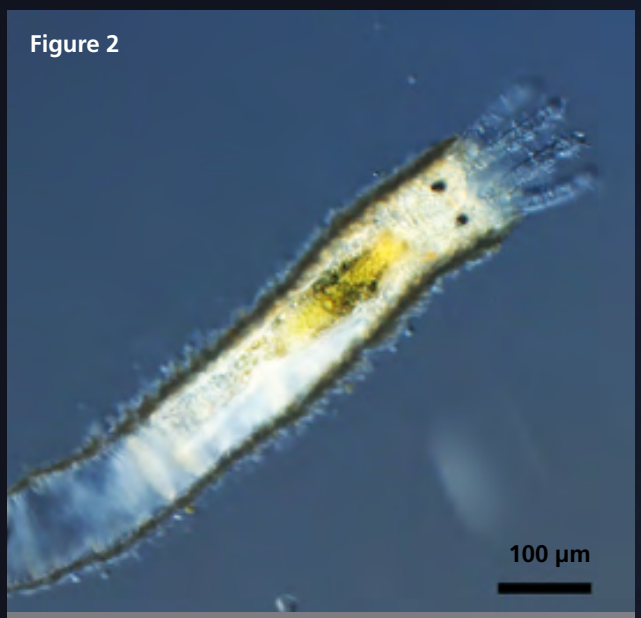
It has recently been shown that it is not just the presence of bacteria that is responsible for inducing metamorphosis of *Hydroides*, but an interaction with bacteriophage tail-like assemblages, named

Figure 1



***Hydroides elegans* larva**
Differential Interference Contrast (DIC) microscopy was used to image the H. elegans larva on a Zeiss inverted microscope. The image was visualized at 20x magnification on a standard microscope slide and coverslip. Scale bar is 100 µm.
Photo credit: Amanda Alker

Figure 2

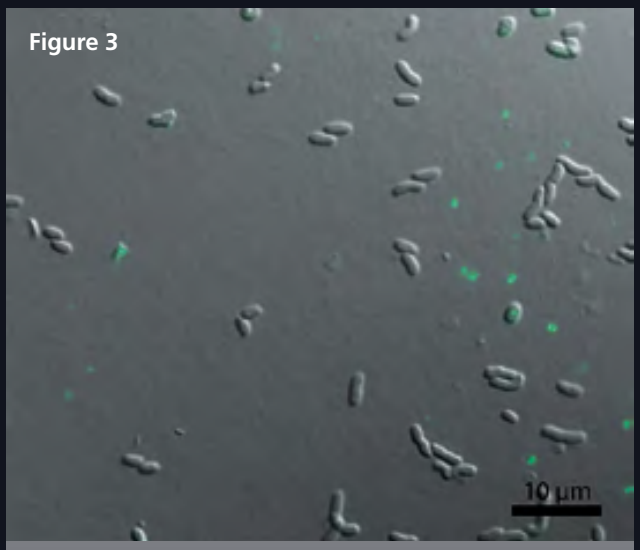


***Hydroides elegans* juvenile**
Differential Interference Contrast (DIC) microscopy was used to image the H. elegans juvenile on a Zeiss inverted microscope. The image was visualized at 10x magnification and newly metamorphosed juveniles were placed on a small glass-bottomed Petri dish with seawater. The transition of larva to juvenile is marked by the loss of cilia and the formation of 'antlers' which help the tubeworm feed. Scale bar is 100 µm. *Photo credit: Amanda Alker*

Metamorphosis-Associated Contractile structures (MACs) produced by the bacterium *Pseudoalteramonas luteoviolacea* (Figure 3). Structural analysis of MACs revealed that they are organized as extracellular arrays of phage tails connected by tail fibres and a hexagonal net (Figure 4). MACs can be classified as one type of Contractile Injection System (CIS), which are homologous to the tails of phage and contain a sheath, tube, tail spike and baseplate complex. Bacteria can wield CISs from within the cell (e.g., Type 6 Secretion Systems) or release them extracellularly (e.g. R-type bacteriocins, MACs) and enable bacteria to effect target cells by their syringe-like action. While the function of some CISs are well characterized to mediate virulence, MACs are the first CIS documented to mediate a beneficial interaction with a eukaryotic organism – by inducing the metamorphosis of a tubeworm.

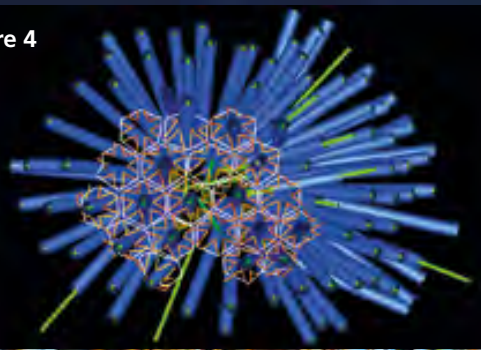
Studying how bacteria stimulate tubeworm metamorphosis promises to provide fundamental insight into beneficial bacteria–animal interactions in many taxa because *Hydroides* share characteristics with other animals that rely on bacteria for metamorphosis, including corals and urchins. *P. luteoviolacea* is also capable of inducing metamorphosis in these animals, making it plausible that MACs are the factor responsible for inducing metamorphosis in other animals that depend on bacteria to induce their metamorphosis.

Figure 3

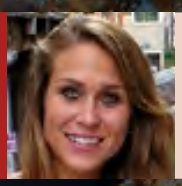


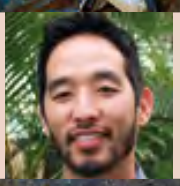
***Pseudoalteramonas luteoviolacea* and MACs**
Epifluorescence microscopy allowed visualization of Metamorphosis-Associated Contractile structures (MACs). The MACs were labelled with Green Fluorescent Protein and imaged at 100x magnification. Aggregations of the green circles indicate that the formation of MACs occurs extracellularly or in conjunction with the lysis of P. luteoviolacea. Scale bar is 10 µm.
Photo credit: Amanda Alker

Figure 4



Model of a MAC array
Electron cryotomography enabled physical representation of the MACs. Individual phage-tail structures are symbolized by green inner tubes and blue outer sheaths. A hexagonal net (shown in white) holds each of the individual tails together, supported by tail fibres (shown in orange), which reinforces the array.
Photo credit: Martin Pilhofer





Amanda T. Alker left
Nicholas J. Shikuma right

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AN ARCHITECTS VISION OF A living

When I first presented my projects to an audience of microbiologists at the Centre for Bacteria Cell Biology at Newcastle University, one from the audience expressed horror that architects were now "*doing microbiology*". It is certainly true that, as someone trained to design buildings, studying and working with bacteria is not an obvious career path but the relationship between architecture and biology is fundamental.

Vitruvius, who wrote the first great architectural textbook in the 1st century BC, suggested that architecture is the imitation of nature. Through biophilia we seek forms in nature which inspire the design of new buildings and through biomimicry we seek a structural understanding of biological systems to inform the engineering of our buildings. What if we could go much further, however? What happens when we become architects of nature?

My own interest in microbiology was triggered by an article on Newcastle University's website. The article (which was also widely covered in the popular press) reported on the success of a team of undergraduate students who had entered a competition called IGEM (International Competition for Genetically Engineered Bacteria). The group had designed and prototyped a bacteria-based system called BacillaFilla, which used an engineered strain of *Bacillus subtilis* to swarm into microscopic cracks in concrete and trigger a process of biomineralization, resealing the cracks and protecting the steel reinforcement from decay. The project caught my attention, not only for its audacity, but I was fascinated by the idea that if we could repair buildings using bacteria – perhaps we could build them as well.

Our buildings are over-engineered – using more materials than is required for them to function because our construction techniques are based on principles of material mass fabrication which suit industrial production, but are not suited for the very specific and unique factors required by every new building we make. An answer to this might be to make our buildings more like biological systems or perhaps to make them living. The idea of living buildings has been part of the architectural imagination for many years but has tended to exist only as speculation, however, advances in biological science have started to make these fantasies a potential reality. My university's IGEM competition entry, it seemed to me, provided a starting point for a new sort of building science and perhaps a new way of constructing buildings.

Bacteria provided a good starting point because there are already relevant applications being developed in labs. For example, we can make self-healing concretes that use *Bacillus megaterium* in its spore form encapsulated into the aggregate to make self-healing materials. When cracks form in the surface of the

building

material, water dissolves a calcium-rich powder, reactivating the bacteria which then produces urease to trigger biomineralization re-cementing the cracks. It is even possible to use the same biomineralization process to create a new sort of cement. A process which involves laying down sand aggregates with urease-producing bacteria to create bricks. This process has already been commercialized.

Six years after the IGEM competition and with a newly minted Master's degree in Synthetic Biology I have started to build a research group to take these ideas much further. What if, we speculated, we could engineer a type of bacterium which would not only make building materials, but do so intelligently only where they are needed. Imagine a column of sand saturated with billions of engineered bacteria cells. As a force is applied to the top of the column, bacteria in the sand detect an increase in pressure. The bacteria respond by synthesizing a material or triggering biomineralization to bind the grains together and resisting the load. The resulting structure would consist of a material where sand grains are only cemented where the forces through the material require. Using this technique we could create building foundations that construct themselves. Through our EPSRC project 'Computational Colloids' we have been able to identify over 100 genes in *E. coli* which are sensitive to moderate levels of pressure (10 atm) and build our gene circuit to increase levels of GFP (Green Fluorescent Protein) production when the bacteria is pressurized. If we are successful with our next round of funding we expect to be able to build our first demonstrator using bacteria suspended in an agarose gel to begin inducing crystals when the gel is put under load.

We are some distance from our application domain but the Computational Colloids project points towards a radical type of engineering and architecture – building a proof of concept where the material itself acts as manufacturer and designer, modelling and responding to its environment. This may be the first step towards buildings which are able to respond to their environment and are composed, in part, of living cells. As I have made the transition from architecture to microbiology, we may be opening a door for a new generation of microbiologists to become architects and civil engineers.

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3D CELL CULTURE MODELS

for investigating virus–host interactions

Infectious disease presents a global challenge to human health. In recent years newly emerging viral infections have been well documented including widespread respiratory infections such as coronavirus and influenza virus, and international outbreaks such as Ebola virus and Zika virus. For many years the study of virus–human interactions has relied on the use of *in vitro* methods, specifically two-dimensional (2D) *in vitro* single cell mono-culture and animal models. *In vitro* conditions vary considerably from those *in vivo* and the mechanisms of infection for many pathogens are species specific; new and emerging viruses can be difficult to propagate, and appropriate animal models are limited. 3D culture systems are used in many biological science disciplines including cell biology, immunology, tissue engineering, and cancer and stem cell research. This technology can assist in the study of virus–host interactions in a setting which better represents *in vivo* physiological conditions; tissue-like constructs which are similar to their equivalents *in vivo* are present allowing for more in-depth, accurate and relevant investigations to occur.

In traditional 2D cell culture, cells are grown in a monolayer on glass or plastic, such as in cell culture flasks, Petri dishes or multi-well plates. 2D cultures support viral infection, and have been successfully used to study the viral life cycle. However, they do not provide the 3D cellular organization required to accurately mimic host physiology. An early form of 3D culture, explant tissue culture, aimed to redress this; however, using tissue directly from a donor had limitations. Samples were limited by the number of donations from the same donor, and tissue was only viable in culture for a relativity short time. Subsequently, 3D systems have been developed which build on established 2D culture systems, requiring only one donation and the use of cryo-preserved cells. These include natural and synthetic scaffold-based systems, aggregate cultures (such as growth of cells as spheroids), hydrogel-based technologies, microfluidic chip technologies and bioreactors. A summary of the advantages, concerns and applications of these systems can be found in Table 1. 3D systems can result in

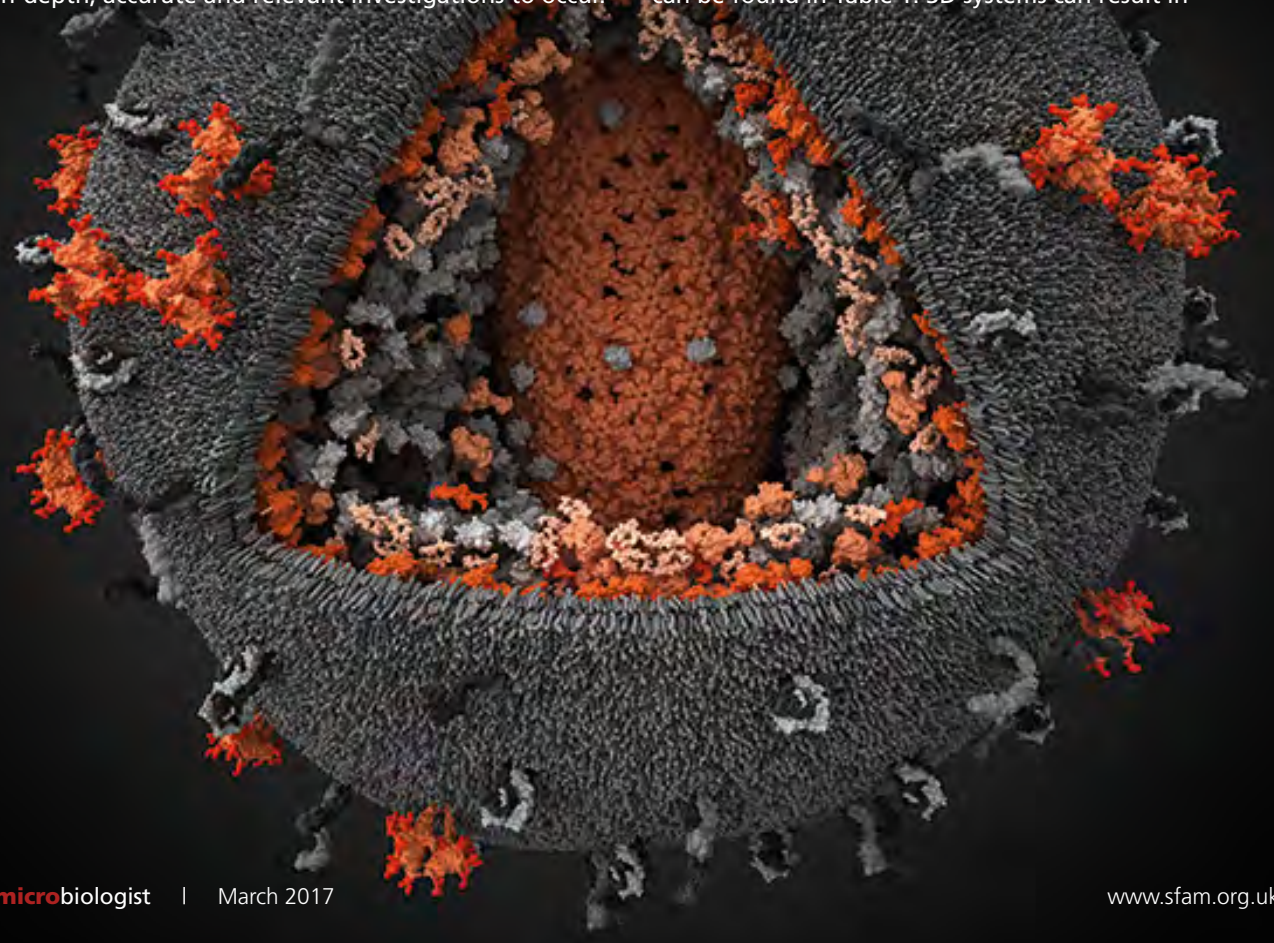


TABLE 1 DIFFERENT EXISTING OPTIONS FOR 3D CULTURE APPROACH*

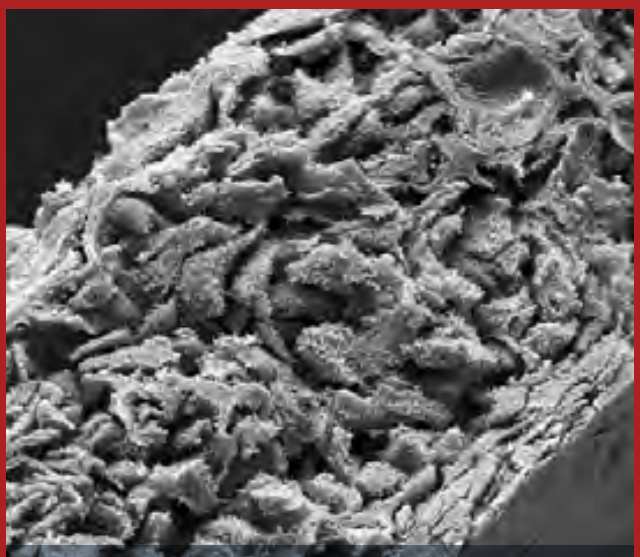
OPTION	ADVANTAGES	CONCERNS	APPLICATIONS
Scaffold-free systems	No added material; consistent spheroid formation; co-cultures possible; transparent HTS capable; compatible with liquid handling tools	No support or porosity; limited flexibility; size of spheroid limiting	Basic research; drug discovery; personalized medicine
In vitro scaffolds for laboratory applications	Large variety of natural and synthetic materials available with various properties; customizable. Co-culture possible	Possible scaffold to scaffold variation; may not be transparent and therefore difficult to image; cell removal may be difficult; HTS options limited	Basic research; drug discovery; cell expansion
Hydrogels	Large variety of natural or synthetic substrates available; customizable. Co-culture possible	Gelling mechanism, gel to gel variation and structural changes over time; undefined constituents in natural gels; may not be transparent; HTS options limited	Basic research; drug discovery
Bioreactors	Several options available; high volume cell production; customizable	Cost; HTS options limited	Basic research; tissue engineering; cell expansion
Microchips	*In vitro* organ-specific systems; high gas permeability; transparent	Commercial availability; required expertise; cost; HTS options limited	Basic research; drug research

HTS – High-throughput screening

** Adapted from Fundamental Techniques in Cell Culture, Laboratory Handbook – Third Edition*

cultures which, to a certain extent, recapitulate the cellular organization found in tissues, mimicking *in vivo* cell-to-cell and cell-to-matrix interactions. Cells grown in 3D systems differ phenotypically from their 2D counterparts including their morphology, polarity, proliferation, gene and protein expression, drug sensitivity and cell-to-cell interactions amongst others (Table 2). Although 3D cultures give a better insight into cellular virus–host interactions, there are still some limitations; for example, many 3D culture systems are not supported by a circulatory system; transport of small molecules and fluid flows which occur naturally *in vivo* are not present.

Currently, 3D cell culture models offer prospective superiority over conventional 2D models for the study of virus–host interactions. They provide a bridge between 2D cell culture and *in vivo* models and the potential to grow cells as cultures of single cell lines, mixed co-cultures of two or more cell lines, physiologically relevant organoid cultures derived from primary isolates or stem cells. The issue of fluid flow can



Scanning electron microscope image of 3D growth in an Alvetex® membrane courtesy of Stefan Przyborski, Professor of Cell Technology, Durham University.

TABLE 2 DIFFERENCES OF BIOLOGICAL FUNCTION AND CELLULAR DIFFERENCES OF 2D AND 3D CULTURES*

CELLULAR CHARACTERISTIC/ FUNCTION	2D	3D
Cell shape	Single layer	Multiple layers
Morphology	Sheet-like flat and stretched cells in monolayer	Form aggregates / spheroid structures
Polarity	Partial polarization	More accurate depiction of cell polarization
Migration	Only one mechanism	Several cell migration strategies
Adhesion	Represents exaggerated stages of dynamic *in vivo*	Generate adhesions comparable with 3D adhesion *in vivo*
Proliferation	Monolayer grown tumour cells grow faster than 3D spheroids	Similar to the situation *in vivo*
Gene / protein expression	Often display differential gene / protein levels compared with *in vivo* models	Gene and protein expression more representative of *in vivo*
Drug sensitivity	Cells are more sensitive to drugs in contrast to 3D cells	Cells are more resistant to anticancer drugs compared with 2D cells
Cell–cell interactions	Limited	*In vivo* like

** Adapted from Bing H. et al. (2016)*

be addressed in microfluidic chip 'lab on a chip' systems, through perfusion pumps such as hollow fibre bioreactors and the Kirkstall 'Quasi-Vivo' system or alternatively, by the lateral approach of encouraging the cell cultures themselves to move through the culture medium.

A system of 3D modelling that employs the latter technique is the rotating wall vessel (RWV) cell culture system, a bioreactor developed by the National Aeronautics and Space Administration (NASA), which has been widely used to investigate virus–host interactions. Conventional cell culture can generate shear (unaligned) forces which may damage cells and hamper differentiation. In addition, insufficient oxygenation and nutrient supply in these processes can also contribute to cell death. To resolve these issues NASA developed a bioreactor which provides a 'low fluid-shear' environment with minimal turbulence and randomized gravitational vectors which promote cell growth. The RWV is a suspension culture vessel that has been optimized to promote cell growth, allowing oxygen and nutrients to diffuse across cell aggregates. It consists of a rotating cylinder that is full of culture media allowing easy manipulation of culture conditions. Cells can be initially grown in a 2D monolayer, they are then removed from the substrate, re-suspended and placed within porous extracellular matrix-coated micro-carrier beads to encourage aggregate growth. During incubation, due to the rotation of the cylinder, the cells constantly fall through the media which is nutrient rich and oxygenated. Many studies have shown that these RWV systems can produce 3D cultures that closely mimic tissue *in vivo* in cellular polarity, differentiation and proliferation, and complex cell-to-cell interactions. These models are particularly good for the study of infectious diseases and may be used to

Resin-embedded 3D Spheroids of A549 lung carcinoma cells (ECACC 86012804) grown on Ultra Low Attachment (ULA) plastic (Corning) PAS stained for Mucins (MUC5AC) counterstained with H and E. Image courtesy of ECACC.

investigate virus entry and virus–host interactions in addition to viral replication.

An example of this is use of the RWV system in the study of severe acute respiratory syndrome coronavirus (SARS-CoV). Investigation of respiratory viruses often focuses on the respiratory epithelium which forms a barrier in the host to protect against infection. Traditional 2D cell culture techniques are often used for these studies, however, they lack the barrier features which would be present *in vivo*. These include mucin expression, a highly glycosylated protein that is a constituent of mucus (forms a physical barrier to protect epithelial cells from damage and pathogen entry *in vivo*), microvilli and tight cell–cell junction proteins. Tight junctions limit the movement of molecules and ions between adjacent cells. In the case of SARS-CoV, initial studies suggest that 3D human bronchotracheal epithelial cell aggregates, formed in an RWV, represent a more physiologically relevant model which is species specific. Characterization of such aggregates has identified cellular differentiation, collagen IV, mucin 1 and tight junction proteins at levels similar to those seen *in vivo*. The model therefore provides the virus with the specific cellular structures required for attachment and entry to cells, as well as allowing for polarized orientation with receptors. It is hoped that models such at this will be able to assist in the investigation of other emerging respiratory viruses such as Middle East respiratory syndrome (MERS-CoV).

In conclusion, 3D cell culture systems can be a useful tool in the investigation of virus–host interactions. They provide *in vitro* platforms which can support a variety of cell types as single cell lines or complex co-cultures and they closely mimic the physiological *in vivo* environment of the body, as seen through the expression of cellular and structural features not seen in 2D culture. 3D systems have allowed the study of fastidious, difficult to cultivate viruses and will certainly have a role in the understanding of new and emerging viruses. There is scope for these technologies to be used to enhance antivirus drug development, therapy studies, and vaccine development and evaluation.

Resin embedded 3D Spheroids of A549 lung carcinoma cells (ECACC 86012804) grown on Ultra Low Attachment (ULA) plastic (Corning) immune-stained for Mucin (MUC5AC) counterstained with H and E. Image courtesy of ECACC.

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Ayuen Lual left

External Communications, Culture Collections, Public Health England

Jim Cooper right

Cell Biology Applications Scientist, the European Collection of Authenticated Cell Cultures (ECACC), Culture Collections, Public Health England

London's MICROBIOTA

A series on applied microbiology themes in the capital

Wee Willie Harris, Britain's legendary wild man of rock 'n' roll from the 1950s, is not Bermondsey's only contribution to the long march of human progress, and, to be fair, probably not the most important. On a visit to Bermondsey, you may encounter the occasional Epicurean seeking out Manze's famous Eel and Pie shop in Tower Bridge Road, or possibly architecture enthusiasts viewing the art deco Alaska Factory, a former sealskin works now converted into expensive flats, but sadly the area is a less frequented part of the London tourist trail and its role in the history of applied microbiology is almost forgotten.

The Alaska Factory points to the long period Bermondsey spent as a centre of the tanning and leather trade. This alone might merit a mention in this column since tanning leather is a notable microbiological process, particularly in the 'bating' stage where microbial enzymes digest proteins to help stabilize and soften the pelt. Nowadays the enzymes used are produced commercially by large-scale microbial fermentation but in the past the same ends were achieved by a natural fermentation which was initiated by pounding dung or a solution of animal brains into the hides; an unpleasantly aromatic procedure that led to the industry being banished downriver and downwind from the sensitive noses of the more affluent classes upstream. However, it is in the field of food preservation that Bermondsey has a unique claim in the annals of microbiology. Under the eaves of the caretaker's house of a school in Southwark Park Road is a plaque commemorating the fact that on this site Bryan Donkin FRS and John Gamble produced the first canned foods in 1812.

The principle of heat preservation of food in sealed containers had been established some time earlier by the Frenchman Nicolas Appert who used glass jars sealed with corks and heated in a water bath. Another Frenchman, Phillipe de Girard, patented the use of more robust and lighter tinned iron containers through

It is in the field of food preservation that Bermondsey has a unique claim in the annals of microbiology

his English agent, Peter Durand, in 1810, and he then sold the rights to Donkin. Bryan Donkin was a Northumbrian engineer who had been an apprentice at the Dartford Iron Works owned by John Hall. He had an extremely varied and successful career. Having already developed a profitable papermaking machine before his foray into canned foods, he worked on numerous manufacturing and civil engineering projects, eventually becoming Vice President of the Institution of Civil Engineers and a Fellow of the Royal Society in 1838.

Donkin's original cans were made from three pieces: the body, a single piece of tinplate rolled into a cylinder with a soldered seam, the base and the lid. The empty can was filled with product and the flanged lid soldered on. The lid had a small hole through which topping up liquid could be added. The hole was then covered with a cap soldered on before processing. The cap had a small hole, known as a brog hole through which steam could escape during heating. When this was deemed complete the cap was cooled with a cold wet rag and the hole sealed with solder. The cans were originally heated in a boiling water bath for up to six hours, although later in the century water was replaced with calcium chloride solution which allowed much higher heating temperatures and reduced processing times.

The canning process was developed long before the work of Pasteur and for many years the belief persisted that it preserved the food by expelling air and creating a vacuum. There was no understanding of the role that heat played in killing microorganisms particularly the mesophilic spore formers whose elimination is necessary to assure shelf stability and safety from botulism. The success of the process was determined simply by storing products for a month or more in a warm chamber (32–40°C) and discarding those that swelled with gas production. Detailed study of the thermal death kinetics of bacterial spores and elaboration of the 'botulinum cook' standard for low-acid canned foods took place more than a century after Donkin's factory started production.

Initially, the products were relatively expensive and had a more specialist market supplying the navy and finding particular favour on voyages and expeditions around the world. Celebrity endorsements were sought including a visit by Donkin and John Gamble (the factory manager) to Kensington Palace in 1813 where the Prince Regent, later George IV, tried and approved of samples of canned meat and milk. Support also came from notables such as Lord Wellesley, later the Duke of Wellington, and Sir Joseph Banks, President of the Royal Society.

The factory in Bermondsey was never solely concerned with food canning and this part of the operation was later taken over by Crosse and Blackwell and moved elsewhere. The residual engineering activities on the site moved north to Chesterfield in 1890 where a company still exists today bearing Donkin's name and manufacturing valves and fittings for the gas and water industries.

Times change, and although the school caretaker is now the 'facilities manager' the plaque to Donkin remains on his house. As far as I know, there is no comparable memorial to Wee Willie Harris, other than a brief mention in the Ian Dury song, '*Reasons to be cheerful (Part 3)*'.

Martin Adams
SfAM *President 2011–2014*

WHERE HAVE ALL THE **ANTIMICROBIALS** GONE?

And how do we find more?

We are facing a global problem – one which will affect us all. The threat of antimicrobial resistant infections is a clear and present danger and we risk returning to the pre-antibiotic era, where simple infected wounds may kill, management of chronic illness may become impossible and routine surgery is impractical due to the infection risk. Whilst increasing antibiotic stewardship and reducing antimicrobial use in farming are undoubtedly essential, we are still short of viable alternative drug molecules that can be used in the clinic. The recent publication of the final '*The Review on Antimicrobial Resistance*' report which was chaired by economist, Jim O'Neill, has some stark findings and recommendations. We must begin to act on these recommendations – one of which is the need to develop new antimicrobial drugs.

Since the days of Selman Waksman and the discovery of streptomycin, soil has always been seen as a great resource for discovering antibiotics and later, a broad range of bioactive natural products that not only have antibiotic (antibacterial) activity but also antifungal, antihelminthic, anticancer and immunosuppressive activity. The majority of these specialized metabolites that are used in human and animal health come from bacterial genera belonging to the phylum, Actinobacteria. The most prolific genus being *Streptomyces*, which alone is responsible for over two-thirds of these clinically useful molecules, with many being discovered in the 'Golden Era' of antibiotic discovery in the 1950s and 1960s. However, the global crisis in antimicrobial resistance has led us to re-evaluate how we find novel drug molecules from these and other microorganisms.

Seek and you will find... but we need to be innovative

Novel environments yield novel strains and novel strains may yield novel metabolites that may find utility in medicine. During the Golden Era of antibiotic discovery,

We risk returning to the pre-antibiotic era, where simple infected wounds may kill

Streptomyces strains

soils were mined extensively for their *Streptomyces* and related bacteria. However, after a period of time, the same metabolites began to be re-discovered regularly and the rewards for searching diminished. In recent years this has led scientists to search in unique environments for strains that may harbour novel specialized metabolites. The marine environment has proved a useful hunting ground with the so-called 'rare actinobacteria' such as *Salinispora* and *Verrucosispora* yielding metabolites with great medical potential, such as the salinosporamide and the abyssomicins, respectively (Fiedler *et al*., 2005; Udwary *et al*., 2007). The high-altitude deserts of Chile, such as the Atacama Desert, have also yielded interesting organisms with fantastic biosynthetic potential such as *Streptomyces leeuwenhoekii* which produces the novel antimicrobials, the chaxalactins and chaxamycins (Busarakam *et al*., 2014).

The chemical diversity of natural products from microbial sources is vast, and we struggle to characterize them, due to the sheer volume of these molecules, using modern molecular biology and chemical techniques that are currently available. Conservative estimates suggest that the genus *Streptomyces* alone has the capability to produce over 150,000 natural products, and even after ~70 years of study we have characterized less than 5% of these (Walsh, 2015). The development of high-throughput sequencing methods was revelatory in our understanding of *Streptomyces* natural product biosynthesis. Completion of the whole-genome sequence of *Streptomyces coelicolor* in 2002 revealed that despite being a well-studied organism, which was known to produce three natural products (Actinorhodin, Undecylprodigiosin and a calcium-dependent antibiotic), this strain was actually capable of producing more than 20 specialized metabolites (Bentley *et al*., 2002). Rather than being unusual, this phenomenon is repeated throughout the genus and beyond in related organisms as we sequence more genomes. The so-called 'metabolically talented' strains of Actinobacteria are capable of producing over 30 specialized metabolites from large, co-ordinately regulated, gene clusters that direct the biosynthesis of these complex molecules (biosynthetic gene clusters). The difficulty in studying these molecules is that very few are produced under laboratory conditions and a key area of study within the field now is finding ways to activate these 'silent' biosynthetic gene clusters so we can study the products that they encode the biosynthetic enzyme for. There are many ways to do this from simply growing bacterial strains in a range of conditions to encourage expression, chemical induction of biosynthetic gene clusters and the use of synthetic biology-type approaches to activate or enhance production of specialized metabolites. Our ability to clone large fragments of DNA, containing entire biosynthetic gene clusters has increased in recent years allowing whole clusters to be introduced into heterologous hosts for biosynthesis. This approach has the advantage of removing much, if not all, global transcriptional control of pathway expression allowing expression of 'silent' pathways.

Another approach which is yielding interesting results is the dysregulation of specialized metabolite production. Each biosynthetic gene cluster has specific regulatory proteins that act as pathway-specific regulators – either repressing or activating gene expression within the gene clusters to co-ordinately regulate expression of the genes within a biosynthetic pathway. Recent work has shown that 'silent' biosynthetic pathways can be 'switched on' via rational deletion of pathway-specific transcriptional repressors, particularly of the ArpA-like family. This approach led to the discovery of a new family of specialized metabolites called gaburedins (Sidda *et al*., 2014). This approach was also recently applied to microbisporocin, a potent lantibiotic molecule from *Microbispora corallina*, where constitutive expression of a transcriptional activator (MibR) increases production, but also overexpression of

The global crisis in antimicrobial resistance has led us to re-evaluate how we find novel drug molecules

The development of high-throughput sequencing methods was revelatory in our understanding of *Streptomyces* natural product biosynthesis

the novel pathway-specific extracytoplasmic function sigma factor can also result in precocious overexpression of a normally poorly expressed molecule (Fernández-Martínez *et al*., 2015).

The converse approach may also be taken, where activator proteins, which are well described in streptomycete-specialized metabolite biosynthesis, can be cloned and expressed using strong constitutive promoters and introduced into strains to achieve pathway activation. This recently yielded the discovery of the stambomycin antibiotics (Laureti *et al*., 2011) illustrating the utility of such approaches.

Given that there is an urgent need to develop novel antimicrobials, basic microbial science is yielding novel strategies to allow us to be innovative in how we realize this goal. There is an enormous wealth of biosynthetic potential out there in the environment and to be discovered in the genomes of novel organisms, we just need to be clever in how we access and exploit this biosynthetic potential for human use.

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Lorena T. Fernández-Martínez left
Department of Biology
Edge Hill University

Paul A. Hoskisson right
Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde

The MICROBIOME and HUMAN HEALTH Meeting

where

The Bloomsbury Hotel
16–22 Great Russell St
LONDON WC1B 3NN

when

12 April 2017

Registration from **10:00 am**

why

Since we discovered that microbes cause infectious diseases, we've largely focused on keeping them under control. As we come to better understand these organisms, there's growing evidence that an imbalance in those microbes can affect our well-being and may contribute to a range of chronic conditions.

who

Anne Neville
Wellcome Trust Sanger Institute, UK

Thomas Clarke
Imperial College London, UK

Lesley Ogilvie
University of Brighton, UK

Simon Cutting
Royal Holloway, University of London, UK

Janneke Van De Wijgert
University of Liverpool, UK

Rob Read
University of Southampton, UK

John Cryan
University of Cork, Ireland

and more!

how

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why

Join us as we showcase original research conducted by amazing early career scientists, with a skills building session in the afternoon. The ECS Research Symposium provides individuals with a forum to share developing ideas, theories and results across a broad range of microbiological topics.

who

Presentations and posters by early career microbiologists.

BIOINFORMATICS WORKSHOP hosted by

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The James Hutton Institute, UK

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University of Birmingham, UK

how

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ANNUAL APPLIED MICROBIOLOGY 2017 CONFERENCE

New insights into Food Safety

BALTIC Centre for Contemporary Art in Gateshead | 3–6 July 2017

*Sf*AM would like to invite all scientists with an interest in food microbiology to attend and participate in the Annual Applied Microbiology Conference 2017

Fees before 2 June (includes accommodation):

Full Member	**£250**
Student Member	**£200**
Student Non-Member	**£400**
Non-Member	**£600**

INDIVIDUAL DAY RATES WITHOUT ACCOMMODATION ARE AVAILABLE

Deadline for abstract submissions and Studentship Grant applications: **10 March 2017**

Foodborne diseases are a chief concern of many microbiologists as they not only affect people's health and well-being, but also have major impacts for countries' economies too.

While there have been some successes in the reduction of foodborne disease caused by particular pathogens, the level of foodborne disease caused by microbial agents remains unacceptably high, and is a major cost and burden to society.

This conference will look at our current understanding of the key pathogens that are causing the greatest risk to our health and our economy. There'll be a focus on new insights into these individual agents that aid our understanding of the problems they cause.

New issues such as the transmission of antibiotic resistance through the food chain will also be presented, as will new techniques for reducing levels of disease through approaches to control and food safety education.

Speakers include:

Sarah J. O'Brien University of Liverpool, UK
Foodborne disease - the current UK situation

Sandra Hoffmann USDA, USA
The cost of foodborne disease

Paul Cook Food Standards Agency, UK
Antimicrobial resistance risks in the food chain

Ellen Evans Cardiff Metropolitan University, UK
Tailoring food safety education

Mike Peck Institute of Food Research, UK
Clostridium botulinum, Clostridium perfringens and Clostridium difficile

Suresh D. Pillai National Center for Electron Beam Research, USA
Photons to electrons: the rapidly evolving food irradiation technologies and consumer perceptions

Paula Bourke Dublin Institute of Technology, School of Food Science and Environmental Health
Cold plasma technology

Rob Kingsley Institute of Food Research, UK
Salmonella

To book and for further details:
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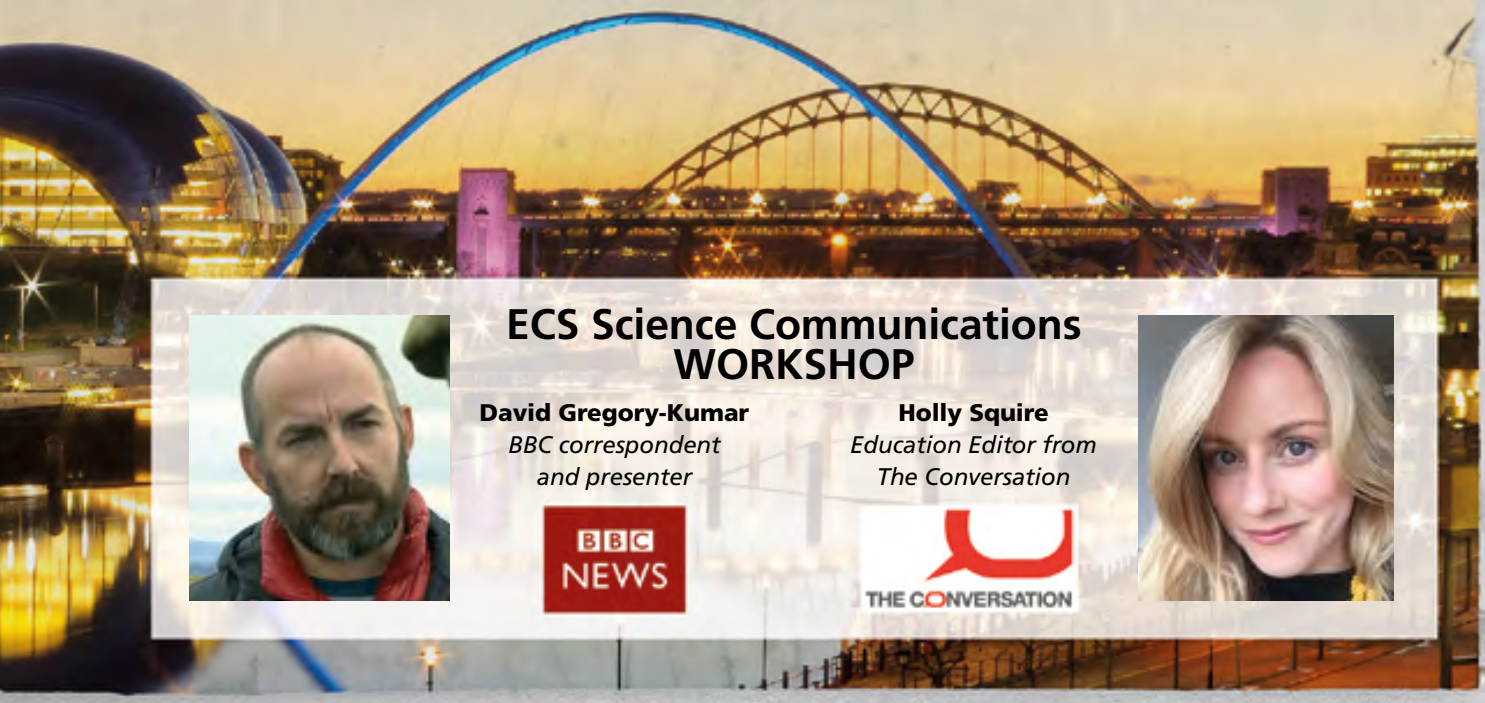


ECS Science Communications WORKSHOP

David Gregory-Kumar
BBC correspondent and presenter

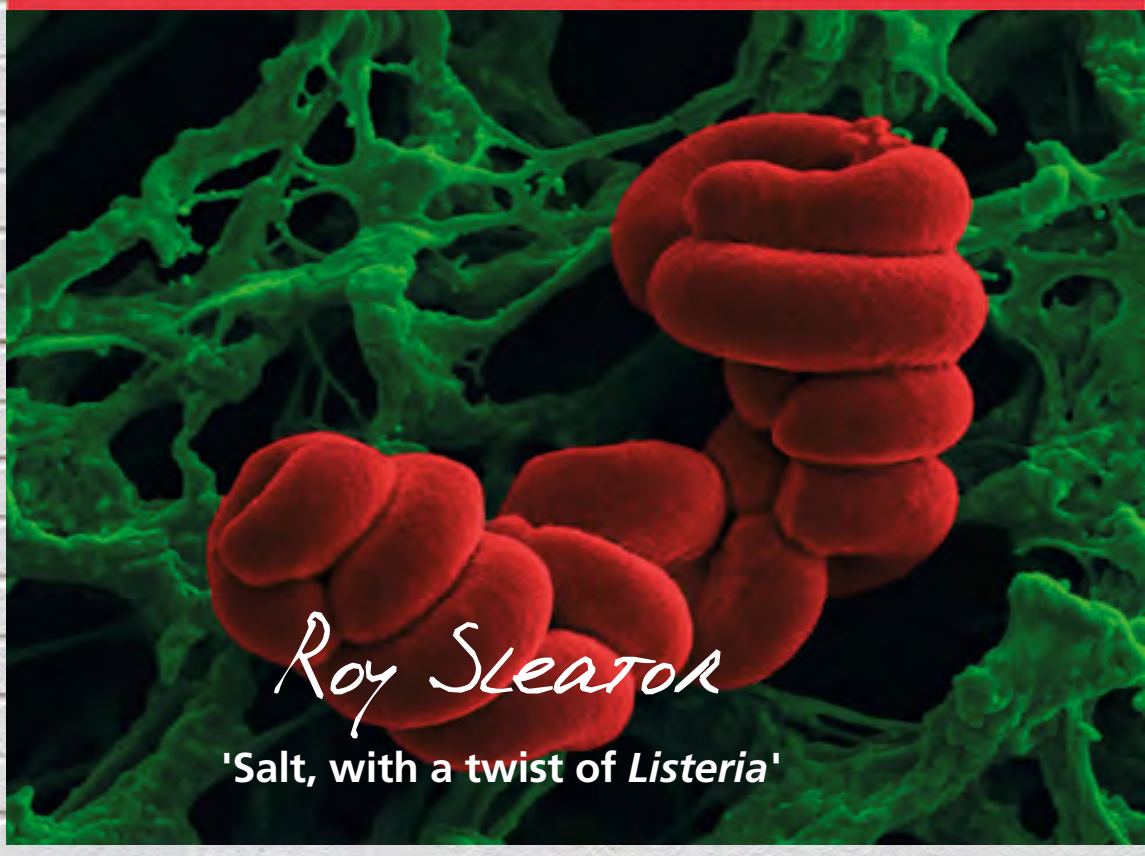
BBC NEWS

Holly Squire
Education Editor from The Conversation

THE CONVERSATION

2016 IMAGE COMPETITION

SfAM WINNER



'Salt, with a twist of *Listeria*'

RUNNERS UP

'In The Zone'

'Microbiology Rocks!'

FACEBOOK WINNER

Helen Hookway

'Micrasterias rotata'

FINALISTS

Marta Simões

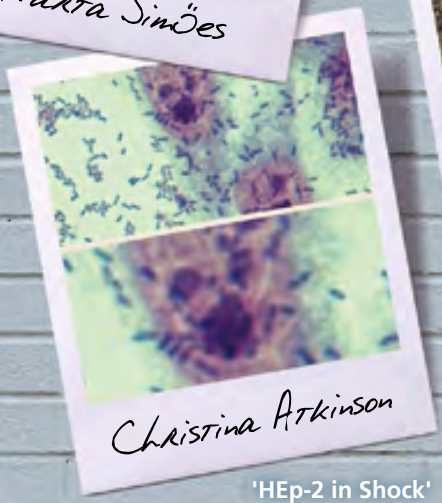
'Autumn – The End of the Tunnel'

Tasha Sturm

'Unknown Shoe Swab'

Manoj Pradhan

'Father of Modern Microbiology'



Christina Atkinson

'HEp-2 in Shock'

Nicole Jackson

'Fluffy *Scytalidium dimidiatum*'

Alexandra-Eliza Bujor

'London Landscape'

Rahul Jain

***'Penicillium* in Focus'**

Samantha Wilson

'British Bacteria'

Emmanuel Adukwu

The beginning

I didn't plan to be a microbiologist. After starting university as a medical student in Nigeria, I spent nearly three years in medical school. Following a change in location and after a year out of university, I changed courses too.

I chose a biomedical science degree at Coventry University. This choice was thanks to Dr Elaine Green, who was willing to listen and get me onto the programme. Undergraduate life was fraught with the challenges associated with having two jobs; working full-time while studying to pay fees. Navigating university without knowledge of the systems and the services? Pure madness!

My final year project set the tone for what became my love for microbiology. I became fascinated by the idea that natural compounds were potential antimicrobial agents and proceeded to investigate the effects of honey as an antimicrobial. This led to my interest in an MRes after a year of job searching and interviews.

I was fortunate to meet Professor Val Edwards-Jones by chance whilst in Manchester and the rest is history. Our encounter ended in a dispute over who would fund the project. I expected to work and pay for my studies. For Val, that was unacceptable! To cut a long story short, she funded me.

I planned to return to medical school. However, following advice from Val and other physicians at my new workplace, ICON plc, I decided to study for a PhD. ICON was then the fourth largest clinical trial company globally and an organization involved in biopharma and drug development.

My role was as a Clinical Trial Co-ordinator and while at the company, I co-ordinated over a dozen high-profile clinical trial projects. As we know, antimicrobial drugs and antibiotics are not always a priority for drug development.

I studied for my PhD at the University of Northampton, as a mature and ready candidate under the supervision of Professor Carol Phillips. My project was focused around community-acquired infections (CAIs), which at the time were a big issue in the US. Infection outbreaks of epidemic hypervirulent *Clostridium difficil*e and Panton Valentine Leukocidin (PVL) MRSA were causing significant healthcare issues in the UK and Europe too.

My PhD experience was brilliant. I enjoyed research and was in the lab every day; I loved my work. My MRes experience prepared me for the rigours of the PhD and I would often advise young undergraduate students to try a Master's degree first before considering a PhD.

Opportunities

Early in my PhD, I received advice from Dr Katie Laird, Senior Lecturer at De Montfort University and an active S*f*AM Member. She encouraged me to join the Early Career Scientist Committee (ECS) and acquire teaching qualifications. Those two actions, coupled with support from my mentors, enhanced my opportunities tremendously.

I joined the ECS events team and later became the Chair of the Committee as well as Observer on the Main

Executive Committee, serving in that role for three years. Before completion of my PhD, I was also an Associate Fellow of the Higher Education Academy. I was able to unpack my learning experiences and develop a teaching philosophy which is central to my practice today.

The basis of a good PhD programme is the breadth of opportunities on offer for personal and technical development as a researcher. I attended over 15 national and international conferences during my PhD, presented my research at global institutions and published during my PhD. I also met most of the experts I had cited in my thesis, including Dr Rodney Donlan, Team Lead at the Biofilm Division at the Centers for Disease Control and Prevention, Georgia, USA, who I consider a great role model. All of these enhanced my confidence and belief in my ability and belonging to the field.

With a teaching qualification, I was able to secure some teaching roles; an Associate Lecturer at the University of Northampton, Academic Tutor at Coventry University College and an academic post at UWE Bristol.

On reflection, my experience has been diverse. I have worked in eight different job sectors including the commercial sector, honing my communication, persuasion and presentation skills, working as a salesperson and more than five years in the entertainment industry. As a result, I have developed excellent links with industry and won innovation grants due to my knowledge of the commercial sector and how businesses work. This now contributes significantly to the development of my undergraduate and postgraduate students.

New adventures

Lately, my career has taken a new spin. I co-founded a platform Aspiring Professionals Hub (APH) with Dr Amara Anyogu (academic, fellow S*f*AM Member and former ECS colleague). The APH is a global platform, aimed at developing and supporting young students and early to mid-career professionals, especially PhD and graduate students, worldwide.

We have a widely read blog with readership in nearly 170 countries and our goal is to support, mentor, train and enable young individuals at different stages of their careers, especially those in hard-to-reach areas. Information about the hub can be found at **www.aspiringprofessionalshub.com** and we welcome written contributions. Please email us at **info@aspiringprofessionalshub.com**.

So, would I say a microbiology career is rewarding or worth doing?

Definitely! It is diverse, flexible and the skills are transferable and translational. Some of the careers that life science graduates can pursue are described in the Further Reading resources. Typical routes can include teaching, lecturing, postdoctoral and other research, working as a research scientist in industry, scientific and medical communications, medical writing, scientific recruitment, life science and medical sales, biomedical scientists, laboratory technicians and the civil service. Atypical routes include working as life science solicitors, finance managers, or in data management, business development, project management, Government and politics. Better still, you can run your own business!

What lessons have I learned?

- Hard work does not kill and enthusiasm can take you a long way.
- Networking is important – 'Your network is your net worth'.
- Good mentors are golden. Listen to their advice and be humble.
- Failure is relative and resilience is important. Attend an emotional resilience course if you can.
- Learn new skills, both scientific and non-scientific.
- Create, innovate and dare to be different.
- Diversity and inclusivity are important! Workforce diversity and inclusion are key drivers of innovation and business growth (Forbes Insights, 2011).

I wish you success in your career.

FURTHER READING

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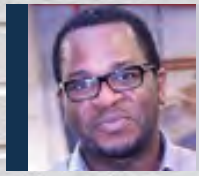


Emmanuel Adukwu

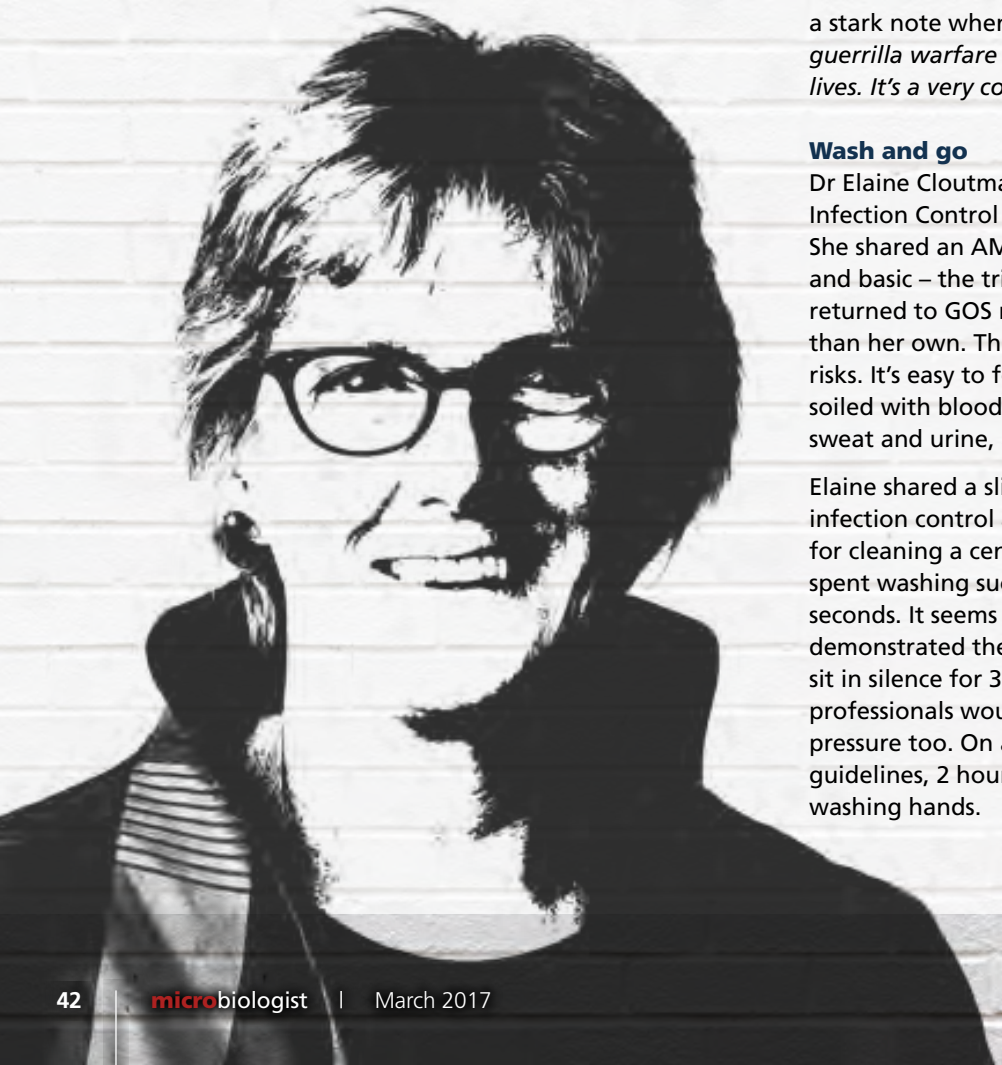
Senior Lecturer in Biomedical Science and Employability Lead, University of the West of England

Finding solutions to a threat on WORLDWIDE PUBLIC HEALTH

Last November, the Society for Applied Microbiology held its second conference on antimicrobial resistance. The objective was to view AMR from the perspective of finding solutions in terms of infection control, improved diagnostics, and the development of new and novel compounds to address the 'discovery void'.

The event was a huge success and the Society will be holding a two-day conference during the latter part of 2017, with one day focused on wastewater and another devoted to diagnostics and sensitivity testing.

The event was held at the neo-classical One Great George Street, global headquarters of the Institution of Civil Engineers. Guests arrived and enjoyed refreshments in the Great Hall, under twinkling chandeliers and an awesome ceiling.



Reality check

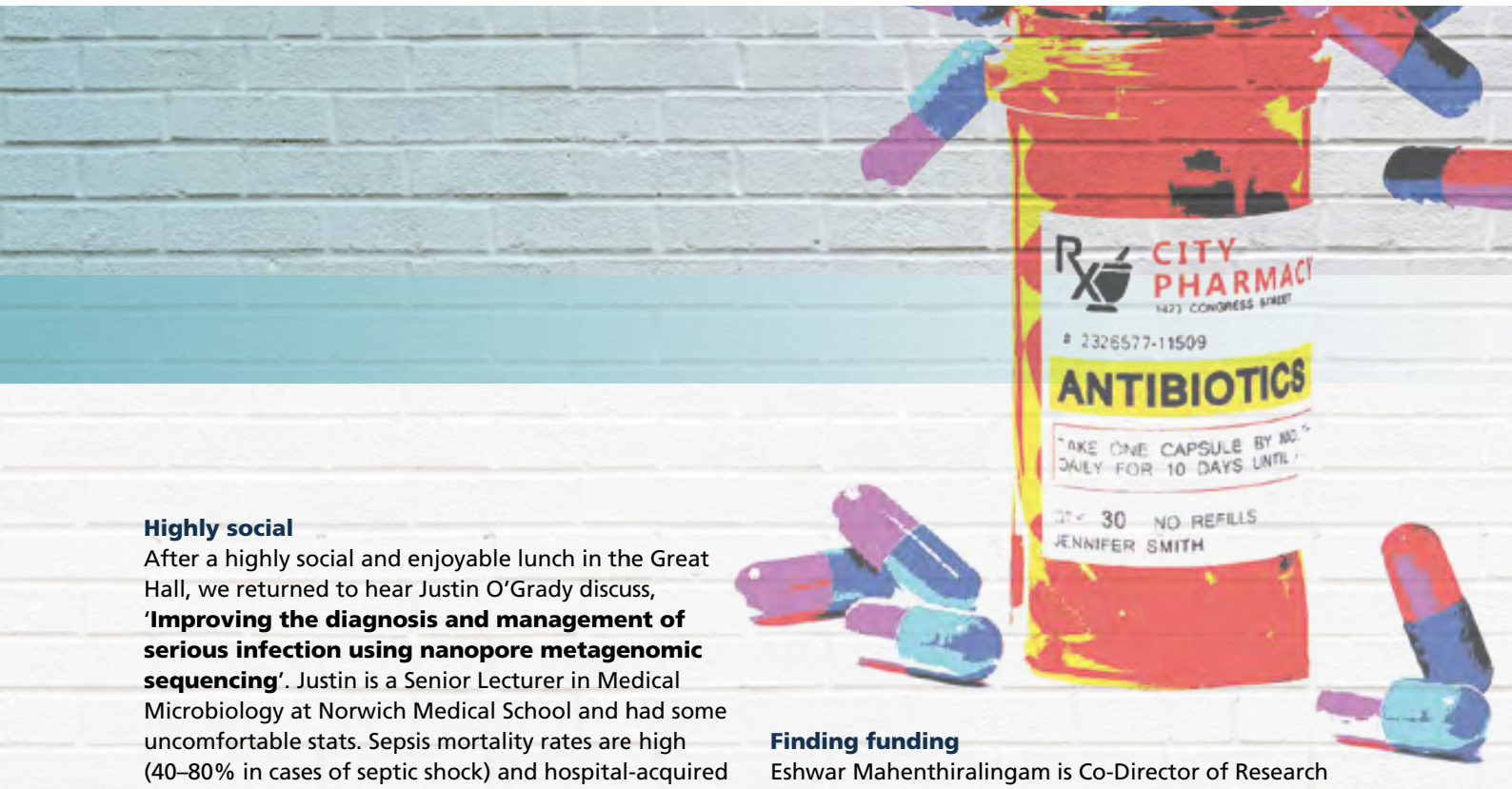
Professor Dame Sally Davies was our first and keynote speaker. Appointed Chief Medical Officer in 2010, she acts as the UK Government's principal medical adviser and is the professional head of all directors of public health in local Government. Her presentation gave credit to the progress achieved in the AMR fight, but also highlighted the serious challenges the global community faces.

To highlight the speed at which AMR occurs, Dame Sally showed '*The Evolution of Bacteria on a Mega-Plate Petri Dish*' – a film from Harvard Medical School. Their experiments are thought to provide the first large-scale glimpse of bacteria as they encounter increasingly higher doses of antibiotics and adapt to them. It's a sobering, visual insight into AMR and might be the scariest movie of last year. Dame Sally ended on a stark note when she admitted: "*This is going to be guerrilla warfare for our lives and our grandchildren's lives. It's a very complex problem, but we can do it.*"

Wash and go

Dr Elaine Cloutman-Green is a Clinical Scientist in Infection Control at Great Ormond Street Hospital. She shared an AMR challenge that felt both critical and basic – the trials of laundry. Clean laundry that's returned to GOS may have come from hospitals other than her own. This presents a range of potential health risks. It's easy to forget that hospital laundry may be soiled with blood, wound exudates, sputum, saliva, sweat and urine, as well as vomit and faeces.

Elaine shared a slide featuring the PHE guidelines for infection control and prevention – most notably, advice for cleaning a central venous catheter line. The time spent washing such equipment should be at least 30 seconds. It seems a tiny measure of time, but Elaine demonstrated the epic reality by making the audience sit in silence for 30 seconds. She reminded us that health professionals would be feeling the weight of time pressure too. On average, if a nurse sticks to the guidelines, 2 hours in any day would be spent washing hands.



Highly social

After a highly social and enjoyable lunch in the Great Hall, we returned to hear Justin O'Grady discuss, '**Improving the diagnosis and management of serious infection using nanopore metagenomic sequencing**'. Justin is a Senior Lecturer in Medical Microbiology at Norwich Medical School and had some uncomfortable stats. Sepsis mortality rates are high (40–80% in cases of septic shock) and hospital-acquired pneumonia (HAP) accounts for 25% of infection in the intensive care unit. He also discussed the difficulty of getting a decent DNA reading: "*We're having a lot of trouble with sputum*."

Ioannis Katis spoke on working '**Towards AMR testing using paper-based diagnostic sensors**'. He talked us through the sensors, which are fabricated via laser-based technology. They are apparently cheap, easy-to-use and allow rapid testing of either pathogens or their resistance to antibiotics. It was cheering to hear how the kit could be posted, allowing patients to do a test at home. A doctor would be able to assess the results and diagnose and prescribe accordingly.

Tim Bull vs TB

Tim Bull from St George's spoke of '**Rapid diagnostics of TB in relation to AMR**' – a fascinating, if concerning dip into the issues related to this disease. Professor Dame Sally Davies had reminded us at the beginning of the day that London is the TB capital of Europe. Parts of the city have higher rates of TB than Rwanda, Iraq or Guatemala.

"*We can kill things*," Tim Bull reminded us; "*but not TB and we can make TB grow faster*".

Paul Hoskisson delivered an inspiring address when he spoke on '**Future prospects: inspiring STEM undergraduates to tackle the AMR crisis**'. Specifically, he spoke of using AMR as a springboard to engage the public in the scientific process, using pop-up events, such as gathering soil samples. The real-time thrills and benefits of social media were highlighted by Paul when he suggested students engage with journal authors via Twitter.

Finding funding

Eshwar Mahenthiralingam is Co-Director of Research at Cardiff University and his lab studies the pathogenesis and ecology of bacterial opportunistic pathogens with a major focus on *Burkholderia cepacia* complex bacteria. *Pseudomonas* and *Burkholderia* bacteria continue to cause devastating infections in people with cystic fibrosis. Using molecular biology and genomic approaches, Eshwar and his team monitor their ability to spread between patients, resist antibiotics and cause lung disease.

This work led to them finding novel polyketide antibiotics with potent activity against major pathogens such as *Acinetobacter spp*. and *Mycobacterium tuberculosis*. Unfortunately for Eschwar, the long (unfunded) road from discovery to funding proved frustrating.

Funding the future

Lucky Cullen of Kingston University dazzled at the ECS Symposium last year and certainly didn't disappoint at this event either. She shared her research looking at the ability of *E. coli* MG1655 to evolve *de novo* antimicrobial resistance and through mutational analysis determine whether the evolutionary pathways to *de novo* resistance can be predicted.

The day ended with a panel discussion hosted by Professor Mark Fielder, S*f*AM's Vice President and featuring most of the speakers. It was a provocative and informative debate that proved an enlightening end to a hugely successful and stimulating day.

Stewart Cumiskey
S*f*AM *Press and Media Officer*

Membership CHANGES

We would like to warmly **welcome** the following new Members to the Society.

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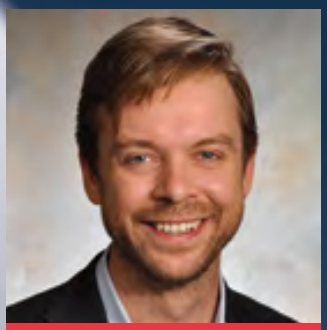


Jack Gilbert 2016

?

Nicola Stanley-Wall 2015

Vasilis Valdramidis 2014

Lori Snyder 2013

Brian Jones 2011

Mark Webber 2010

Paul Cotter 2008

Nominations Open

This prestigious prize is awarded each year at the Annual Applied Microbiology Conference to a young microbiologist (under 40!) who has made a substantial contribution to the science of applied microbiology. It is worth £3000! The award was instituted in 1984 by the directors of Oxoid to commemorate the life and works of the late W H (Bill) Pierce, former Chief Bacteriologist of Oxo Ltd and a long-time Member of the Society. Application is through nomination by Full Members of the Society only. To nominate a candidate please contact the *Sf*AM office, including a full CV of the nominee and a letter of support. The closing date for applications is 13 May 2017.

sfam society for applied microbiology

JournalWATCH

Highlights and featured articles from the *Sf*AM journals

Journal of Applied Microbiology

www.journalappliedmicro.com

Metabolic engineering of Cyanobacteria and microalgae for enhanced production of biofuels and high-value products

M. A. Gomaa, L. Al-Haj and R. M. M. Abed

A lot of research has been performed on Cyanobacteria and microalgae with the aim to produce numerous biotechnological products. However, native strains have a few shortcomings, like limitations in cultivation, harvesting and product extraction, which prevents reaching optimal production value at lowest costs. Such limitations require the intervention of genetic engineering to produce strains with superior properties. Promising advancements in the cultivation of Cyanobacteria and microalgae have been achieved by improving photosynthetic efficiency through increasing RuBisCO activity and truncation of light-harvesting antennae. Genetic engineering has also contributed to final product extraction by inducing autolysis and product secretory systems, to enable direct product recovery without going through costly extraction steps. In this review, we summarize the different enzymes and pathways that have been targeted thus far for improving cultivation aspects, harvesting and product extraction in Cyanobacteria and microalgae. With synthetic biology advancements, genetically engineered strains can be generated to resolve demanding process issues and achieve economic practicality. This comprehensive overview of gene modifications will be useful to researchers in the field to employ on their strains to increase their yields and improve the economic feasibility of the production process.

http://onlinelibrary.wiley.com/doi/10.1111/jam.13232/full

Shoe soles as a potential vector for pathogen transmission: a systematic review

T. Rashid, H. M. VonVille, I. Hasan and K. W. Garey

Shoe soles are possible vectors for infectious diseases. Although studies have been performed to assess the prevalence of infectious pathogens on shoe soles and decontamination techniques, no systematic review has ever occurred. The aim of this study was to perform a systematic review of the literature to determine the prevalence of infectious agents on shoe bottoms and possible decontamination strategies. Three electronic bibliographic databases were searched using a predefined search strategy evaluating prevalence of infectious pathogens on shoe bottoms and decontamination strategies. Quality assessment was performed independently by two reviews with disagreements resolved by consensus. Thirteen studies were identified that supported the hypothesis that shoe soles are a vector for infectious pathogens. Meticillin-resistant *Staphylococcus aureus*, *Clostridium difficile* and multidrug-resistant Gram-negative species among other pathogens were documented on shoe bottoms in the healthcare setting, in the community and among food workers. Fifteen studies were identified that investigated decontamination strategies for shoe soles. A number of decontamination strategies have been studied of which none have been shown to be consistently successful at disinfecting shoe soles. In conclusion, a high prevalence of microbiological pathogens was identified from shoe soles studied in the healthcare, community and animal worker setting. An effective decontamination strategy for shoe soles was not identified. Studies are needed to assess the potential for contaminated shoes to contribute to the transmission of infectious pathogens.

http://onlinelibrary.wiley.com/doi/10.1111/jam.13250/full

Letters in Applied Microbiology

www.lettersappliedmicro.com

Rapid and accurate identification of *Xanthomonas citri* subspecies *citri* by fluorescence *in situ* hybridization

D. W. Waite *et al*.

Xanthomonas citri subsp. *citri* (Xcc) is an aggressive and hardy pathogen of citrus plants worldwide. Outbreaks are difficult and costly to contain and the establishment of citrus canker results in restricted trade. In order to extend the existing toolkit for identification of Xcc we developed a novel diagnostic approach based on fluorescence *in situ* hybridization. Our approach is of comparable specificity and sensitivity to existing methods but can be performed directly on infected tissue making it significantly faster than existing PCRs, and requiring fewer laboratory resources.

http://onlinelibrary.wiley.com/doi/10.1111/lam.12624/full

Reducing time to identification of aerobic bacteria and fastidious microorganisms in positive blood cultures

J. Intra *et al*.

Bloodstream infections are serious conditions with a high mortality and morbidity rate. Rapid identification of pathogens and appropriate antimicrobial therapy have a key role for successful patient outcome. In this work, we developed a rapid, simplified, accurate and efficient method, reaching 99% identification of aerobic bacteria from monomicrobial-positive blood cultures by using early growth on enriched medium, direct transfer to target plate without additional procedures, matrix-assisted laser desorption ionization-time of flight mass spectrometry and the SARAMIS database. The application of this protocol allows to anticipate appropriate antibiotic therapy.

http://onlinelibrary.wiley.com/doi/10.1111/lam.12682/full

Microbial Biotechnology

www.microbialbiotech.com

Progress on lipid extraction from wet algal biomass for biodiesel production

F. G. Naghdi *et al*.

Lipid recovery and purification from microalgal cells continues to be a significant bottleneck in biodiesel production due to high costs involved and a high energy demand. Therefore, there is a considerable necessity to develop an extraction method which meets the essential requirements of being safe, cost-effective, robust, efficient, selective, environmentally friendly, feasible for large-scale production and free of product contamination. The use of wet concentrated algal biomass as a feedstock for oil extraction is especially desirable as it would avoid the requirement for further concentration and/or drying. This would save considerable costs and circumvent at least two lengthy processes during algae-based oil production. This article provides an overview on recent progress that has been made on the extraction of lipids from wet algal biomass. The biggest contributing factors appear to be the composition of algal cell walls, pre-treatments of biomass and the use of solvents (e.g., a solvent mixture or solvent-free lipid extraction). We compare recently developed wet extraction processes for oleaginous microalgae and make recommendations towards future research to improve lipid extraction from wet algal biomass.

http://onlinelibrary.wiley.com/doi/10.1111/1751-7915.12360/full

Antibiotic drug discovery

W. Wohlleben *et al*.

Due to the threat posed by the increase of highly resistant pathogenic bacteria, there is an urgent need for new antibiotics; all the more so since in the last 20 years, the approval for new antibacterial agents had decreased. The field of natural product discovery has undergone a tremendous development over the past few years. This has been the consequence of several new and revolutionizing drug discovery and development techniques, which is initiating a 'New Age of Antibiotic Discovery'. In this review, we concentrate on the most significant discovery approaches during the last and present years and comment on the challenges facing the community in the coming years.

http://onlinelibrary.wiley.com/doi/10.1111/1751-7915.12388/full

Environmental Microbiology

www.env-micro.com

Field-based evidence for copper-contamination-induced changes of antibiotic resistance in agricultural soils

H.-W. Hu *et al*.

Bacterial resistance to antibiotics and heavy metals are frequently linked, suggesting that exposure to heavy metals might select for bacterial assemblages conferring resistance to antibiotics. However, there is a lack of clear evidence for the heavy metal-induced changes of antibiotic resistance in a long-term basis. Here, we used a high-capacity quantitative PCR array to investigate the responses of a broad spectrum of antibiotic resistance genes (ARGs) to 4–5 year copper contamination (0–800 mg kg^{-1}) in two contrasting agricultural soils. In total, 157 and 149 unique ARGs were detected in the red and fluvo-aquic soil, respectively, with multidrug and β-lactam as the most dominant ARG types. The highest diversity and abundance of ARGs were observed in medium copper concentrations (100–200 mg kg^{-1}) of the red soil and in high copper concentrations (400–800 mg kg^{-1}) of the fluvo-aquic soil. The abundances of total ARGs and several ARG types had significantly positive correlations with mobile genetic elements (MGEs), suggesting mobility potential of ARGs in copper-contaminated soils. Network analysis revealed significant co-occurrence patterns between ARGs and microbial taxa, indicating strong associations between ARGs and bacterial communities. Structural equation models showed that the significant impacts of copper contamination on ARG patterns were mainly driven by changes in bacterial community compositions and MGEs. Our results provide field-based evidence that long-term copper contamination significantly changed the diversity, abundance and mobility potential of environmental antibiotic resistance, and caution the unperceived risk of the ARG dissemination in heavy metal polluted environments.

http://onlinelibrary.wiley.com/doi/10.1111/1462-2920.13370/full

Environmental filtering decreases with fish development for the assembly of gut microbiota

Q. Yan *et al*.

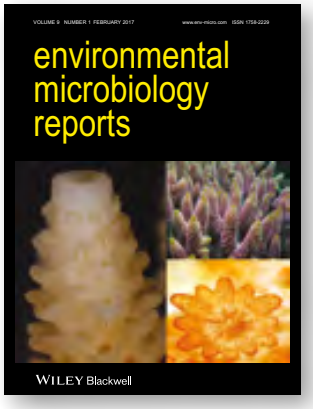
Gut microbiota typically occupy habitats with definable limits/borders that are comparable to oceanic islands. The gut therefore can be regarded as an 'island' for the assembly of microbial communities within the 'sea' of surrounding environments. This study aims to reveal the ecological mechanisms that govern microbiota in the fish gut 'island' ecosystem. Taxonomic compositions, phylogenetic diversity and community turnover across host development were analysed via the high-throughput sequencing of 16S rRNA gene amplicons. The results indicate that the Shannon diversity of gut microbiota in the three examined freshwater fish species all significantly decreased with host development, and the dominant bacterial taxa also changed significantly during host development. Null model and phylogenetic-based mean nearest taxon distance (MNTD) analyses suggest that host gut environmental filtering led to the assembly of microbial communities in the fish gut 'island'. However, the phylogenetic clustering of local communities and deterministic processes that governed community turnover became less distinct as the fish developed. The observed mechanisms that shaped fish gut microbiota seemed to be mainly shaped by the gut environment and by some other selective changes accompanying the host development process. These findings greatly enhance our understanding of stage-specific community assembly patterns in the fish gut ecosystem.

http://onlinelibrary.wiley.com/doi/10.1111/1462-2920.13365/full

Environmental Microbiology Reports

www.env-micro-reports.com

Nitrate- and nitrite-dependent anaerobic oxidation of methane



C. U. Welte *et al*.

Microbial methane oxidation is an important process to reduce the emission of the greenhouse gas, methane. Anaerobic microorganisms couple the oxidation of methane to the reduction of sulfate, nitrate and nitrite, and possibly oxidized iron and manganese minerals. In this article, we review the recent finding of the intriguing nitrate- and nitrite-dependent anaerobic oxidation of methane (AOM). Nitrate-dependent AOM is catalysed by anaerobic archaea belonging to the ANME-2d clade closely related to *Methanosarcina* methanogens. They were named '*Candidatus* Methanoperedens nitroreducens' and use reverse methanogenesis with the key enzyme methyl-coenzyme M (methyl-CoM) reductase for methane activation. Their major end product is nitrite which can be taken up by nitrite-dependent methanotrophs. Nitrite-dependent AOM is performed by the NC10 bacterium '*Candidatus* Methylomirabilis oxyfera' that probably utilizes an intra-aerobic pathway through the dismutation of NO to N_2 and O_2 for aerobic methane activation by methane monooxygenase, yet being a strictly anaerobic microbe. Environmental distribution, physiological and biochemical aspects are discussed in this article as well as the co-operation of the microorganisms involved.

http://onlinelibrary.wiley.com/doi/10.1111/1758-2229.12487/full

Changes in the rumen microbiome and metabolites reveal the effect of host genetics on hybrid crosses

Z. Li *et al*.

The rumen microbiota plays important roles in nutrient metabolism and absorption of the host. However, it is poorly understood how host genetic variation shapes the community structure of the rumen microbiota and its metabolic phenotype. Here, we used sika deer (*Cervus nippon*) and elk (*Cervus elaphus*) to produce the following two types of hybrid offspring: *sika deer* ♀ × *elk* ♂ (SEH) and *elk* ♀ × *sika deer* ♂ (ESH). Then, we examined the rumen microbiome and metabolites in the parents and their hybrid offspring. The rumen microbiota in the hybrids differed from that in their parents, suggesting a significant effect of host genetics on the rumen microbiome that may have resulted from vertical transmission. The rumen metabolites displayed patterns similar to the structure of the rumen microbiome, with changes in the amounts of volatile fatty acids and metabolites of amino acids. The alanine, arginine, proline and phenylalanine pathways were enriched in the rumen of hybrid animals. The enriched metabolites in the above pathways were positively correlated with the bacteria *Prevotella* spp., *Acetitomaculum* spp., *Quinella* spp., *Succinivibrio* spp. and *Ruminobacter* spp. These results suggest that host genetics has a major impact on the rumen microbiome and metabolites in hybrid animals.

http://onlinelibrary.wiley.com/doi/10.1111/1758-2229.12482/full

Melissa McCulloch
Wiley-Blackwell

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Details for the next BMS Masterclass released

BioConnections are pleased to announce that the next Biomedical Science Masterclass will be held on the 6th April, 2017 at Charles Darwin House in Central London.

The topic for this one day event will be 'Cystic Fibrosis & other sticky problems' with a series of lectures focusing on both the medical microbiology and infection prevention/control aspects of patient care.

Delegate rates include discounted fees for IBMS and S*f*AM members.

Full details including programme and online booking form are available from the BioConnections news website at: www.bioconnections.net

Further Information

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Celebrating 45 years of making pre-prepared microbiological media

Back in November 2016 Cherwell Laboratories based in Bicester, Oxfordshire celebrated its 45th birthday. The founder and owner Lawrence Whittard, started the business in what was essentially a large greenhouse as a veterinary diagnostic laboratory. Cherwell quickly expanded into the fledgling industry of pre-prepared media. From those humble beginnings, the current head office and manufacturing facility, still based in Bicester, can produce up to 7,000 plates per batch and as few as 20 depending on the order size.

Offering an extensive selection of both industry standard products and those with a unique formulation or presentation, the Redipor® range provides a flexible solution for environmental monitoring, sterility testing of products, operator validation and process validation. The range includes petri dishes (55mm, 90mm and 140mm) and contact plates, plus gamma irradiated media, bottled media, broth bags and ampoules, with all products subjected to a full array of QC tests, including comprehensive growth tests.

For more information about Cherwell's Redipor® range of media, SAS microbial air sampler product range and cleanroom decontamination solutions from Mar Cor Purification, which includes the new Minncare®Dry Fog 2 system, please visit www.cherwell-labs.co.uk.

Further Information

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First Installation of the New Whitley Microaerobic Workstation

Following the successful launch of the Whitley M35 Workstation last year, there has been tremendous interest from customers in clinical and food applications, as well as in academic research.

The Whitley M35 is the most advanced microaerobic workstation available. It is ideal for the study and isolation of Campylobacter spp, Helicobacter pylori and other similarly fastidious organisms. This is a 4-gas system with built-in gas sensing technology that allows you to programme precise gas concentrations. Options include a removable front for easy access to the entire chamber for thorough cleaning between experiments and a humidification system that prevents agar drying out. The M35 has an intuitive colour touchscreen interface with PIN-code protected user access levels and is Ethernet-enabled for remote access. Accommodating up to 600 x 90mm Petri dishes, this workstation is perfect for manipulating samples in a sustainable microaerobic environment.

One of the first UK units sold was installed at The University of Nottingham. The laboratory staff are very pleased with their new workstation and it is being used on a daily basis. The first unit sold overseas went to a customer in Germany who is using the workstation to cultivate *Campylobacter*.

Whitley M35 Workstation at the University of Nottingham

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Practical Carcass Swabbing

Current meat hygiene regulations (such as European Regulation No. 2073/2005) require regular microbiological testing of carcasses at abbatoirs. To avoid damaging and devaluing the carcass by the excision of plugs of flesh, it is possible to sample the surface using a sponge swab dragged along the length of the carcass. Polywipes™ Carcass Swabs with Peptone Saline have been specially designed to allow the collection of compliant samples. Polywipe Carcass Swabs are blue sponge swabs premoistened with peptone saline (conforms to ISO 17604 & ISO 6887), 10cm wide (as required) and ready to use. They are supplied with gloves for sterile handling, resealable bags for transport to the laboratory, and preprinted labels to record essential details such as farm, species, length of carcass, and reference number. The bright blue colour helps easy retrieval if the sponge should be dropped.

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NCIMB extends patent deposit service

NCIMB has extended its patent deposit service to include filamentous fungi, in addition to bacteria, yeasts, plant seeds and plant cell tissue cultures.

Patents offer assignees exclusive rights to their inventions in exchange for detailed disclosure of the invention. In the case of inventions that are, or require the use of biological material, this involves the deposit of the biological material in a recognised institution.

NCIMB is a recognised institution for patenting purposes and holds the status of International Depositary Authority (IDA) under the Budapest Treaty. This means that biological material deposited with NCIMB under the Treaty meets the deposit requirements of patent offices in many countries around the world, and it is not necessary to submit material in every country in which patent protection is sought.

In addition to patent deposits, NCIMB also offers a range of ISO9001:2008 accredited storage solutions for biological material up to ACDP category 2 and ACGM class 1. Whether you would like to store a single box of ampoules to provide back-up cultures for a university research project, or you are looking for dedicated, high security vessels for off-site cGMP storage of valuable manufacturing strains, we can tailor a package that suits your needs.

For more information contact Terry Dando
t.dando@ncimb.com

Further Information

Visit: www.ncimb.com
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NCTC: New bacterial strains in 2016

We made a record number of bacterial strains available in 2016. In total, 98 new strains from 20 families were added to the collection, a quarter of which were Type strains. Many strains contain information on antimicrobial resistance and susceptibilities. Most are from clinical samples, or are bacteria with the capacity to cause human illness that were isolated from environmental, food or water samples including:

- **Unique strains** from outbreaks
- **WHO panel** of *Neisseria gonorrhoeae* control strains for antimicrobial susceptibility testing
- '**Pre-antibiotic era**' strains of *Klebsiella pneumoniae* (Murray collection) which can be used to map pathogen evolution
- **Type strains** of the Staphylococcaceae family

Whole genome sequencing (WGS) data is available for many of the strains through the NCTC 3000 project (undertaken in partnership with the Sanger Institute and PacBio) and many more strains are currently being analysed. All 98 new strains can be found on the NCTC website: www.phe-culturecollections.org.uk/newbacterialstrains

If you have isolated a new or interesting strain and would like to deposit with us, please contact us: www.phe-culturecollections.org.uk/deposit-strains-with-nctc

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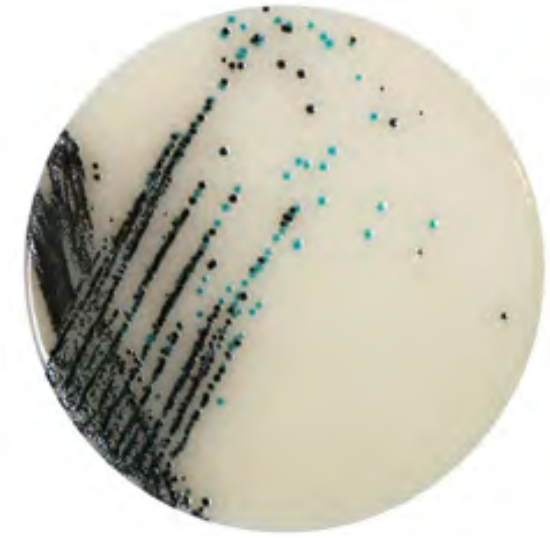
Email: culturecollections@phe.gov.uk

Neogen Develops Superior Chromogenic Media for *Salmonella*

Neogen´s Lab M has developed a unique chromogenic media that offers a superior ability to simultaneously detect numerous strains of *Salmonella* of concern to the food and animal feed industries, while inhibiting or minimizing other organisms.

This new Chromogenic Agar for *Salmonella* Esterase (CASE) uses a proprietary dual chromogenic system to differentiate between Salmonella and non-target organisms that grow on the agar and is suitable for use within the ISO 6579 protocol – the international standard for testing food and animal feed for *Salmonella* species.



"Currently available *Salmonella* chromogenic media typically produce pink purple colonies that are sometimes hard to distinguish – whilst this new agar gives turquoise-blue and black colonies that are very easy to identify" said Steve Chambers, Neogen's European sales and marketing director. "CASE is also able to detect specific *Salmonella* serovars that are often missed by existing media, including non-motile and weaker strains such as *S*. Dublin, reducing the risk of reading false negative results."

Additionally the formulation of CASE means growth from background flora is significantly reduced and closely related *Enterobacteriaceae*, such as *Citrobacter* and *Enterobacter*, are clearly defined. This makes difficult matrices easier to read and can significantly reduce the amount of unnecessary confirmations required which can be costly and time-consuming.

Further Information

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Thermo Fisher Scientific offers efficient and flexible testing solutions for laboratories that conduct food pathogen and quality analysis. All our food testing PCR assays are optimized and validated for use with the Applied Biosystems™ 7500 Fast Real-Time PCR instrument and Applied Biosystems™ RapidFinder™ Express Software.

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Further Information

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