MICROBIOLOGY TODAY

QUARTERLY MAGAZINE OF THE SOCIETY FOR GENERAL MICROBIOLOGY 37:1 FEBRUARY 2010

SYSTEMS MICROBIOLOGY

TB – A SYSTEMS APPROACH

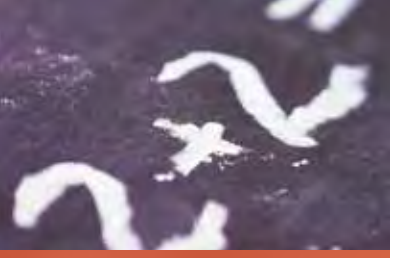
PHAGE MODELLING

VIRUSES AND GEOMETRY

MODELLING PROTEIN LOCALIZATION

HYPHAL GROWTH

SYSTEMS & MATHEMATICS



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EDITOR
Dr Paul Hoskisson

EDITORIAL BOARD
Dr Kim Hardie
Professor Mark Harris
Professor Jo Verran

MANAGING EDITOR
Janet Hurst

EDITORIAL ASSISTANT
Yvonne Taylor

DESIGN
Ian Atherton

ADDRESS
SGM HQ, Marlborough House, Basingstoke Road, Spencers Wood, Reading RG7 1AG
TEL. 0118 988 1809
FAX 0118 988 5656
EMAIL mtoday@sgm.ac.uk
WEB www.sgm.ac.uk

ADVERTISING
David Lancaster, Ten Alps Publishing, London Office, 10 Savoy Street, London WC2E 7HR
TEL. 0207 878 2316
FAX 0207 379 7118
EMAIL david.lancaster@tenalpspublishing.co.uk

ISSN 1464-0570

PRINTED BY
Latimer Trend & Co. Ltd, Plymouth, UK

NEW LOOK FOR MT

Microbiology Today has had a make-over! After 5 years of the previous design, it was time to take a fresh look at the page layouts and fonts. Design Manager Ian Atherton has used his creative talents to produce some striking, colourful designs for the articles and features. He says:

'The previous design has served us well for the last 20 issues, and I am still quite fond of it. The main articles worked well with their clean and crisp layouts, and that deliciously fine typeface for the titling! But some parts of the magazine were starting to look tired, and last autumn Janet and I discussed the possibility of a make-over to reinvigorate the design. Once I started thinking about how to approach this project, it became apparent that the 'make-over' was rapidly developing into a full-blown redesign from front to back, using new typefaces and a more up-to-date and challenging approach to integrating images, text and colour, whilst still trying to retain some sobriety. And here it is – the first issue of the new-look MT. Of course, like any new design, it will continue to evolve and any weakspots can be improved, but I have to say I'm really rather pleased with it so far, and I hope it will serve to enhance your enjoyment of this highly regarded magazine.'

The sections remain pretty much unchanged, but if you have ideas for new ones, do let us know. Feedback on the new design will be welcome (mtoday@sgm.ac.uk).

SGM is social networking!

www.twitter.com/SocGenMicro
www.facebook.com/pages/Society-for-General-Microbiology/188529991077

President Obama's doing it, Stephen Fry was doing it and now the SGM is doing it too! Since the last issue of *Microbiology Today*, SGM has signed up to *Facebook* and *Twitter* to improve our communications with existing members and reach new audiences.

Once a teenager-only domain, social networking sites are now being used by businesses, educational institutions and professional individuals, as well as mums, dads and grandparents worldwide. The most popular social networking site, *Facebook*, has more than 350 million users and is completely transforming online communications.

Rather than simply providing a larger audience to broadcast to, social networking sites represent real-time discussion forums for global users who share a common interest. The SGM's mission is promoting modern microbial science and our job is to spread the word about the importance and excitement of microbiology both within and beyond the scientific community. Social networking offers an exciting new way to do this and will also let us collaborate more easily with our supporters.

As the SGM embraces this new phenomenon, we will be using *Facebook* and *Twitter* to alert you to the microbiology stories that make the news and giving you details of our activities, including upcoming scientific meetings and education outreach events. Users will be able to participate in these events virtually, through photos and videos on *Facebook*, and by following our real-time updates on *Twitter*. Since the SGM's *Facebook* page was launched in November it is gaining new 'fans' daily – with a total of over 200 when *Microbiology Today* went to press.

Most importantly, we are encouraging you to help the SGM carry out its mission by using these tools to share your thoughts on microbiology with other users, to seek help or information from them, to advise us on our current projects and to share ideas for new ones. So start spreading the word! Get in touch with me any time with your suggestions or feedback.

LAURA UDAKIS (email l.udakis@sgm.ac.uk)

Prize & Awards 2010

Marjory Stephenson Prize Lecturer

PROFESSOR JAN TOMMASSEN (Utrecht) will deliver his prize lecture, entitled '*Assembly of outer membrane proteins in bacteria and mitochondria*' on Wednesday 31 March 2010 at the Society's meeting at the Edinburgh International Conference Centre. The Prize Lecture has been awarded for his major contributions to the understanding of bacterial membrane biology and significant service to SGM.

PROFILE

Jan studied biology and chemistry at Utrecht University in the Netherlands. He graduated in 1978 with a major in microbiology, followed in 1982 by a PhD on the PhoE protein of E. coli *K-12 gained under the supervision of Ben Lugtenberg. Lugtenberg moved shortly thereafter to Leiden University, and Jan took over his post at Utrecht. Since 2001, he has been Professor in Prokaryotic Microbiology there. Throughout his career, Jan has studied transport processes in the cell envelope of Gram-negative bacteria. Currently, he is researching the transport of outer membrane proteins and lipopolysaccharides and their assembly in the outer membrane, structure/function relationships of outer membrane proteins, protein secretion systems, and the development of a vaccine against* Neisseria meningitidis. *Jan's main hobby is marathon running and he was national masters champion in 2004 and 2007.*

Peter Wildy Prize for Microbiology Education

DR SUE ASSINDER, Director of Education at the Liverpool School of Tropical Medicine, has been awarded the 2010 Peter Wildy Prize. She will deliver her lecture on 8 September 2010 at the SGM Autumn Meeting in Nottingham. Her profile will appear in a future issue of *Microbiology Today*.

Heatley–Payne and Hayes–Burnet Awards

These schemes are offered jointly with the American Society for Microbiology and Australian Society for Microbiology, respectively. They support the reciprocal exchange of one postgraduate student member to present their research at the other society's main conference and a visit to a research laboratory in that country. The awards have been developed to strengthen long-lasting bonds between the SGM and the two other major international societies. They are designed to benefit PhD students in the partner countries by giving them the opportunity to present their work overseas and experience the best of microbiology in the exchange country.

The Heatley–Payne Award for 2010 has been made by the SGM to **ANDREJ TRAUNER** of Imperial College London, who will present his work at the American Society for Microbiology Meeting in San Diego at the end of May. Andrej works on *Mycobacterium smegmatis*. **JOHN HARRINGTON**, the US-based recipient of the Heatley–Payne Award, and **JEFF BUTLER**, the Australian recipient of the Hayes–Burnet Award will be joining us at the Edinburgh Meeting at the end of March to present their research.

THE LATEST ON SOCIETY ACTIVITIES, MICROBIOLOGY AND MICROBIOLOGISTS

Fleming Lecturer

DR STEVE DIGGLE (Nottingham) will deliver his lecture '*Microbial communication and virulence: lessons from evolutionary theory*' on Tuesday 30 March 2010 at the Society's meeting in Edinburgh. The Fleming Lecture is awarded for outstanding research by a microbiologist in the early stages of their career. Steve writes:

I began my career by leaving school early to become a rock star (failed). To fund this habit I worked for several years as a laboratory technician in a variety of places, including the Paterson Institute for Cancer Research. Here I met my wife who persuaded me to study for a degree in Biological Sciences at the University of Salford. After completing my studies, I undertook a PhD with Professors Paul Williams and Miguel Camara at Nottingham which focused on quorum sensing and the regulation of virulence in the opportunistic pathogen Pseudomonas aeruginosa. *I further developed this during a period of postdoctoral work and focused on understanding the role of 2-alkyl-4-quinolone quorum sensing molecules in the virulence of* P. aeruginosa *and other species. During this period I became interested in why such systems exist in micro-organisms rather than simply how they work, which led to me obtaining a 5-year Royal Society Research Fellowship in 2006. This has led to collaborations with evolutionary biologists and a more conceptual approach to studying quorum sensing. My work now combines evolutionary theory with empirical studies of interest to both evolutionary biologists and microbiologists. It is hoped that by combining traditional approaches with evolutionary theory, we can begin to address questions such as what factors influence cooperation and the evolution of virulence in microbes and can we exploit these to develop new antimicrobial strategies?*

Out of the lab, I enjoy reading and talking (a lot) about the history of plague, and also playing bass in my band Abbey Street *in a variety of local hostelries. We are available for bookings!*

Council nominations

PROFESSOR MIKE BARER, **DR RICHARD HALL** and **DR CATHERINE O'REILLY** retire from Council in September 2010. Under the new Articles of Association adopted at the AGM on 9 September 2008, there are two vacancies to fill, for which nominations are invited from Ordinary Members. All nominations must include the written consent of the nominee and the names of the proposer and seconder, both of whom must be Ordinary Members. Members submitting nominations should indicate the main area of microbiological interest of their nominee, who must have been a member of the Society for at least 2 years. Nominations should be sent to the SGM General Secretary, Dr David Blackbourn (d.j.blackbourn@bham.ac.uk), or c/o SGM Headquarters to arrive no later than **30 APRIL 2010**.

Stockxpert / Jupiter Images

NOVEMBER COUNCIL MEETING HIGHLIGHTS

PRESIDENT'S BUSINESS

PROFESSOR HILARY LAPPIN-SCOTT chaired her first meeting of Council in the role of President. Not only did Council have a new President, but it also had a new look because it was the first meeting of the reconfigured, streamlined body. Several changes have reduced the size of Council, thereby increasing the contribution of each member. The Editors-in-Chief of the four SGM journals (*IJSEM*, *Journal of General Virology*, *Journal of Medical Microbiology*, *Microbiology*) no longer sit on Council, but instead are represented by the Publications Officer, currently **PROFESSOR HOWARD JENKINSON**. There is no longer a separate International Secretary as the General Secretary has subsumed that role. Education and Public Affairs have been combined in one officer post, ably filled by **PROFESSOR JOANNA VERRAN**. In due course, there will be only 6 Elected Members.

Professor Lappin-Scott suggested that Council meetings should include opportunities to discuss the future development of the Society. Council is cognizant of potential threats to SGM income and therefore its stability, for example from falling membership in the current economic climate and reduced revenue from SGM journals through competition from open access journals. These are not problems unique to SGM, but affect many learned societies and associated publishers.

HONORARY MEMBERSHIP

Council agreed unanimously to support the nomination of outgoing President **PROFESSOR ROBIN WEISS** for Honorary Membership. Robin was in office from 2006 to 2009. He is a world-leading virologist and has been a keen supporter of SGM throughout his career.

SGM PRIZES

Council agreed on the recipients of the Marjorie Stephenson Prize Lecture, the Fleming Lecture and the Peter Wildy Prize.

The Marjory Stephenson Prize is awarded biennially for an outstanding contribution of current importance in microbiology.

The annual Fleming Prize is awarded to recognize outstanding research in any branch of microbiology by a microbiologist in the early stages of his/her career.

The Peter Wildy Prize is awarded annually for an outstanding contribution to microbiology education, without restriction on the area of microbiology in which the award is made. See p. 3 for details of the winners.

SGM MEETINGS

PROFESSOR CHRIS HEWITT has taken over from Professor Lappin-Scott as Scientific Meetings Officer. The Spring 2010 meeting at the Edinburgh International Conference Centre will be the third under the new organizational structure.

The Autumn 2010 meeting will be held in Nottingham, with the theme of *Metals and Microbes* and arrangements for the Spring 2011 meeting are already well underway; it will be held in Harrogate and the main theme will be *Intracellular Life*.

SGM FINANCES

In these difficult economic times, SGM's finances have not been untouched by the recession. Nevertheless, SGM is financially stable thanks to careful stewardship led by **RICHARD NOBLE**, Finance Manager, and **PROFESSOR COLIN HARWOOD**, Treasurer. Spending on grants and education remained healthy.

EDUCATION ACTIVITIES

In her new officer role, **PROFESSOR JO VERRAN**, has set up the Education and Public Affairs sub-committee. This committee has a broad remit that will evolve with time; one aim will be to increase membership.

One of the most important activities of SGM is to raise and improve the profile of microbiology to the public and that includes facilitating teaching our subject to the highest standards in schools and beyond, to tomorrow's microbiologists. **DARIEL BURDASS**, Education Manager, was congratulated on the excellent new microbiology education website she is developing (www.microbiologyonline.org.uk) which will help to further these objectives.

FEEDBACK

In providing governance to the SGM, Council seeks to accommodate the requirements and wishes of members in all aspects of Society activities. Members are welcome to get in touch with me or other officers directly about any matters that they would like to raise.

DAVID BLACKBOURN, General Secretary
(email **d.j.blackbourn@bham.ac.uk**)

***Geobacter metallireducens*, an anaerobic bacterium that can oxidize organic compounds using iron oxide or other metals as an electron acceptor.** *Derek Lovley / Science Photo Library*

2010 Divisional Committee Elections

Under the system for planning SGM's scientific meetings (described in the November 2007 issue of *Microbiology Today*, p. 146), members of Divisional Committees serve for 4 years. Replacements are now required for members of the Committees due to retire in September 2010. There are two routes: the Divisional Committees themselves may nominate candidates, and Ordinary Members of the Society may make nominations. For the Virology, Eukaryotic Microbiology and Prokaryotic Microbiology Divisions. nominations must be in the cross-cutting theme in which the vacancy arises. The Irish and Education Divisions do not have cross-cutting themes. All nominees must be members of the Society.

Nominations are now invited for the following vacancies:

Division:	Virology	Eukaryotic Microbiology	Prokaryotic Microbiology
Cross-cutting theme:			
Microbial diversity & evolution	1 vacancy	1 vacancy	1 vacancy
Fundamental microbiology	1 vacancy	1 vacancy	1 vacancy
Translational & applied microbiology	1 vacancy	1 vacancy	1 vacancy
Infectious disease	1 vacancy		1 vacancy

Division:	Education	Irish
	1 vacancy	1 vacancy

All nominations should be seconded by another Ordinary Member of the Society, and include a statement that the candidate is willing to stand, and which Division and where appropriate, cross-cutting theme the nomination is for. A nomination form is available on the Society website at **www.sgm.ac.uk/meetings/divisions.cfm**. Where the number of nominations from the Divisional Committees and Ordinary Members exceeds the number of vacancies, elections will be held.

Nominations should be sent to the **Chief Executive, Dr Ron Fraser, at Society for General Microbiology, Marlborough House, Basingstoke Road, Spencers Wood, Reading RG7 1AG** (email **r.fraser@sgm.ac.uk**), to arrive no later than **16 April 2010**.

A list of current members of Divisional Committees is available on the Society website at **www.sgm.ac.uk/meetings/divisions.cfm**

Let it snow, let it snow, let it snow!

Karen Rowlett

Normal proceedings at Marlborough House were disrupted by the severe weather both before and after Christmas for several days. Heavy snow and ice, unheard of this in this neck of the woods for decades, brought the area to a standstill. Many staff could not get into work at all, although others were able to struggle in on foot or by taxi, and the building was never actually closed. The biggest problem we had once the roads had become passable, was that the car park was a foot deep in snow and cars could not get in. The road outside was already clogged by abandoned vehicles, so there was nothing for it but to dig ourselves in! Many hands make light work, as the proverb says, and enough space was cleared for some cars to park. Several staff organized car shares for their journey and others took to public transport, once the buses were running again. Work soon resumed as usual, but we apologize for any delays in responding to you. More photos of the snowy scene are on the SGM Facebook page.

SGM staff (*L to R:* Laura Udakis, Jane Westwell, Melanie Scourfield, Pauline Stevenson and Rachel Walker)digging their way back to work. *Karen Rowlett*

TRAVEL & MEETINGS

Postgraduate Student Conference Grants

All Postgraduate Student Associate Members are eligible to apply for a grant to support their attendance at one SGM meeting each year. Grants contribute towards travel, registration and accommodation expenses. The student need not be presenting their research so it is an ideal introduction to scientific meetings at little or no cost to themselves or their supervisor's budget. Applicants must be PG Student Associate Members resident and registered for PhD in an EU country. Closing date for EICC meeting: **26 March 2010**.

President's Fund for Research Visits

Up to £3,000 is available to support early-career microbiologists who are planning a short research visit to another laboratory (minimum visit 4 weeks, maximum visit 3 months). Closing dates for applications: **19 March** and **24 September 2010**.

Retired Member Grants

Cover accommodation and the Society Dinner at one SGM meeting a year. Closing date for EICC meeting: **26 March 2010**.

Scientific Meetings Travel Grants

Support for early-career microbiologists wishing to present work at a scientific meeting in the UK or overseas. Graduate research assistants and lecturers (within 3 years of first appointment in both cases), postdoctoral researchers (within 3 years of first appointment) and postgraduate students are eligible to apply. Retrospective applications are not considered.

SfAM/SGM Short Regional Meeting Grants

Contribution of up to £2,000 towards the costs of running a regional microbiology meeting.

Technician Meeting Grants

All Associate Members who are technicians are eligible to apply for a grant to support their attendance at one SGM meeting each year. Applicants need not be presenting work at the meeting. Some microbiology technicians who are not members of SGM may also apply for grant to attend a Society Meeting. Closing date for EICC meeting: **26 March 2010**.

MEDICAL MICROBIOLOGY SUPPORT GRANTS

Elective Grants

Funding for medical/dental/veterinary students to work on microbiological projects in their elective periods. The closing dates for applications in 2010 are **19 March** and **24 September**.

Trainee Support Grants

Funding for SGM members carrying out small lab-based microbiology projects during either foundation or specialty postgraduate medical training. Up to £3,000 is available towards the consumables costs of a project. The closing dates for applications in 2010 are **19 March** and **24 September**.

EDUCATION & DEVELOPMENT

NATIONAL

Education Development Fund

Small grants to members for developments likely to lead to an improvement in the teaching of any aspect of microbiology relevant to secondary or tertiary education in the UK. Up to £1,000 is also available to support public engagement activities.

GRADSchool Grants

Postgraduate Student members who are not eligible for a free place on a Vitae (www.vitae.ac.uk) personal development course (National GRADSchool) may now apply for a grant from SGM to cover full course fees. Retrospective applications are not considered.

Seminar Speakers Fund

Small grants to cover the travel and other expenses of up to two speakers on microbiological topics in annual departmental seminar programmes.

Student Society Sponsored Lectures

These cover the travel and other expenses of up to two speakers on microbiological topics per society each year at student society meetings.

INTERNATIONAL

International Development Fund

The Fund exists to provide training courses, publications and other help to microbiologists in developing countries. Closing dates: **19 March** and **24 September 2010**.

The Watanabe Book Fund

Members who are permanently resident in a developing country may apply for funding to acquire microbiology books for their libraries. These annual awards are available as a result of a generous donation from Professor T. Watanabe of Japan. In 2009 an award was made to **DR TIM CUSHNIE**, Faculty of Science, Mahasarakham University, Thailand. Applications for 2010 are invited. Closing date: **24 September 2010**.

GRANTS

SGM has a wide range of grant schemes to support microbiology. See www.sgm.ac.uk for details.

Any enquiries should be made to the:

Grants Office
SGM
Marlborough House
Basingstoke Road
Spencers Wood
Reading RG7 1AG
tel. 0118 988 1821
fax 0118 988 5656
email grants@sgm.ac.uk

Check out the current schemes, to ensure that you don't miss any deadlines.

PEOPLE

CONGRATULATIONS TO...

SIR LESZEK BORYSIEWICZ FRS, Chief Executive of the Medical Research Council and knighted in 2001 for his research into vaccines, who is to become the new Vice-chancellor of Cambridge University in October.

DR GAIL FERGUSON, a senior lecturer in medical microbiology at the University of Aberdeen, has been presented with the Wain Medal, named in memory of the late Louis Wain, an honorary professor at the University of Kent, which is awarded annually to a young scientist who excels in biochemistry. Dr Ferguson is currently researching bacteria that thrive on the seabed.

TIM WREGHITT OBE (left), Regional Microbiologist for the Health Protection Agency (East of England) and Honorary Consultant Virologist at Addenbrooke's Hospital who has won the Department of Health's *Healthcare Scientist of the Year Award 2009*. The Award was presented by Dr Sue Hill, the Department's Chief Scientist and Sir Roland Jackson, Chief Executive of The British Science Association at a ceremony in London on 24 November. Dr Wreghitt, based at the HPA's Cambridge laboratory said, *'I'm amazed and delighted to receive this award. I am so proud of all the excellent work Healthcare Scientists do in hospitals and the community'*.

Staff

Two new Senior Staff Editors have been appointed in the SGM journals office. One vacancy has arisen following the decision of **CHRIS SINCLAIR**, who has managed *Microbiology* for many years, to reduce her working hours. Staff Editor **RACHEL WALKER** (left) has been promoted and will run *Microbiology*. The other post has arisen because the management of *JMM* and *IJSEM* are to be split; up to now **MELANIE SCOURFIELD** has been Senior Staff Editor for both. She will now run *JMM* and Staff Editor **KAREN ROWLETT** (below) has been promoted to take over *IJSEM*. Congratulations to them both and we hope that Chris will enjoy her extra leisure hours.

Welcome to **SUSAN LEONARD** (left) who takes over as Scientific Conferences and Events Manager from **JOSIANE DUNN** when she retires in April. Susan started work in January, to enable a gradual handover of duties. She has a great deal of experience in events management, particularly in the pharmaceutical sector, and has also previously worked for a charity. Delegates will be able to meet Susan at the Spring conference in Edinburgh.

DEATHS

We regret to announce the deaths of two very longstanding members of the Society.

DR ELLEN I. GARVIE, who joined SGM in 1948 died in October. She worked formerly at the National Institute for Dairying at Shinfield, near Reading. **DR W.J. BRINLEY MORGAN**, a member since 1953 died in May. He worked until retirement at the Central Veterinary Laboratory, Weybridge and was editor of *The Veterinary Journal* from 1988 to 1991.

NamesforLife

BrowserTool takes expertise out of the database and puts it right in the browser

The list of validly published names of *Bacteria* and *Archaea* changes roughly 15 times each week. Invalid and trivial names appear in the literature and public databases at a rate more than three times higher. A small number of experts work to keep pace; meanwhile the rest of community is left alone to make sense of an onslaught of names. All agree that the correct name is essential for accurate communication, but which name is it? And if a name changed, why did it change?

What does this mean as you read the literature? Do you stop reading to check on the taxonomic state of play? Do you look it up later? Are you sure that your knowledge is current?

There is a solution. *NamesforLife*, in partnership with the SGM and the International Committee on the Systematics of Prokaryotes, extracts all relevant information from the taxonomic literature for *Bacteria* and *Archaea*. This information is then presented, with additional annotation, for any text that is readable in a web browser (starting with Firefox, but expanding to other browsers in the near future), on-demand. Never again need a reader be ill informed about the status or meaning of a name.

The archaeon *Pyrococcus furiosus*. *Eye of Science / Science Photo Library*

The *NamesforLife* philosophy is that online annotation must be sufficiently authoritative and persistent for other systems to rely on them rather than reinvent them. Those services must work not only for the ad hoc human user, who after all has fail-safe alternatives, but also in third-party applications. *NamesforLife* identifies service objects using the now familiar digital object identifiers (DOIs) and makes them reliably citable and reusable. The objects then become formally structured micropublications. How is it done? *NamesforLife* employs expert curators to index the literature as a sequence of interrelated taxonomic, nomenclatural, and organismal events, all tied to previously recorded events and to the literature.

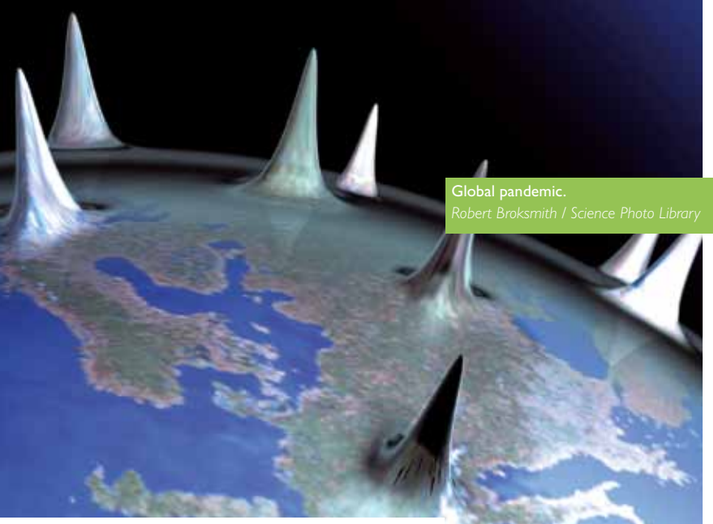
The result is not simply a database to search. The *NamesforLife* BrowserTool takes the expertise out of the database and puts it right in the browser! Expert annotation is presented via a menu that collocates with the occurrence of a name on a web page. The menu links to other resources and to *NamesforLife* Taxonomic Abstracts, which aggregate key information and track changes.

An example of the *NamesforLife* BrowserTool in action.

The BrowserTool will launch at the SGM Spring Meeting 2010 in Edinburgh and will be free for registered use.

Every validly published bacterial and archaeal name that is viewed in the browser is highlighted (automatically or on demand) and serves as a direct link to encapsulated information about its past and present status as well as key references and other online resources, all with the simple click of a mouse.

GEORGE GARRITY, Michigan State University
(email garrity@namesforlife.com)



Global pandemic.
Robert Broksmith / Science Photo Library

Interactive 'flu tracking

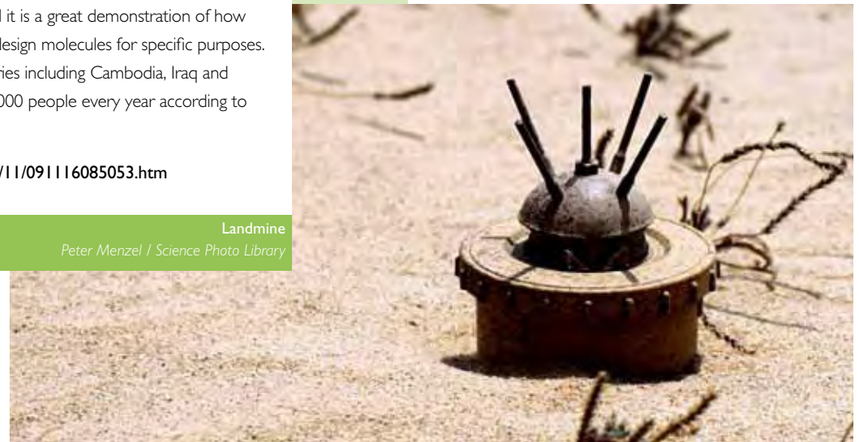
The power of supercomputers has been harnessed by Ohio State University scientists to create a comprehensive interactive map of how avian influenza has spread around the world. Mapping the spread of viruses in this way will help experts better predict the behaviour of pandemic 'flu strains such as H1N1. The team took huge amounts of genetic data on avian influenza strains from the last 12 years and used bioinformatics to work out their evolutionary relationships. From this they have developed a web-based tool for health officials and the public to visualize how the virus emerged and spread globally. Despite its complexities, the interactive map is extremely user-friendly. People can choose to search for transmission pathways in a particular region rather than seeing them all at once. Colour-coded lines indicate whether the virus is incoming or outgoing from a particular location, and also show how much evidence there is to support it. The visualizations and application are available at **http://routemap.osu.edu**

Cladistics (2009) doi:10.1111/j.1096-0031.2009.00297.x

Bespoke bacteria detect landmines

Bacteria that glow green in the presence of explosives could offer a cheap solution to detect landmines, according to scientists. The engineered bacteria can be sprayed in a colourless solution onto suspected danger sites from the air and will form glowing green patches within a few hours if explosives are present. The researchers at the University of Edinburgh created the bacteria using a new technique called BioBricking that allows the microbes to be custom-built from a range of tiny parts. Alistair Elfick who supervised the student-led project said it is a great demonstration of how new techniques can be employed to design molecules for specific purposes. Landmines are present in many countries including Cambodia, Iraq and Afghanistan and injure or kill up to 20,000 people every year according to the charity Handicap International.

www.sciencedaily.com/releases/2009/11/091116085053.htm

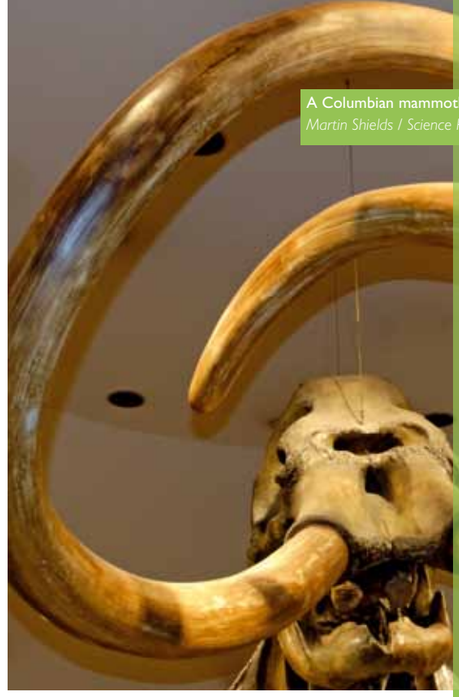


Landmine
Peter Menzel / Science Photo Library

Speed limit of evolution

While we have a sound knowledge of how Darwinian evolution occurs, until now we have known little about how fast it happens. Researchers from the University of Pennsylvania have developed a mathematical model to determine how quickly a population will evolve using a catalogue of 'evolutionary speed limits'. Understanding the speed of evolution could help combat antibiotic resistance and assist in the preparation of vaccines against rapidly evolving viruses such as influenza. One of the major findings of the work is that for some organisms, including humans, increasing numbers of genetic mutations will not necessarily mean increased fitness. In such organisms, while early mutations may be very advantageous, they also dampen the beneficial effects of later mutations. The theoretical model was validated against two decades-worth of *E. coli* data. The team described 14 sets of conditions, or 'landscapes', that influence the speed and pattern of genetic mutations in an organism. This in turn determines how a population's overall fitness changes over time.

www.pnas.org/content/106/44/18638.full.pdf+html?sid=31b83f12-9926-4160-8a5f-995f3757bbb5



A Columbian mammoth skeleton (*Mammuthus columbi*).
Martin Shields / Science Photo Library

Fungal clues to mammoth extinction

Fungal spores found in mammoth dung are providing insight into how the great beasts became extinct, and suggest that scientists may have to revise their theories. Researchers from the University of Wisconsin examined *Sporomiella* spores preserved in the sediment in a riverbed in Indiana. By looking at the quantity of spores in different layers of sediment, they were able to work out the number of great mammals that roamed the environment at any given time. Some experts think that mammoths became extinct 13,000 years ago at the start of the Clovis period, when humans were making stone tools to hunt large animals. However, the study shows that populations of great mammoths started declining 1,000 years prior to this. If humans were involved in their demise, it must have been pre-Clovis settlers. The study also rules out theories that extinction came about by an asteroid hitting the earth, also around 13.000 years ago.

www.sciencemag.org/cgi/content/abstract/326/5956/1100

OUR PICK OF SOME RECENT MICROBIOLOGY STORIES — LAURA UDAKIS

Bacterial beacons for climate change

Bacteria in Arctic rivers could be used as markers for climate change in the polar regions. A 3-year study showed that the movement of the bacterial communities in six Arctic river ecosystems correlated to seasonal changes in environmental conditions. The University of Maryland researchers showed that the bacterial communities in the rivers were remarkably similar and that their movement was synchronous. The research suggests that a divergence in the normal shift patterns could serve as a sensitive indicator of climate change.

www.pnas.org/content/early/2009/11/24/0906149106.full.pdf+html?sid=2e500133-f0e4-4635-be53-05073ba43574

Aerial photograph of the Yukon River in central Alaska. *Dr Robert Spicer / Science Photo Library*

Plasma power

Bactericidal plasma cocktails that stop MRSA and other drug-resistant bacteria in their tracks could soon replace good old soap and water as the main defence against hospital-acquired infections. Research in the new field of 'plasma medicine' by scientists at the Max Planck Institute for Extraterrestrial Physics has led to the development of a new prototype device to rid bacteria from human skin in hospitals and public places. A 12 second exposure is enough to reduce the incidence of bacteria, viruses and fungi on the skin by a factor of a million. Plasma is the fourth state of matter after solids, liquids and gases and is defined by its ionized state. Plasma is found in the cosmos, where high-energy processes strip atoms of their electrons. It is known to be lethal to bacteria, viruses and fungi, and is already used to disinfect surgical tools. Potentially, the bactericidal properties of plasma could be used to treat a range of problems from gum disease to body odour.

www.iop.org/EJ/abstract/1367-2630/11/11/115019

MICROSHORTS

DELIVERING MODERN MICROBIAL SCIENCE
WWW.SGM.AC.UK/MEETINGS

Adenovirus. *Russell Kightley / SPL*
Network. *Stockxpert / Jupiter Images*

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  email c.j.hewitt@lboro.ac.uk
- **Deputy Scientific Meetings Officer**
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  email evelyn.doyle@ucd.ie
- **Education Division**
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  email s.assinder@liverpool.ac.uk
- **Eukaryotic Microbiology Division**
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  email n.gow@abdn.ac.uk
- **Irish Division**
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  email j.mcgrath@qub.ac.uk
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  email i.r.henderson@bham.ac.uk
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  email m.harris@leeds.ac.uk
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Suggestions for topics for future symposia are always welcome.

society for general microbiology
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SPRING 2010

Edinburgh International Conference Centre
29 March–1 April 2010
www.sgmeicc2010.org.uk
Systems, Mechanisms and Micro-organisms

Programme Preview
A booklet giving details of the programme and a summary of each session is enclosed with this issue of *Microbiology Today*. Further information, including poster titles, will be published on the SGM website as it becomes available.

Who should attend?
Anyone who wants to keep up to date with modern microbial science, no matter what their field or stage of their career. The conference will also provide a great opportunity for networking.

Where is it?
Located in the heart of historic Edinburgh, the International Conference Centre has excellent facilities. There is plentiful overnight accommodation close by. Edinburgh has convenient rail, air and road transport links.

Accommodation
Rooms to suit all pockets are available from Reservation Highway. Book through the meeting website.

Welcome workshop for early-career microbiologists
Improve your conference experience by attending this interactive event, with supper and a drink, on the Sunday evening (28 March).

Grants
Conference grants are available to SGM Associate Postgraduate Student Members.

Deadline for earlybird registration
26 February 2010

Conference highlights
Prize Lectures
Trade exhibition
Gala Dinner at Our Dynamic Earth
Poster sessions with drinks

Sessions

Systems & cells
Signalling and systems biology
Environmentally induced morphogenesis
Gene function analysis
Regulatory networks
Small regulatory RNAs
Applications of 'omics

Clinical & Medical Microbiology
Parasites and pathogens: how to hijack the host and evade the immune response
STIs: now!
Gut microbes and health: from molecular to metabolic impact
Workshop:
FRC Path and Beyond
Virus workshops:
Epidemiology and modelling
Global challenges of virus infection

Environment
Microbiology of oceans

Industry
Renewables (*joint with IChemE Biochemical Engineering Subject Group*)

Virology
The 'omics revolution: elucidating the pathways of virus infection
The global challenges of virus infection
Workshops:
Positive-stranded RNA viruses
DNA viruses
Retroviruses
Global challenges of virus infection
Negative-stranded RNA viruses
RNA viruses
Epidemiology and modelling

SGM Prize Medal
Lecturer:
Sir Paul Nurse FRS
Prize Medal Symposium:
Controlling the cell cycle

Education & Personal Development
Innovations in microbiology learning & teaching
(*joint with HEA Centre for Bioscience*)
Infection trainees' workshop
Workshop for early career microbiologists:
Effective presentation skills

FUTURE

Autumn 2010
University of Nottingham
6–9 September 2010
Metals and Microbes
www.sgmnottingham2010.org.uk

IRISH DIVISION

Spring 2010
National University of Ireland, Galway
15–16 April 2010
New insights into molecular microbiology through the manipulation of protein structure and function
Organizer: Gerard Wall
(email gerard.wall@nuigalway.ie)

Autumn 2010
University of Maynooth
2–3 September 2010
Insect-mediated microbial diseases of humans and animals: current problems and future threats
Organizer: Kevin Kavanagh
(email kevin.kavanagh@nuim.ie)

Spring 2011
Queen's University Belfast
Phages

Autumn 2011
University of Cork
Marine biotechnology

For details of all Irish Division activities, contact John McGrath (email j.mcgrath@qub.ac.uk)

OTHER EVENTS

SGM is supporting the following meetings:

British Yeast Group Meeting
17–19 March 2010
St Anne's College, Oxford
email timothy.humphrey@rob.oc.ac.uk

Fourth European Congress of Virology
7–11 April 2010
Villa Erba Congress Center, Cernobbio, Lake Como, Italy
www.eurovirology2010.org

Systems microbiology

How can the principles and techniques of systems biology be applied to microbiology?

DOUGLAS B. KELL

"Systems methods are at the heart of modern microbiology, and are already revolutionizing how we work."

I DEFINE AS A SYSTEM anything consisting of entities that can interact with each other. These can then be described in terms of graphs (networks) of 'nodes' (the entities) interacting via 'edges'. This rather general definition recognizes that tools for describing and understanding biochemical networks can equally well be applied to problems of ecology and population biology in which there are fluxes of matter, energy and information.

To describe properly the properties of such a system – I use metabolic networks as an example – requires four steps, in order: (i) determining the qualitative or topological structure of the network in terms of 'who talks to whom' – these are the kinds of networks observed on laboratory wall charts, and the reconstruction relies on genomic, biochemical and literature data; (ii) determining whether the interactions are direct (as in an actual reaction that transforms substances chemically) or indirect (such as where an entity modifies that step, e.g. by activating or inhibiting it); (iii) adding the kinetic rate equations for each of the steps; (iv) determining their parameters (mainly kinetic and binding coefficients). The first two steps are qualitative, the last two quantitative.

Given such information, preferably encoded using a standard such as the Systems Biology Markup Language SBML (www.sbml.org), it is then possible to provide a stochastic or ordinary differential equation model of the entire metabolic network of interest, and to 'run' that model to provide the time evolution of the system variables (typically metabolic fluxes and concentrations). There are then many other things one might do with such a model, including comparing the predicted variables with those measured experimentally, seeking to estimate the parameters from the measured variables ('system identification' or 'solving the inverse problem') or seeing which changes in the network might beneficially change the system, e.g. for biotechnological purposes. A particularly important set of techniques known as sensitivity analysis seeks to determine the relative importance or contribution of all the various steps in the network to the variables measured, since this allows experimenters to concentrate on those that matter.

Imagine a network with 1,000 enzymes. If knocking out just three of them would give a huge increase in a desirable flux, it should be a simple piece of molecular biology to effect this. The problem is that there are more than 100 million ways of choosing three from 1,000. However, the combination of sensitivity analysis and 'what if?' modelling allows one to search huge areas of the search space of possible networks *in silico* when seeking rational improvements in bioprocesses, and 100 million is not then a large number. This is the way to do business.

To conclude, systems methods are at the heart of modern microbiology, and are already revolutionizing how we work. The needs are user-friendly bioinformatics tools to integrate the many kinds of data, including high-throughput sequencing data, 'omics data and biochemical network properties that together will help us solve the problems of systems microbiology.

DOUGLAS B. KELL is Professor of Bioanalytical Sciences at the School of Chemistry and the Manchester Interdisciplinary Biocentre, University of Manchester (email dbk@manchester.ac.uk)

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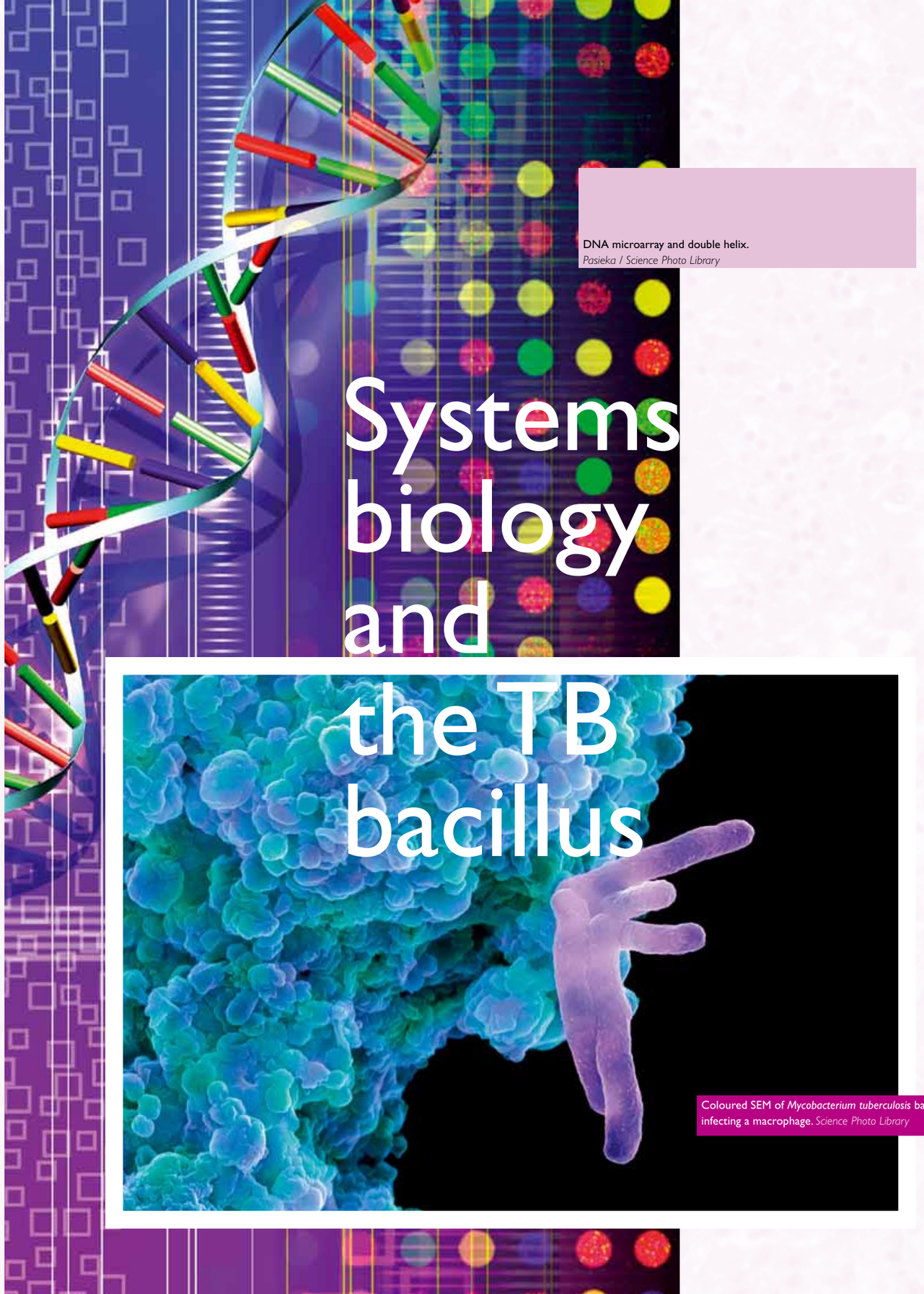
Backgrounds *Stockxpert / Jupiter Images*

JOHNJOE McFADDEN

Systems biology and the TB bacillus



DNA microarray and double helix. *Pasieka / Science Photo Library*

Coloured SEM of *Mycobacterium tuberculosis* bacteria infecting a macrophage. *Science Photo Library*

Using a systems approach to unravel the function of genes could be key to understanding pathogenesis

WHAT IS A GENE?

Microbial genome sequencing projects have released a flood of genes for most medically and industrially important microbes, including the TB bacillus. Much effort in microbial genetics is directed towards identifying the functions of these genes, particularly 'orphan genes' that lack a functional homologue in other organisms. Identifying a function for a gene often involves a naming process when a nondescript gene designation is replaced by a neat acronym such as '*adh*' or '*icl*', implying a function as discrete as the name itself. But recent studies challenge the concept of a discrete gene and are potentially turning reductionist biology on its head.

The first clues turned up in a study of the cell's metabolic pathways. These pathways are like Britain's road networks that bring in raw materials (substrates) and transport them to factories (enzymes) where the useful components (molecules) are assembled into shiny new products (more cells). A key concept was the 'rate-limiting step', a metabolic road under strict traffic control that was thought to orchestrate the dynamics of the entire network.

Biotechnologists try to engineer cells to make products, but their efforts have often been hindered by the tendency of the key genes controlling the rate-limiting steps to reassert their own agenda. Scientists fought back by genetically engineering these genes to prevent them taking control. When they inserted the engineered genes back into the cells, they expected to see an increase in yields of their products. But they were often disappointed. The metabolic pathways slipped back into making more cells, rather than more products.

Geneticists were similarly puzzled by an abundance of genes with no apparent function. Take the 'prion gene'. This is the normal gene that in mad cow disease is transformed into the pathogenic brain-destroying protein. But what does it normally do? The standard way to investigate what a gene does is to inactivate it and see what happens. But geneticists who inactivated the mouse's prion gene found that the mutant mice were perfectly normal. The prion gene, like many other genes, seems to lack a function.

But a gene without function isn't really a gene at all. By definition, a 'gene' has to make a difference; otherwise it is invisible to natural selection. Genes are those units of heredity that wrinkled Mendel's peas and are responsible for making your eyes blue, green or brown. A century of reductionist biology has tracked them down, through Watson and Crick's double helix, to the billions of A, T, G and C gene letters that are spewed out of DNA sequencers. But now it seems that genes, at the level of DNA, are not the same as genes at the level of function.

"Recent studies challenge the concept of a discrete gene and are potentially turning reductionist biology on its head."

THE ROLE OF SYSTEMS BIOLOGY

The answer to these riddles is being unravelled by systems biology. Let's return to that road network. We may identify a particular road, say the A45, that takes goods from Birmingham to Coventry and call it the BtoC road, or BtoC gene. Blocking the A45 might be expected to prevent goods from Birmingham reaching Coventry. But of course it doesn't because there are lots of other ways for the goods to get through. In truth the 'road' (or gene) from BtoC isn't just the A45, but includes all those other routes.

Rather than having a single major function, most genes, like roads, probably play a small part in lots of tasks within the cell. By dissecting biology into its genetic atoms, reductionism has failed to account for these multitasking genes. Systems biology pioneers, such as the late Reinhart Heinrich, replaced the concept of rate-limiting steps in metabolic pathways with one of distributed metabolic control. So the starting point for systems biologists isn't the gene, but rather a mathematical model of the entire cell. Instead of focussing on key control points, systems biologists look at the system properties of the entire network. In this new vision of biology, genes aren't discrete nuggets of genetic information, but more diffuse entities whose functional reality may be spread across hundreds of interacting DNA segments.

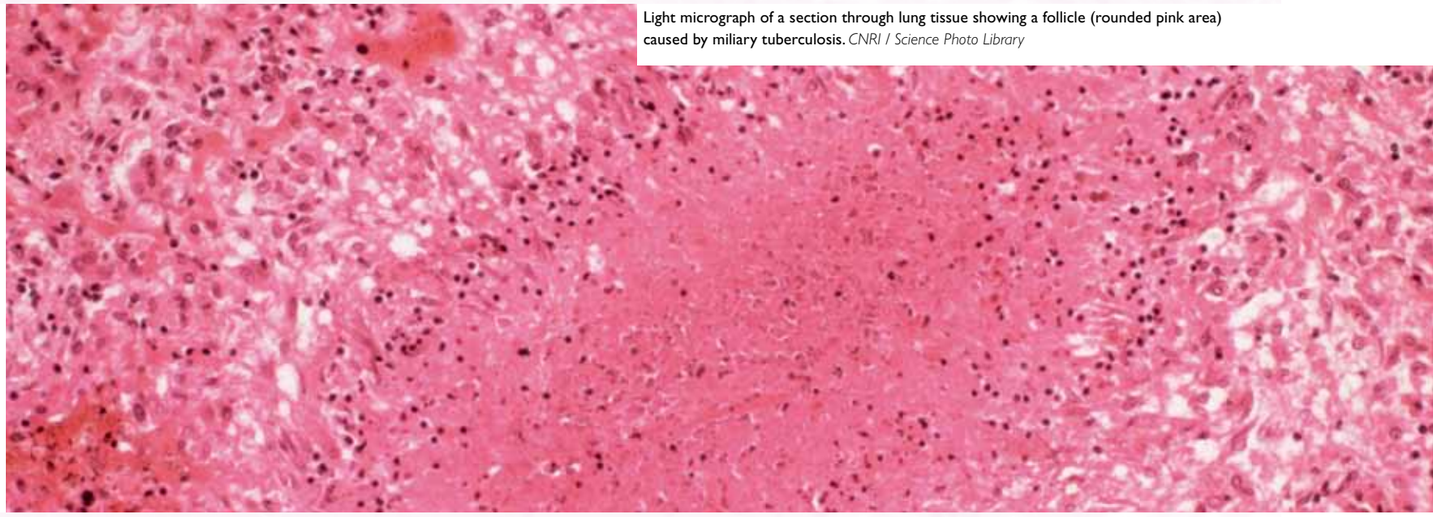
MICROBIAL MODELS

Systems biology courses are infiltrating curricula in campuses across the globe, and systems biology centres are popping up in cities from London to Seattle. The BBSRC has recently announced the creation of three Systems Biology centres in the UK, two of which are largely targeted towards the study of microbes. Microbes are ideally suited for systems-level approaches for a number of important reasons. First, they have small genomes. This is particularly important in systems biology research because of the combinatorial explosion. In a genome of n genes, the number of possible intragene binary interactions increases as $n(n-1)/2$ and the number of possible binary states of the system increases as 2^n. Modelling of possible interactions within complex organisms with tens of thousands of genes is far beyond existing computing power. Modelling of simpler microbial cells is a more tractable problem.

Another microbial advantage is the ability to precisely control their growth. This is vital to systems biology approaches, such as flux balance analysis (FBA), that derive models of the internal physiological state of the cell. These models can be used to predict the flux through metabolic pathways, but only work for systems in steady-state. This is experimentally feasible for microbes growing in continuous culture in a bioreactor vessel (chemostat), but is very difficult or impossible to achieve for multicellular organisms.

TB – A CASE IN POINT

Many questions in TB research may be most effectively tackled by a systems-led approach. One of the most important of these is the problem of persistence. The tubercle bacillus is able to survive in the host for years or decades in a rather mysterious physiological state known as persistence. The existence of this state is a major problem for TB control since TB treatment has to be maintained for 6 months to kill persistent organisms. Drug regimes that efficiently kill persistent cells would revolutionize TB control, but very little is known about the physiological state of the organism during persistence. A few clues, such as the finding that the enzymes isocitrate lyase and nitrate reductase seem to be necessary for persistence, indicate that a key component of the pathogen's shift towards persistence is a change in primary metabolism. The requirement for isocitrate lyase suggests the bacterium scavenges host lipids during infection (since the glyoxylate shunt is essential for growth on fatty acids). However, recent metabolic studies have indicated that isocitrate lyase may have additional metabolic roles, including oxidation of glucose by 'hungry' *Escherichia coli*. The role of the enzyme in intracellular *M. tuberculosis* is therefore less clear and needs to be approached at a systems level.



Light micrograph of a section through lung tissue showing a follicle (rounded pink area) caused by miliary tuberculosis. *CNRI / Science Photo Library*

"Now it seems that the genes, at the level of DNA, are not the same as genes at the level of function."

At the University of Surrey we have been studying the TB bacillus at the systems level. A key resource for our work is the ability to grow the pathogen in continuous culture in a chemostat, allowing application of steady-state modelling methods, such as flux balance analysis (FBA). The first step was to measure the macromolecular composition of the organism, since this is a key component of metabolic models. Our studies indicated that this depends on the organism's growth rate, once again pointing towards a shift in metabolic activity. The macromolecular composition data has been incorporated into a genome-scale metabolic model of the TB bacillus which can be interrogated by FBA online and is a useful tool for systems biology studies of the TB bacillus (http://sysbio.sbs.surrey.ac.uk/tb/). The model has been used to investigate the metabolic changes associated with the switch from fast to slow growth in the chemostat which may be relevant to persistence in the host.

JOHNJOE McFADDEN is Professor of Molecular Genetics, Faculty of Health and Medical Sciences, University of Surrey (email j.mcfadden@surrey.ac.uk)

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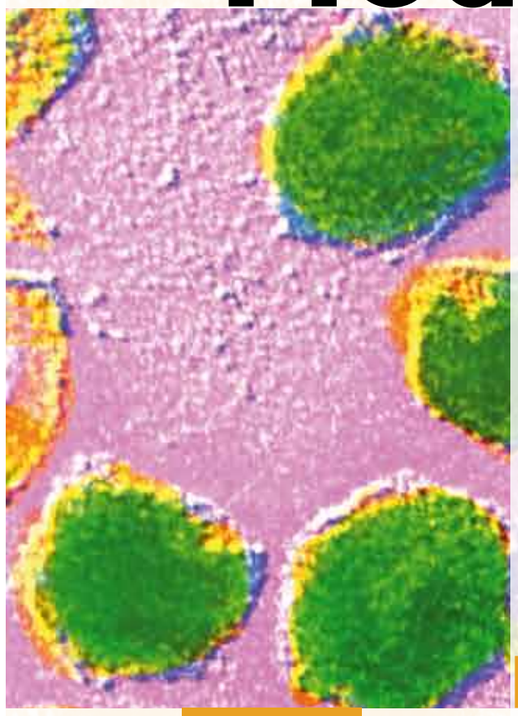
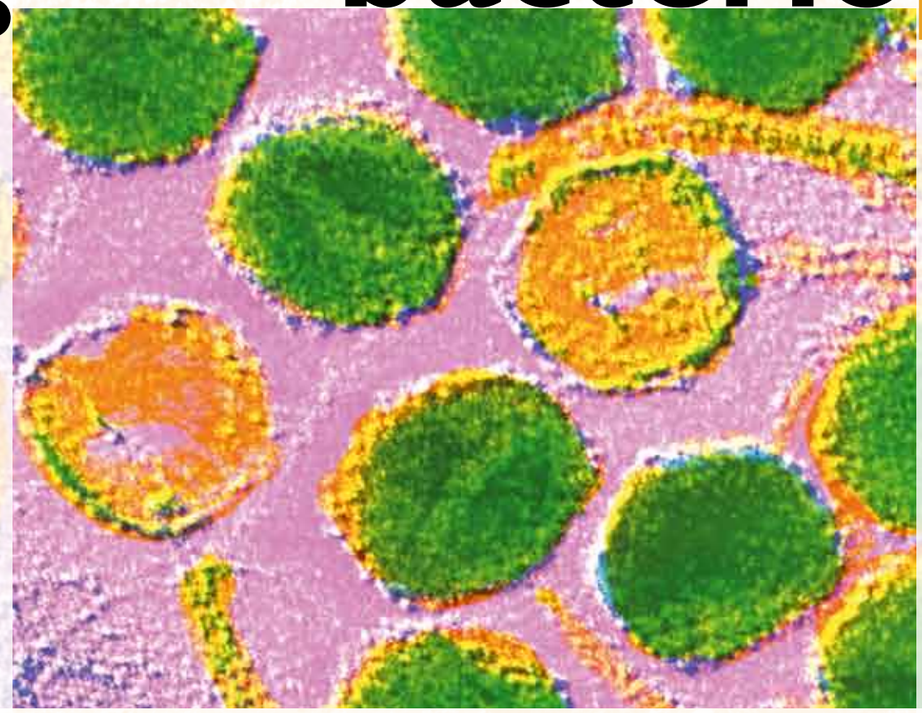
Modelling bacteriophage





False-colour TEM of lambda bacteriophage.
CNRI / Science Photo Library

ROSALIND ALLEN

BACTERIOPHAGE, or viruses that infect bacteria, are believed to be the most abundant and the most diverse organisms on Earth. During an evolutionary 'arms race' with their bacterial hosts over billions of years, phage have evolved an impressive arsenal of tactics. After outwitting bacterial defence mechanisms, phage can hijack the bacterial replication machinery to make new phage which burst out of the now defunct host cell. Alternatively, 'temperate' phage can lie dormant inside their bacterial hosts for many generations, until triggered to suddenly replicate themselves and kill the (apparently) unsuspecting bacterium. A typical bacterium, whether living in the ocean or in the human colon, has a good chance of being blown up by a phage before successfully reproducing. Phage are a rich source of novel genes, proteins and regulatory mechanisms with potential applications in biotechnology which are only just beginning to be recognized. They are also a huge factor affecting the growth, survival and evolution of microbes in human and animal hosts and in the environment. If we aim to use mathematical modelling to understand, predict and ultimately control microbial populations, we could do much worse than starting with phage.

PHAGE LAMBDA: THE CLASSIC MODEL SYSTEM

Phage lambda, discovered in 1950, infects sensitive strains of *E. coli*. For a genome of only 48.5 kb, packed into a particle of only 50 nm diameter, this phage has attracted a lot of attention. Phage lambda became one of the key model organisms on which modern molecular biology was built. Over a period of intense study lasting 40 years, the genes in the phage lambda genome, the proteins encoded by them and the interactions between these genes and proteins were investigated in great detail. The humble phage lambda was the source of discoveries such as repression and activation mechanisms for gene regulation, chaperone proteins, DNA recombination and restriction enzymes, which microbiologists and many others now take for granted. This huge body of knowledge makes it the ideal test case for systems biology modelling.

Mathematical models typically rely on kinetic parameters: one needs to specify the rate constants for DNA binding reactions, transcription, translation, etc. Often, these parameters have not been measured for the system we are trying to model and we are forced to guess – or, worse, we may be tempted to choose parameters that give us the outcome we are hoping for! Phage lambda is one of the few cases where we do not have this problem: it is so well characterized biochemically that almost all the important protein–DNA and protein–protein interactions have been quantified. Not only this, but the biology of phage lambda has been studied with great precision.

Lambda is a temperate phage: when it infects an *E. coli* cell, it makes a choice between immediately replicating and killing the cell (lysis) or integrating its genome into the *E. coli* chromosome and lying dormant for many generations (lysogeny), before eventually emerging to kill the cell. Both the decision whether to embark on lysis or lysogeny after infection, and the choice of when to emerge from lysogeny are governed by random chance: identical phage infecting identical cells will not necessarily follow the same path. Correctly predicting the fraction of cells which follow the lytic versus lysogenic paths, and how long the lysogens lie dormant before killing the host,

Phage lambda has been a mainstay of molecular biology research for over 40 years, and has provided answers to many fundamental questions. So, where better to start looking for solutions to important problems in systems microbiology than this humble bacterial virus.

"If we aim to use mathematical modelling to understand, predict and ultimately control microbial populations, we could do much worse than starting with bacteriophage."

requires advanced mathematical modelling techniques. These models have to take into account the randomness of chemical reactions, and must also be able to cope with 'rare events', such as the transition from lysogeny to lysis, which happen very infrequently but are crucial when they do happen. Phage lambda provides an important test system for mathematical models. If the models can get the right answer for the humble phage lambda, we can be reasonably confident that they will also work for less well characterized systems where we do not know the answer in advance.

PHAGE AS PREDATORS

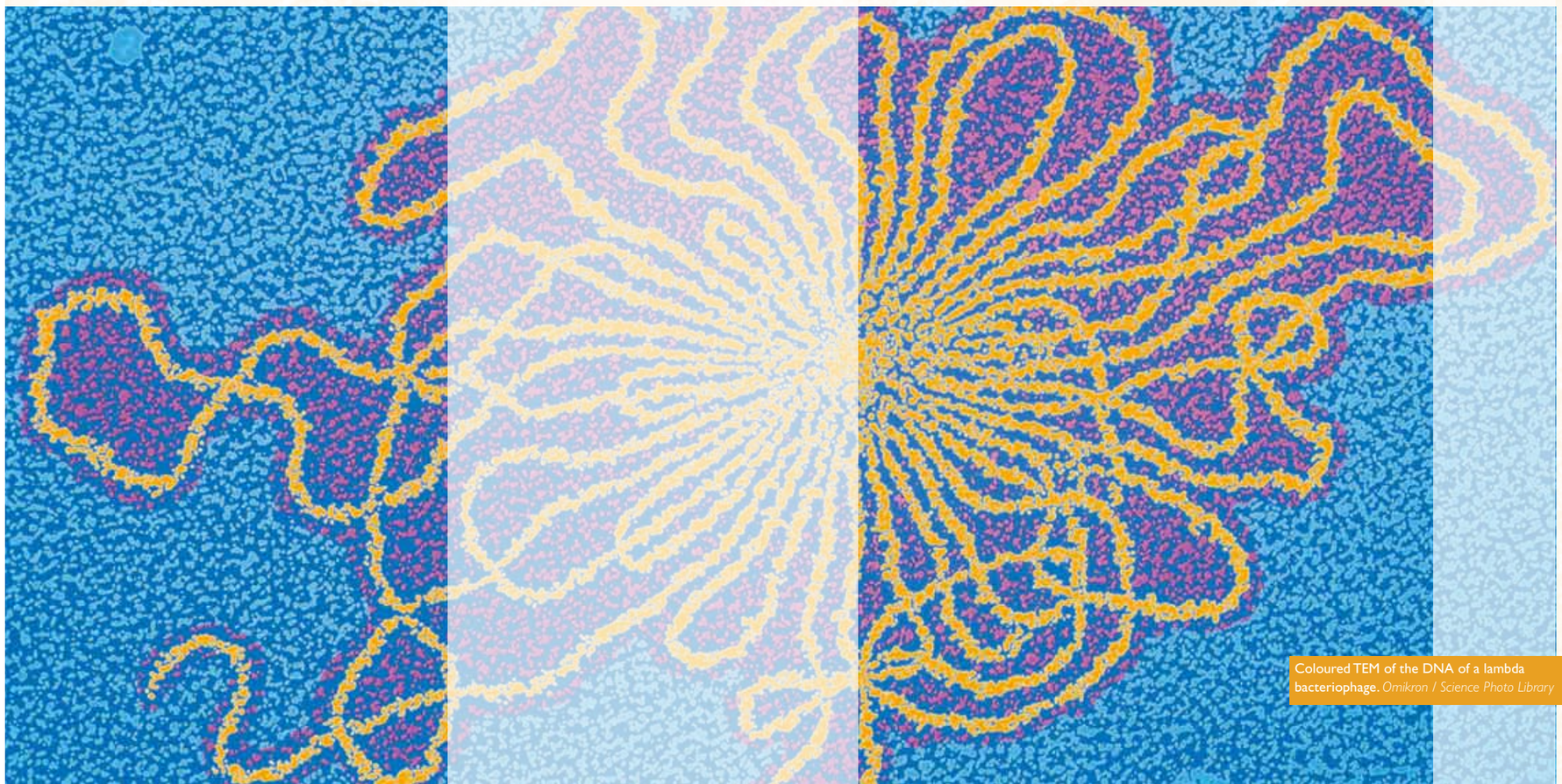
How do phage affect bacterial populations in the environment? Just as foxes prey on rabbits, so phage prey on bacteria. Mathematical modellers have been inspired by this analogy to write down equations for phage and bacterial populations that are based on models developed for animal ecosystems. These models describe how the growth of the predator (phage) population is influenced by the prey (bacterial) population, and vice versa. Under some circumstances the models predict that the predator and prey populations will oscillate in time, while in other cases the predator becomes extinct, or both species become extinct, or the two species can co-exist. These models can help us to understand the factors controlling bacterial and phage populations in the environment. And bacteria and phage are also ideal for testing these ecological models and theories, since, unlike foxes and rabbits, they can be grown under well-controlled conditions in the lab, well within the timescale of a PhD project.

In real environments, however, life is more complicated. Different chemical transformations are carried out by different microbial 'ecotypes', which can inhabit different zones within a microbial ecosystem. For example, methane is produced by methanogens in anaerobic zones and consumed by methanotrophs in aerobic zones. Within these zones, many different methanogens and methanotrophs compete for the same resources. Microbial ecologists aim to understand how diversity is maintained in these ecosystems: why do we find many co-existing methanogens and methanotrophs rather than just one 'winner'? Is it possible that phage could play a role? Phage can promote diversity in simple model systems. If two bacterial strains compete for the same resource, the faster-growing strain will out-compete the other. However, both experiments and theory show that if phage are added, both strains can co-exist, providing the slow-grower is more resistant to the phage. Could this principle also apply, on a grander scale, to more complex ecosystems with many microbial species and many ecotypes? Modelling has an essential role to play in helping us to answer this and a host of other questions about the dynamics of microbial ecosystems.

PHAGE AND EVOLUTION

Understanding evolution is one of humankind's most important objectives – but evolution experiments with animals and plants are generally long and expensive, with the result that theory is often far ahead of measured data. Phage have short generation times, are easy to manipulate in the lab, and have small genomes which are cheap to sequence – making them ideal model systems for studying evolution. For example, in recent work by Kerr *et al.*, bacteria and phage populations were allowed to evolve in 96-well microplates, using a robot to transfer samples between communities in different wells. Different 'migration patterns' turned out to lead to different evolutionary outcomes, as predicted by a computer simulation model.

Mathematical models can also be used to understand how phage have influenced the evolution of bacterial genomes. Phage can sometimes transfer bacterial genes from one bacterium to another. While some people believe that this 'horizontal gene transfer' has played a crucial role in the evolutionary history of bacteria, others consider it much less important. Computer simulations can potentially make a useful and novel contribution to this debate, since in a simulation, we can turn on and off phage-mediated horizontal gene transfer and see what difference it makes.



Coloured TEM of the DNA of a lambda bacteriophage. *Omikron / Science Photo Library*

A MODEL IS JUST A MODEL

Modelling can never replace biological knowledge and intuition. A mathematical model is only as good as the biological insight that is used to build it, and as accurate as the parameters that it contains. But a good model can predict outcomes that would take a long time to measure in the lab, and can sometimes even show what causes those outcomes. So modelling in combination with experiments is very powerful, and there is no better system to start with than bacteriophage.

ROSALIND ALLEN is a Royal Society University Research Fellow at the School of Physics and Astronomy, Edinburgh University (email rallen2@ph.ed.ac.uk)

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VIRUSES AND GEOMETRY

WHERE SYMMETRY MEETS FUNCTION

REIDUN TWAROCK & TOM KEEF

Background: Surface structure of a Norwalk virus particle. *Laguna Design / SPL*

THE SIMPLEST VIRUSES are nanometre-sized particles consisting of genomic RNA or DNA surrounded by protective protein containers. Like Trojan horses, these containers, or capsids, provide protection and transport for the viral genomes between hosts. One of their remarkable features is the wealth of well-ordered patterns in which capsid proteins are arranged in these containers. It makes you wonder… is there more to this display of beauty than mere aesthetics?

Symmetry makes viruses more than pretty – it makes them incredibly efficient and sophisticated.

A CODING MATTER?

Crick and Watson argued in 1956 that viruses should display symmetry due to coding constraints. By using symmetry, viral particles can be encoded by only one, or a few, types of protein, which are then repeatedly synthesized and used as building blocks for the capsid. This constrains the organization of the capsid proteins, to either helical structures or spherical particles. There are only a finite number of incarnations of symmetry in three dimensions, which are embodied by a set of geometric shapes, called Platonic solids (see Fig. 2). Simple spherical viruses, i.e. viruses containing a protein shell surrounding a nucleic acid, exhibit icosahedral symmetry. That means they have the same symmetry properties as the icosahedron, a shape formed from 20 triangles. Since the corner of each triangle accommodates a protein, as demonstrated in Fig. 1(a), capsid proteins organized according to this symmetry must occur in multiples of 60 unless located on a symmetry axis.

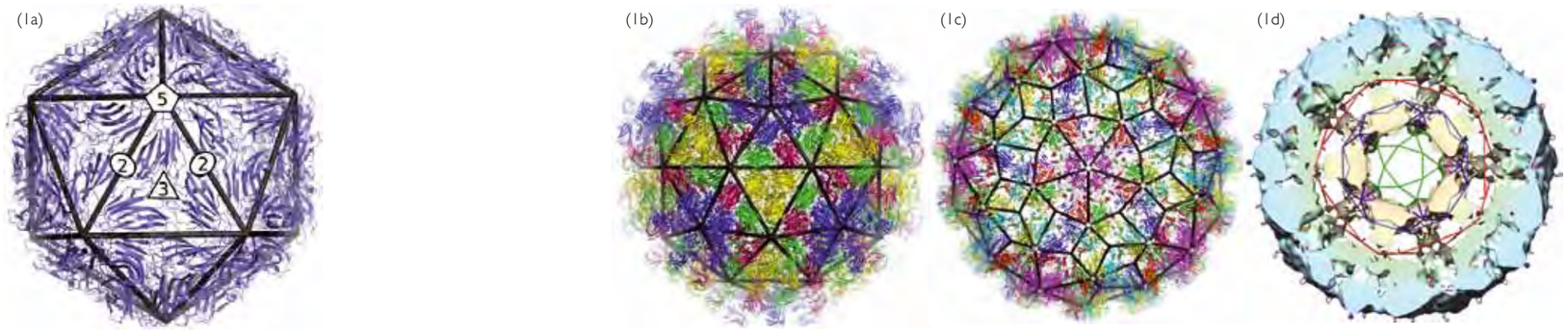


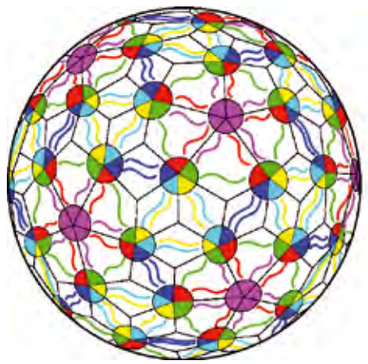
Fig. 1 *(above)*. (a) Viruses have the same symmetry properties as the icosahedron, sharing 2-, 3- and 5-fold axes of rotational symmetry with this Platonic solid. This virus (STMV, PDB-ID 1a34) is composed of 60 capsid proteins that are located in the corners of the triangular faces of the icosahedron superimposed in black. Numbers indicate the locations of the 5-, 3- and 2-fold axes of icosahedral symmetry. (b) A *T*=4 virus (Providence Virus, PDB-ID 2qqp) can be modelled by subdividing each face of the icosahedron into four smaller triangles. In this way, hexagonal protein clusters are formed around the sites where six triangles meet. (c) The tiling model for SV40 (PDB-ID 1sva) accounts for the locations and relative orientations of the pentamers that form the capsid. Sites marking the locations of pentamers are indicated by white spheres. (d) A slab of about 40Å through the cryo-EM density of the viral capsid and the genomic RNA of bacteriophage MS2, with different layers of material modelled by our new 3D symmetry principle. *Neil Ranson, University of Leeds*

QUASI-EQUIVALENCE THEORY

Viruses do indeed dance to this tune of symmetry as subsequently shown by Don Caspar via X-ray crystallography. However, the requirement of being confined to only 60 copies of a capsid protein places severe size restrictions on viral capsids and their genomes. It is therefore not surprising that most viruses are composed of more than 60 capsid proteins. Don Caspar and Aaron Klug argued in a seminal paper in 1962 that more than 60 capsid protein subunits can be accommodated in the capsid if additional copies are organized according to quasi-equivalence. From a mathematical point of view, quasi-equivalent conformations of capsid proteins can be obtained by dividing the triangular faces of the icosahedron into smaller triangles, as shown in Fig. 1. The number of small triangles per icosahedral face is called the triangulation number *T* and

(2)

(3a)



(3b)

Fig. 2. The Platonic solids, encoding tetrahedral, octahedral and icosahedral symmetry. Viruses share their symmetry properties with the icosahedron.

Fig. 3. (a) Diagrams showing the locations of proteins in the SV40 capsid, with different colours denoting proteins that are related to each other by icosahedral symmetry. Viral Tiling theory predicts the locations and relative orientations of the 72 pentamers in the capsid. (b) Kite shaped tiles represent trimer interactions, whilst diamond shaped tiles, called rhombs, encode dimer interactions.

Fig. 4 (*opposite page*). Two tessellations in terms of diamond-shaped tiles called rhombs. The tessellation in terms of 6-fold clusters (left) can be obtained from one shape of rhomb and repeats periodically; the tessellation admitting 5-fold clusters (right), a patch of a Penrose tiling, is given by a small and a large rhomb and is not periodic.

All images R. Twarock and T. Keef

only specific values T=1,3,4,7… are geometrically possible. Since six triangles meet in a hexagonal arrangement, Caspar and Klug's theory predicts that capsid proteins occur in clusters of six (hexamers), except for 12 clusters of five (pentamers) located at the particle 5-fold axes. This is a very powerful result and has been shown to be in excellent agreement with a plethora of viral capsid structures. It forms the basis of modern structural virology, and is a cornerstone of image reconstruction techniques.

FROM HEXAGONS TO PENTAGONS

Given the success of quasi-equivalence theory, it was therefore surprising in 1982 that Ivan Rayment and colleagues discovered a virus that does not follow this rule. Indeed, a number of viruses such as *Polyomaviridae* and *Papillomaviridae* are formed entirely from pentamers. An example is Simian Virus 40 (SV40), shown in Fig. 1(c). Zooming closer into its surface one sees that adjacent pentamers are connected via C-terminal arm extensions of the proteins, and that these occur in two different ways, either in groups of three (trimer interaction) or two (dimer interaction) (see diagram in Fig. 3). The local environments around different pentamers are hence not identical and the capsid is therefore not quasi-equivalent in the sense of Caspar–Klug theory. Moreover, 60 of the pentamers are located in positions where hexamers would be expected – as Liddington and collaborators said in their article in *Nature* in 1991: '*The puzzle is how do the … pentamers fit into the hexavalent holes?*'

AS PHYSICS…

This structural puzzle is akin to a problem that surprised the physics community in the 1980s. It is known in mathematics that periodic arrangements formed from pentagons cannot exist, and it was therefore widely accepted that alloys don't have atoms arranged according to 5- or 10-fold symmetry. However, Dan Shechtman and collaborators discovered alloys that do… and called the new structures quasicrystals. How can the occurrence of 5-fold symmetry in quasicrystals be understood? The answer was given by a mathematical approach called tiling theory, that investigates how space can be tessellated in terms of a number of basic shapes called tiles. Aperiodic tilings, of which the Penrose tiling discovered by Sir Roger Penrose from the University of Oxford is one of the most famous examples, embody tessellations that can accommodate 5-fold symmetry at the expense of periodicity. As Fig. 4 demonstrates, it is possible to arrange diamond-shaped tiles, known as rhombs, with local 6-fold symmetry in a periodically repeating pattern, whilst local 5-fold symmetry can only be accommodated if periodicity is lost.

…SO BIOLOGY

We have used a similar concept in three dimensions to describe the structures of spherical viruses. The new theory, called Viral Tiling theory, investigates how a set of basic shapes can tessellate icosahedral surface lattices. This approach generalizes the hexagonal surface lattices of Caspar–Klug theory to tessellations also containing pentagonal arrangements. The interpretation of these tessellations, as in Caspar–Klug theory, is that proteins are predicted to be located in corners of the tiles. For example, in the case of SV40, the tiling pinpoints the locations of all 72 pentamers. What is more, the two types of tiles, rhombs and kites, encode the two different types of interactions between protein subunits: kites indicate the locations of trimer interactions, whilst rhombs indicate dimer interactions (Fig. 3). This extension of Caspar–Klug theory to include protein clusters with pentamers instead of hexamers is similar to the extension of crystallography by quasicrystals: a logical next step in the mathematical rule set that provides the blueprints for these structures.

A THREE-DIMENSIONAL WORLD

Both Caspar–Klug theory and Viral Tiling theory model virus structures in terms of surface lattices, and their predictive power is therefore confined to pinpointing the locations and relative orientations of the protein clusters in the capsid. Information on the thickness of the capsid, the structural folds of individual capsid proteins, and the organization of the viral genome within the capsid cannot be predicted in this way. A dimension is missing. We therefore asked the question – is there a wider mathematical framework that both addresses the full three-dimensional structure of a virus, and contains within it the results of Caspar–Klug theory and Viral Tiling theory as special cases? We were able to show that the three-dimensional blueprints of viruses can be understood via a classification of suitable extensions of the icosahedral symmetry group, mathematical structures that encode how icosahedral symmetry manifests itself at different radial levels of a structure. The new theory acts like a mathematical microscope and predicts the geometric constraints that impact on all viral components collectively.

"The 3D blueprints of viruses can be understood via a classification of suitable extensions of mathematical structures that encode how icosahedral symmetry manifests itself at different radial levels of a structure."

So, symmetry seems to be even more important in virology than previously appreciated. But what is the reason for all this symmetry in the zoo of viral particles? Again, the answer is function. Symmetry goes hand in hand with stability. Symmetric configurations are usually more stable, a feature that is important for viruses when transporting their genomic material between hosts. However, controlled destabilization is crucial for the release of the genome and hence for infection. Do the many asymmetric features observed in viruses therefore imply a functional role for symmetry breaking in viruses? And do the boundary conditions implied by symmetry place constraints on the evolution of viral particles, ensuring an outcome important for function? The occurrence of symmetry in viruses also raises a number of other important questions, but one thing seems certain – symmetry in viruses is more than a beautiful caprice of nature.

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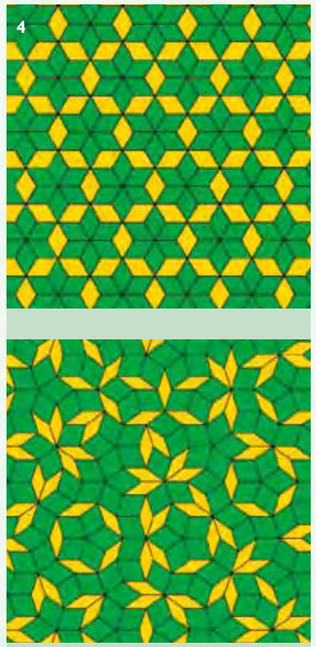

REIDUN TWAROCK is Professor of Mathematical Biology & **TOM KEEF** is a Postdoctoral Research Assistant in the Department of Mathematics, University of York (email rt507@york.ac.uk)
This research is funded by a Leverhulme Trust Research Leadership Award.

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Using modelling to understand protein localization in bacteria

LEENDERT HAMOEN

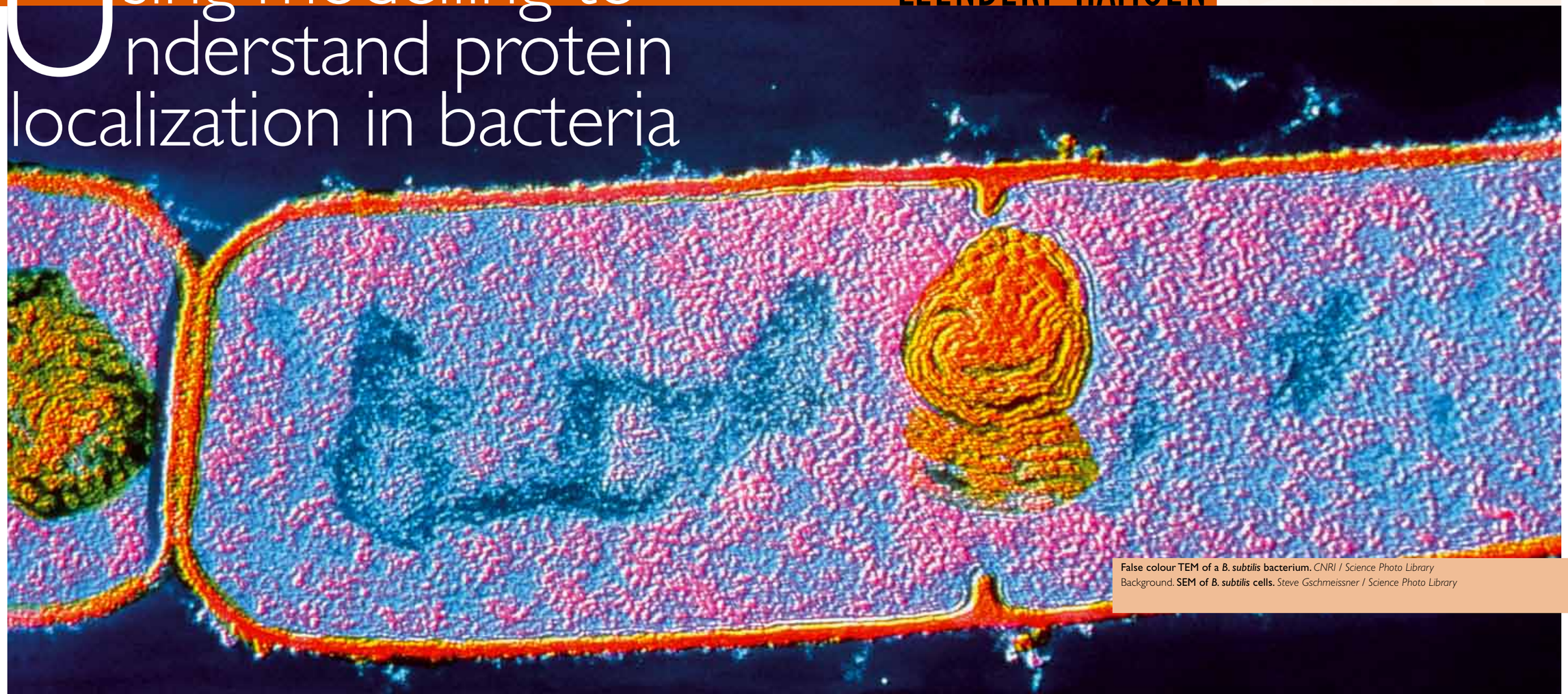
How do bacterial proteins find their destination in the cytoplasm of the cell? A multidisciplinary approach and some computer modelling provided many of the answers to this question.

THE ORGANIZATION of the bacterial cytoplasm is surprisingly complex. Some proteins accumulate near the cell poles, and others are only found at mid-cell. Certain bacterial proteins form spirals, whereas others oscillate between the cell poles. What is so intriguing about this organized distribution of proteins is that bacteria do not contain membranes to compartmentalize their cytoplasm, and they do not have a dedicated cytoskeleton that transports proteins to certain regions in the cell as eukaryotic cells do. How all these bacterial proteins find their proper destination in the cytoplasmic space is a major question in bacterial cell biology, and this problem has intrigued me for a long time. Eventually, when there was an opportunity to work in this field, I decided to study the polar localization of the protein DivIVA (pronounced as 'div-4-a') in the model organism *Bacillus subtilis*. This brought me to the laboratory of Jeff Errington which was then in Oxford.

Using fluorescence microscopy and GFP-labelled DivIVA, Jeff's lab had shown that this protein localizes at mid-cell when cell division is initiated, and also accumulates at the cell poles (Fig. 1). But more importantly, they had found that DivIVA shows a comparable localization pattern when expressed in an unrelated bacterium like *Escherichia coli*, and even in the fission yeast *Schizosaccharomyces pombe*. This suggested that the localization characteristic of DivIVA is an intrinsic property of the protein, and this made DivIVA an ideal model system to study protein localization in bacteria.

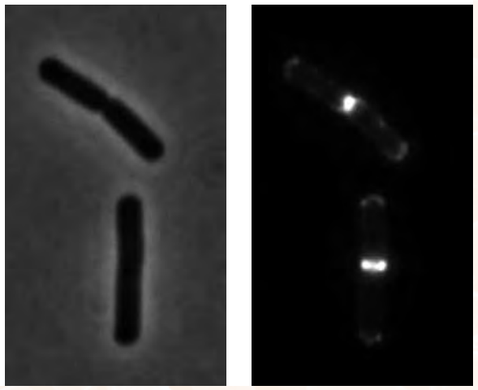
REACTION-DIFFUSION SYSTEMS

Searching the literature for processes that could explain how spatial distributions of proteins could spontaneously emerge, I came across 'reaction-diffusion' systems. In a famous paper published in 1953, entitled '*The chemical basis of morphogenesis*', the well-known mathematician Allen Turing had shown that two diffusing components (e.g. proteins), which influence the production of each other, can form stable patterns of cells producing one component separated by cells producing the other component. It turned out that these principles can also be applied to certain chemical reactions, and over the years reaction-diffusion principles have been used to model the specific distribution of proteins within cells, including the oscillation of the Min proteins in *E. coli*. So reaction-diffusion system could explain the localization pattern of DivIVA.



False colour TEM of a *B. subtilis* bacterium. *CNRI / Science Photo Library*
Background. **SEM of *B. subtilis* cells.** *Steve Gschmeissner / Science Photo Library*

Fig. 1 (*below*). **Localization of DivIVA-GFP in *B. subtilis*. Phase contrast (left) and fluorescence light (right) images are shown.** *L. Hamoen*



One afternoon in Oxford I had a discussion with Martin Howard, a biophysicist with experience in modelling reaction-diffusion systems. This was time well spent and these discussions made it clear that my ideas were too simplistic. However, the main problem was arriving at a sensible reaction partner for DivIVA that could make a reaction-diffusion system work for DivIVA localization.

MEMBRANE CURVATURE MODEL

Yet there was an alternative model: membrane curvature at division sites and cell poles that could guide DivIVA to its proper localization. This assumption posed two problems. First, how do you prove this *in vivo*, and second, how could it work? If DivIVA did bind to curved surfaces, it is probable that the protein has an affinity for the cytoplasmic membrane. So this was the first thing to test, and indeed purified DivIVA binds specifically to phospholipid bilayers. However, could we prove that the protein binds to curved lipid membranes? It took more than 4 years to come up with a satisfying experiment as somehow we needed to manipulate the curvature of the cell membrane so that only the change in curvature could account for any effect on the localization of DivIVA.

Fig. 2 (*right*). **Localization of DivIVA-GFP in *B. subtilis* (top), in *E. coli* cells (middle), and in an *E. coli* murein hydrolase mutant (bottom). Upper frames show phase contrast, middle frames show fluorescent membrane stain, and lower frames show GFP fluorescence (deconvoluted images). A schematic representation of division sites / cell poles is presented above the microscopic images. DivIVA-GFP is indicated in green.** *L. Hamoen*

"Now that we had shown that DivIVA indeed binds to curved membranes, we needed to understand the mechanism."

When expressed in *E. coli*, DivIVA-GFP binds to the periphery of the oval-shaped cell poles and forms an arc-like fluorescent signal (Fig. 2). Now, there is a way to make these oval poles flat. To separate daughter cells after division, bacteria use specific cell wall hydrolases, and when these hydrolases are absent, *E. coli* grows in long chains and the cell poles are flattened (Fig. 2). This results in a rather sudden transition from the lateral wall to the cell pole, thus introducing a strongly concave, curved cell membrane. It turned out that DivIVA-GFP binds primarily to these areas of strong 'negative' curvature (Fig. 2).

ELUCIDATING THE MECHANISM

Now that we had shown that DivIVA indeed binds to curved membranes, we needed to understand the mechanism. An obvious explanation would be that DivIVA binds specific lipids that accumulate at curved membranes. Cardiolipin is one such lipid. This lipid is cone-shaped and therefore it is energetically more favourable for this molecule to float in areas of the membrane that are curved. Unfortunately, in *B. subtilis* mutants that do not produce cardiolipin the localization of DivIVA was not affected. If no other protein or lipid is involved in the binding of DivIVA to curved membranes, could it be that DivIVA itself senses membrane curvature? Electron microscopy had shown that DivIVA forms very large elongated oligomers of about 22 nm long that assemble into a complex meshwork. Could these oligomeric structures fit into the corners of curved membranes? This would only work if the DivIVA oligomers themselves adopt a curved configuration, maybe inflicting the deformations in flat lipid membranes. We used transmission electron microscopy to see whether purified DivIVA causes bends in artificial liposomes, but the results were negative. So the conclusion must be that DivIVA oligomers do not recognize curved membranes by forming a curved arrangement.

THE ROLE OF OLIGOMERS

None of the conventional mechanisms seemed to be able to describe why DivIVA accumulates at curved membrane regions. Consequently, I wondered whether the clustering of DivIVA oligomers is favoured in these regions. The size of these protein clusters is limited by the quantity of oligomers that detach from the surface, such that clusters formed on a membrane surface result in fewer oligomers detaching, especially when the protein cluster is cornered by two membranes (Fig. 3). Of course, a division septum does not make a sharp 90° angle with the side wall, and EM images showed that in *B. subtilis* the curvature at the septa has a radius of around 50 nm. Moreover, DivIVA oligomers are huge, so maybe when these oligomers cluster they can 'bridge' this curved area (Fig. 3). Due to a lack of knowledge of the biophysics of protein interactions, I was not sure whether my reasoning was correct, and I had no way of testing the model. It became evident that I needed to collaborate with someone from a biophysical background.

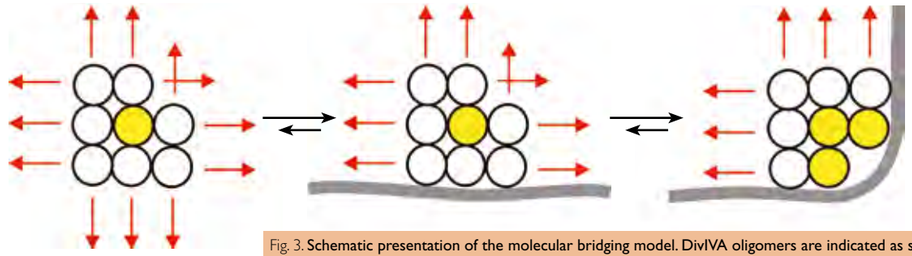


Fig. 3. **Schematic presentation of the molecular bridging model. DivIVA oligomers are indicated as spheres that form a free-floating cluster (left), a cluster that attaches to the cell membrane (middle), and a cluster that fills the corner of a curved membrane (right). Oligomers that can detach (red arrows) are indicated in white.** *L. Hamoen*

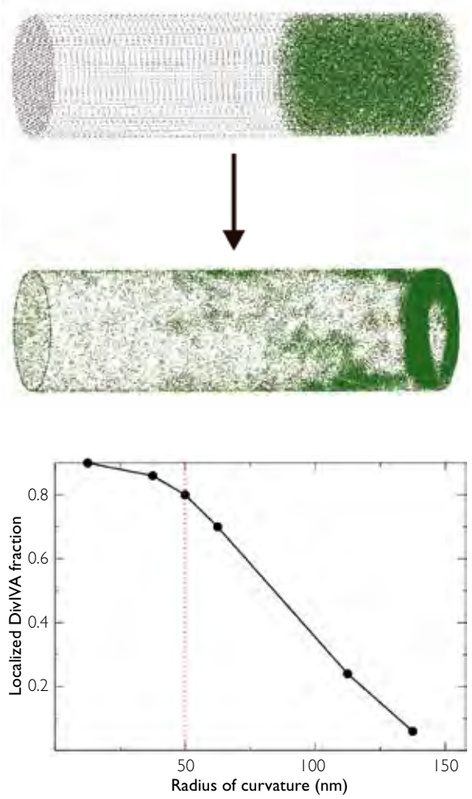


Fig. 4. Monte Carlo simulation of 200 DivIVA oligomers (green dots). The membrane curvature at the end of the cylinder has a radius of 50 nm. The graph presents the polar localization of spheres for different membrane curvatures. To reduce computing time we started with an asymmetric distribution. *L. Hamoen*

MONTE CARLO SIMULATIONS

After some inquiries I contacted Davide Marenduzzo, a biophysicist at the University of Edinburgh. It was a great surprise when he replied suggesting that the model might actually work! He was even willing to run some Monte Carlo simulations to test it too. Such simulations are not trivial as a single one can take more than a day of computing time, even when DivIVA oligomers are simulated as simple spheres. After a few inspiring months, we were able to show that, using relevant parameters, the spheres do accumulate at the surface areas that are most strongly curved (Fig. 4). It was satisfying that after almost 6 years we finally had a model that could explain why DivIVA binds to negatively curved membranes.

Unfortunately, some referees of the paper needed more persuasion. Their argument was that we used spheres in our simulations and that the contact sites on the spheres were not defined; not a very realistic situation. We had to agree and tried to simulate more natural DivIVA oligomers by translating DivIVA oligomers into rigid stacks of four small spheres, whereby only the top and bottom sphere could make contact with other oligomers or the membrane. The effort was worth it; the simulations gave a better localization pattern (Fig. 5), a pattern that is reminiscent of the fluorescence signal observed at the site of cell division in *B. subtilis*. Many questions still remain, and our 'Molecular Bridging' requires extensive testing. However, the combination of *in vivo* experiments with Monte Carlo simulations proved very fruitful and will also provide an excellent framework for further testing.

"The combination of in vivo experiments with Monte Carlo simulations proved very fruitful."

The collaboration with Davide Marenduzzo has been a great experience. Modelling was extremely valuable when experimental testing became impossible. My experience has also been that it is not necessary to have an in-depth knowledge of each other's disciplines in order to communicate the subject of study, as long as the research question is clear.

LEENDERT HAMOEN is a Wellcome Trust Career Development Fellow at the Institute for Cell and Molecular Biosciences, University of Newcastle (email l.hamoen@ncl.ac.uk)

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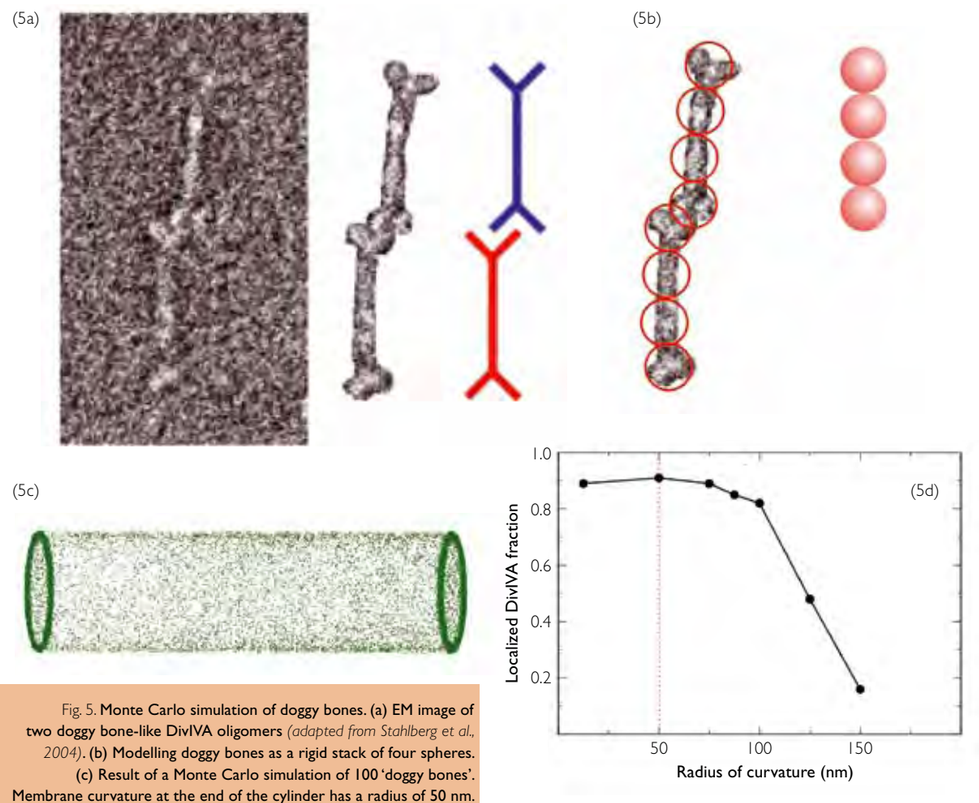


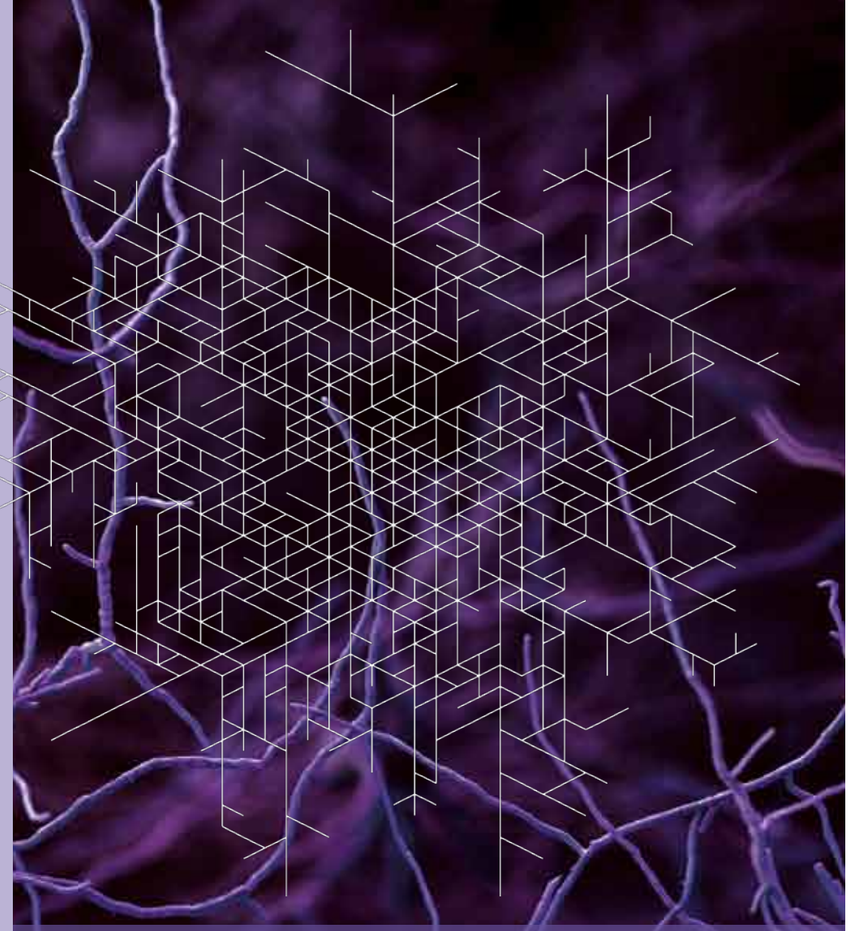
Fig. 5. Monte Carlo simulation of doggy bones. (a) EM image of two doggy bone-like DivIVA oligomers *(adapted from Stahlberg et al., 2004)*. (b) Modelling doggy bones as a rigid stack of four spheres. (c) Result of a Monte Carlo simulation of 100 'doggy bones'. Membrane curvature at the end of the cylinder has a radius of 50 nm. (d) Fraction of polar localized doggy bones as a function of different membrane curvatures. *L. Hamoen*

Background. **Coloured SEM of hyphae of *Aspergillus niger*.** *Eye of Science / Science Photo Library*
Far right. **Model fungal mycelium.** *Reproduced with permission form Boswell et al. (2007)*

Mathematics has long been known as a powerful tool for describing the physical world. An example of just how important mathematics is becoming in helping us to understand the natural world is its application to modelling hyphal tip growth.

A blueprint for polarized growth

FORDYCE DAVIDSON



GROWTH BY cell elongation is a morphological process that transcends taxonomic kingdoms. Examples include hyphal tip growth in actinobacteria and filamentous fungi, plant root-hair formation and the development of neurons in animals. Such structures have developed almost certainly because they afford an evolutionary advantage – producing a growth habit well-suited to physically complex environments, facilitating the (internal) redeployment of nutrients or enabling the transfer of information over long spatial scales. The biology involved in producing this polarized growth form is clearly very different in plant, bacterial, fungal or mammalian cells. But its ubiquitous nature suggests that certain 'rules' are being followed. Moreover, if we compare fungi and actinobacteria, the foci of this article, it is clear that these rules are 'scalable': tip growth is similar, irrespective of the orders of magnitude difference in cell size. It appears that these rules form a blueprint for polarized growth.

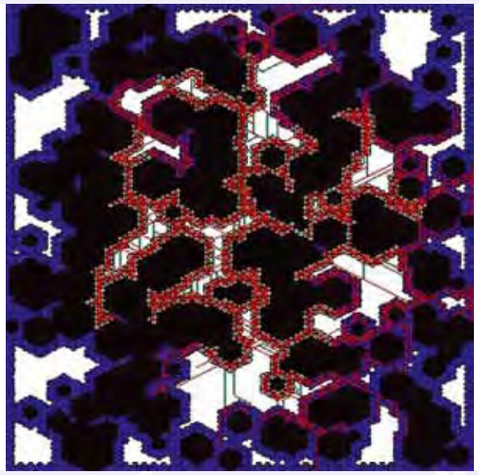
That the physical world can be described using mathematics has been known for millennia. Rather surprisingly, the mainstream use of mathematics to understand biological phenomena is a much more recent trend. The blueprint for polarised growth must be based on the laws of physics and hence describable by mathematics. If we could understand these rules, then we have the opportunity to make significant headway towards understanding this complex growth habit and hence control it to our advantage.

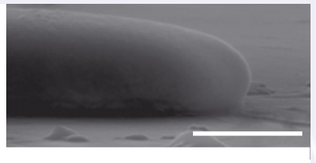
HYPHAL TIP GROWTH

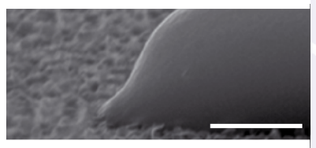
From a mechanical point of view, hyphal tip growth in filamentous fungi and actinobacteria is closely related, and a suite of mathematical techniques has been developed that provides insight to its common morphology in these otherwise unrelated organisms. To describe hyphal growth requires the complex biological processes to be abstracted to a level where key biophysical components associated with tip formation can be isolated and their interaction investigated. At a base level this requires descriptions of (i) the cell wall and (ii) the delivery of materials that maintain the cell wall and produce new, polarized growth. To investigate the functional consequences of tip growth requires further layers of abstraction and the incorporation of information across a range of spatial scales. Individual hyphae branch and anastomose to form a mycelium, which interacts in both a local and global manner with its micro-environment. Thus further considerations are (iii) network formation and (iv) (environmental) stimuli and signal processing.

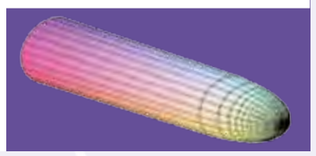
DESCRIBING THE TIP – OR HOW TO MAKE A HYPHA USING WHAT'S ON YOUR DESK

Constructing a meaningful mathematical description of tip formation is in itself a considerable challenge. Several approaches have been developed, some species-dependent and others more generic. Despite the biological differences, the basic mechanics of tip formation and extension in filamentous fungi and actinobacteria are similar – a soft region in the cell wall is located at









Right. **Model for fungal mycelium (red) growing in a computer-generated soil (black) with water film (blue).** *Reproduced with permission from Boswell et al. (2007)*

Far right. **Normal (top) and micro-tip (middle) morphologies). Bars, top 5 µm, middle 1 µm.** *Reproduced with permission from Bowen et al. (2007).* **The diagram at the bottom shows a geometric model for normal hyphal tip morphology.** *F. Davidson*

the apex. This soft tip is stretched by internal forces and thus driven forward. A combination of turgor pressure, the developing cytoskeleton and the structure of the cell wall itself make up the driving forces. Sub-apically, the wall stiffens and a tube is formed. (A nice mental picture can be conjured by imagining blowing up a balloon inside a wire basket desk tidy with the bottom cut off – as soon as the balloon pokes out the bottom, you slip on another band of desk tidy.)

To describe this process mathematically, both geometrical and biomechanical models are being developed. The former allows for the most basic, but qualitatively accurate description of possible self-similar 'tip-like' shapes, given that experimental observations show wall expansion is normal (at right angles) to the tip surface. More detailed biomechanical models take account, for example, of the balance of forces on the cell wall, which is assumed to be a thin, differentially elastic membrane. (Here, the mental picture can be of one of those party balloons that skilled people can twist into animal shapes.) In these models, the tip shape is not predetermined, rather it evolves naturally through the mathematical rules for elastic materials.

MAINTAINING POLARIZED GROWTH

The biological processes that form and maintain the tip shape – the supply and integration of wall building materials – add another layer of complexity. Not much is known about this in actinobacteria, but experimental results suggest that turgor pressure is a main player. For filamentous fungi, a considerable amount of modelling has been developed to address this problem. Two main hypotheses have developed in parallel over the past two decades. The steady-state (SS) theory proposes that plastic wall material is continually deposited at the hyphal apex and cross-linked into a more rigid form over time. The second hypothesis revolves around the concept of a vesicle supply centre (VSC) or Spitzenkörper. This theory predicts that the VSC or equivalent structure, acts as a distribution point for vesicles containing cell-wall-synthesizing materials. It suggests that a gradient of exocytosis would be created at this vesicle assembly point, which moves with the growing hyphal tip. This gradient is hypothesized to be responsible for the shape of the apical dome. There is still debate over these mechanisms, but it appears that they are both right and a model combining elements of the VCS model, to explain the spatial organization of the fungal tip, and the SS model, to account for the temporal control of wall flexibility, presents the most likely answer. These theories have been (and could only have been) developed and tested using mathematical modelling. They continue to motivate experimental investigations.

SCALING UP AND SCALING DOWN – THE REAL CHALLENGE

The comments above give a small glimpse into the complexity of what appears at first glance to be a relatively 'simple' process – the formation of a polarized cell. Although tip formation is central to the growth habit, a tip-scale model for fungi or bacteria is, in isolation, unlikely to yield useful information about the large-scale form and function of these organisms. On the other hand, the tip-scale model does not explicitly include details of specific gene transcription–translation pathways, which will be central to hyphal formation and processing of environmental signals. On scaling up or scaling down from the tip, the indeterminate nature of these filamentous organisms ensures that the complexity of the growth dynamics remain the same, almost fractal-like.

So how does one attempt to construct meaningful, quantitative links across these scales? It is not the goal of the mathematical modeller to devise an extremely complex system of equations to capture the dynamics of all processes across all scales. Even if this were possible, which is highly unlikely, all that it achieves is the replacement of one form of impenetrable complexity with another. Instead, the aim is to reduce a complex (biological) system to a simpler (mathematical) system where the rigorous, logical structure of the latter can be used to identify, isolate and investigate key properties. However, as Einstein is famously quoted, '*everything should be made as simple as possible, but no simpler*'. Hence, mathematical modelling is not about what to include, but what can be omitted, where the art is in achieving a meaningful balance between the two.

It is therefore advantageous to attempt to construct models that operate at a range of scales by the transfer of information across scale boundaries. Here, information is only passed up (or down) in scale where and when it is needed. This has huge benefits for computation time and savings in complexity. This so-called multi-scale modelling of biological systems is currently the subject of intense interest. Those of us involved in this are developing techniques similar to those designed to study physical problems such as the 'atom to continuum' models used in materials science. Models for the development and function of fungal mycelia have been constructed where the interaction of the tip with its micro-environment is scaled-up as 'movement probabilities' in the mycelium-scale model. For example, this allows us to model the development of fungal mycelia in a computer-generated soil in order to test hypotheses regarding growth dynamics, acidification of the micro-environment and physical 'bio-barrier' properties of growth.

CONCLUSION

Mathematical modelling is a powerful tool, which compliments experimental studies of microbial growth and function across a huge range of spatial scales from gene transcription to nutrient turnover in agricultural soils. Future studies will continue to make use of specific models designed to address key questions at selected scales. However, if we are to make genuine progress in linking gene to tip to function, then multi-scale modelling approaches are most likely to produce the answers.

"It is not the goal of the mathematical modeller to devise an extremely complex system of equations to capture the dynamics of all processes across all scales."

FORDYCE A. DAVIDSON is a Reader in the Division of Mathematics, University of Dundee (email fdavidson@maths.dundee.ac.uk)

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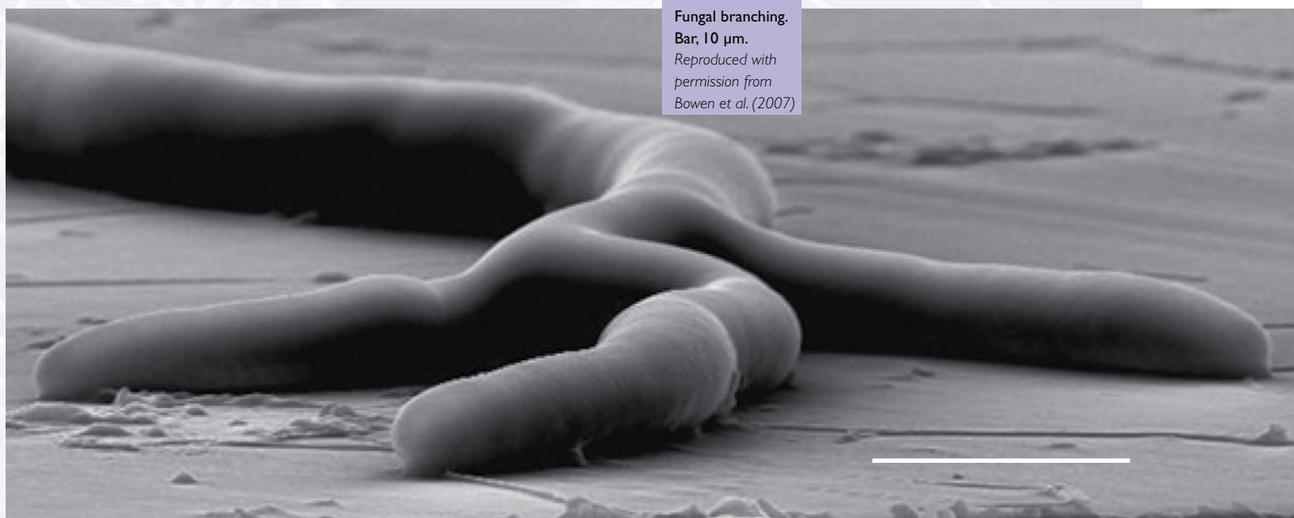
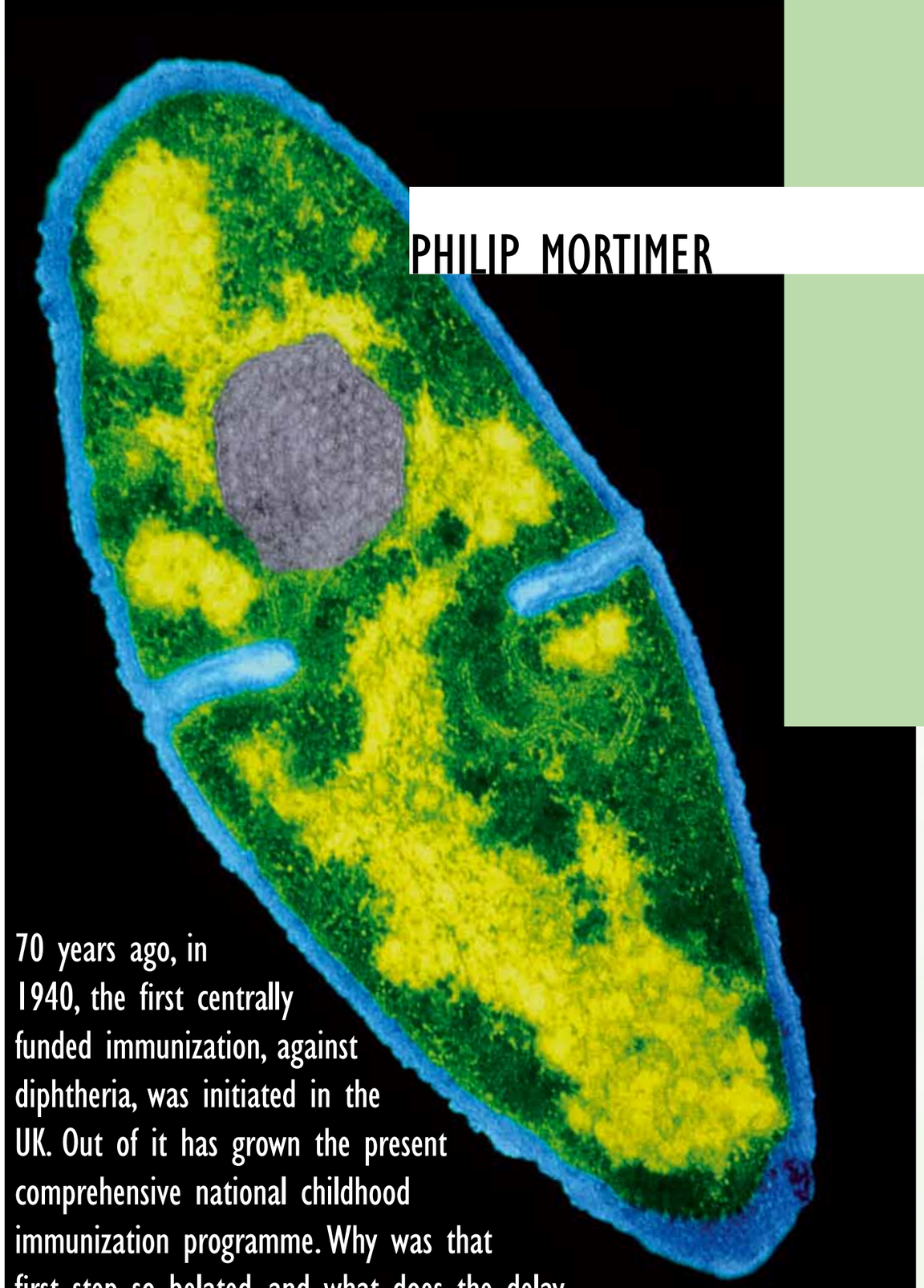


Fungal branching. Bar, 10 µm. *Reproduced with permission from Bowen et al. (2007)*

PHILIP MORTIMER

Diphtheria and the origins of the UK childhood immunization programme



70 years ago, in 1940, the first centrally funded immunization, against diphtheria, was initiated in the UK. Out of it has grown the present comprehensive national childhood immunization programme. Why was that first step so belated, and what does the delay tell us?

Coloured TEM of a section through a *Corynebacterium diphtheriae* bacterium, the cause of diphtheria in humans. *Kwangshin Kim / Science Photo Library*

DELAY AND INDIFFERENCE characterized the interwar period of British public health provision, at least in respect of diphtheria prophylaxis. The two decades witnessed a gradual decline in numbers of diphtheria cases and deaths, mainly attributable to the increasingly effective use of diphtheria antitoxin; but the UK signally failed to take advantage of the opportunity that, from the mid-1920s, diphtheria toxoid (i.e. vaccine) offered to eliminate the disease. The failure was, at its root, an administrative rather than a scientific or professional one, and the emergency measures of 1940 that repaired the lapse in effect acknowledged that.

The story begins in the late Victorian era. By the mid-1890s, German and French researchers had prepared antitoxin against *Corynebacterium diphtheriae*, and by the turn of the century antitoxin was also being raised in horses at the Lister Institute in London and, for instance, in New York. Diphtheria antitoxin, given early in disease and to contacts of cases, was effective, but its overall impact was limited both because of its lack of value in established disease and because of delays in its universal implementation. The other forms of serotherapy in use at the time also meant that serum sickness and even anaphylaxis were sometimes associated with this form of diphtheria treatment.

THE TOXOID VACCINE

The 1900s saw a new approach in the form of attempts to modify the exotoxin of *C. diphtheriae* by removing its toxicity while retaining its immunogenicity. By the early 1920s balanced mixtures of toxin and antitoxin were being widely used, and the toxin was being chemically modified. In particular, Gustave Ramon at the Pasteur Institute in Paris was promoting a formalized toxin which he called 'anatoxine'.

Nowhere was anatoxine (i.e. toxoid) used to better effect than in Ontario. In Toronto, in 1915, the Connaught Laboratories had been founded to produce diphtheria antiserum and in 1925 production of diphtheria toxoid began there. John Fitzgerald, who was both the Director of the Toronto Institute of Hygiene and of the Connaught Laboratories, instigated a programme of childhood immunization with toxoid that was startling in its impact (Fig. 1).

By 1930 it was evident that an effective diphtheria vaccine was readily available, and data were also beginning to emerge from its use in large cities in North America that 'herd' immunity could be achieved once three-quarters of children had been immunized, either in the case of pre-school children with toxoid or in the case of older, possibly sensitized, children with toxoid/antitoxin mixtures. Diphtheria in the community was preventable.

WHY DID BRITAIN DITHER?

The British response to these international advances in diphtheria prophylaxis was dilatory to say the least. British microbiologists were expert in diphtheria diagnosis and British companies were capable of preparing the toxoid. Technically, the ability to immunize the main at-risk age group (pre-school and primary school children) existed. An MRC special report in 1934 described the successful use of toxoid and toxoid/antitoxin floccules in a residential school at Greenwich where between 1928 and 1932 about a thousand boys were successfully immunized. But because no British town or city adopted this approach, none achieved what US city health departments, European

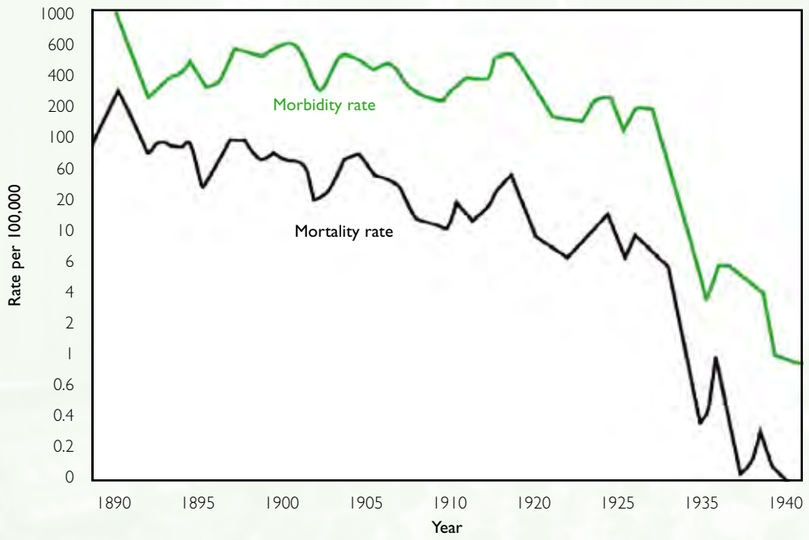


Fig. 1. **Morbidity and mortality from diphtheria in Toronto, Canada, 1890–1940. Note the fall attributable to the introduction of toxoid immunization after 1925.** *Adapted from Cruickshank (1942)*

cities and all of Canada did during the 1930s, i.e. controlled diphtheria by immunization. 'Private' immunizations and better use of antitoxin made some impact on the incidence of disease in Britain, but her record was worse than that of other developed countries. Each year about 2,500 British children died of diphtheria.

The reasons for this lapse continue to be instructive. First, a vocal minority of professional and lay people in Britain distrusted vaccinations, an attitude dating back to the anti-Jennerian movement of Victorian times. There was growing popular opposition, in the absence of epidemic smallpox, to compulsory infant vaccination, and there was a new professional awareness of post-vaccinal encephalitis (first fully described at the London Hospital by Turnbull in 1922). Added to this was an insular attitude towards a French-inspired advance in vaccine practice.

Second, the approach of the British scientific community to diphtheria prophylaxis had got bogged down in technicalities, with groundless anxieties being raised such as whether incomplete vaccine coverage would increase the number of carriers. This seems to have become an excuse for inaction.

Third, and most important, was the lack of funding to pay for other than private immunizations. Ever since 1853, infant smallpox vaccination had been done if not by private medical practitioners, then by locally employed vaccination officers (depending on the social class of the patient). By the 1930s, municipalities were funding TB dispensaries and other schemes, like infant welfare clinics. There was little appetite for assuming the further financial burden of diphtheria immunization, no matter how much individual medical officers might argue for it in council committees.

U-TURN, AND A PRECEDENT SET

Then in 1940, the threat of a wartime epidemic and the mass of scientific argument in favour of diphtheria immunization combined to force a policy innovation. Ministry of Health Circular 1307 advised municipalities to immunize children against diphtheria and, significantly, offered central funding to pay for it. Some towns and cities responded very rapidly, others did not; but by the end of 1942 half of Scottish children and a third of English children had been fully immunized against diphtheria. Local compliance continued to grow and by the time the National Health Service was introduced in 1948, diphtheria was a distinctly uncommon disease (Fig. 2).

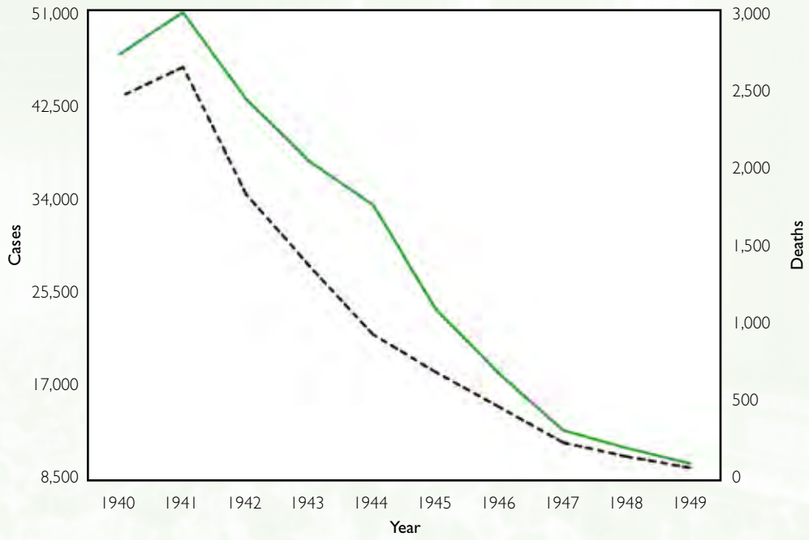


Fig. 2. **Cases (solid green line) and deaths (broken black line) due to diphtheria in England and Wales 1940–1949.** *Data taken from Table II, Chapter 3, in 'The Control of Communicable Diseases' (published by Harvey & Blythe, London, 1952).*

"A vocal minority of professional and lay people in Britain distrusted vaccinations, an attitude dating back to the anti-Jennerian movement of Victorian times."

The refectory of the Greenwich Hospital School where diphtheria toxoid immunization was successfully introduced in 1928 ('herd' immunity could in fact be attained by compliance rates considerably lower than the MRC study achieved there). *Reproduced from MRC Special Report Series (1934)*

Thereafter, both diphtheria and other immunizations remained matters for national as opposed to local funding. Decisions about widening the childhood immunization programme have by now long since been taken by central government, guided by an expert advisory committee. As yet, at least, devolution has not changed that UK consensus. The development of the programme has reached a point that could only have been dreamed of by those who in the interwar years despaired at the inability simply to institute diphtheria immunization.

CONCLUSION

Keeping the UK programme abreast with modern advances in vaccinology has become a complex and costly undertaking; but the principle that decision-making should be central, and not left to local initiatives, is firmly established. As has often been said, infectious diseases do not recognize administrative boundaries. By the same token, immunization needs almost always to be pursued nationwide if a universal prophylaxis is to be attained.

PHILIP MORTIMER has recently retired from the Health Protection Agency, Colindale (email philip.mortimer@community.co.uk)

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Let's get practical

Concerns are often raised about the lack of practical investigations in schools and the poor laboratory skills of students. Microbiology is a very practical subject, requiring a particular range of manipulative skills that can only be acquired by repetition. Despite all the doom and gloom of politicians and the media, experimental work is being carried out in our schools. **DARIEL BURDASS** explains why practical work is important and describes how it is taught today, along with information about the services that SGM offers to promote hands-on microbiology. Our members too can work directly with schools as **JANE WESTWELL** and **DERREN READY** describe.

The Role of Practical Work in Schools and Colleges

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Several studies over time have collected teachers' views on the aims of practical work. Work by Kerr in 1964, Beatty & Woolnough published in 1982 and Swain and colleagues in 1998 all showed that four aims remained constant with teachers, regardless of the kind of practical work being done:

- To encourage accurate observation and description
- To make phenomena more real
- To arouse and maintain interest
- To promote a logical and reasoning method of thought.

These aims should still apply to practical work done in schools today.

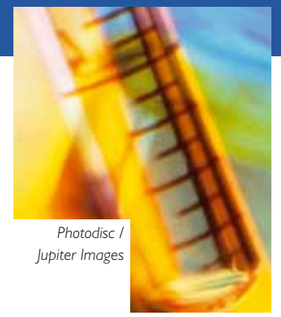
However Hodson had a different approach when reviewing the effectiveness of practical work and used the following headings:

Motivation – Students find practical work both stimulating and enjoyable. The hands on approach sets it apart from other subjects although one study found that enjoyment decreased with age.

Acquisition of skills – in the laboratory and in field work

Learning scientific knowledge – Explanation of a scientific concept to reinforce learning and to enable understanding. I listen – I forget, I look – I remember, I do – I understand.

Methods of science – To give insight into the 'How Science Works' element of the curriculum students need to recognize how scientists identify, investigate and solve problems and learn that their work is not a static process and is constantly evolving. They also should realize that scientific research is constrained by the ethical and moral views of Society.



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Scientific attitudes – To develop open-mindedness, objectivity and the willingness to suspend judgment.

The type of practical work done in schools is often limited to fair-testing. It has been reported that over 80% of investigations in England and Wales are of the fair-test variety where students focus on the control of variables. It is important that students are exposed to a full range of investigations, such as pattern seeking, classifying, surveys, comparisons and modelling if they are to acquire a well-rounded view of practical science, together with the development of good skills and an understanding of 'How Science Works'.

If investigations are being used to highlight Methods of Science, then it is important that the investigation is open-ended. If the outcome of the investigation is already known due to the nature of the theory being tested, the students are

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not testing a theory, they are demonstrating it. Many students, particularly as they move into secondary school, carry out practical exercises that are similar to following a recipe and this could be one of the reasons for a decline in interest in practical work with age – the students need to feel a sense of ownership and control to feel motivated.

Practical work can often become stifled in schools by the need to get the 'correct answers' to back up what they have read in the text books. Both teachers and students, when put in this situation, often find they obtain conflicting results that do not support the concept they are trying to understand. This can be very problematic. Nott & Smith suggest that teachers faced with this situation usually respond in one of three ways:

- Talking their way out of it – assign blame, e.g. to the equipment
- Rigging it – where the teacher uses his experience to manipulate the variables to obtain good results
- Conjuring it – manipulation of materials or apparatus to produce good results.

According to Hodson, conjuring is most prevalent when practical work is concerned with the learning of science, when outcomes are essential to good understanding. Teachers justify their actions in terms of the learning benefits the students gain. However, this is at odds with Methods of Science or How Science Works.

Students need to learn the following practical skills that are common to many procedures:

- Planning the investigation
- Use of apparatus and measuring instruments
- Observation of outcomes
- Recording of data
- Interpretation of data
- Performance of investigation
- Communication

It is important that students see these skills as transferable and not just linked to a specific investigation they are personally involved with. As much of learning comes from talking about what has been done, it is important that adequate time is given to the students to discuss their results either in groups or with the whole class.

Simulations, for example on DVD, may be of value where real practical investigations are restricted due to expense or lack of laboratory time. However, they should not be seen as a replacement for hands-on practical activities.

THE ROLE OF POLICYMAKERS

Although teachers play a big part in enhancing practical science in schools, they can only do so within the constraints of education policy. The Government and its agencies could strengthen good quality practical science in schools and colleges in several ways, such as providing greater numbers of specialist subject teachers for biology, chemistry and physics in secondary schools and ensuring that science budgets reflect the huge expense that is involved in carrying out good-quality practical work. Putting proper training in place for school technicians is important to ensure that they are well qualified, respected and paid members of the school community, as without good technical support practical work would be even more limited. The Government also needs to ensure that investigations are not straightjacketed by the National Curriculum and there is opportunity for open-ended work.

SGM MEETS THE CHALLENGE

Learned societies such as SGM can help to influence policymakers by lobbying and responding to consultations, but they can also play a significant role in directly promoting practical science in schools. The SGM firmly believes in this approach and, in partnership with its members, offers a range of activities and resources to promote practical microbiology in schools.

The Society runs highly subsidized basic and advanced practical microbiology courses for teachers and technicians to help ensure that they are confident to carry out practical work with micro-organisms. We are continuing to meet the needs of new teachers by offering a limited number of courses to PGCE students, which we hope to expand over time. The SGM provides, free to schools, practical investigations specially tailored for use by school students, together with a helpline for those who need advice. The Society also funds ten Nuffield Bursaries in microbiology to give post-16 students the opportunity to join a real research project with practising scientists in any area of the subject.

Today practical work is taught beyond the lab and encompasses complementary activities such as science-related visits, presentations and role play, case studies and analysis and evaluation of the reliability of science in the news. There are now some excellent websites that provide online global news services that feature health, science and technology reports from leading universities, hospitals, journals, agencies and companies engaged in research (**www.eurekalert.org/**; **www.sciencedaily.com/news**).

The SGM also offers an up-to-date service that highlights microbiology in the news – **www.sgm.ac.uk/news** Most stories are linked to the full newspaper article and where appropriate the original research.

See **www.microbiologyonline.org.uk** for details of all these activities or email **education@sgm.ac.uk**

DARIEL BURDASS,
Education Manager

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Sara checks out a specimen under a microscope. *Aldrington Primary School*

OUT OF SCHOOL AND IN

SGM members describe their different approaches to telling children about the exciting world of microbes.

Mini-microbiologists

Have you ever entertained the idea of delivering practical microbiology workshops to over 90 primary school children in your teaching labs? SGM member **BOB RASTALL** did just that in September last year when 3 classes of 9–11-year-olds went on an outing to the Department of Food & Nutritional Sciences at University of Reading. **JANE WESTWELL** from the External Relations Office tells more…

Four years ago I visited my daughters' school to deliver some hands-on microbiology to support the KS2 microbes unit. Although the pupils loved the workshop, I could only visit one out of three year groups. Two class teachers observed my workshop then delivered it to the remaining pupils who enjoyed the lessons, but it didn't have the same level of excitement as having a visitor. Talking about it later we wondered how we could teach all 90 pupils at the same time. The solution was obvious – take the classes to the experts. It didn't take much effort to persuade my husband Bob Rastall to get involved (he has had a

long-standing interest in public engagement, we have often worked on this type of activity and our second daughter would be in a future group of children to benefit!).

PREPARATION IS THE KEY

In 2007 (the curriculum is taught on a 2-year rolling basis), we delivered the first large-scale workshop to three groups of 30 pupils in adjoining labs. On the day, it required enthusiastic postgrad and postdoc volunteers to adequately staff the labs, and three workshop leaders. Beforehand, it required adaptation of tried and tested SGM activities and a few meetings with school curriculum leader Terri Gregory. We completed hazard assessment forms for the activities. The school form identified crossing the road en route to the campus as the highest risk factor! All pupils loved the day (as evidenced by the crowds of admirers when Bob was next in the playground) but we did identify a few areas for improvement. The consensus was to run the workshops again in 2009 but with some modifications.

THE IMPROVED VERSION

It is amazing how quickly 2 years can pass; last summer we started talking to the school again about the next visit and we began making preparations for a visit at the end of September (to give the school a chance to deliver some of the curriculum, but before the labs would be needed for undergraduate teaching). This time, the workshop content was better balanced and we focused on activities that couldn't be delivered in the classroom. I had a prior commitment, so postdoc Sofia Kolida stepped in, made meticulous preparations and then Bob and postdocs Annett Klinder and Adele Costavile led the groups.

A few days before the visit, the children came in from the playground and were provided with a nutrient agar plate and a worksheet. They labelled the plate, according to instructions, then placed two fingers on one half of the agar. After washing their hands, they placed the same two fingers on the other half. The plates were then sealed with sticky tape and collected that afternoon. for incubation. Sofia patiently wrapped each one with film to prevent prying fingers gaining access and the plates were set aside for each child to examine.

SCIENTISTS FOR A DAY

On the big day, the children walked to the university and picnicked on campus before joining Bob in a lecture theatre for a safety briefing and distribution of lab coats and safety glasses. Sofia had sourced a supply of disposable lab coats which, given the nature of the activities, the children were able to take home as souvenirs. After going to the labs the classes launched straight into the first activity: '*Investigating the effect of temperature on the growth of yeast*'. This is simple to deliver and builds on the SGM '*Yeast Power*' activity by using water baths which are not available in a typical classroom. The children incubated yeast, sugar and water in test tubes for 30 minutes at 70°C, 35°C and in iced water. Balloons on the test-tubes traps CO_2, and the children would be able to quantify growth by measuring the circumference of the balloons (with a piece of string and a ruler). Obviously, great care was taken to keep the children away from the hot water to reduce scalding hazards.

Measuring the circumference of a balloon inflated by yeast power! *Aldryngton Primary School*

Bob Rastall lectures to 90 primary school children, squashed into a teaching lab. *Aldryngton Primary School*

Example of one of the culture plates inoculated by the children. *Aldryngton Primary School*

Whilst the yeast incubated and volunteers set up the next activity, Bob delivered a brief PowerPoint presentation on microbes. He kept it simple and brief to keep the children focused and used lots of images. He also recruited a critical proof-reader (one of our daughters) to make sure that the talk was pitched correctly and the language was suitable. At the end of the presentation he was questioned closely by the enthusiastic audience. Then it was back to the labs for the next activities: examination of mushroom gills, blue cheese fungi, stained yoghurt bacteria and yeast cells using microscopes, and inspection of the agar plates from the previous week. The children were given a worksheet to make observational drawings of the colonies they saw and describe the shapes and colours. Light and electron micrographs were available for comparison along with a simple key which outlined the appearance of microbes that might typically have appeared on their hands. The children could clearly see the benefit of thorough hand-washing and a few guilty grubby hands were exposed! After inspection, all plates were rounded up for safe disposal. In order to minimize the potential risks of this activity, the children were briefed on the necessity of not opening them and they were well supervised by teachers, university volunteers and parent helpers.

The afternoon ended with measuring the balloons of the incubated (and cooled) test tubes, and the children were asked to suggest how the temperature might have affected yeast growth. A final round of supervised hand-washing preceded the departure of 90 very excited mini-scientists.

Two days later, a big batch of thank you letters arrived. It was clear that many of the children learnt lots whilst having fun that day and being in proper lab had made a big impact.

Word has got out and Bob is currently in discussion with another local primary school about the possibility of delivering practical microbiology to their pupils.

These workshops have been great fun to deliver and although cheap in terms of consumables costs they do need a group of enthusiastic and well-briefed helpers to make the experience worthwhile for the children.

We could not have managed without the support of willing university staff and PhD students: Sandra Tejero, Heidi Urwin, Antonis Ampatzoglou, Ubaldina Szulc and Eddie Deaville, not to mention the parent-helpers who accompanied the school party.

JANE WESTWELL, is External Relations & Grants Administrator at SGM Headquarters

View from the other side

TERRI GREGORY, Deputy Head of Aldryngton Primary, shares her impressions.

Making science exciting at primary school is sometimes a challenge. Children have a fantastic natural interest in the world about us and giving them hands-on experience without fully equipped labs and resources is very difficult. At Aldryngton we are very fortunate to have parents willing to share their expertise, who very bravely offered to host '90' 9–11-year-olds at the university labs. The school staff visited the labs and met with Bob and Jane to work out logistics and a detailed plan of the day.

The children loved the experience of meeting in a lecture theatre, and wearing the lab coats and glasses was a firm favourite. We were then able to study and analyse bacterial samples that we'd taken in school earlier in the week using some very powerful microscopes.

Carrying out the yeast experiment with the temperature baths was another activity which could not have been done easily at school, and could certainly not in groups of three with everyone really involved in a range of scientific skills.

Bob's lecture and presentation were very informative and useful in that we have a large cohort of very able children who asked the type of questions that sometimes had Bob having to find out later! They also loved the statistics about amounts of poo and elephants!

The children's feedback was massively positive and science – particularly the trip – was identified as a favourite part of our *Discoveries – Big and Small* topic. Facts about microbes also featured very highly in the '*What have you learnt this term?*' question. The trip had many benefits: a unique experience of a lab at a very young age; a look into what the world of science can offer; a hands-on experience; access to expertise and finally a great day out for children, staff and parents involved.

Go on … give it a try!

If you would like to share your enthusiasm about microbiology, you could not ask for a more receptive audience than primary school children. All you need is lab space and plenty of helpers (who would surely love to expand their skills on their CV?). I have copies of the work sheets that were developed for this practical and you can obtain them by emailing **j.westwell@sgm.ac.uk**

Images – Aldryngton Primary School

Children learning about dental plaque during an 'outreach' activity. *Derren Ready*

Microbiology in the classroom

On the other hand, Derren Ready has been going out to schools …

Over the last few years I have been involved in a variety of school 'outreach' activities and overall I can say that I've found it a very enjoyable and rewarding experience. The SGM staff has been incredibly supportive and they have supplied me with stickers, pens, pencils, notepads, rulers, bars of soap and little fluffy microbes. Without doubt, regardless of the age of the children, from 5 to 18, there's nothing as good as a freebie at the end of a lesson!

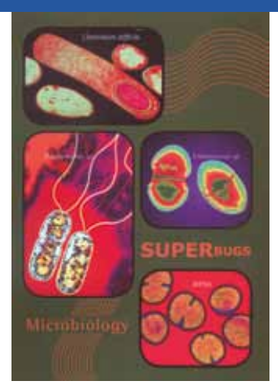
So what have I been doing? I've tried out a range of activities from just giving an interactive talk to various practical sessions. We have had fun using yeast to blow up balloons and making dental plaque with children (out of children!). With some of the older children we have carried out serial dilutions, and used a magic full stop to show how little our microbial companions are. Children hate washing their hands, so I have looked at the spread of infection and the importance of hand washing using a UV lamp, fluorescent gel and a very long line of children – they were shocked to discover how easily we can spread microbes!

I have also linked up with a local school and together we organized an after-school science workshop with another scientific parent volunteer. We had a great turn out with over 100 pupils attending, and they could make rockets, solve a mystery using chromatography, see how penguins stay warm in cold conditions using a blubber glove and icy water, carry out pH testing on different drinks, make a spinning 'Tardis' and of course learn some microbiology too.

Many of these are activities which are already available to you on the SGM website. The website has links and documents which can help you to get started and to give you some ideas for you to carry out your outreach session. Generally I've found that a session of about 45 minutes, with a little bit of chatting and then a few practicals always works well with younger children; also, the younger children generally like time for questions and it helps to give them a worksheet. The older children tend to like more detail in their talks, but still really enjoy a practical session and surprisingly still like to wear the fluffy sticky microbes even when they are 18!

DR DERREN READY is a Clinical Scientist and Honorary Lecturer in Microbial Diseases at the Eastman Dental Hospital in London (email d.ready@eastman.ucl.ac.uk)

In brief



SUPERBUGS

The latest SGM briefing for schools and the public lays it on the line in simple terms about superbugs such as MRSA, *C. difficile*, vancomycin-resistant enterococci and *Pseudomonas aeruginosa*. The 4-page, brightly coloured leaflet also explains what antibiotic resistance is and how it is caused, together with the means by which superbugs can be stopped in their tracks. Less well-known problems, such as multi-drug resistant *Acinetobacter baumannii* (MDR-AB) and extended-spectrum beta-lactamases (ESBLs) are also covered.

FOLLOWING IN DARWIN'S FOOTSTEPS: SCHOOLS COMPETITION

A group of UK students could be about to follow in the footsteps of Charles Darwin on a voyage to the Galapagos Islands. The trip is first prize in a competition being organized by the Wellcome Trust to celebrate the end of Darwin 200, the bicentenary of Darwin's birth. Students are required to find the most imaginative way to explain the science behind its *Survival Rivals* experiments. These three kits have been distributed free of charge to state secondary schools across the UK and are targeted at different ages: *I'm a Worm, Get Me Out of Here*, *Brine Date* and *The X-Bacteria*. The kits explore themes of natural and sexual selection, and antibiotic resistance in bacteria. Students are being asked to record the results of their experiments creatively via film or photography. For further information on the competition, visit **www.survivalrivals.org**

Stockxpert / Jupiter Images

Conferences: talking the talk – *with style*

LOVE IT OR LOATHE IT, presenting work is a vital part of your development as a researcher. There is little point in pushing back the frontiers of knowledge if you don't communicate your findings. Not surprisingly, many people are daunted by the thought of delivering a paper to a crowd of (sometimes critical) strangers. At SGM we believe that our conferences should provide plenty of opportunity for early-career members to hone their presentation skills in a supportive environment. Many of the sessions include slots for offered papers which are often given by postgrads and postdocs.

Speak up at Edinburgh

Not only do we provide the opportunity to give talks, we are also keen to help you develop your communication skills. On **Monday 29 March**, at the forthcoming SGM Conference in Edinburgh, **Paul Hoskisson** (Lecturer at Strathclyde University and SGM Council Member) will be delivering a lively interactive workshop on presentation skills for early-career microbiologists. Paul will share his knowledge and demonstrate how to give a memorable talk and avoid pitfalls.

Meet and be greeted

If you are coming to the meeting, even if you are not speaking, the prospect can be quite scary. To give you confidence and help you to make the most of the conference, why not come along to the Welcome Workshop for early-career microbiologists on Sunday 28 March? A mere £10 registration fee will gain you entry to two hours of fun activities to improve your communication skills and add value to your experience as a delegate. Jo Heaton (University of Lancashire and SGM Education Division Member) will lead the workshop which will also include your supper and a drink.

In my view ...

Rich Boden, 2008 winner of the *SGM Young Microbiologist of the Year competition*, shares his experience with Gradline readers.

I was talking recently with a friend who, nearing the end of his PhD, was about to register for a large conference in the USA. He mentioned how much he hated lugging poster tubes around airports. I asked '*Why don't you apply to give a talk?*' and heard the unfortunately too frequent answer, '*Because I'm only a PhD student*'. But, if you are a PhD student (or postdoc) you really should apply to give conference talks. Even if you aren't selected, you'll most likely be offered a poster – so you have nothing to lose by applying. Giving talks at conferences is really useful for many reasons – first and foremost to promote your research (and yourself!) to other researchers, but also in terms of gaining the all-important skill of public speaking and disseminating information to an (often varied) audience.

The first conference I spoke at was a Gordon Research Conference in the USA towards the end of my PhD. I'd submitted an abstract for a poster and this was 'upgraded' to a talk a few weeks before the conference. I duly wrote my slides and practised my talk a few times to get the timing right then flew out to the conference. Just before lunch on the first day, I discovered that the conference schedule had been changed and my talk was timetabled for that evening, not the third day as I had expected. This gave me just a few hours to practise some more and perfect it. Well, nothing quite like a baptism by fire! I remember feeling absolutely terrified, though once I'd got past the first few minutes, it was quite good fun. From the feedback I was given, the talk went well and, more importantly, people seemed interested in my work, which was very nice.

An advantage of giving a talk versus presenting a poster is that you have a captive audience! The downside of a busy poster session is that people can't always view everything that interests them. I certainly find that it's very rare that I manage to look at more than a dozen or so that I have identified from the abstracts. The other massive advantage is in terms of networking – people recognize you after the talk and they connect your face to your work. Networking at conferences is one of my weaknesses, as (like many others) I find it very hard to approach a total stranger and start a conversation, but if you have seen someone give a talk, it's suddenly so much easier to open a dialogue.

During the final months of my PhD, I gave four conference presentations and won prizes for two of them. As a result, I was invited to deliver a session to PhD students and postdocs at Warwick entitled *How to give talks at conferences*. When I started writing it, I realized that my presentation technique is to adapt styles from good talks that I have seen and avoid things that I think look bad or have irritated me as an audience member.

Rich's top tips for a successful conference presentation

- **Pitch it correctly** – your audience might all be biologists or even microbiologists but they probably won't be experts in your area of research so make sure you talk at a level that everyone can understand.
- **Make it easy on the audience** – keep your slides simple and tell the story in a logical order. This will help keep the attention of audience members who have jetlag / conference fatigue / a hangover / information overload or just aren't too interested in your particular subject area!
- **Avoid PowerPoint's default 'themes'** – nothing says '*I spent 5 minutes throwing this together*' quite like the dark blue background with yellow and white text! Avoid busy background graphics too. Black text in an easy-to-read font (e.g. Arial or Times New Roman, not Comic Sans!) on a plain-coloured background works well.
- **Use colour wisely** – if you decide to use different colours for headings and bullets etc, there is some great software at **www.colorschemer.com** that does all the work for you. White text on a black background is tiring to read, so I avoid it. Also, bear in mind that cyan, yellow and light green don't show up properly on most projectors.
- **Avoid animations** – they slow down the flow of your talk and can look naff.
- **Check your videos carefully** – if you have a video in your talk, check that it plays correctly on the conference system – nothing is more embarrassing than a video that won't play.
- **Microphones** – if the conference uses a clip-on microphone, make sure you're wearing something it can easily be clipped onto so that it doesn't fall to the floor mid-talk!
- **Avoid 3D graphs** – they're hard to interpret from a distance.
- **Get the timing right** – nothing worse than being told you're out of time!
- **Avoid cue-cards** – continually having to look down at a stack of cards or a script interrupts the flow of your talk. Use your slides as your cue-cards but don't just read out what is written on the slides - the audience can read that themselves.
- Most importantly of all: **have confidence in your work** – ultimately, you are the world expert in your own research.

- **Age** 31
- **Present occupation** Postdoctoral Research Fellow at the University of Warwick
- **Education**

  PhD University of Warwick: *Metabolism of dimethylsulfide in the Bacteria*

  I studied the biochemistry and physiology of bacteria – mainly isolated from marine systems – that are capable of metabolising the volatile organosulfur compound dimethylsulfide (DMS). DMS is a horrible chemical to work with – smells like boiled cabbage – but it is also thought to be central in climate control and is one of the many chemicals responsible for the smell of the sea. People have thought for years that bacteria degrade more than 90% of DMS produced in the oceans but no one has really known much about it. So the main questions that I asked (and at least partially answered!) were who's doing it, how are they doing it and why do they do it?

  BSc King's College London: Biochemistry
  (and before that, about half an MSci Chemistry)

Q What influenced your decision to do a PhD?

A My undergraduate career was a bit unusual. I started reading an MSci Chemistry at King's College London, but towards the end of the first year, it was announced that the department would be closing. I started thinking about doing something else but I never really got round to it until the second year of the degree when I moved to the biochemistry department because I had been enjoying the environmental and medical-related modules.

I decided to start a BSc Biochemistry from scratch as it would be less stressful than trying to jump into the second year of something I had no grounding in. Part of the biochemistry course was chemistry and the course co-ordinator noticed I'd already sat most of the chemistry modules so I had to do something else instead. Due to timetabling, the only options available were 2nd and 3rd year modules and I ended up doing a final year project (in my first year) in neuroimmunology (which eventually lead to my first publication a couple of years later). I was well and truly bitten by the research bug by now and did another project with a different supervisor in the second year. I stayed with the same supervisor in the final year: working on isolating methylated amine-metabolizing bacteria from the River Thames. We eventually published this work.

Towards the end of my degree, I knew I wanted to carry on doing research and a PhD was the only way forward. I was already working with methylotrophic bacteria and I saw a PhD project at Warwick working on dimethylsulfide – mainly with methylotrophs – so again, that seemed like the obvious choice.

Q What was the most rewarding aspect of PhD research?

A Lots! One thing I love about research in general is that you are always learning – whether it's new techniques and methodology or getting results. A great feature of my current lab (where I also did my PhD) is the cross-feeding of ideas. Everyone is from vastly different backgrounds so there much to learn from others.

Rich Boden

Microbial mat composed mainly of methanotrophic and chemolithoautotrophic bacteria and fungi, floating on the surface of the lake in Movile Cave, Romania. *Dr Alexandra Hillebrand, 'Emil Racovita' Institute of Speleology, Romania*

Q What did you find most challenging?

A Reigning in my work! I've always been at my best when I have multiple foci so I tend to follow many different lines of investigation at once.

Q How did you get involved in the SGM *Young Microbiologist of the Year Competition?*

I had a couple of posters at the SGM Meeting in Edinburgh in Spring 2008 and there were 'do you want to be considered' forms for the prize on the poster boards, which, of course, I ticked (there was £500 at stake!). One of my posters was selected as 'best poster' from the environmental section and I went on to give a talk in the September 2008 meeting in Dublin on my work on *Methylophaga thiooxidans* – a marine methylotroph that can oxidize dimethylsulfide to tetrathionate.

Q How did you find the experience?

A Fitting a big chunk of research into a 10 minute talk geared at an audience of non-specialists was certainly an experience! I had various personal commitments the week of the conference in Dublin so I flew in to give my talk and then flew back out again a couple of hours later. I confess I only saw a few of the other competitor's talks (the ones before mine) as I had to leave early. The next day a friend, who was at the conference, emailed to tell me I'd won. I didn't believe it until I received the official letter a few days later – I was convinced he was having me on!

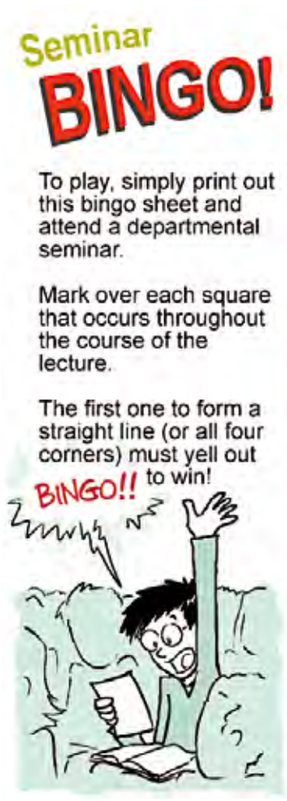
Q Why did you opt for postdoctoral research?

A Similar reasons to those for wanting to do a PhD – I want to do research for a living. My main research interests relate to sulfur-oxidizing bacteria and I was very fortunate to be appointed as an NERC-funded postdoc working on the microbiology of Movile Cave, which is a very unusual ecosystem located in Romania that seems to be entirely driven by methane and sulfur oxidation.

Q How do you see your future?

A I hope to stay in academia, working in the field I enjoy…well, everyone has to have a dream!

RICH BODEN can be contacted at
rich.boden@warwick.ac.uk



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A STITCH IN TIME SAVES LIVES – RAISING AWARNESS OF HIV AND AIDS

World AIDS Day is 1 December. Each year has a theme, with the aim of raising public awareness of the current status of the disease. This year, one of the themes was 'Respect and Protect'. People living with HIV still face discrimination, but treatment is improving and life expectancy is increasing (www.WorldAIDSDay.org). In the UK, there are over 80,000 people living with HIV, and numbers continue to rise each year. Over one-quarter of these do not know that they are infected. Raising public awareness of the disease is vital. JO VERRAN *and* LYNN SETTERINGTON *got together to mark the event in some innovative ways.*

Lyn Setterington (*left of centre*) and Jo Verran (*right of centre*) with two MMU students embroidering the banner in the foyer at the university. *Jo Verran*

THE MICROBIOLOGIST'S VIEW

Oscar Burriel / Science Photo Library

I have recently, set up a '*Bad Bugs Book Club*', where a group of scientists and non-scientists meet to discuss books in which infectious disease forms a major part of the plot (**www.sci-eng.mmu.ac.uk/intheloop**). On the list was *Dorian* by Will Self, which has the additional title of *An Imitation*, since it uses Oscar Wilde's *Picture of Dorian Gray* to underpin a tale of decadence and HIV transmission in the early 1980s, and we decided to hold the club meeting on World AIDS Day. I try to couple the Book Club meetings with an additional cultural event, and remembered a colleague of mine, Lynn Setterington, whom I had met through some community engagement work she had done using quilting and embroidery. Lynn and I talked about making an AIDS quilt, and possible collaboration, resulting in us applying to SGM's Public Engagement with Microbiology Fund, for the production of a quilted banner, designed by Lynn, but produced during various community events – with the final event being the Book Club meeting.

Lynn used the words '*Respect and Protect*' as the theme for the banner, with the background being embroidered in red, on white material, using cross-stitches and AIDS ribbons. The design placed a white cross (representing the 'and') in the centre of the banner, providing a focus for the piece. Lynn took the banner to events at various locations, including Whitworth Art Gallery, a local school, a local community group and the University. Many people contributed – even I had a go, despite being worried about my needlework skills. It was actually a wonderfully soothing and engaging activity to be sewing and talking to people across the banner. The final piece is really beautiful. The cross stitches, looking like lots of kisses, all done by different hands interweave between the ribbons, which give the appearance of cascades of drops of water, or of blood.

During the embroidery session at MMU in the entrance foyer (on the coldest day of 2009!), the new SGM HIV/AIDS information booklet was launched, and posters designed by Sahrish Mir, one of my undergraduate project students, made an informative backdrop to the activity.

Numb-fingered, we then moved to a warmer room and watched a screening of the 2007 TV documentary *HIV and Me*, presented by celebrity and actor Stephen Fry. One of the HIV consultants who appears on the documentary, Ed Wilkins, answered questions on the programme, and gave some really positive updates on the current status of treatment regimes and life expectancy in UK HIV cases. However, in order for treatment to be given, diagnosis is essential, and individuals with 'multiple and concurrent' partners are particularly at risk.

The Book Club meeting finished off the day. *Dorian* is a difficult book to read: it addresses some very sensitive issues in a fairly confrontational way. The story is very much about the time in which it is set, but we were able to bring information from the previous screening to the discussion, enabling us to consider HIV education in a broader context.

It was great doing this interdisciplinary activity. I learnt a lot from the community-orientated work that Lynn has done, and we are both really proud that we managed to organize, design and complete such a new project so successfully. Lynn and I would like to thank SGM for providing the funding for the banner and refreshments for the Book Club meeting. The banner gave real focus to our World AIDS Day events, and it will eventually be displayed to the general public.

JO VERRAN **is SGM Education Officer and Professor of Microbiology at Manchester Metropolitan University (email j.verran@sgm.ac.uk)**

THE NEEDLEWOMAN'S VIEW

Having got to know Jo Verran via the MMU community group meetings and hearing about some of her endeavours, I realized we shared some interests and ambitions, even though our academic backgrounds were very different. So when Jo suggested working together on a project for World AIDS Day, I envisaged an interesting and new challenge. This was in late October and with such a quick turn around for completion on 1 December, I knew we had to act quickly; so following research that first evening I emailed Jo with a design that would fit the brief and incorporate a 2009 campaign slogan '*Respect and Protect*'.

In terms of public engagement, which was key to raising awareness about AIDS, and knowing the time and effort involved in setting up workshops and venues, I settled on a total of six sewing sessions. These finally evolved into two in university, two with local community groups, one in a public art gallery/museum and one at a local high school with a large percentage of pupils whose first language was not English (largely with African and South-east Asian backgrounds). I had worked with some of the groups before, so a level of trust and understanding was already in place, whilst the rest were new initiatives. All the workshops were well-attended with a total of 100–150 people taking part, spanning all ages and a broad mix of social and ethnic backgrounds. Some of the conversations as ever in such events were telling: the school children wanted to know if I had worked with any celebrities, the Whitworth Art Gallery drop in included a midwife who worked with women from Africa and a session in the MMU library

discussed the soothing aspects of hand stitching and taking a less hurried approach.

The final 'stitch up' on World AIDS Day itself was an interesting mix, combining my own art students and colleagues, along with Jo's science students and fellow academics, and despite the cold the quilt was finished on time. It is a delight now the quilt is complete to see the vast range of hand writing, in the form of the stitched crosses, big and small in all shades of red thread and ribbon. The final stage is finding a suitable home for the piece so that the general public and all those involved can come and view the wonderful collaboration.

LYNN SETTERINGTON **is a Public Engagement Fellow and Senior Lecturer in Embroidery at Manchester Metropolitan University (**email **l.setterington@mmu.ac.uk)**

Lynn and Jo and the quilt. *Jo Verran*

For information on how you can obtain funding for your microbiology public engagement activity, see **www.sgm.ac.uk/grants**

FLEMING ANNIVERSARY CELEBRATIONS

Last year was the 80th anniversary of the publication by Alexander Fleming of his discovery of penicillin, the first antibiotic. JANET HURST *describes an event held to commemorate the event.*

The official photographer, Mike Scott, snaps Hugh Pennington musing on Fleming's achievements. *Ron Fraser*

Fleming was born at Lochfield Farm, near the little Ayrshire town of Darvel and on 13 November 2009 local MP Des Browne and the SGM worked with the Darvel Improvement Group, Darvel Community Council and East Ayrshire Council to present a range of activities to celebrate the penicillin anniversary.

The day dawned bright and sunny, a good omen for the success of the whole event. An audience of science students from surrounding high schools and members of the local community, alongside local government officials and dignitaries, packed the newly refurbished Town Hall at Darvel. After an introduction by Des Browne, well-known microbiologist and former SGM President Professor Hugh Pennington delivered an entertaining lecture on Alexander Fleming and antibiotics and used the occasion to urge the young people present to consider taking up a career in the exciting science of microbiology. A lively question and answer session followed and then Hugh presented trophy cups, one a piece, to the Kilmarnock and Loudoun Academies, which both have strong connections with Alexander Fleming. SGM sponsored these with the stipulation that they should be awarded annually in each school to the student judged to have excelled in biosciences. The cups were accepted on behalf of Kilmarnock Academy by pupils Joanne Craig and Stephanie McMahon, and on behalf of Loudoun Academy by pupils Elaine Cochrane and Alistair Smith.

The audience was then able to inspect the displays put on at the back of the hall that marked different aspects of the penicillin story and Fleming's life. Kevin Brown, curator of the Fleming Museum at St Mary's Hospital, Paddington, where the famous mould was first discovered contaminating a culture plate of staphylococci, brought along some precious artefacts as well as an informative display panel. Phil and Heather Scott, who now own Lochfield Farm, which they have restored, and who are very proud of their home's association with the famous microbiologist, also fielded an exhibit. Modern antibiotic development was shown by a team of microbiologists from the University of Strathclyde in

The packed Town Hall at Darvel. *Ron Fraser*

Des Browne MP talks to the students in Darvel Town Hall. *Ron Fraser*

Students looking at the SGM resources. *Ron Fraser*

Students at Kilmarnock and Loudon Academies with their new SGM trophies along with (*from left to right*) Janet Hurst (SGM), Hugh Pennington, John Campbell (Deputy Provost of East Ayrshire), Des Browne MP and Ron Fraser (SGM). *Mike Scott*

Local dignitories and organizers of the event at the rededicated bust in the Fleming Memorial Garden, Hastings Square, Darvel. *Mike Scott*

The new Clydesdale Bank £5 note. *From left to right:* Elaine Shaw (Clydesdale Bank), Des Browne MP, Hugh Pennington and George Armstrong (Clydesdale Bank). *Ron Fraser*

Hugh Pennington, Janet Hurst and Ron Fraser in front of the SGM banner. *Mike Scott*

Glasgow. The students crowded round their exhibits and plied Iain Hunter, Paul Hoskisson and Geoff Coxon with questions. The SGM had a big pile of leaflets and freebies in the form of notebooks, pens and fluffy 'bugs' up for grabs that soon disappeared. Darvel Improvement Group has amassed a large collection of documents, photographs and news clippings about Alexander Fleming and his association with the area which they were pleased to show to people. Also in the Hall were representatives of the Clydesdale Bank, who on the following Monday were to launch a new £5 note featuring a portrait of Fleming to honour his remarkable medical achievements. Unfortunately, none were available on the day for free distribution!

Then it was time to leave the Town Hall and cross the road to Hastings Square, where the Fleming Memorial Garden, set up in 1960 is sited. It has grown a little shabby over the years and in particular the stone bust of the great man has suffered from erosion by the weather. East Ayrshire Council, with support from the SGM and the Darvel Improvement Group are refurbishing the area and on the day, Hugh Pennington re-dedicated the memorial bust which had received a facelift.

SGM was delighted to be associated with this event and Chief Executive Ron Fraser and his Deputy Janet Hurst much enjoyed their part in making the arrangements and being present on the day. We were very proud not only to honour a great man and his achievements, but also to be able to enthuse and inform a whole new audience about microbiology.

In the words of Des Browne MP, '*The success of the Fleming Memorial Lecture and all of the celebrations that took place to mark this son of Darvel's global, life-changing discovery can only be attributed to the innate sense of hard work and inspiration that still beats strongly in the heart of his community today. This was an event very worthy of such a great Scotsman as Sir Alexander.*'

JANET HURST **is Deputy Chief Executive of the SGM and heads the External Relations Department (email j.hurst@sgm.ac.uk)**

Dirty fingernails under UV light. *E. Stevenson*

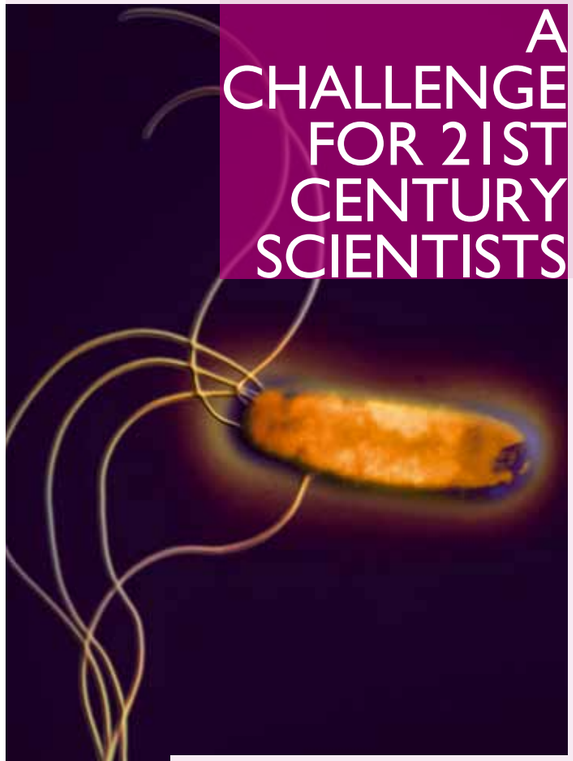
SUPERBUGS:

A CHALLENGE FOR 21ST CENTURY SCIENTISTS

Superbugs in general and Burkholderia cepacia in particular are the focus of a Wellcome Trust funded public engagement project in Scotland. ELIZABETH STEVENSON tells us about the initiative.

The issue of 'superbugs' is rarely far from the headlines with much of the focus tending to be on hospital-acquired infections such as MRSA and *C. difficile*. Lurking in the rogues' gallery of bacteria with superbug status is *Burkholderia cepacia*, a microbe which can have a devastating effect on the lives of individuals with cystic fibrosis. The bacterium was first discovered by plant pathologists, not medics, as a cause of sour skin onion rot. It can be used to prevent both 'damping off' disease in seedlings and moulding of fruit and also to degrade groundwater contaminants. However, it also causes disease in humans and is the superbug which eats penicillin for breakfast!

In the project, we explore some of the issues surrounding superbugs, antibiotic resistance and hygiene through a combination of hands-on workshops and discussion activities.



TEM of negatively stained *Burkholderia cepacia*. *Kwangshim Kim / Science Photo Library*

For example, one of the workshops involves the use of a non-toxic hand gel which glows under UV light. Workshop participants apply the hand gel and then wash their hands as they would do normally. Under UV light, any remaining gel fluoresces and indicates those areas on the hands which have not been properly washed. These areas are recorded by participants on a worksheet printed with hand 'shapes'. It is interesting to note that the same areas, i.e. nailbeds and insides of thumbs keep occurring. Participants then try washing their hands again to remove the remaining gel. Then they design a handwashing protocol which they believe would address the problems they encountered in the workshop.

The school pupils of today will become the doctors, nurses and other healthcare professional and research scientists of tomorrow and the 'superbugs' project enables them to explore simple aspects of hand hygiene, antibiotic resistance and the ethical issues associated with the treatment of individuals who are affected by these nasty microbes.

The project team consists of Dr Elizabeth Stevenson (PI), Dr Janet Paterson and Dr Iona Beange (science communicator employed on the project), all of whom have considerable public engagement experience.

In addition, key members of the project team are Professor Emeritus John Govan (College of Medicine and Veterinary Medicine) and Dr Dominic Campopiano (School of Chemistry), both from the University of Edinburgh. John Govan and Dominic Campopiano were team members of the UK Cystic Fibrosis Microbiology Consortium, which brought together scientists and clinicians with complementary expertise, and was funded by grants from the Big Lottery Fund and the Cystic Fibrosis Trust.

The project highlights the collaborative research spanning many disciplines within science and medicine and the variety of approaches necessary to combat the resistance and spread of these antibiotic resistant organisms. We provide opportunities for researchers in the Schools of Chemistry, Biology and Medicine to become involved in delivering the workshops with the researchers and science communicator thus providing valuable opportunities for training and experience in public engagement.

Please contact me for further details of project.

DR ELIZABETH STEVENSON **works on outreach activities for the School of Chemistry at the University of Edinburgh (email e.stevenson@ed.ac.uk)**

Speed typing

The bacterium *Clostridium botulinum* produces small proteins that are extremely toxic to humans and other animals. These botulinum neurotoxins (BoNT) cause the condition botulism. The bacteria are common in soil, and hence are found in natural products and food. However, they only thrive and produce the toxins in totally oxygen-free surroundings, so the disease is actually very rare. Deep wounds and tinned food where the canning process has gone wrong, are classic situations for botulism.

Only a few thousand millionths of a gram (nanograms) are needed to kill a person. The toxins act to paralyse muscles by making them stay relaxed and therefore weak. This effect can gradually progress through the body and without medical treatment can cause death if it prevents breathing. Symptoms appear within hours or at most one week, depending on the exact nature of each case. It is therefore important to treat patients promptly, but also to identify the source of the botulism, for example to prevent illness in other people from contaminated food. Unfortunately, this can take some time and identifying the type of toxin is an important step.

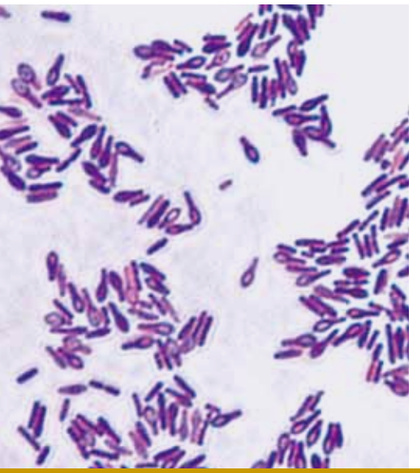
Satterfield, B. A., Stewart, A. F., Lew, C. S., Pickett, D. O., Cohen, M. N., Moore, E. A., Luedtke, P. F., O'Neill, K. L. & Robison, R. A. (2010). A quadruplex real-time PCR assay for rapid detection and differentiation of the toxin genes A, B, E and F. *J Med Microbiol* 59, 55–64.

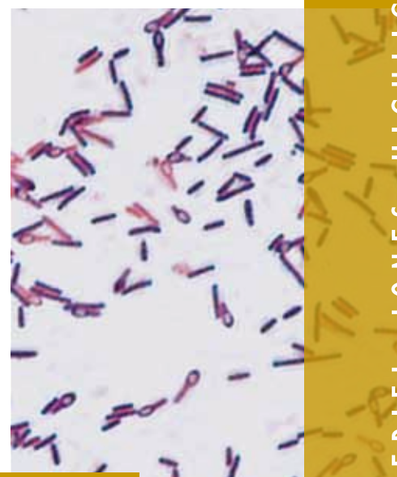
Between them, strains of *C. botulinum* produce at least seven distinct toxins that come in several distinguishable sub-types. Researchers at Brigham Young University, in collaboration with the Utah Department of Health, have now reported a rapid method to identify the four types of toxin that affect humans. As the team point out, a mouse bioassay taking up to 4 days is the current 'gold standard' for confirming the toxin type. There are obvious ethical concerns about this method, in addition to the time needed.

These researchers have developed an assay based on the genes behind the toxins. Others have already tried this, but the group from Utah has produced a method to test for four toxin genes simultaneously in one tube. The similarity between the genes meant that the researchers had to take particular care to ensure that the assay was absolutely specific for each. Remembering the situations in which botulism occurs, they also made sure that the assay still worked when the bacteria were mixed with food, soil or faeces. The final sensitivity of the assay meant that they could detect as few as 10–100 bacteria. They tested the assay on *C. botulinum* isolates supplied by either the American Type Culture Collection or the Utah Department of Health, and which had been toxin-typed using the mouse bioassay. They also used some other gene assays as a further check.

The results were either an exact match, or there was an obvious reason for a discrepancy. The bacteria can lose the ability to produce toxins when they are stored for many years, and in one strain, repeating the mouse bioassay when the gene assay had been unable to detect toxin genes showed that the strain did indeed no longer produce toxin. For another, where the genes identified differed from those recorded for the strain, running the mouse assay again gave a result that matched with the genes. The only major problem that the researchers ran into was that the genes in the bacteria were not released during the assay preparation if faecal material was present.

The researchers believe that they have made a significant advance with this rapid and robust assay to the methods available to detect all human-disease-causing BoNTs that would be encountered in a natural disease outbreak. They hope that clinicians and researchers will try it as a swift and reliable means of determining BoNT type, which will aid control of this disease.





Gram stains of two *Clostridium botulinum* isolates clearly showing the spores this organism makes. *Richard A. Robison / Brigham Young University*

Surgical instruments. *Liquidlibrary / Jupiter Images*

How clean is your scalpel?

Ever since the need for microbe-free surgical instruments to prevent infections became apparent in the 19th century, hospital staff have struggled to keep them free from potential pathogens. Some pathogens, such as mycobacteria, fungal spores, non-enveloped viruses and the prions that cause new variant Creutzfeldt–Jakob disease (vCJD), are surprisingly tolerant to disinfection. Even physical methods, like prolonged exposure to temperatures well above boiling point in an autoclave, may be insufficient to inactivate them securely, as exemplified by highly resistant prions. In addition, high temperatures or the alternative of disposable surgical instruments are not always practical as surgical procedures advance to involve more complex and delicate, electronic equipment. There is a need for new disinfection and cleaning methods, especially methods that do not result in proteins becoming stuck to the surface of instruments.

Researchers at the Robert Koch-Institut in Berlin who work on infection control and hospital hygiene and with spongiform encephalopathies, fungi and highly pathogenic bacteria and viruses had already identified a mixture of the detergent SDS and strong alkali NaOH that was highly effective against prions. This also had the important property of removing prion proteins from surfaces as well as making them inactive. These researchers have now tested whether adding an alcohol makes a solution that is effective against a very broad range of relevant pathogens. Mixtures of chemicals can take advantage of the different properties of each one to make something that is more effective than each alone. Although the three chemicals are potentially toxic, they are frequently encountered in everyday life. For example, SDS is included in some handwash liquid detergents, and NaOH, as caustic soda, is sold for unblocking drains in hardware stores. Alcohols are used in much higher concentrations in hand disinfectants. For the tests, the researchers coated steel wires or other model carriers with bacteria, fungal spores, viruses or prions suspended in blood or brain homogenate, to mimic surgical instruments after use. In addition to tests for viable microbes or infectious prions, after the contaminated carriers had been submerged in the potential disinfectant solutions for 20 minutes at room temperature, the researchers added a stain for protein to see whether this had been successfully cleaned away or whether disinfection was mediated by inactivation without cleaning.

After working through a series of bacterial, fungal and viral pathogens that are particularly difficult to disinfect, they determined that a mixture of 0.2 % SDS, 0.3 % NaOH and 20 % n-propanol inactivated all these infectious agents without fixing proteins to surfaces. This mixture is milder than the solutions of single chemicals currently recommended for prion decontaminations, since the different actions of the three components reinforce and broaden their effects. Modern medicine relies on using clean, sterile materials during operations, and this type of painstaking research is needed to ensure that disinfection methods keep up with the challenge of new surgical instruments and pathogens.

Beekes, M., Lemmer, K., Thomzig, A., Joncic, M., Tintelnot, K. & Mielke, M. (2010). Fast, broad-range disinfection of bacteria, fungi, viruses and prions. *J Gen Virol* 91, 580–589.

Freshwater systems inhabited by *Polynucleobacter cosmopolitanus*. Left, **Tropical Lake Wamala, Uganda;** top right, **temperate Lake Mondsee, Austria;** bottom right, **lake on the Tibetan plateau located at >5,000 m.** *M.W. Hahn & Q.L. Wu.*

All over the world

Opportunities to study non-pathogenic bacterial strains from around the world of what turns out to be a novel species are not so common, but in his work with bacteria from lakes, Martin W. Hahn has built up an extensive network of contacts and collaborators. A recent issue of *IJSEM* contains a report from several of these researchers about the distribution and properties of the novel species *Polynucleobacter cosmopolitanus*. It appears that *P. cosmopolitanus* has a worldwide distribution crossing continents and climate zones. Amongst other places, they identified it in the Hawaiian Archipelago, water from the Loire in France, Lake Victoria in Uganda, a lake in New Zealand and a pond high in the Tibetan Plateau. Fortunately, the bacterium could be isolated from natural waters and maintained in the laboratory, allowing both its physiology and molecular characteristics to be studied. It was clearly a bacterium of freshwaters, although in the laboratory it tolerated mildly saline conditions.

The researchers focused on five strains for detailed studies. The cells were very small curved rods. The first member of this genus, *P. necessarius*, was identified in the 1980s living within small freshwater ciliates. Unlike *P. necessarius*, *P. cosmopolitanus* lives freely in lake water and many of its cells are too small to be eaten by protozoa. Individual strains vary slightly in the nutrients that they can consume, but on this basis are indistinguishable from *P. necessarius*. However, all *P. cosmopolitanus* strains are identical in highly conserved regions of genes used for bacterial identification and these differ from *P. necessarius*. Although the molecular genetic data showed that *P. necessarius* and *P. cosmopolitanus* were 96–97 % similar, this is enough to mean that they must be considered as separate species. The cells of *P. cosmopolitanus* also have several short fatty acids that *P. necessarius* lacks.

For scientists working on macro-organisms like mammals or higher plants, the cosmopolitan distribution of a single species in habitats with different climatic conditions and other environmental parameters is quite uncommon. However, for bacteriologists this observation fits quite well with the 'everything is everywhere' hypothesis, which assumes global distributions of (free-living) species of micro-organisms due to high dispersal rates. It is likely that detailed investigations on the genetic makeup and ecophysiological adaptation of *P. cosmopolitanus* strains isolated from geographically distant and limnologically different lakes could reveal larger differences in adaptive traits between the strains. This could indicate that strains of this species occupy distinct ecological niches and that they represent analogues of closely related species in higher organisms. This could raise the question of how comparable are species described according to rules based on species concepts for micro- and macro-organisms.

Hahn, M. W., Lang, E., Brandt, U., Lünsdorf, H., Wu, Q. L. & Stackebrandt, E. (2010). *Polynucleobacter cosmopolitanus* sp. nov., free-living planktonic bacteria inhabiting freshwater lakes and rivers. *Int J Syst Evol Microbiol* 60, 166–173.

Tularaemia – detecting a understanding and potential threat

Tularaemia is an uncommon disease caused by *Francisella* bacteria, affecting a few hundred people each year worldwide. It can be treated successfully with antibiotics, but the symptoms of ulcers, sore throat, diarrhoea and pneumonia occur in other diseases so diagnosis can be delayed and the disease can be lethal.

The infection can be acquired from more diverse sources than any other illness. These include contaminated food or water, inhalation and via bites by infected ticks. These are found in rural areas and *Francisella* is known to survive in water sources like ponds and lakes for over a year. Fortunately, it cannot be transmitted from person to person, but the fact that as few as 10 bacterial cells can cause tularaemia means that it has potential in biological warfare.

One intriguing aspect of *Francisella* is that it can evidently multiply, or at least survive, in a wide range of habitats that include human macrophages, arthropods, natural waters and soil. Scientists anticipate that bacteria sense and adapt to these very different situations by changing the complement of proteins that govern cellular activity. *Francisella* has a relatively small number of genes and appears to lack several that would be expected to be involved in these regulatory processes. Many bacteria cope with a lack of nutrients by using a process called the stringent response that protects protein synthesis. It is often very important in the life cycle and virulence of intracellular bacterial pathogens. This usually involves proteins called RelA and SpoT, and *Francisella* has genes for both. Researchers at Porton Down have checked what RelA does in *F. novicida*.

They disrupted the *relA* gene from *F. novicida* and discovered that the cells could no longer synthesize the polyphosphate compound that is key to the stringent response. This affected global gene regulation, but the consequences differed from those in many other bacteria, since the *F. novicida* cells multiplied even better than normal in liquid culture and on surfaces. However, the structure of the cells changed, probably because the bacteria could no longer respond appropriately once nutrients began to run out. This impaired responsiveness became much more apparent when the researchers tested how well the mutant bacteria grew within mice and in mouse cells. The bacteria grew less prolifically and were over 100-fold less effective in causing an infection. Indeed, most mice developed high levels of immunity against wild-type *F. novicida* after a mild infection with the mutant.

The implication is that RelA is crucial to the survival of *F. novicida* in the nutrient-poor and hostile environment of animal cells, and thus is important in the virulence of this pathogen. This insight, and particularly the way that the mutant bacteria provided some protection against tularaemia, will help in developing improved detection methods for this species.

Dean, R. E., Ireland, P. M., Jordan, J. E., Titball, R. W. & Oyston, P. C. F. (2009). RelA regulates virulence and intracellular survival of *Francisella novicida*. *Microbiology* 155, 4104–4113.

False-colour TEM of *Francisella tularensis* bacteria. *Eye of Science / Science Photo Library*

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  tel. 0141 548 2819; email **paul.hoskisson@strath.ac.uk**
- **Dr Catherine O'Reilly** Dept of Chemical and Life Sciences, Waterford Institute of Technology, Cork Road, Waterford, Ireland
  tel. +353 51 302858; fax +353 51 378292
  email **coreilly@wit.ie**
- **Dr Karen Robinson** Centre for Biomolecular Sciences, University of Nottingham, University Park, Nottingham NG7 2RD
  tel. 0115 823 1094; email **karen.robinson@nottingham.ac.uk**
- **Dr Gary Rowley** School of Biological Sciences, University of East Anglia, Norwich NR4 7TJ
  tel. 01603 592889; email **g.rowley@uea.ac.uk**

Interdisciplinary Reviews: Systems Biology and Medicine

Editors J.H. Nadeau & S. Subramaniam
Publisher John Wiley & Sons Ltd (2009)
Details Online issue | ISSN 1939-5094
Reviewer Johnjoe McFadden, University of Surrey

This new journal aims to address the need for more dialogue between medicine and systems biology by commissioning reviews, publishing opinion, and by inviting 'pedagogic material' in the field of systems biology and medicine. The first issue includes reviews on a diverse range of topics, including stem cell differentiation, dynamics of MAPK signalling, systems biology of cancer, NF-κB signalling, quorum sensing in bacteria and eukaryotic chemotaxis. The reviews are clearly written by experts in the field and are well-illustrated. The reviews explain many difficult concepts, such as multiscale modelling or the role of positive and negative feedback on system dynamics. What I found particularly interesting and useful was the reviews of areas, such as the lung physiome or modelling of the eye, which are less familiar to a systems biology audience. The journal will be a valuable resource for anyone with an interest in the application of systems biology to medicine.

Photos.com / Jupiter Images

Editor M. Schaechter
Publisher Elsevier (2009)
Details £690.00 | pp. 4,600 | ISBN 978-0-12373-944-5
Reviewer John Heritage, University of Leeds

It was a great privilege to be asked in July to review the *Encyclopedia of Microbiology* online version. For a number of reasons, I have been delayed in preparing this review. This has had the advantage of highlighting technical issues relating to online books. In July, I was given a username and password to access the *Encyclopedia*. I was impressed with the range of topics and with the quality of the authors who had contributed to the project. The major topic areas covered include: Industrial applied microbiology; Agro/food applied microbiology; Archaea; Bacteria; Cell structure and chemical composition; Environmental microbiology and ecology; Evolution and systematics; Fungi; Genetics, genomics; History and culture (and biographies); Mutualism and commensalism; Pathogenesis; Physiology; Protists; Public issues; Techniques; and Viruses. The number of articles range from a single paper on archaea to nearly 50 articles on pathogenesis, which includes articles on the major groups of antibiotics. This raises my first concern: it is not always obvious where one can find articles.

My next concern is of a technical nature. While using the standard setting on my browser, everything worked well, but this will be accessed by people with visual difficulties. It was disappointing, therefore, to find that when I used larger fonts than standard, the page layout did not cope well and there were overlaps of text, making accessibility somewhat problematic. This was only a minor annoyance, since all online articles are duplicated as PDF files. The web-browser issue aside, I found most of the articles that I sampled were authoritative and interesting, although some were much better presented than others – an inevitability in a project of this size.

I was disappointed by the quality of some of the illustrations. These have a fairly standard presentation, a thumbnail linked to a full-sized image that opens on following the link. Some diagrams were of very poor quality. Given that this is an electronic resource and free from many of the constraints of paper publications, this is a major problem. My next, and probably greatest concern, is the variable quality of editing. Because of a desire to buy a fine sweet wine for the festive season, and hoping to learn more on the noble rot, I explored the article on wine and was interested to learn about 'Nobel mold' [sic.]. I was not aware that the inventor of dynamite had an interest in oenology – you learn something new every day! That was the most glaring error that I could identify – there were others. I also had one more major technical issue. I was granted access via a username and password. After a break, I tried to re-access the system using the 'Forgotten your User Name or Password' facility. As expected, the response to that request was almost instantaneous, but sadly my access remained barred to all but the outline material. Given the technical difficulties I have experienced and the price of access, I can only offer lukewarm support for what should be an excellent resource.

Systems Biology: Methods in Molecular Biology 500

Editor I.V. Maly
Publisher Humana Press (2009)
Details £73.50 | pp. 500 | ISBN 978-1-93411-564-0
Reviewer Conrad Nieduszynski, University of Nottingham

Systems biology probably has almost as many definitions as practitioners. This volume considers systems biology in the broadest terms: the integration of experimental and mathematical approaches to biological systems with the aim of gaining both predictive and explanatory power. Therefore, systems biology is an approach that can potentially be applied to any field of modern biology, from an individual biochemical pathway to a whole ecosystem. Thus the challenge for this volume is the breadth of the field. Individual chapters describe particular biological systems, with the majority dealing with mathematical modelling approaches. In addition there are two chapters detailing experimental approaches at the cellular level.

Predominantly, the methods are clearly explained and well-illustrated, although some may be inaccessible to the non-specialist. Several chapters include lengthy sections of code and this volume would have therefore benefited from a companion website. In summary, the diversity of topics covered and the range of styles employed mean that only certain chapters are likely to be of value to individual biologists. Therefore, this volume will generally be of most value as an institutional purchase.

Food Science and Technology

Editor G. Campbell-Platt
Publisher John Wiley & Sons Ltd (2009)
Details £44.99 | pp. 520 | ISBN 978-0-63206-421-2
Reviewer Andrew Allsebrook, University of Abertay of Dundee

This book is a very welcome addition to the category. The Editor has covered a wide range of topics, including those which support the traditional Food Science category, such as Food business management and Product development, in a very consistent manner. The book finds the correct balance between academic knowledge and its application to the wider food industry, for example the consideration of cleaning and sanitizing within Food engineering. In addition to accuracy and detail, the chapters are all very readable. There are a few minor areas which could be ironed out for updates – food fermentation is covered in both Food microbiology and Food biotechnology chapters, while HACCP, key to food safety management, is discussed only briefly within Food microbiology. These comments are far outweighed by the positives of the book, in particular its accessibility, breadth of topics and the supporting online material. This book is highly recommended for any food-related degree course.

Photodisc / Jupiter Images

Study & Communication Skills for the Biosciences

Authors S. Johnson & J. Scott
Publisher Oxford University Press (2009)
Details £19.99 | pp. 256 | ISBN 978-0-19921-983-4
Reviewer Jane Westwell, External Relations Office, SGM

Study and communication skills are often taken for granted by students – they either assume that there is little value in learning how to learn and communicate effectively or that they can do it already. The authors counter this negative view with an excellent introduction and by always putting their subject into context.

The intended readership is undergraduate students, so the book covers a range of topics, including how to make the most of lectures, finding and using information sources (paper and electronic), citations, avoiding plagiarism, basic writing skills, revision technique, essay and report writing. The authors also give attention to delivering effective presentations and preparation of academic posters. Their advice is clear, comprehensive and no-nonsense. The book is structured so that the user can dip into chapters as needed, but it is easily read from cover to cover.

Although aimed at readers new to higher education, I think the book has a great deal to offer postgraduate students too; the information on good listening skills can just as easily be applied to conference talks and good communication skills are essential whatever the level of a presentation.

I liked this book very much – pity it wasn't around when I was a student.

Phagocyte–Pathogen Interactions: Macrophages and the Host Response to Infection

Editors D.G. Russell & S. Gordon
Publisher American Society for Microbiology (2009)
Details US$179.95 | pp. 610 | ISBN 978-1-55581-401-4
Reviewer Cyril J. Smyth, Trinity College Dublin

This book could reasonably be subtitled *Everything you ever wanted to know about macrophages and much more*. The 78 microbiologists/immunologists/geneticists/cell biologists/molecular biologists/molecular pathogenicity experts drawn from laboratories around the world have contributed reviews, averaging about 15–20 pages in length, to a volume that is encyclopaedic in content, up-to-date and educative. Lest the subtitle delude the reader into thinking that this book concentrates solely on macrophages in terms of phagocyte–pathogen interactions, the reality is quite the opposite. The opening three chapters deal with neutrophils, macrophages and dendritic cells. The first review on 'Neutrophils forever' immediately engages the reader with delightful titles to sections such as '*Neutrophilic granulocytes, what is in a name?*' and '*TLR and NLR signalling: who is calling?*'. By the end of the review on dendritic cells, I felt confident to lecture on these professional antigen-presenting cells that had always been somewhat of a mystery to me.

Sections II and III deal with all aspects of phagocytosis. If you want to read a comprehensive review on C-type lectins, integrins, toll-like receptors or on signalling for phagocytosis, membrane trafficking or actin-based motility, the information is all to hand. The chapter on functional analysis of the intraphagosomal environment in relation to *Salmonella* and *Mycobacterium* illustrates how much, and how little, is known about phagosomal function, and reviews the use of fluorescent reporters that allow measurement of pH, enzyme activities and phagosome lysosome fusion, which may lead to a better understanding of this phagocyte–pathogen interface.

The fourth section of this book deals with bridging between the innate immune response and the acquired immune response. The six reviews embodying these aspects of phagocyte–pathogen interactions lead the reader through the complexities and roles of lipoxins and cytokines. My complete ignorance of the fact that not all activated macrophages are identical and that different populations of macrophages with distinct physiologies develop in response to different stimuli was erased in an afternoon's read. I also learned that NEMO is not just the name of a clownfish in an animated film, but a protein that allows the interaction of modulators of NF-κB, resulting in its correct function! If you haven't heard of the 'tether-and-tickle mechanism' for apoptotic cell uptake, chapter 21 should take your fancy!

As one who has studied various aspects of microbial pathogenesis for most of my working life, section V on Pathogens of the professional phagocyte was compulsive reading. The contributions dealing with bacteria, yeasts, protozoa and helminth infection are all written by internationally recognized researchers in these fields. Having chapters dealing with such a variety of micro-organisms brings out parallels and differences effectively.

The final section of the book deals with models of host–pathogen interactions. I found the chapter on *Dictyostelium discoideum* to be particularly stimulating and thought-provoking. By the time I had finished reading this chapter, the authors had more than convinced me of the relevance of this model system. Contributions on *Drosophila melanogaster* and *Danio rerio* as model systems for phagocytosis and the study of phagocyte–pathogen interactions were likewise refreshing and interesting. The final contribution links whole-genome RNAi screening in *Drosophila* macrophage-like cells with new insights into macrophage function.

The Editors of this treatise are to be congratulated on bringing together a wealth of information. This is a comprehensive text of use to final-year undergraduates, postgraduates, postdoctoral scientists and experienced researchers. In spite of the price, it represents excellent value for the money – highly recommended.

Reviews on the web

Reviews of the following books are available on the website at **www.sgm.ac.uk/pubs/micro_today/reviews.cfm**

Antimicrobial Drug Resistance: Vol 1: Mechanisms of Drug Resistance
Editor D.L. Mayers
Publisher Humana Press (2009)
Details £104.50 pp. 678
ISBN 978-1-60327-592-7

Microbial Pathogenomics
Editor H. de Reuse & S. Bereswill
Publisher S. Karger AG (2009)
Details US$290.00 pp. 214
ISBN 978-3-8055-9192-8

Yeast Functional Genomics and Proteomics: Methods and Protocols
Editor I. Stagljar
Publisher Humana Press (2009)
Details £59.99 pp. 300
ISBN 978-1-93411-571-8

Guide to Signal Pathways in Immune Cells
Author E.N. Wardle
Publisher Humana Press (2009)
Details £90.00 pp. 415
ISBN 978-1-60327-537-8

National Institute of Allergy and Infectious Diseases, NIH: Volume 2 Impact on Global Health
Author V. St Georgiev
Publisher Humana Press (2009)
Details £135.00 pp. 810
ISBN 978-1-60327-296-4

Pathogens and Toxins in Foods: Challenges and Interventions
Editor V.K. Juneja & J.N. Sofos
Publisher American Society for Microbiology (2009)
Details US$189.95 pp. 524
ISBN 978-1-55581-459-5

To join our panel of book reviewers, email **y.taylor@sgm.ac.uk**

Roger Stanier and the SGM

ROGER STANIER (1916–1982), was perhaps the most versatile microbiologist of his generation. The organisms that he worked on included *Pseudomonas*, *Streptomyces*, *Cytophaga*, blue-green bacteria and a chytrid. He was very skilful in obtaining pure cultures, and his studies on them included taxonomy, fine structure, and the paths of aromatic breakdown and carotenoid synthesis. He was the senior author of a very influential textbook, *The Microbial World*, published in the UK as *General Microbiology*, which in the course of 30 years had five editions. Born in Canada, he retained Canadian citizenship throughout his life, although the University of California, Berkeley, and the Pasteur Institute were the sites of most of his research. Honours which came in the 1970s included Chevalier de la Legion d'Honneur, FRS and Foreign Associate of the National Academy of Sciences, USA. He became a member of the SGM in 1946, during a short period in the UK.

Stanier's move from the University of California to the Pasteur Institute in Paris was in 1971. It occurred to me that with the increasingly international membership of the SGM an overseas Council Member would be a good idea, and that travel from Paris would be no more difficult and expensive than that for some of our UK Council Members. So in 1974 I put forward Stanier for election to Council, with our International Secretary Tony Rose seconding the proposal. At that time I lived closer to Reading than any other Council Member, so regularly participated with the Executive Secretary, Gerard Sheldon, in vote counting for Council Elections. The vote by SGM members for Stanier was the most decisive that I ever saw.

Stanier proved an active member of Council (1974–1978), but developed a brain tumour which was operated upon. After the operation he remarked that it was not often that a hole in the head did anyone any good but that he was an exception. Returning to Council meetings, he dismissed sympathetic enquiries with the cheerful assertion that there was nothing wrong with him. Alas there was, and he died of cancer a few years after his term on Council ended.

In recognition of his great contributions to science and his service to the SGM, he was elected an Honorary Member in 1978.

The SGM had reprinted Stanier's important 1966 paper on the classification of *Pseudomonas*, and then did the same for his 1979 paper on the classification of blue-green bacteria. The reprinting of the *Pseudomonas* paper was profitable, as every bacteriologist needs to know about *Pseudomonas*, but by comparison the number of microbiologists that need to know about the blue-green bacteria is small. Stanier's last letter to me expressed anxiety that the SGM would make a loss over the reprinting. Stanier was not only a great microbiologist, but also a brave man and a loyal member of SGM.

Roger Stanier's obituary was published in *J Gen Microbiol* (1983) **129**, 255–261, and is available online at **http://mic.sgmjournals.org**

MICHAEL CARLILE was a Council Member from 1972 to 1976 and Meetings Secretary from 1977 to 1980

LETTER

MICROBIOLOGY TODAY, BUT MICROBIOLOGY TOMORROW?

DEAR SIR

Keith Gull's piece in the November 2009 issue of *Microbiology Today* (vol. 36, part 4, p. 240) explained clearly the case to consolidate the viral research of the Institute for Animal Health at the Pirbright site. As anyone with present or past connections to IAH will know, redevelopment of IAH is long overdue.

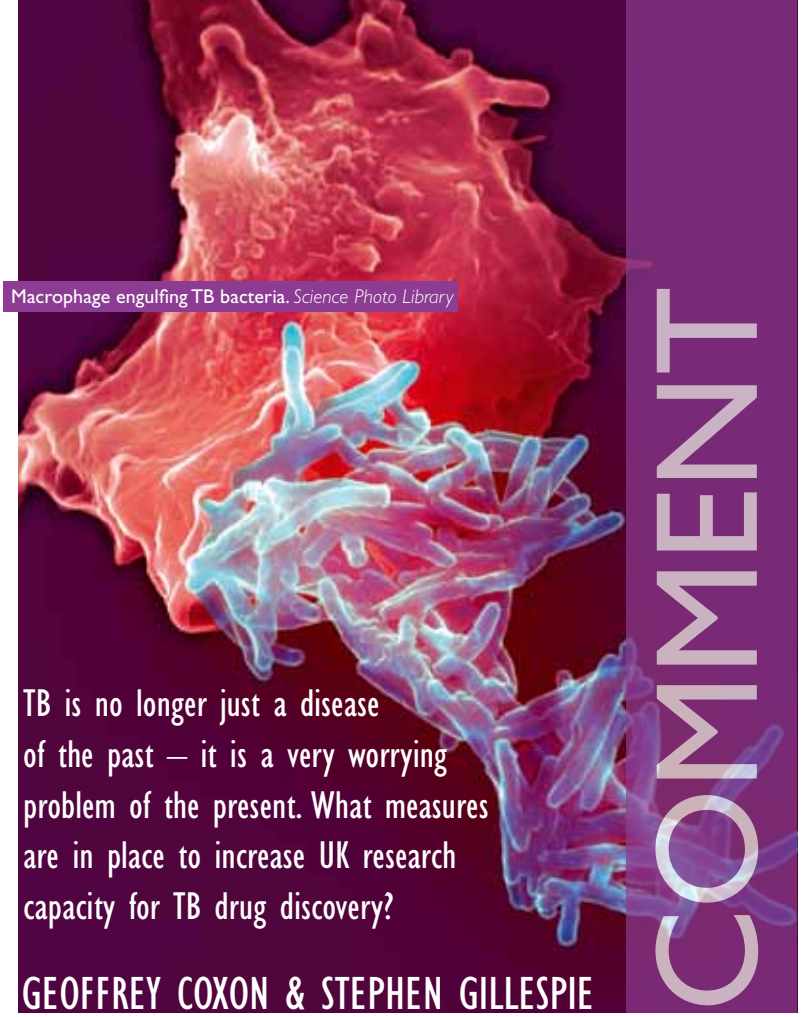
However, the article slides over the fact that work on bacteria will cease at IAH. The justification for this can be found in the press release from IAH Director Martin Shirley that states

> *'Most of the diseases that have emerged in the last 25 years have been viral. There is no reason to believe that emerging diseases in the coming decades will be any different.'*

This statement is extraordinary in two ways. Whilst it is true that emerging diseases have been viral in the recent past, this has not always been the case. The acquisition of a new trait that allows an organism to establish in a new animal or human niche can happen, and has happened, with bacteria as well. Second, it implies that only emerging diseases are worthy of research. This is strange considering the continuing burden of bacterial disease in both animals and humans (e.g. MRSA and *C. difficile* to name but two), and surely embarrassing as the press release was around the time that the last *E. coli* O157:H7 farm outbreak was prominent in the news.

Bacteria remain of tremendous significance in medicine, dentistry and veterinary medicine: basic and applied bacterial research has contributed to huge advances in biology, and to improvements in human and animal well-being. The apparent perception amongst some that bacterial disease, and research into its causes, is no longer so important is worrying and dangerous.

ALISTAIR LAX
Department of Microbiology, King's College London Dental Institute, London SE1 9RT



Macrophage engulfing TB bacteria. *Science Photo Library*

TB is no longer just a disease of the past – it is a very worrying problem of the present. What measures are in place to increase UK research capacity for TB drug discovery?

GEOFFREY COXON & STEPHEN GILLESPIE

A GLOBAL pandemic of tuberculosis (TB) has afflicted mankind for many centuries. TB is a debilitating and chronic disease caused when *Mycobacterium tuberculosis* (Mtb) is spread by coughing, sneezing or even talking. It is mistakenly considered by most to be a disease of the past, yet currently it kills approximately 2 million people every year. It infects one-third of the world's population and at any given time up to 13 million people globally will be suffering from an active TB infection.

The problem is a growing threat because of an inadequate drug regime, lasting for 6 months, based on drugs discovered over 40 years ago. This has caused patient non-compliance, which in addition to an epidemiological co-existence between HIV/AIDS sufferers and the inadequacies of healthcare in the developing world, has resulted in rampant multiple drug resistance.

To control this problem we need new tools, of which the most important are new drugs. There are significant barriers to overcome. Although much information about Mtb has been gained over the last decade, including the complete sequencing of its genome, it is not understood how this relates towards developing new, faster-acting TB drugs. The drug discovery process is also complex and expensive. It takes between 10 and 20 years to deliver a new drug to the clinic from an initial scientific concept, and can cost in excess of £400 million. Owing to rigorous safety evaluation and the scientific complexities associated with Mtb, this means that only a tiny percentage of new compounds identified in the early stages will ever make it to the clinic.

Given the high risks and costs involved, the ultimate question is: who really should be funding TB drug discovery? There is an insufficient commercial market for new TB drugs as 94% of cases are in the developing world where drugs must be delivered at low cost. Understandably, this may prove very unattractive to the pharmaceutical industry.

The strategy being adopted to address this issue is the integration of academic institutions, not-for-profit organizations and governments into a working partnership. Some pharmaceutical companies have also even begun to integrate their efforts in this way over the last decade. In the USA, Johnson & Johnson, GlaxoSmithKline and Bayer have led the way in partnership with the Global Alliance for TB Drug Development (GATB).

So what is the state of TB drug discovery in the UK? Britain was once a leader in finding new antibiotics, notably with the discovery and development of the very first antibiotic, penicillin, and there is no doubt that we should be making a significant contribution. To this end, UK scientists researching new treatments for TB have formed TB Drug Discovery UK (TBD-UK). The initiative aims to align its expertise and form partnerships with like-minded scientists working on drugs for other diseases such as cancer and obesity. Funded by the Medical Research Council, over the next two years TBD-UK aims to identify mechanisms by which new drugs can be developed. It will specifically involve bringing microbiologists, biochemists, geneticists, organic chemists, medicinal chemists, process chemists, X-ray crystallographers, molecular modellers and clinicians to identify routes to combine their diverse skills and increase their capacity for TB drug discovery. Already this approach has led to the identification of a new class of anti-TB agent, the 2-aminothiazolecarboxylates, by combining integrated medicinal chemistry expertise with that of those involved in the development of the fluoroquinolones and their clinical evaluation. More are on the way!

TBD-UK aims to work with government, not-for-profit organizations such as GATB, charities and industry in order to maximize the UK's research potential in the search for new TB drugs. Embracing such a multidisciplinary strategy is the only way to make sure that the UK makes a full contribution to the overall global effort to eradicate TB.

GEOFFREY D. COXON and **STEPHEN H. GILLESPIE** of TBD-UK are a lecturer in Medicinal Chemistry at the University of Strathclyde (email geoff.coxon@strath.ac.uk), and Professor of Medical Microbiology at University College London (email sgillespie@medsch.ucl.ac.uk), respectively (http://tbd-uk.org.uk).

FURTHER READING

Al-Balas, Q, Anthony, N.G., Al-Jaidi, B., Alnimr, A., Abbott, G. & others (2009). Identification of 2-aminothiazole-4-carboxylate derivatives active against *Mycobacterium tuberculosis* H37Rv and the β-Ketoacyl-ACP Synthase mtFabH. *PLoS ONE* 4, e5617. doi:10.1371/journal.pone.0005617