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celebrating life
DNA DOUBLE HELIX 1953-2003

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Above: Computer representation of a molecule of DNA. *Alfred Pasieka / Science Photo Library*

Vol. 30, Part 1, February 2003

DNA50 Special issue

celebrating life
DNA DOUBLE HELIX 1953-2003

In this special issue we commemorate the 50th anniversary of the publication of the structure of DNA by James Watson and Francis Crick in *Nature* in 1953. Micro-organisms have always played an important role in DNA studies and this issue of *Microbiology Today*, which focuses on modern molecular microbiology, celebrates the momentous discovery. It forms one of SGM's contributions to the DNA50 programme of events in 2003 which is being co-ordinated by the Medical Research Council, the Royal Society and *Nature* (for details see www.dna50.org.uk).

The Society's President, Sir David Hopwood, FRS gives an overview of the topics covered (p. 3) and notes the enormous amount of progress made in our knowledge of molecular biology over the past half century. Articles on DNA repair in bacteria (pp. 8–10), gene therapy, which today is most effective using viruses (pp. 14–15), and RNA replication and host plant defence (pp. 12–13) show the range of current understanding. Microbial genomics has made a huge impact in recent years and this features in two articles by members of the Pathogen Sequencing Unit of The Wellcome Trust Sanger Centre (pp.16–21).

The SGM's scientific meeting at UMIST in September is the Society's other major contribution to DNA50 events. An outline of the programme appears on pp. 34–35 and further information is available on the SGM website. The Main Symposium 'Exploiting Genomes: bases to megabases in 50 years' is described in detail on pp. 6–7.

Other articles look back, one to the state of microbiology 50 years ago (pp. 4–5) and another to the controversy about smallpox vaccination in the 19th century (pp. 22–24). Rabies is a present-day issue of concern which Mary Warrell addresses in 'Comment' on p. 52.

These articles appear in addition to all the regular features and reports of Society activities.

Articles

Regular Features

Other Items

The views expressed by contributors are not necessarily those of the Society; nor can the claims of advertisers be guaranteed.

PublicAffairs

The Society has been very active in the public affairs arena in recent months and has many exciting activities planned for the future. Input from members is always welcome, particularly if they are willing to be included in our database of experts and provide advice and information on specialist areas of microbiology when needed by the media or for responses to consultations. Email **pa@sgm.ac.uk**

Biosciences Federation

The Biosciences Federation is born!

Readers will have learned from the August 2002 issue of *Microbiology Today* (p. 134) of plans to form a federation of UK life sciences learned societies to enable them to speak with a more unified voice on matters of concern covering the whole spectrum of biology. Following the events referred to in that article, a working party with representatives of some of the larger societies was convened by Sir John Arbuthnott and charged with bringing the concept to reality. This duly occurred on 26 November 2002 – The Biosciences Federation now exists, as a Company Limited by Guarantee, Number 4600861. Colin Blakemore is the first President, John Arbuthnott the Honorary Secretary and Nancy Rothwell the Honorary Treasurer, with seven other Council members, two of whom – Nancy Lane and John Whittaker – join the three officers to form an Executive Committee. Simultaneously, the UK Life Sciences Committee, which previously carried out some of the functions to be taken on by the Biosciences Federation, but for only a part of the biological spectrum, ceased to exist.

As a matter of legal convenience, the founding members were limited to the Biochemical Society, British Ecological Society, British Pharmacological Society, Linnean Society, Nutrition Society, Physiological Society, Society for Endocrinology and the SGM, but it is hoped that many others will quickly join and all will have an equal status. Several societies are indeed doing so already, including, importantly, the Institute of Biology – a complicated move for them in view of their special position in British biology and their Chartered status. It is expected that very soon the total number of biologists adhering to the Federation via their membership of one of the federated societies will exceed that of the chemists and physicists represented by their professional bodies.

The primary aim of the Federation is to be a national forum that promotes, represents and advances the UK's expertise in the Biosciences nationally and internationally. It plans to do this by promoting liaison and dialogue on common issues relating to research and teaching, by providing opinion and information to assist the formulation of public policy on biological issues, and to promote debate about practical and ethical issues in biology both between biologists and with the wider public. The hope is that the government and others will welcome the Federation as something of a 'one stop shop' for authoritative information and guidance on the many biological issues that hit the media every day.

The SGM welcomes the formation of the Federation and expects to be fully involved in helping to carry out its aims, especially concerning microbiology, as a complementary portal to its own successful activities. The Society plans to play a leading role in the proposed Education Group of the Federation, just as we did when this was part of the UKLSC. There are many practical matters to settle, finances to raise and working relationships with member societies to sort out, but I am confident that this will happen, given the enthusiasm of member societies. We wish the fledgling Federation well.

■ ***David Hopwood, SGM President and member of The Biosciences Federation Council***

Consultations

SGM has recently responded to the following consultations:

- The Royal Society Inquiry into *Measuring Biodiversity*
- Department of Health: *Interim Guidelines for Smallpox Response and Management in the Post-eradication Era*

Responses are being collated to the following consultations

- House of Commons Science and Technology Committee: *The Scientific Response to Terrorism*
- Department for Environment, Food and Rural Affairs: *A Proposed Strategy for Enhancing Veterinary Surveillance in the UK*
- Department for Environment, Food and Rural Affairs: *National Scrapie Plan – Scrapie National Flocks Scheme*
- The Scottish Executive: *Health Protection in Scotland*

Microbiology Awareness Campaign

The new campaign is beginning to take shape, with an event planned in Edinburgh to promote relevant local microbiological issues to Scottish parliamentarians and civil servants. It will take the form of short presentations and an exhibition, over a lunch at a central venue in the city close to the Scottish Parliament.

Women in science

The recently published *Set Fair Report*, compiled by Baroness Greenfield for the Department for Trade and Industry, focuses on the retention and progression of women in science, engineering and technology (SET). It concludes that under-representation of women in SET is an issue for society, for organizations and for employers as well as for the individual. Despite the many bodies and programmes that exist to promote the participation of women in SET, their efforts are fragmented and do not always fully achieve their objectives. Amongst a series of recommended actions, the Report suggests the formation of a Working Science Centre to provide information and to bring initiatives together and to reduce duplication. The full report can be downloaded from **www.set4women.gov.uk/set4women/research/greenfield-report.pdf**

The Athena Project, which aims to promote the advancement of women in science in higher education, has announced the winner of the first Athena Awards. Queen's University of Belfast will receive a substantial cash prize at a ceremony at the Royal Society in February. The award was made for their Gender Initiative which has sparked a culture change across the whole university.

WISE (Women into Science and Engineering) have produced a colourful A3 poster which aims to encourage girls to choose careers in SET. Email **wisecampaign@emta.org.uk** for further information.

DNA 50: then and now

David Hopwood

Fifty years ago, on 25 April 1953, James Watson and Francis Crick published their paper in *Nature* on the double-helical structure of DNA that became the most familiar biological icon of all time. It pervades the representation of both academic and applied biological science – consider how many research institutes, university departments, congresses and biotech companies include some allusion to the double helix motif in their logo. And how our understanding of the biological world would have developed without it. Added to its scientific significance, the 'race' to determine the structure of DNA has other elements needed to ensure its popular appeal, including the perceived betrayal of a tragic figure in the story, Rosalind Franklin (see p. 46), and, at least for a British public, the conquest of Everest and the coronation of Queen Elizabeth in the same year.

Along with countless other organizations, the SGM is recognizing the 50th anniversary, in our case with this special issue of *Microbiology Today* and with the Society's 153rd meeting, at UMIST in September, largely devoted to the scientific legacy of the Watson and Crick discovery. Petra Oyston and her co-organizers describe the main symposium at that meeting – *Bases to Megabases in 50 Years*. It should be a great meeting. It happens to be my last as President of the Society and I hope lots of people will recognize it as a 'must', either to catch up on new developments for their own research or to fill in gaps for their course teaching.

The SGM has recently begun to include a History of Microbiology lecture in the programme of its September meetings, and Colin Howard, who gave the first of these lectures in 2000, has summarized his theme in this issue of *Microbiology Today*. Before this, John Postgate, almost a household name for his book *Microbes and Man*, wrote the only comprehensive account of the history of the Society on the occasion of its Golden Jubilee in 1995. It is therefore completely appropriate that he introduces this special issue with a retrospective account of the first link between Watson and Crick – in the person of a young Jim Watson – and the SGM. It seems that it didn't go too well but, not for the first time and certainly not for the last, the occasion was rescued over alcoholic drinks in the evening! For those who would like a definitive history of the post-war events that led to the DNA structure and from there to the rise of the Laboratory of Molecular Biology in Cambridge as a world leader in the new field of science, Soraya de Chadarevian's book *Designs for Life: Molecular Biology after World War II*, which I review on page 46, is highly recommended. She will be giving this year's History of Microbiology lecture at the UMIST meeting, fitting in perfectly with the meeting's theme.

This issue contains articles that resonate with the Watson and Crick discovery in several interesting ways. As Peter Strike points out, the basic mechanisms of DNA replication and mutation were famously adumbrated in the classic 1953 papers, but DNA repair was not. He traces the development of our understanding of this key aspect of the genetic material of all cells. It parallels the amazing growth in our understanding of molecular biology in general and still has its share of unsolved mysteries. Again, as Mike Mayo reminds us, RNA replication was hardly covered in 1953, yet it is central to the existence of a clear majority of viruses. It is much less faithful than DNA replication, probably accounting for the choice of DNA by all (complete) organisms, but is exploited by viruses to aid their phenomenally rapid evolution. And gene therapy of human disease, to be rational and effective, depends on a knowledge of the genomes of viruses – the vectors for introduced genes – as well as the host. As Stacey Efstathiou tells us, this is one of the most challenging fields for applying the legacy of Watson and Crick, for both scientific and ethical reasons, but things are certainly happening.

Today there is a flood of whole microbial genome sequences hitting the databases at an ever-increasing rate. Stephen Bentley puts a numerical perspective on this and conveys some of the excitement of entering a genomic Aladdin's Cave and switching on the floodlights. Once the DNA of any microbe is sequenced it is hard to imagine working on its genetics without it. What about our ability to make sense of all this information? Many people have written suites of software to make this possible, and most of them certainly have things to offer the microbiologist who is not a genomics specialist but wants to find out as much as possible about the genetic endowment of their favourite microbes, including the genetic relationships with sequenced relatives. Some of the best 'free' packages have come out of the Sanger Institute, and members of SGM have been fortunate in 2002 to have been able to attend hands-on courses about two such packages, Artemis and the Artemis Comparison Tool, from the Sanger experts. As Nick Thomson describes, the courses provided excellent occasions for learning, and it is gratifying to read that the instructors felt that they had also benefited from the chance to discuss the software with users knowledgeable about some of the microbes whose genomes they had annotated. For my own part, I am especially pleased that this new SGM-sponsored initiative has fulfilled a dual aim of the Council: to do our bit in the genomics field, and to kick off a new policy of holding workshops and other events in the regions. There will be more regional genomics workshops in 2003. Watch this space for news of other regional activities that are in the planning stage.

● *Sir David Hopwood, FRS, is SGM President and his group has recently collaborated with the Sanger Institute to sequence the Streptomyces coelicolor genome. He may be contacted at John Innes Centre, Norwich Research Park, Colney, Norwich NR4 7UH, UK.*
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ABOVE:
Computer representation of a molecule of DNA.
ALFRED PASIEKA / SCIENCE PHOTO LIBRARY

Microbiology and me in 1952

John Postgate

Former SGM President and distinguished writer John Postgate looks back at the state of microbiology in 1952, the year when Jim Watson made a presentation at an SGM meeting.

In that year the microbiological scene was buzzing with activity. As usual, progress was driven by new experimental techniques. New ways of disrupting bacteria without denaturing their constituent proteins had greatly facilitated the preparation of active cell-free enzyme preparations. The traditional Warburg manometer was obsolescent, albeit still useful in special contexts, and cumbersome analyses by microbiological or enzymic assays had been widely replaced by paper chromatography. This could be rendered semi-quantitative by ingenious gimmicks such as photometric or densitometric scanning of chromatographs, or weighing cut-out spots, but the truly quantitative partition chromatography, and its ion-exchange analogue, were coming into use. Many biochemicals labelled with radioactive isotopes for use as tracers were now available from dealers; centrifuges had diminished in size and improved enormously in quality; optical colorimetry and spectroscopy were being displaced by electronic devices.

In consequence, papers exploiting such techniques to determine the minutiae of bacterial and microfungal metabolism had been dominating the contents pages of *J Bacteriol* and *J Gen Microbiol* for 3 or 4 years, and many pathways of catabolism, respiration and fermentation had been elucidated. 'Simultaneous adaptation' was illuminating more specialized degradation pathways, such as the breakdown of aromatics by pseudomonads. Pathways of biosynthesis of carbohydrates, of amino acids, haems and micronutrients, for example, were hot research topics, the major research tools being radioactive tracers, metabolite analogues (to block pathways), and examination of syntrophies among related auxotrophic mutants. At a more holistic level, electron microscopy had come of age and was giving reliable information about the structure of viruses and the interiors of bacterial cells; the existence of an osmotic barrier, somewhere beneath the cell wall and associated with a semi-permeable surface zone, was clear, and strong evidence was accumulating for subcellular compartmentation. Despite its featureless appearance under the microscope, the bacterial cell could no longer be regarded as an amorphous bag of enzymes.

I was then a newly fledged full-time research microbiologist, 4 years after completing my doctoral research at Oxford, employed by the Department of Scientific and Industrial Research (DSIR) at the Chemical Research Laboratory, in the enclave of the National Physical Laboratory, at Teddington outside London. I was part of a little team of four scientists headed by a desk-bound K.R. Butlin, one of the handful of groups in the world who studied sulphate-reducing bacteria. It may seem odd that a tiny microbiology unit existed among all those chemists and physicists, but that is how things were. Microbiology may by then have gained recognition as a distinct discipline in academe, but not among the administrators of the DSIR. To them it was a fringe pursuit, an aberration of medicine, or perhaps something to do with brewing. They did not know quite how to fit microbiologists into their scheme of things, and rather wished they would go away.

I worked with traditional equipment for growing strict anaerobes: tubes with plugs soaked in pyrogallol, and Knight & Fildes anaerobic jars. I calibrated my Warburg manometers. I used paper chromatography backed by old-established chemical analyses, a 'modern' but jittery centrifuge suspended on rubber coated springs, and so on; my main concern was how sulphate reduction was linked to substrate catabolism. Viruses, protein synthesis and nucleic acids were remote from such smelly pre-occupations, so I was more an observer and exploiter of the great developments that were taking place (a few years later I was able to tip in my own two-pennyworth, but that's another story). Yet I was well aware of the big questions of the day: what were viruses?

RIGHT:
Practical microbiology ca 1952. The author inoculates specimens of iron and steel with a laboratory culture of sulphate-reducing bacteria before burial. They will be exhumed in later years, as part of a field study of anaerobic corrosion.
COURTESY J. POSTGATE

'Luria's absence thrust upon me the job of describing the recent work of the American phage workers. There was no need to put together a speech. Several days before the meeting, Al Hershey had sent me a long letter from Cold Spring Harbor summarizing the recently completed experiments by which he and Martha Chase had established that a key feature of the infection of a bacterium by a phage was the injection of the viral DNA into the host bacterium. Most important, very little protein entered the bacterium. Their experiment was thus a powerful new proof that DNA is the primary genetic material.

Nonetheless, almost no-one in the audience of over 400 microbiologists seemed interested as I read long sections of the letter... Moreover, when it came out that I was an American, my uncut hair provided no assurance that my scientific judgement was not equally bizarre.'

Those are the words of J.D. Watson in *The Double Helix*. In fairness to his audience one must add that his diction (head down, reading passages from a letter in not the easiest of mid-West accents), and the hall's poor acoustics, had much to do with his lack of audience response; but even in 1952, scepticism about the genetic role of DNA was still widespread...

Excerpt from *Fifty Years On* by John Postgate (1995), Society for General Microbiology, Golden Jubilee Brochure.

How did they originate? And what controlled the replication and heredity of bacteria? Nucleic acids? Autocatalytic enzymes? Specialized proteins?

The SGM's meeting on the *Nature of Virus Replication* at Oxford in the spring of 1952 promised a degree of enlightenment, as well as the prospect of gleanings for my own research – not to mention the opportunity to meet old microbiological chums. The overt theme of the meeting, set up by the distinguished plant virologists N.W. Pirie and E.C. Bawden, was how did viruses multiply when they had, or seemed to have, no metabolism of their own? It was a timely, forward-looking theme, for consensus was badly needed on what a virus was; whether it was fundamentally a rogue protein, a rogue nucleic acid, a degenerate bacterium, or a rogue cluster of genes – whatever the latter might mean in the days when the chemical nature of genes was in doubt. Yet most microbiologists already felt that the rogue gene cluster idea matched up best with the general behaviour of viruses, and that therefore study of their multiplication would yield valuable information about heredity in general. Bacteriophage multiplication and lysogeny seemed to offer a relatively simple model system for virus action; yet even here at least one scientist argued passionately at the meeting that bacteriophages were endogenous lytic products of the bacterium, not viruses, so such studies were irrelevant.

Overshadowing the whole meeting was a wholly non-microbiological affair. An invited speaker from the USA, bacteriophage expert S.E. Luria, was not present, because at the last moment the US authorities, then in thrall to Senator McCarthy's Committee on Un-American Activities, had confiscated his passport – they suspected Luria of holding communistic views. (His written paper was nevertheless published in the SGM symposium volume). Jim Watson, a peripatetic American post-doc then working at Cambridge, UK, deputized for Luria and took the opportunity to read to the meeting a long letter from A.D. Hershey, which described Hershey's and Chase's now famous experiment demonstrating that phage DNA, and not phage protein, was the infective material which initiated virus synthesis. Essentially Hershey and Chase had prepared T2 phage labelled with radio-S (marking the protein component) or radio-P (marking the DNA component), and demonstrated that, when infection of the host bacteria was interrupted mechanically using a blender, the radio-P remained in the bacterial cells, in which phage multiplication continued, and the radio-S washed off the cells and could be precipitated and recovered. The controls were proper, and the work was powerful evidence that phage heredity resided in its DNA. Watson, thrilled by the letter, recorded in *The Double Helix* his disappointment with the Society's response (though for my part I am not sure how well his message got through; see box) and the hurt was still there in 1993 (see Watson's *A Passion for DNA*, OUP, 2000, p. 23).

However, the message certainly registered where it mattered. Roger Stanier took me to a gathering that evening in one of the rooms of Lady Margaret Hall, where the conferees were billeted, and I was able to be a fly-on-the-wall while pundits in the infant field of viral molecular genetics cross-examined Watson, aided by a bottle of calvados which Roger had imported from France. Details of the discussion, and the names of the participants, have long vanished from my ageing memory, but I well recall the sense of excitement in the room, childish pleasure even, as Watson parried the company's interrogation and the elegance and plausibility of Hershey and Chase's experiments were revealed. History has confirmed that it was not just the calvados!

● *Professor John R. Postgate, FRS was President of the SGM 1984–1987. His popular books have helped to enthuse and inform many members of the public about microbiology. 'Microbes and Man' is in its 4th edition. He may be contacted at Houndean Lodge, 1 Houndean Rise, Lewes, East Sussex BN7 1EG, UK.*
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Exploiting genomes: bases to megabases in 50 years

Petra Oyston & Dave Kelly

The Symposium *Exploiting genomes: bases to megabases in 50 years* is being organized by H. Jenkinson, P. Oyston, I. Sutcliffe, J. Parkhill and D. Kelly and will take place on Monday 8 and Tuesday 9 September 2003 at the 153rd Meeting of the SGM, at UMIST, Manchester. See www.sgm.ac.uk/meetings for the full programme, and to book online.

The whole ofthis meeting is a major SGM contribution to the DNA50 programme.

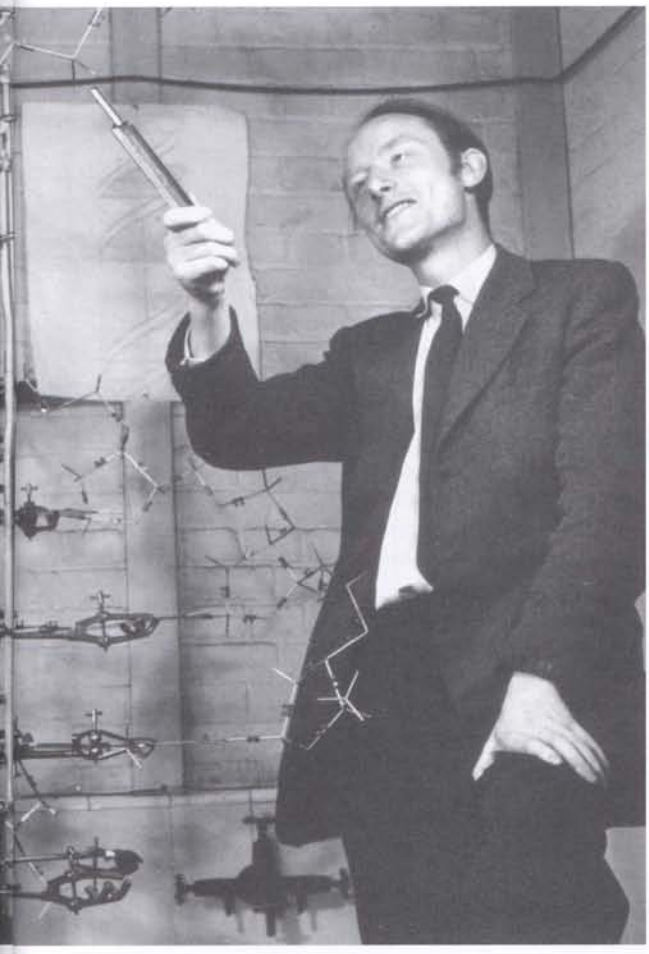
celebrating life
DNA DOUBLE HELIX 1953-2003

It is 50 years since Crick and Watson published in *Nature* the structure of DNA, and the SGM has planned a symposium to be held at the September 2003 meeting at UMIST, Manchester, to celebrate the impact that this discovery has made on microbiology. What little progress could have been made in microbiology without the ability to examine and manipulate microbial DNA, skills we now take for granted, seems obvious to us now in 2003. Using the tools of molecular biology, we can clone and mutate genes, express proteins to high yield in large-scale fermenters, determine the evolutionary relatedness of any given strain, and even identify microbes that are impossible to grow in the laboratory. Indeed, it is obvious that microbiology has been transformed by molecular biology in ways that must have been unimaginable 50 years ago.

Once the structure of DNA was known, it was only a relatively short time before the organization of genes and (in bacteria) operons was understood. However, due to the early cumbersome chemical sequencing techniques it was some time before a complete genome was sequenced. The first DNA genome to be sequenced was that of bacterial virus ϕX174 by Fred Sanger's group at Cambridge in 1977, and for a long time sequencing of only the small genomes of viruses could even be contemplated. The advent of high throughput sequencing technology has since revolutionized microbial genomics. Genome sequence data have allowed the entire genetic repertoire of an organism to be examined, rather than just individual genes in isolation. An introductory perspective on 'Genomes and beyond' will be provided in the opening lecture of the symposium, to be given by G. Weinstock. The world was rather taken by surprise when *Haemophilus influenzae* was the first bacterium to be completely sequenced by Fleischman *et al.* in 1995, as most people had expected *Escherichia coli*, the laboratory workhorse, to claim that honour. But although the sequences of several small-genome, specialized pathogens were published in rapid succession after 1995, larger microbial genomes soon followed. There are currently 103 completed bacterial genome sequences (although this number will be out of date by the time this article is published!), and over 150 sequencing projects at different stages of completion. At the Symposium, some of the applications of this mass of genome data will be reviewed by Julian Parkhill (Sanger Institute). Siv Andersson (Uppsala University) and Emilio Garcia (Lawrence Livermore National Laboratory) will talk in more detail about the recent sequencing of *Bartonella* and *Yersinia* (two interesting and important pathogenic bacteria), respectively. Nowadays, the ability to sequence whole genomes is almost routine, so that now there are examples of several strains of a species being sequenced for comparison.However, the publication of a genome sequence is still a matter of particular excitement, not only for researchers working on that organism, but often for a wider audience of microbiologists who can see relationships with their own work. Rather than the genome sequence being an end in itself, it is the start of a huge amount of work to put the information into context with regard to the biological significance of the organism. For example, sequence data is being exploited to reveal how species have evolved, the basis of strain diversity and how pathogens have both acquired virulence genes and lost non-essential genes in their adaptation to their hosts.

A key discipline which has been essential to the success of genomics is that of bioinformatics, by which the likely identities of genes and structures of gene products can be inferred and their evolution traced (T. Gaasterland, Rockefeller University). Predictions can also be made about the level of expression of genes from sequence information (D. Ussery, Denmark). An interesting project called the Minimal Microbial Genome which will be outlined by C. Hutchison (TIGR, USA) is taking a novel approach to analysing the significance of each gene in an organism. They are asking the question, 'How few genes does a bacterium actually require for viability?' To answer this, they intend to strip down an existing genome to a minimal set of essential genes, creating, in effect, a new organism.

In addition, genomics has allowed the rapid development of other areas, such as transcriptomics and proteomics, whereby the expression of all of the genes and proteins, respectively, in an organism can be monitored in response to varying stimuli. Infection results in massive changes in protein expression in both the micro-organism and the host. Viruses, by their very nature, hijack the machinery of the cell for their replication, so it is unsurprising that viral infection results in dramatic changes in cellular gene expression. This topic will be covered in two talks (P. Ghazel, Edinburgh University and P. Kellam, UCL), and



LEFT:
James Watson (b. 1928) on the left and Francis Crick (b. 1916) on the right with their model of part of a DNA molecule in 1953.
PHOTO A. BARRINGTON BROWN / SCIENCE PHOTO LIBRARY

herpesvirus genomics will be reviewed by A. Davison (University of Glasgow). However, until recently the effect of bacterial infection on cellular gene expression has been less well understood. The availability of fully annotated bacterial genomes represents a powerful resource to help understand the complex biology of host–pathogen interactions for a range of medically important bacterial pathogens. The use of microarrays to monitor whole-genome expression in bacteria (for example, talks by Phil Butcher, St George's Medical School and Brendan Wren, London School of Hygiene and Tropical Medicine) is a powerful approach, and is resulting in identification of differentially expressed genes important in pathogenesis, as well as providing useful targets for the rational design of new drugs and vaccine candidates for important bacterial pathogens. The study of transcripts by array technology is complemented by proteomics. David O'Connor (Southampton University) will describe the most recent developments in the field of protein identification and quantitation, using *Salmonella enterica* var. Typhimurium as his model. The technology of proteomics is moving ahead rapidly, with new software and automated systems of protease digestion and mass spectrometry for protein identification. Linking proteome maps to genomic databases will create an invaluable resource for future studies of many microbial species.

Whole-genome screening techniques, such as identifying promoters necessary for *in vivo* gene expression (Paul Rainey, Oxford) or following the fate of individually tagged mutants in mixed pools during infection are proving a powerful way of coupling genetic techniques to genomics. Approaches like these will allow us to apply some hypotheses to the vast amount of data that has been generated in recent years. In fact, if there is one criticism of the 'genomic era' it is that data generation may have over-shadowed efforts to understand the biological significance of the information. Even storing data, such as proteome maps and microarray files, in an accessible yet controlled way is a challenge that is just starting to be addressed.

Many pharmaceutical companies have invested heavily in genome sequencing and this reflects the contribution that the data will have in the search for novel antimicrobial targets and vaccine antigens. Historically, identification of antigens suitable for sub-unit vaccines or finding targets which when inactivated would result in attenuation, were reliant on luck as much as anything. With the availability of genome and proteome data, a more logical and informed approach can be followed. *In silico* antigen prediction allows the best candidates from the whole protein complement of the pathogen to be identified (R. Rappuoli, IRIS Research Centre). Likewise, targets which would be suitable for inhibiting with a new generation of antimicrobials can be identified from genome data (P. Rathod, University of Washington).

The organizers hope that this symposium will not only be a celebration of the remarkable progress that has been made since the discovery of the structure of DNA, but will give an overview of cutting-edge research in this area, as well as providing a useful perspective with which to view the current and future development of microbial genomics. We therefore strongly encourage SGM members to participate in this historic symposium at UMIST.

●*Dr Petra Oyston is in the Department of Microbiology, Dstl Biomedical Sciences, Porton Down, Salisbury SP4 0JQ, UK.*
●*Professor Dave Kelly is Chair of Microbial Physiology in the Department of Molecular Biology and Biotechnology at the University of Sheffield, Western Bank, Sheffield S10 2TN, UK.*

BELOW:
The scrolling display at the Wellcome Trust Sanger Institute, Hinxton, Cambridge, UK.
COURTESY RICHARD SUMMERS, WELLCOME TRUST SANGER INSTITUTE

Representations of the double helix

A collection of structural models of DNA is on display at the Whipple Museum of the History of Science, Cambridge, throughout 2003. It is part of an exhibition to celebrate the scientific and cultural impact of the DNA double helix. A star attraction is the full-size reconstruction of the first Watson and Crick model. See www.hps.cam.ac.uk/whipple

Bacteria and DNA repair – 50 years together

Peter Strike

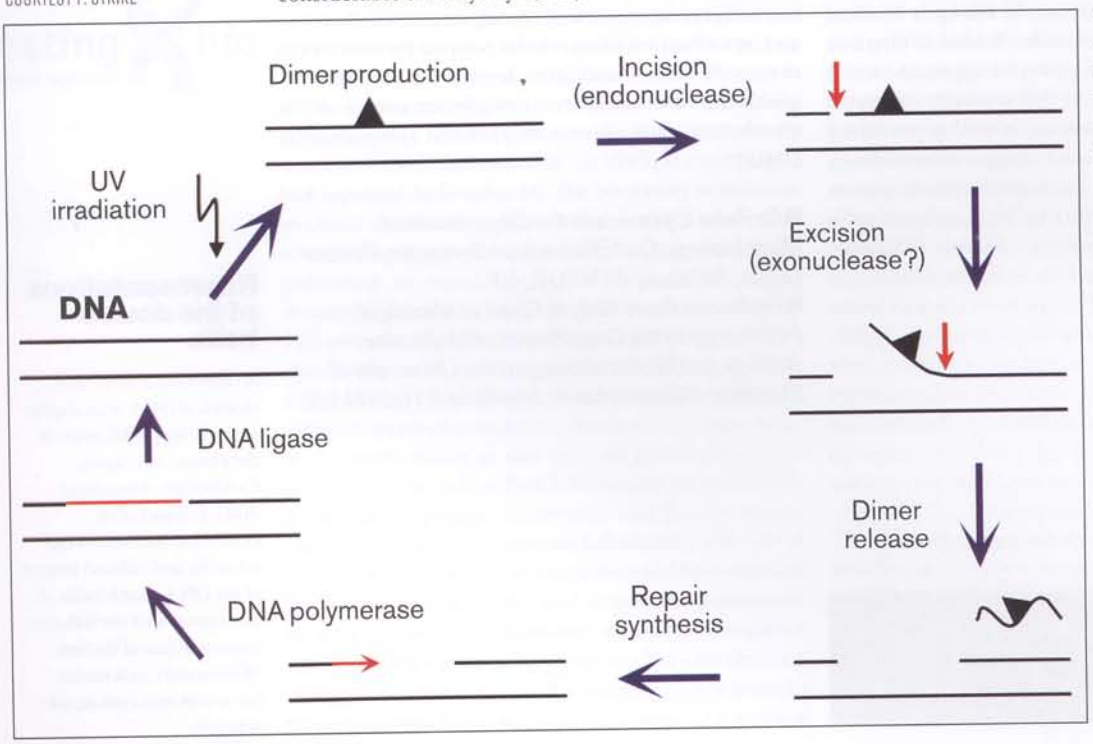
From the discovery of the double helix it has taken 50 years of intense study to understand DNA repair. Nearly all key breakthroughs have come from work with bacterial cells.

DNA repair now sits centre stage, along with DNA replication and the cell cycle, as one of those key processes essential to the function of every living cell. It is of course inaccurate to describe it as a single process – it is a comprehensive suite of functions, able to deal with almost every environmental challenge thrown at our DNA, maintaining the molecule's structure and genetic integrity. Defects in repair impact on survival, mutation, cancer, antibody production, reproduction, meiosis, mitosis ... the list is endless. And yet, not too long ago, DNA repair was considered an odd little corner of biology, largely studied in a rather oblique manner by the 'radiobiologists'. The subject was generally outside mainstream interests, and indeed it could be considered that a general realization of the importance of repair processes really only came with the demonstration of the unequivocal link between mismatch repair and colon cancer in the 1980s. Almost no biochemical analysis of repair functions was even attempted until the 1960s, although good genetics had begun to indicate the presence of these processes somewhat earlier.

Early discoveries

The study of repair started as a consequence of the fascination in the early 20th century with the biological effects of radiation. Herman J. Muller's pioneering work, generating mutants of *Drosophila* with X-rays, led to a more general interest in radiation of all kinds, with UV becoming a firm favourite because of its ease of use and considerable efficacy. By 1941, Alexander Hollaender was reporting the mutagenic effects of ultraviolet light on micro-organisms, and indeed reporting that that the optimum wavelength for mutation coincided with the peak of absorbtion for nucleic acids. Doubt, however, was still prevalent that DNA could be an important molecule. Max Delbruck, for example, is quoted as acknowledging that while much evidence pointed to DNA as the genetic material, '*it was believed that DNA was a stupid substance, a tetranucleotide which couldn't do anything specific*'.

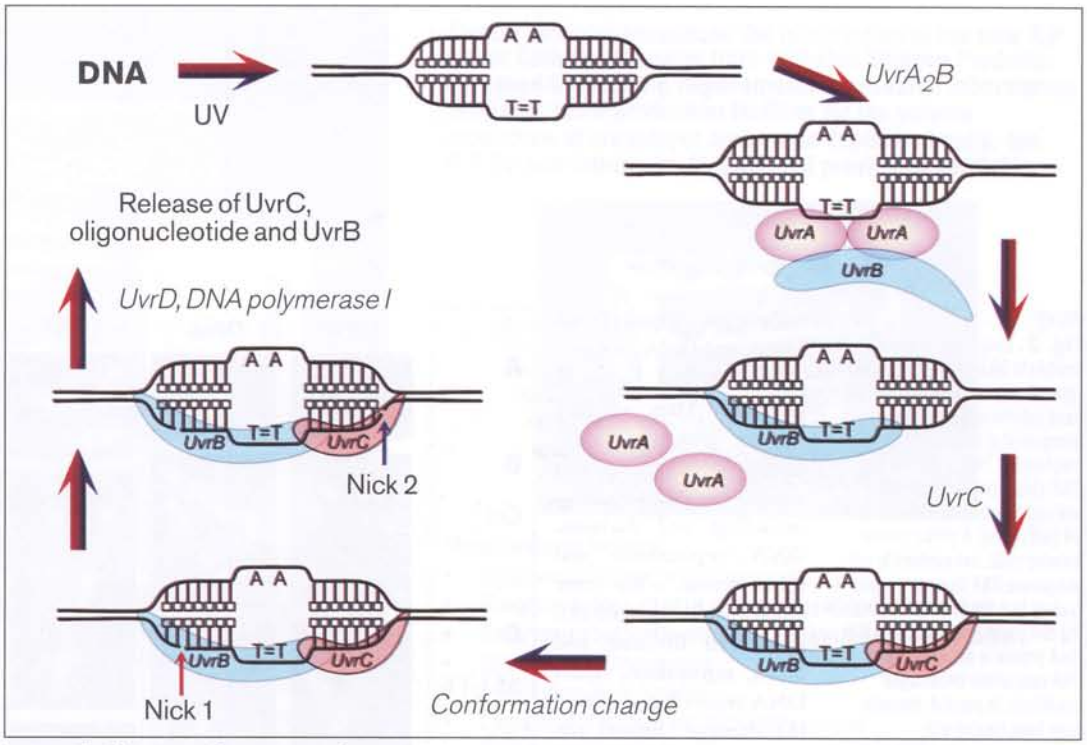
What began to change things was of course the discovery of that structure, the beautiful double helix that suggested to its discoverers not only '*an obvious mechanism for its replication*', but also a mechanism for spontaneous mutation '*due to a base occasionally occurring in one of its less likely tautomeric forms*'. The possibility of DNA repair was not immediately inferred from the structure, but became current in the early 1960s from the work of Bob Haynes and others as a theoretical explanation for a variety of phenomena including 'liquid holding recovery', in which it was observed that cells (of bacteria or yeast), if held in starvation medium for increasing periods following irradiation, showed remarkable levels of recovery. By 1964, Haynes and Philip Hanawalt were sufficiently sure of their ground to point out that the redundancy inherent in the double helix provided a means by which, if one strand of the DNA helix was damaged, '*the information in that portion could be retrieved from the complementary strand*'. Such thoughts were current in a number of laboratories and, from one of these (Dick Setlow's), a biochemical description of the first repair pathway to be understood at this level was about to appear. That pathway was nucleotide excision repair.



BELOW:
Fig. 1. Typical 1960s model of nucleotide excision repair, based on the observations of P. Setlow, P. Howard-Flanders, P. Hanawalt and others. Assignment of enzymes to particular steps is speculative, but the overall picture of events proved to be remarkably accurate.
COURTESY P. STRIKE

Repair in microbes

The Haynes and Hanawalt suggestion has to be set in the context of the elegant genetic and physiological work, done primarily with bacteria and bacteriophages, but also with eukaryotic micro-organisms, which showed beyond doubt that DNA repair was occurring. And more, much more than this – the bacteria did it their way! First, there was light-dependent repair, or photoreactivation, discovered by Albert Kelner in '*the fungus*'



Streptomyces griseus. Then excision repair, discovered initially through the phenomenon known as 'host-cell reactivation', in which the damage done to UV-irradiated bacteriophages could be repaired upon infection into repair-proficient bacterial cells. The demonstration that host-cell reactivation was truly due to a repair process required one key ingredient – a mutant bacterial strain in which repair was defective. This key ingredient came from the laboratory of Ruth Hill, with her isolation of the UV-sensitive bacterial strain *Escherichia coli* B_{s-1}. This strain, some 100 times more sensitive to UV light than the parental strain, provided the vital tool with which to investigate the putative process of excision repair, allowing as it did a direct comparison at the biochemical level of the differences between mutant and wild-type parent. Many labs had by this time predicted how excision repair might work, but it was Dick Setlow who provided the proof, demonstrating that damage-containing oligonucleotides were released from high-molecular-mass DNA in wild-type *E. coli*, but not in the sensitive B_{s-1} strain.

E. coli leads the field

Discoveries from *E. coli* now came thick and fast. Paul Howard-Flanders' group isolated the excision-repair defective *uvr* mutants in *E. coli* K12, allowing a thorough genetic analysis to be undertaken. Dean Rupp and Howard-Flanders showed that a second type of dark repair, termed post-replication repair, occurred in excision-repair-defective mutants. Mutants defective in recombination were isolated by John Clark, and shown to be defective in this newly identified repair process. Mismatch repair was discovered, this elegant mechanism exploiting delayed methylation of newly replicated DNA to direct repair of mismatched bases to the newly synthesized strand. The concept of excision repair was extended to base excision repair (removal of a single damaged base rather than an oligonucleotide), a mechanism involving different initiating enzymes from those identified in the *uvr* mutants, but sharing many later steps. The *uvr*-based mechanism was now renamed 'nucleotide excision repair' to distinguish it from this new mechanism. Studies of mutation resulted in the isolation of a number of classes of 'non-mutatable mutants', confirming that mutation too was an enzyme-mediated process, and culminating in the proposal of error-prone trans-lesion synthesis put forward by Evelyn Witkin and Bryn Bridges. In each of these cases, we now have flesh added to the bones. Base excision repair includes a whole set of mechanisms for the removal of different types of damaged (or incorrect) bases from DNA. Why is there no uracil in DNA? Because base excision repair removes it. Mismatch repair is also multi-faceted, a family of processes recognizing different types of mismatched bases and of such importance that closely related enzymes are conserved from bacteria to man. A highlight of the 1980s was the isolation of the three components of the *uvr* excision repair nuclease by Aziz Sancar and Dean Rupp which caused the journal *Science* to nominate DNA repair enzymes as 'molecule of the year' in 1984. Equally stunning was the elucidation of the genetics and biochemistry of the 'SOS response', the environmentally responsive system controlling the expression of many DNA repair and recombination enzymes. A second controlled system, identified initially by John Cairns as the 'adaptive response', allowed the *E. coli* cell to respond to methylation damage. Characterization of this system resulted in the identification of the alkyltransferases, proteins (not strictly enzymes) that could remove alkylation damage from DNA by transferring it to themselves and which, in the case of the Ada protein, also played a key role in the control of the response.

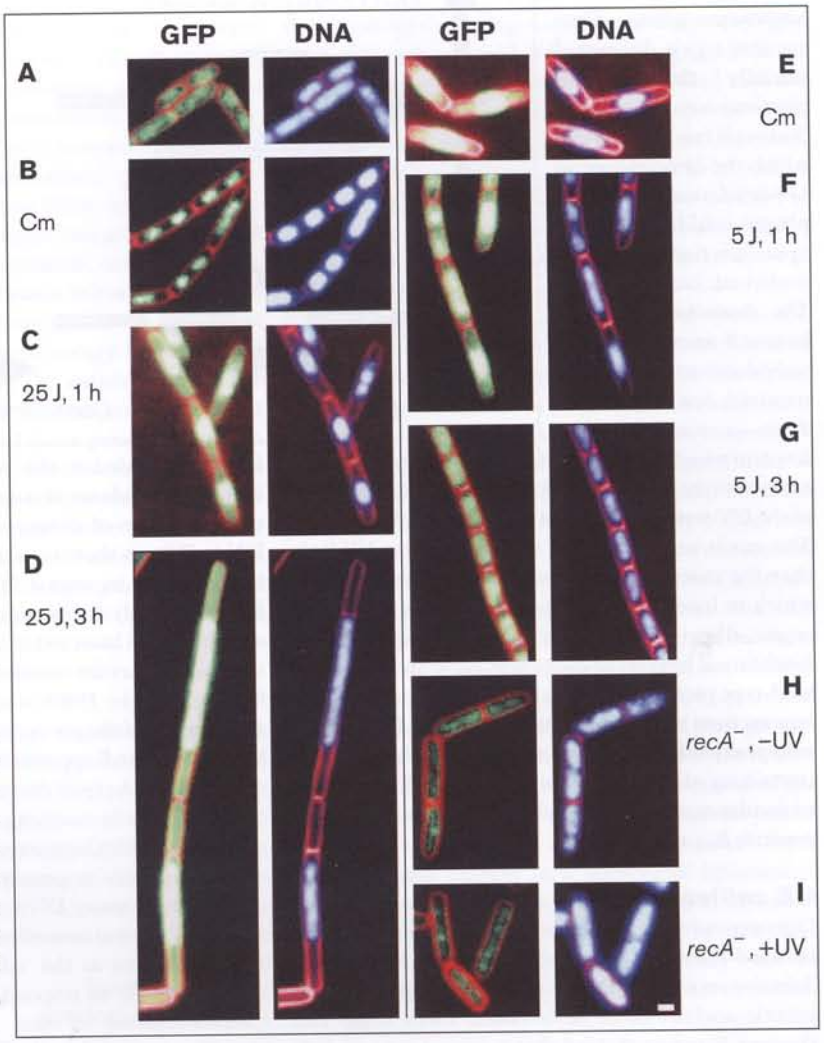
Recent developments

And what has the last 20 years brought us? The concepts of transcription-coupled and strand-specific repair, removing damage preferentially from active genes. A recognition of the importance of oxidative damage, particularly that generated by normal cellular processes. A detailed understanding of many of the enzymes of DNA repair and recombination – the sheer beauty of the branch migration process mediated by RuvABC, and the protein helix formed by RecA as it coats DNA. The unexpected, but perhaps predictable, discovery that *umuDC* gene products, defects in which abolish UV-induced mutation, in fact encode an error-prone DNA polymerase capable of trans-lesion synthesis.

But, perhaps most importantly, they have brought the

ABOVE:
Fig. 2. A simplified model of the incision events of nucleotide excision repair, as we currently understand them. Specific roles for the Uvr proteins have been identified, and the principal difference from the predictions shown in Fig. 1 is that the Uvr enzyme complex actually makes co-ordinated strand breaks at precise positions on both sides of the damage site. The presence of damage is initially detected by a $UvrA_2B$ protein complex scanning DNA for distortions. The UvrB protein is then loaded at the damage site, in a transient complex from which the two UvrA molecules are rapidly lost. The very stable UvrB/damaged DNA complex then attracts one molecule of UvrC to create an incision complex. Recruitment of UvrC results in activation of UvrB to make one single-strand nick 5 bases 3′ to the damage. A further change in conformation activates UvrC to make a second nick 7 bases 5′ to the damage. Subsequently, the combined action of UvrD protein and DNA polymerase I results in the release initially of UvrC, then the damage-containing oligonucleotide, and then UvrB. Repair synthesis then refills the gap so created. The model makes no attempt to show the bend induced in DNA by interaction with the repair proteins, nor does it show any of the interactions with other proteins that direct repair preferentially to active genes.
COURTESY P. STRIKE

realization that DNA repair and DNA recombination do not go on in isolation. They are key cellular processes, integrated with other major aspects of cell function, including cell division, DNA replication and transcription. We now know that a damaged cell stops cell division and DNA replication, until DNA repair has removed the damage. Indeed the bacterial cell seems to radically alter the structure of the nucleoid, so that repair can proceed more efficiently. Should a replication fork hit a damaged site and stall, the replication fork may go into reverse, to generate a 'chicken-foot' structure which may then be processed to allow replication to proceed across the damaged site. A similar response may occur if a replication fork hits an RNA polymerase which has stalled at the site of DNA damage.



RIGHT:
Fig. 3. Responses of *Bacillus subtilis* to DNA damage. The GFP (green)-labelled protein in the left-hand column is UvrA, a key component of the excision repair mechanism. DNA is stained with DAPI (blue) (right-hand column), and cell membranes with dye FM4-64 (red). Panel A shows normal growing cells, not exposed to any exogenous DNA damaging agent. It is clear that the DNA fills most of the cell volume available, and that UvrA protein is associated with DNA even under undamaged conditions. In panel B, the cells have been treated with chloramphenicol, to inhibit protein synthesis. Under these conditions, initiation of DNA replication is inhibited, and the nucleoid adopts a more compact appearance. The UvrA protein is still clearly associated with the DNA. Similar compaction of the nucleoid is seen if the cells are exposed to UV irradiation (panels C and D). UV also induces higher level expression of the *uvrA* gene, resulting in high levels of protein. Cell size increases with time, but the nucleoid fails to fill the space available, and some cells are created that contain no DNA whatsoever. UvrA protein remains tightly associated with the DNA in those cells that contain it. Similar compaction of the nucleoid is observed when cells are treated with the DNA cross-linking agent mitomycin C (panels E and F). At lower UV doses, nucleoid compaction is observed after short incubation times (panel F), but is effectively reversed as repair of DNA damage is completed (panel G). The mechanisms underlying nucleoid compaction are not well understood, but appear to require induction of the SOS response. Compaction is not observed in a *recA* mutant, which cannot induce the SOS response, although association of UvrA with DNA is still clearly maintained (panels H and I).
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What next?

From the discovery of the magic double helix, it has taken 50 years of intense study to come to an understanding of DNA repair that was not, indeed could not be, imagined at the time. Almost all of the key breakthroughs have come from studies on bacterial cells, with an honourable mention for the eukaryotic microbes, particularly *Saccharomyces cerevisiae*. There are undoubtedly more surprises to come. We have yet to explain the extraordinary radiation resistance of the most resistant of all bacteria, *Deinococcus radiodurans*, which is capable of reassembling an intact chromosome following complete fragmentation by exceptionally high doses of ionizing radiation. A new link has become apparent here, in that radiation resistance and resistance to dehydration/rehydration clearly depend on common processes in this organism. All in all, that is not a bad record for a molecule once considered too stupid to be of any interest but which, once its true structure was revealed, became central to all biological thinking.

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Base-pairing in RNA virus replication and host plant defence

Mike Mayo

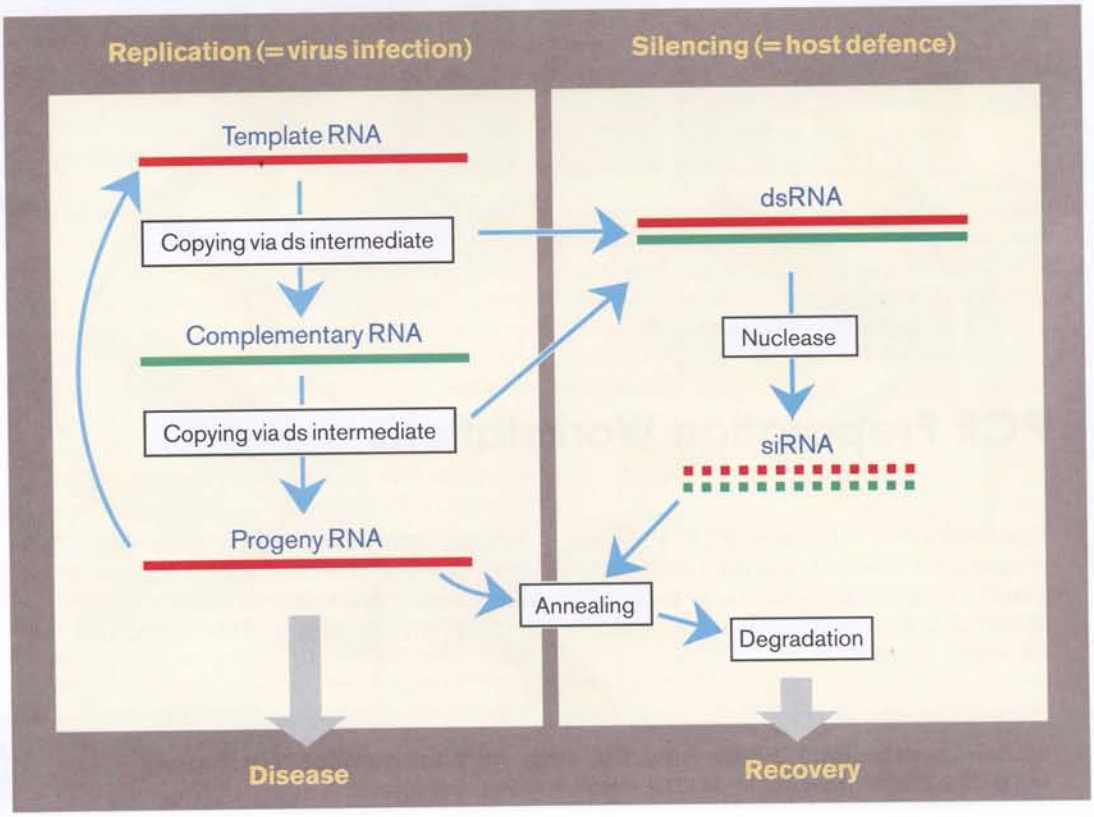
Recent research has shown that host defence against plant virus infection can be 'switched on' by replication of the viral RNA, as Mike Mayo describes.

The fundamental basis of biological replication, for RNA viruses just as much as for their hosts, is base-pairing between complementary nucleotides, pretty much as predicted for DNA by Watson and Crick. Despite their initial doubts, it is clear that ribonucleotides in RNA can base-pair to form double-stranded structures just as deoxyribonucleotides can in DNA. Indeed, we now speak of an 'RNA world' as being the forerunner of the current 'DNA world'; replication based on RNA copying being improved on by evolving to DNA-based copying. However, in virology, RNA-based replication has not been superseded. Depending on the virus species, either RNA or DNA can be the genetic material in virions, or infectious particles, of viruses, with perhaps RNA being the commoner. Of the 245 genera of viruses currently recognized, 147 (60 %) contain viruses with RNA genomes. Mostly this is due to plant virus genera (73 % RNA genomes) compared to 53 % RNA genomes for genera of vertebrate viruses.

RNA genomes

One important difference between DNA-based replication and that based on RNA is that DNA copying is much less error-prone than that of RNA. It is estimated that DNA replication is a million times more faithful than RNA replication. The result is that RNA genomes can accumulate point mutations very much more rapidly (around 10^{-3} per nucleotide position per replication cycle) than DNA genomes. Thus populations of RNA viruses will always contain many variants and are thought of as existing as quasi-species. This may be seen as a disadvantage because of the resulting genetic instability, but one positive effect is that RNA viruses can evolve very rapidly in response to any novel selection pressures or new niche opportunities that may arise – a very useful property to have as a pathogen when hosts are continuously exerting pressure.

However, for RNA viruses there is a law of diminishing returns as genome size increases. The larger a genome is, the greater is the chance of a lethal copying error. Perhaps this is why another difference between viruses with either type of genome is their size. Whereas many species have RNA genomes of around 10 kb in size, and the largest RNA genomes are the 30 kb genomes of coronaviruses, many DNA virus species have genomes of greater than 100 kb and several exceed 300 kb. Possibly, RNA virus genome size has been constrained by the increased hazard of lethal mutation in a large RNA genome. Another way of decreasing this mutation risk would be to divide the genome into several components and this genome design is indeed more common for RNA viruses; with segmented genomes in about 8 % of DNA virus genera but about 36 % of RNA virus genera.



LEFT:
Fig. 1. Diagram illustrating the role of base-pairing in the replication of an RNA virus (left panel) and in the silencing response of the host (right panel). COURTESY SCOTTISH CROP RESEARCH INSTITUTE

RIGHT:
Fig. 2. A *Nicotiana benthamiana* plant about 10 days after infection with *Tobacco rattle virus* that has been engineered so as to carry sequence corresponding to the PDS gene. Regions in which virus replication has stimulated silencing are white because PDS mRNA has also been destroyed. The plant on the left is an uninfected control plant.
COURTESY SCOTTISH CROP RESEARCH INSTITUTE

Infection by RNA viruses

Virus infection of a host can be thought of as what happens when a virus deploys the ability to invade and to multiply in a particular host environment. Multiplication is the result of cycles of replication in which the template RNA, initially in the infecting virion, is copied into a complementary strand that is then copied back into many copies of the virion-sense strand, some of which move out of the cell to infect new cells or new hosts (Fig. 1, left panel). The template and progeny RNA can be either positive-sense (i.e. message-sense) or negative-sense (complementary to message-sense).

During this process the RNAs that are complementary anneal to form double-stranded RNA (dsRNA) and recent research has found that this can provide a switch that provokes host defence against virus infection. In plants (as in fungi, invertebrates and vertebrates) there is a post-transcriptional gene silencing mechanism that involves dsRNA. In essence, the activity results in a nucleolytic attack on dsRNA that generates small interfering RNA molecules (siRNA) that can base-pair with a target (necessarily homologous) RNA. Following this base-pairing, the newly formed dsRNA is destroyed by nucleolytic activity (Fig. 1, right panel). Special nucleases are involved at each of the degradation steps.

Gene silencing

When the initiating dsRNA structure is that of an invading virus, the result is that the host is defended against the virus by its capacity to degrade the template RNA. This effect is silencing. The process can be illustrated dramatically by engineering a virus to contain sequences of a host plant gene. Fig. 2 shows the result of silencing in plants that are infected by *Tobacco rattle virus* that carries part of the mRNA for the plant enzyme phytoene desaturase (PDS). When the silencing activity is stimulated by the virus infection, some of the siRNA is complementary to PDS mRNA. This targets the homologous host mRNA which is destroyed at the same time as the invading virus RNA. Infected cells thus lack PDS and turn white on exposure to light.

Effective silencing would, of course, make all hosts immune to virus infection. This is obviously not so and it has become clear in recent years that at least some viruses encode functions (in some instances, identifiable proteins) that can suppress the gene silencing defence mechanisms of their host plants. Silencing suppressors of different plant viruses differ in their effects and the ways in which they work. So, it is not surprising that those from taxonomically distinct viruses show no phylogenetic similarities; probably suppression has arisen independently during the evolution of distinct virus lineages.

It is thought-provoking that much of the understanding of this novel field in plant biology has been the result of experimentation with genetically manipulated plants and viruses, even though what has been revealed is a process (silencing) possessed by normal plants and one that is possibly fundamental to the functioning and development of the healthy plant.

Conclusions

The process of base-pairing of ribonucleotides to form a double-stranded polynucleotide has turned out to be a key one in several ways. Not only (and unsurprisingly) is it the central event in RNA virus replication, but it also provides the variation needed for evolution by natural selection and it is fundamental to at least one host defence mechanism against infection.

So it is in the end fitting that the 1953 *Nature* papers by Watson and Crick on DNA structure carried acknowledgements of financial support from the National Foundation for Infantile Paralysis, a disease now known to be the result of infection by the RNA genome polioviruses.

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Gene therapy in the treatment of disease

Stacey Efstathiou

Gene therapy offers great potential in treating diseases such as cancer. Stacey Efstathiou explores the current state of knowledge, focusing on the use of viral vectors.

The deduction of the complete nucleotide sequence of the human genome has provided a blueprint of life. Although we are probably many years away from a full characterization of the number, function and regulation of individual genes, it is clear that single gene defects account for over 4000 inherited disorders. Such disorders can lead to severe and often fatal disease early in life or late onset debilitating disease in adults. Linking single gene defects to particular disease syndromes and the rapid development of recombinant DNA and 'gene knockout' mouse technologies have been the central platform on which the emerging science of gene therapy is based. However, although the basic principle of gene therapy is simple, its successful application to the treatment of a variety of disease states is proving a major challenge.

Table 1. Properties of commonly utilized virus vectors

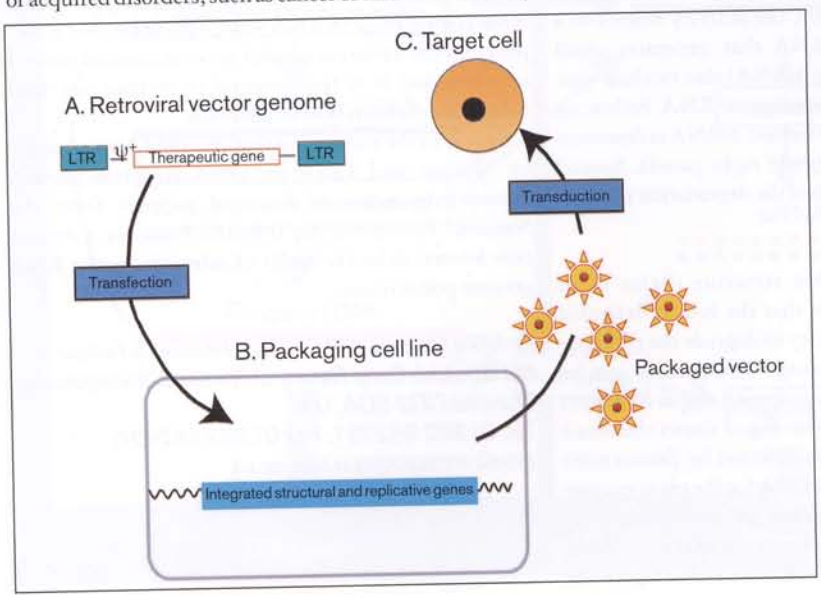
Virus	Advantages	Disadvantages
Murine retrovirus	Stably integrates Straightforward to produce	Can only transduce dividing cells Risk of insertional mutagenesis?
Adenovirus	Can transduce many cell types and incorporate large inserts	Immunogenicity Long-term expression difficulties
Adeno-associated virus	Can transduce many cell types Stably integrates	Can only accommodate small inserts Production difficulties
Herpes simplex virus	Can transduce many cell types and incorporate large inserts Stable retention in neurones	Immunogenic Long-term expression difficulties
Lentiviruses	Stably integrates into both dividing and non-dividing cells Efficient transduction of neurones	Difficult to produce Risk of insertional mutagenesis?

The basic principle of gene therapy

Following the identification and linkage of a specific gene to a particular disorder it should be possible to correct a gene defect by supplying a fully functional copy of the gene in question either directly *in vivo* or *ex vivo*. This strategy is relatively straightforward in the case of recessive single gene defects since insertion of a functional allele of a defective gene is sufficient to reverse a given phenotype. In the case of dominant gene defects or acquired disorders, such as cancer or infectious disease, the situation is more complex and it is often necessary to interfere with the expression of an 'abnormal' gene. Whether one is considering gene therapy of an inherited or acquired disorder the critical first step is efficient gene delivery to a particular cell or tissue type. Thereafter the particular attributes of a gene delivery system will vary depending on the disorder in question. For example in the case of cancer therapy it may be sufficient to induce high level expression of a 'suicide gene' to effectively kill a cancerous cell. In this scenario transient high level expression of a delivered gene is required. In contrast, many genetic abnormalities will require long-term, and in some cases regulatable expression of a therapeutic gene product.

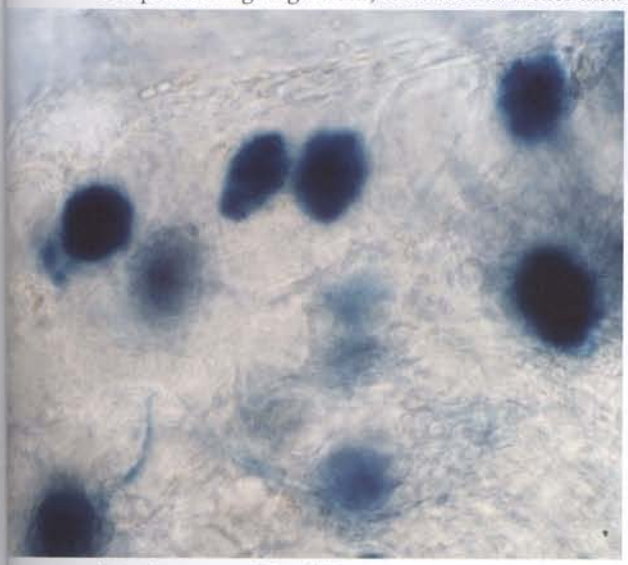
Methods of gene transfer

Delivery of nucleic acid to cells is not straightforward and the most efficient and reliable methodologies involve one of a number of replication-defective virus vectors, each with its own particular set of attributes (Table 1). At the moment viruses have the edge over non-viral, liposome-based or naked DNA delivery systems and advantage is being taken of the fact that viruses have had millions of years to evolve highly efficient mechanisms of cell entry and delivery of nucleic acids to mammalian cells. Of course before a virus can be used with gene therapy in mind it must be made replication-defective, such that it can efficiently transduce a recipient cell with new genetic material in the absence of virus replication



RIGHT:
Fig. 1. Basic principle of gene delivery using a retrovirus vector. (A) A therapeutic gene flanked by replication and packaging sequences is transfected into a mammalian cell line. (B) The helper or packaging cell line expresses structural genes and replication enzymes necessary to replicate and package the incoming virus genome. (C) The packaged vector constitutes a fully formed replication-defective virus, which can deliver or transduce the therapeutic gene into a target cell.
COURTESY S. EFSTATHIOU

or the expression of potentially toxic virus-encoded gene products. Perhaps the most widely utilized vector systems are based on simple murine retroviruses, which can be readily engineered to lack all virus-gene-encoded functions. These virus genes can be replaced by a therapeutic gene and, so long as the gene of interest is flanked by *cis*-acting packaging/replication sequences, virus particles can be generated in helper cell lines (Fig. 1). These helper cell lines provide virus replication enzymes and structural proteins *in trans* and facilitate the production of high titres of the vector in question. Viruses released from such helper cell lines merely constitute packages of nucleic acid, which are morphologically identical to wild-type virus and therefore retain normal infectivity. However, when delivered to non-complementing target cells, transduction rather than



infection ensues. Thus following entry to the cell, reverse transcription of the virus RNA to DNA is followed by stable integration into the host genome where transcription of the delivered gene can take place. The target cell is now stably transduced with foreign genetic material and there is no possibility of generating wild-type virus. Integration is particularly relevant when considering gene delivery to dividing cells and is a particularly useful feature of all retrovirus and adeno-associated virus vector systems. In contrast, the lack of integration as part of the normal life cycles of herpes simplex and adenoviruses would indicate that vectors based on these viruses are best suited to the delivery of genes to non-dividing cells and strategies of cancer immuno- or cytotoxic therapy.

The status of clinical trials

Clinical trials of therapeutic strategies based on gene therapy currently involve in the region of 3,500 patients worldwide with the majority of trials taking place in the USA and Europe. At present the focus is very heavily directed towards cancer therapy which accounts for almost 70 % of all patients with the remainder largely enrolled in trials concerned with single gene defects, infection and vascular disease. Since the majority of trials are in their early stages it is difficult to know just how successful they will be, although, with one or two notable exceptions, there have been few reports of undesirable side effects. A useful source of information regarding the current status of gene therapy and ongoing clinical trials can be located on the *J Gene Med* website (http://www.wiley.co.uk/genetherapy/).

The challenge ahead

The recent promising results obtained in the correction of the recessive X-linked Severe Combined Immunodeficiency Syndrome (SCID-X1) in humans using retrovirus-based vectors and the increasing success rate in the correction of a variety of both genetic and acquired disorders in animal model systems is a reason to be optimistic. Yet, as has been extensively publicized – things can go wrong. There has been one human death associated with the administration of an adenovirus-based vector and the development of leukaemia in a child treated for SCID-X1 is thought to be linked to insertional mutagenesis of the retroviral vector used in this gene therapy trial. There is clearly much to learn and at present many of the current methodologies for achieving effective gene transfer remain unpredictable. Improvements in the safety profile of viral delivery systems are necessary to reduce vector toxicity and immunogenicity. In the case of those vectors that mediate gene delivery by integration a greater understanding of the risks of insertional mutagenesis are required and methods of targeting the site of integration need to be explored. In addition to fully understanding and overcoming these safety issues, further advances towards the design of delivery systems which can target a given cell type and express a therapeutic gene product in a regulatable manner are necessary. Given the rate of progress in the fields of cellular and molecular biology one cannot help but feel that given time, effort and the necessary level of funding, gene therapy will come of age.

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LOWER LEFT:
Fig. 2. Herpes simplex virus (HSV)-mediated gene expression in sensory neurones. A recombinant HSV engineered to express the reporter gene β-galactosidase was used to establish a latent infection within sensory neurones. A sensory ganglion stained for β-galactosidase gene expression is shown. The 'transduced' cells, which express the delivered gene, are visualized as blue cells. The ability of HSV to establish life-long latency in neurones has stimulated interest in the development of this virus as a neuronal gene delivery vector.
COURTESY S. EFSTATHIOU

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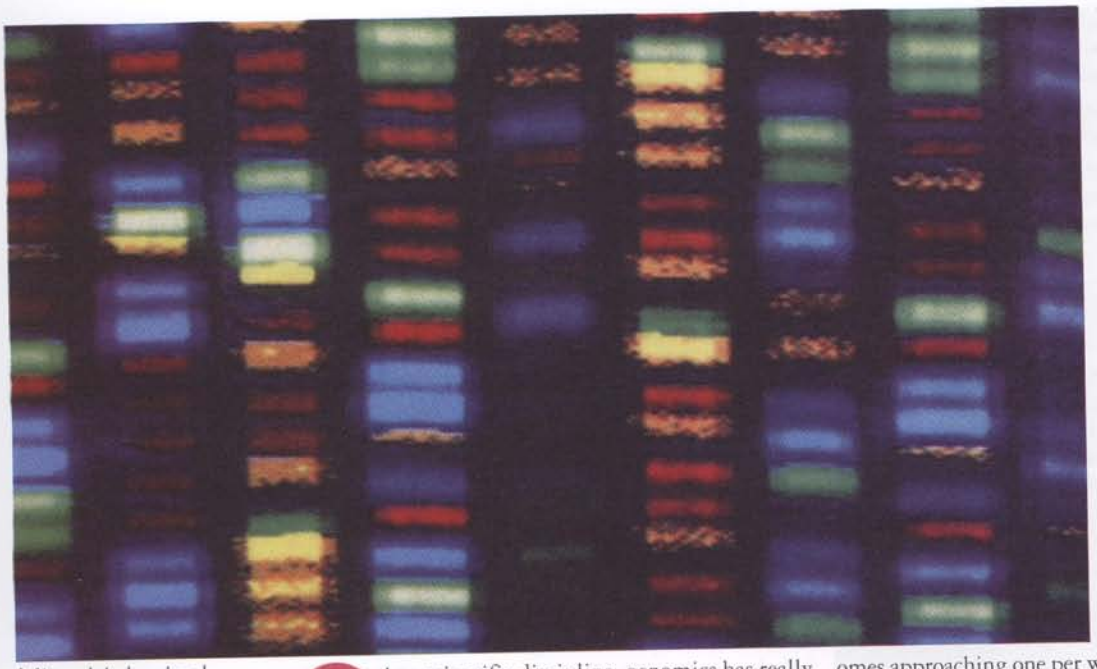
Come the revolution

Stephen Bentley



Microbiological research has been revolutionalized by the recent rapid progress in sequencing microbial genomes. Stephen Bentley explains how this came about and the exciting potential waiting to be realized.

As a scientific discipline, genomics has really burst onto the scene over recent years and caused a rapid revolution in biological research. It has brought full light into the cave where previously our torches could only illuminate discrete parts. Where before our knowledge was restricted to individual genes or clusters of genes representing a small fraction of the genome, for some species we now have the complete catalogue giving a much clearer holistic view. But what triggered the revolution?

Rapid acceleration

Back in 1977 Fred Sanger and his colleagues at the LMB in Cambridge got the ball rolling by working out the fundamental methodology for determining DNA sequences. At that time they determined the 5,386 nucleotide sequence of the bacteriophage ϕX174 – the first complete genome. These were the crucial first steps, but to put things in perspective, using the 1977 'state-of-the-art' DNA sequencing technology it would have taken around a million years to finish the human genome! A decade later, automation of Sanger's technique had brought that figure down to around a thousand years. In the early 1990s huge financial investment was dedicated to elucidating the human genome. The sheer weight of this investment accelerated the advancement of sequencing technology to a point where completing the human genome within 10 years became feasible.

ABOVE:
Colour-coded dyes mean that we no longer need to use radioactive samples in DNA sequencing.
COURTESY WELLCOME TRUST SANGER INSTITUTE

Less is more

So it seems that the genomic revolution was triggered by the quest to sequence the human genome. Now, humans have 24 chromosomes composed of about 3,000 million DNA bases. Prokaryotes, on the other hand, typically have a single chromosome with only a few million bases. This size difference means that many of the large sequencing centres round the world are now easily capable of producing all the raw DNA sequence for a bacterial genome project in a single day! Obviously the full sequencing capacity is not going to be dedicated to microbes alone, but it has meant the opening of a floodgate for microbiology with the current rate of publications on newly sequenced prokaryote genomes approaching one per week. It could be argued that although the human genome project triggered the genomic revolution, microbiology has thus far been the major beneficiary.

The first complete genome sequence of a free-living organism (so discounting bacteriophage and viruses) was that of the Gram-negative pathogen *Haemophilus influenzae* in 1995. By the end of 2002 there were 87 bacterial and 16 archaeal complete genomes in the public databases compared to only 8 eukaryotes. There has been a marked rate of increase since the turn of the millennium. A handful of prokaryotic genomes were completed each year from 1995 to 1999, then in 2000 there were 16, rising to 26 in 2001 and 39 last year. At present there are

around 350 ongoing prokaryotic genome projects. These are remarkable figures and of course don't include work being done in secret by commercial ventures.

The portfolio of genome projects has been dominated by bacterial pathogens. The threat posed by acquisition of antibiotic resistances by known disease agents, emergence of new pathogens and the re-emergence of long forgotten foes has created some urgency in the need to further understand these organisms with the ultimate aim of protecting against infectious disease. Bacterial genomics has accordingly targeted the agents of major diseases such as tuberculosis (*Mycobacterium tuberculosis*), meningitis (*Neisseria meningitidis*), cholera (*Vibrio cholerae*), syphilis (*Treponema palidum*), leprosy (*Mycobacterium leprae*) and plague (*Yersinia pestis*) as well as various causes of gastrointestinal, respiratory, urinogenital and skin infections. Human pathogens currently account for around 65 % of the completed prokaryotic genome projects. The remainder is something of a mixed bag, including model organisms, extremophiles, symbionts, plant pathogens and species of environmental, agricultural and biotechnological interest. An important emerging feature of the microbial genome portfolio is the number of closely related genomes. Multiple members of the same genus and even species appear on the list, with the *Enterobacteriaceae* particularly well represented. Being able to compare a genome with that of a close relative invariably provides extra information that cannot be derived from analysis of each genome in isolation.

Reaping the rewards

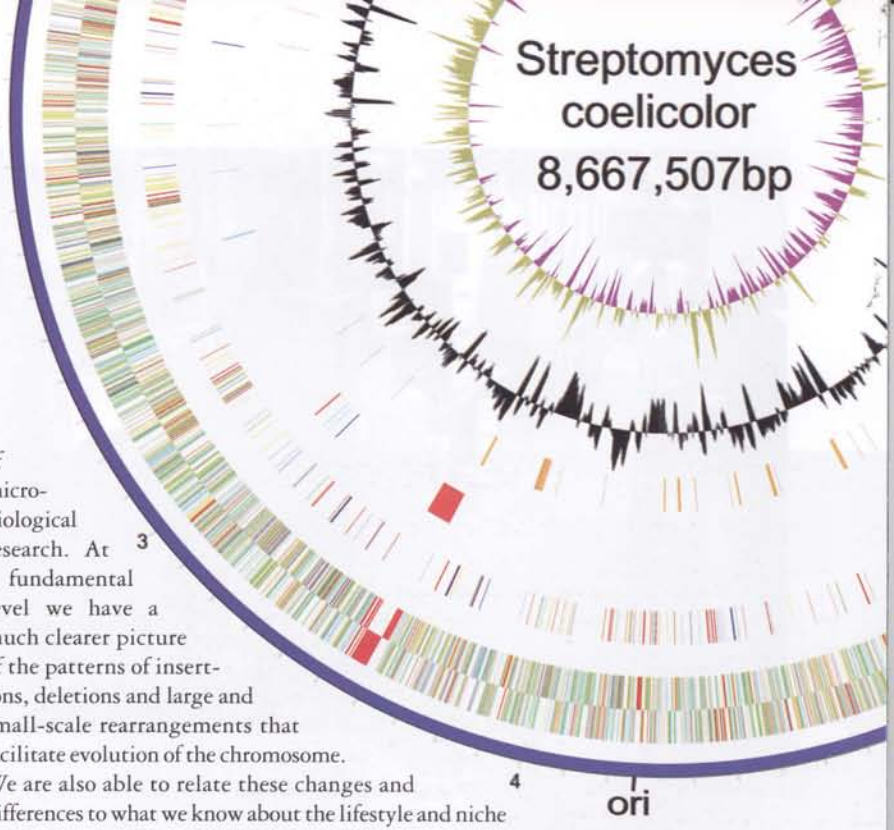
Superficially, genome sequencing may seem like nothing more than genetic stamp collecting, but already analysis of complete genomes has provided new knowledge and given new perspectives to virtually every area of microbiological research. At a fundamental level we have a much clearer picture of the patterns of insertions, deletions and large and small-scale rearrangements that facilitate evolution of the chromosome. We are also able to relate these changes and differences to what we know about the lifestyle and niche of the organism to see how environmental pressures are shaping the genome.

For pathogens we are now able to view their full arsenal of pathogenicity determinants, and by comparing genomes can begin to explain the differing pathogenic processes. By better understanding such processes we hope to find new ways to control the spread and progression of disease. Genomics has also proved to be invaluable in vaccine development. An excellent example of exploitation of genome information has been the identification of promising new candidates for meningitis vaccines from the full complement of likely surface proteins in the genome of *Neisseria meningitidis*. Comparative genomics is also being used in the development of new detection tools crucial to early diagnosis and effective treatment of diseases such as salmonellosis.

The study of biochemistry has been hugely enriched by the sheer number and variety of new enzyme sequences. Fine detail of enzyme function can be elucidated by alignment of similar protein sequences and biochemically adept organisms, such as *Streptomyces coelicolor*, *Pseudomonas aeruginosa* and *Mesorhizobium loti* have shown us the myriad of possible pathways in which they can be employed. Then there are the extremophile enzymes whose sequences may lead us to the secrets of biochemistry at its physical limits. And let's not forget the gene products for which we cannot predict a function – the hypotheticals. These represent uncharted waters, the genotype for which we have no phenotype. Some of these are unique to a particular organism and may be what defines them. Others are found in virtually all genomes and so must represent important biological functions of which we are currently ignorant.

Come join the revolution

So what next? Almost as soon as genome sequencing became feasible people saw the huge potential for exploitation of whole-genome data using other established technologies. Thus genomics begat post-genomics. As well as the rapidly advancing technologies for analysis of transcription (transcriptomics) and



ABOVE:
Circular representation of the *Streptomyces coelicolor* genome.
COURTESY DR S. BENTLEY, WELLCOME TRUST SANGER INSTITUTE

FAR LEFT:
Fred Sanger studying one of his early sequencing gels, Department of Biochemistry, University of Cambridge, 1958.
COURTESY DR F. SANGER

LEFT:
By the 1980's Fred Sanger and his team had refined the DNA sequencing protocols and they were in use in labs worldwide.
COURTESY DR F. SANGER

ABOVE:
Early automatic sequencing machines brought great increases in data output capacity but slab gels still had to be poured and samples were loaded manually.

RIGHT:
State of the art. Samples are now loaded automatically by a small robot arm and separated in fine capillaries (so no need for pouring slab gels).

BELOW:
The Wellcome Trust Sanger Institute is dedicated to genome research with well over a hundred sequencing machines running 24 hours a day, 365 days a year.

PHOTOS COURTESY R. SUMMERS, WELLCOME TRUST SANGER INSTITUTE

protein expression (proteomics) on a global scale, there are many projects aimed at producing mutants for every gene in the genome. These techniques promise exciting prospects for dissection of cellular functions but this is not to say genomics is dead. Although the current genome portfolio is impressive we have only scratched the surface. Where do we stop? A representative genome from every genus or maybe one for each species? And then there is the added value of comparing closely related genomes. So far, each completed genome has brought new knowledge and we can continue to broaden that knowledge. Ultimately, though, the cost must be justified by the benefit, so it's good news that sequencing costs have been falling ever since large-scale projects began. Costs may fall even further if researchers manage to perfect nanopore technology where nucleotide sequences are 'read' as the DNA string passes through a hole in a membrane. There is also talk of amplifying whole chromosomes by a rolling-circle method, bypassing the need to culture the organism and opening up the non-cultureables to genomic analysis.

Genomics is set to infiltrate and hopefully benefit every aspect of microbiological research. As with all new technologies it has a certain level of jargon which may put people off, so it is important that we learn to be comfortable with the language of genomics and familiarize ourselves with the techniques for exploiting the resource. To this end the SGM has teamed up with the Sanger Institute to run courses on a DNA sequence viewing and analysis tool called Artemis (see page 19). This is an excellent starting point for any beginner and is guaranteed to whet the appetite, so why not come and join the revolution?

●*Dr Stephen Bentley studied the molecular genetics of cell division in Escherichia coli and virulence determinants in Erwinia caratovora before discovering genomics as a Senior Computer Biologist at the Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambs CB10 1SA, UK.*
email sdb@sanger.ac.uk

Further reading

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Holden, M., Bentley, S., Sebaihia, M., Thomson, N., Cerdano-Terraga, A. & Parkhill, J. (2003). The magnificent seven. *Trends Microbiol* 11, 12–14. (*This is a monthly column where we try to summarize the salient features of recently published prokaryotic genomes.*)

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Artemis: the Goddess of the Hunt

Nick Thomson

2002 saw the start of a new venture for the SGM and The Pathogen Sequencing Unit (PSU) of the Wellcome Trust Sanger Institute. This partnership was forged by the observation that the public DNA sequence databases have continued to expand, almost exponentially year on year. Luckily for us this trend does not look like changing and the future ahead for whole-genome sequencing appears rosy, with >350 bacterial genome projects currently in progress (see Stephen Bentley's article on p. 16). However, there is an obvious truth that comes with this volume of sequencing. Without appropriate and accessible *in silico* tools with which to meld this mass of information into a more readily interpreted form, we will only ever glance at the surface and never dig deeper into the wealth of data just waiting to be exploited within these public sequence storehouses.

To keep pace with this rate of data generation we need to embrace tools to facilitate whole-genome analysis, as well as utilize software that allows us to compare and extract information from multiple genomes. This will require a move away from trusted software such as GCG and the web-based cut and paste genre of analysis packages, to include more specialized tools.

In an attempt to address this issue we came up with a plan for a series of five one-day regional workshops which would build on our experience of whole-genome analysis. The emphasis was placed on squeezing in as much 'hands-on' experience of our genome analysis tools as was possible in one day. An enthusiastic team of demonstrators (Fig. 1) backed up the practical work, with expertise in bacterial and eukaryotic genomics (ranging from Gram-negative and -positive bugs across to malaria and on to humans and mice), as well as in relevant aspects of computing. In addition to extolling the virtues of whole-genome sequence, we also felt it important to cover some of the possible pitfalls of using these data, and so we also fitted in several short talks to deal with, for example, the differences between draft and finished sequence, automated versus manual annotation and so on.

Artemis and the Artemis Comparison Tool (ACT)

The computer programs featured in these workshops, Artemis and ACT, were both developed 'in-house' by Kim Rutherford and represent the core software for the analysis of both prokaryotic and eukaryotic genomes within the PSU. Artemis is a genome viewer program, which allows the user to get away from the relatively faceless EMBL- and GenBank-style database files, or reams of printed sequence marked with a highlighter pen (based on my previous experiences), and view the genome in a graphical and highly interactive format (Fig. 2). Context is probably the most important facet of whole-genome analysis and Artemis is designed to present multiple lines of evidence within a genomic context. This manifests itself as the ability to zoom in to look for fine DNA motifs as well as being able to zoom out and bring into view operons, several kilobases of the genome or in fact to view the entire genome in one screen. It is also possible to perform quite sophisticated analysis and store the output within the 'Artemis environment' to be accessed later. This is a real bonus for people, like myself, with a paper to desk weight ratio approaching 1 : 1.

Artemis has also proven to be an invaluable 'hands-on' tool for teaching concepts such as gene structure and organization at all levels:

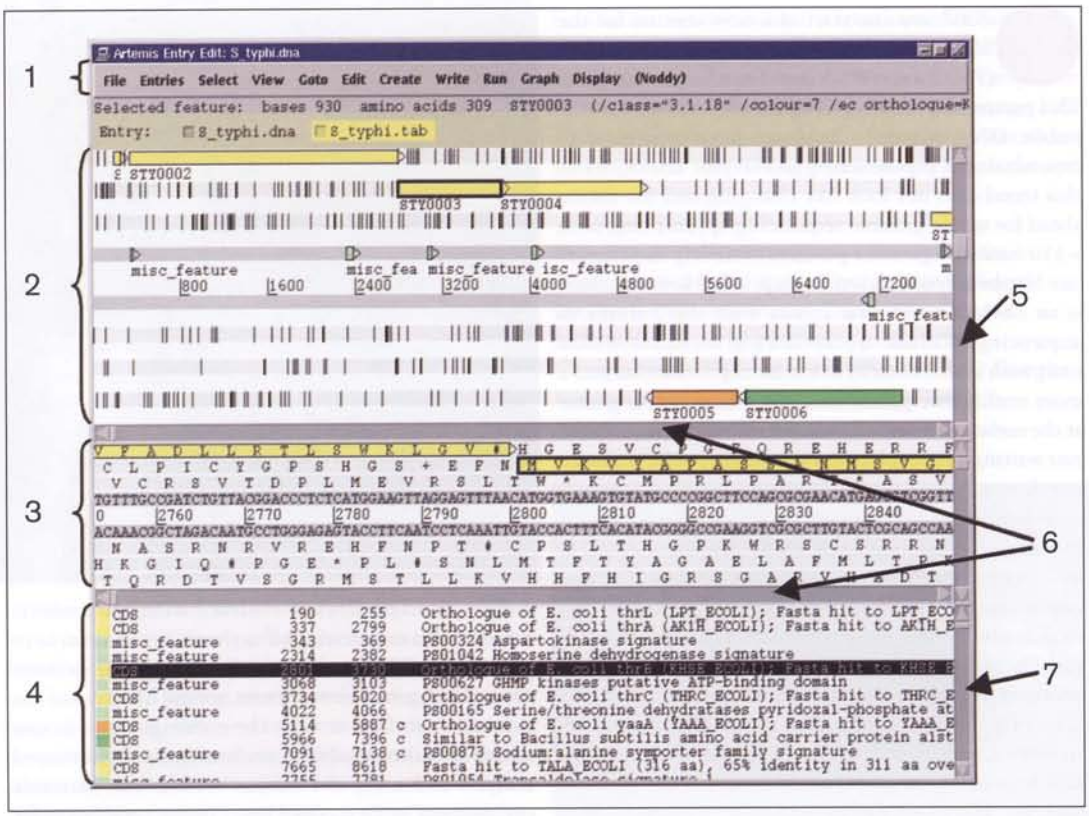
> *'Since the workshop we have incorporated Artemis and ACT into both undergraduate and postgraduate teaching. These programs provide excellent tools for active learning in terms of the investigation of microbial genomes, a field of self-evident importance though not necessarily easy to teach. The visual appeal and dynamic nature of the user interface go beyond what can be readily achieved on the Web.'*
>
> *Dr Peter Miller (University of Liverpool)*

The comparative genomic tool, ACT, is essentially composed of three layers or windows (Fig. 3), depending on the number of genomes. The top and bottom layers are essentially mini Artemis windows (with their inherited functionality), showing the linear representations of the genomes with their associated features. If the upper and lower layers represent the bread, then the middle window is the meat in the sandwich, showing red blocks which span the middle layer and link conserved regions (Fig. 3). Consequently, if you were comparing two identical genome sequences you would see a solid red block extending over the length of the two sequences in the middle layer. If insertions were present in either of

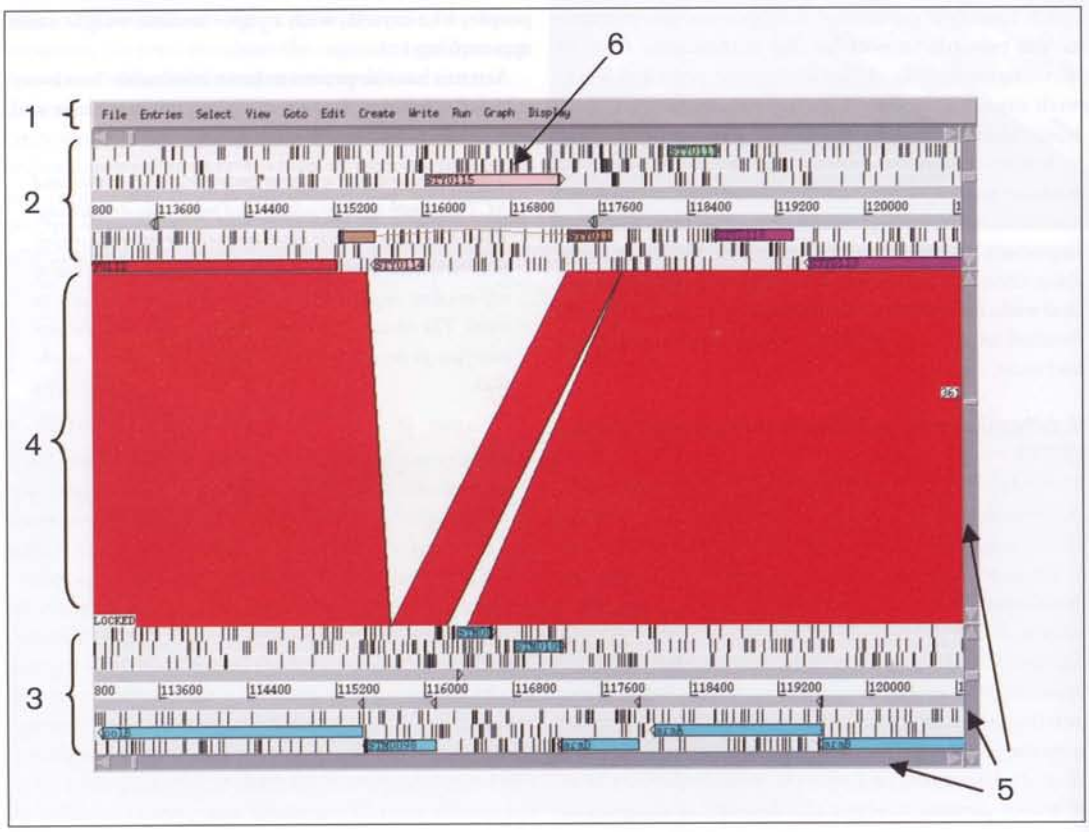
Recently the SGM and the Wellcome Trust Sanger Institute have held some very successful bioinformatics workshops. Nick Thomson, one of the tutors, explains what went on.

ABOVE:
Fig. 1. The PSU demonstrators and the hosts of the Bristol workshop. *From left to right:* Nick Thomson, Kim Rutherford, Mohammed Sebaihia, Howard Jenkinson (SGM organizing representative), Matthew Holden, Julian Parkhill and Matthew Avison (local host). Those members of the PSU not pictured include Arnab Pain, Rhian Gwilliams, Ana Cerdêno-Tarraga.
COURTESY N. THOMSON

RIGHT:
Fig. 2. Artemis. (1) Drop-down menus. (2) Main Sequence View panel showing two central grey lines representing the forward (top) and reverse (bottom) DNA strands. Above and below the DNA strands are the three forward and three reverse reading frames. Stop codons are marked as black vertical bars. Genes and other features (e.g. Pfam and Prosite matches) are displayed as coloured boxes. (3) This is a zoomed-in view of the main panel (2) showing individual nucleotides and amino acids. (4) List of the various features in the order that they occur on the DNA as shown in the other windows. (5–7) Sliders for scrolling and zooming in/out.
COURTESY N. THOMSON



RIGHT:
Fig. 3. ACT. (1) Drop-down menus applying to both sequence windows. (2 and 3) Artemis style view panels showing the sequences being compared. (4) Comparison layer displaying regions of conservation as red blocks. (5) Sliders that allow you to align and move along the genomes and optimize the view. (6) The insertion of an IS element in the upper sequence, disrupts a gene (brown) and appears as a break in the red comparison layer (4).
COURTESY N. THOMSON



the genomes, they would show up as breaks between the solid red conserved regions. Data used to draw these red blocks and link conserved regions is generated by running pairwise BLASTN, or TBLASTX, comparisons of the genomes (details of how this is done can be obtained from the ACT user manual: http://www.sanger.ac.uk/Software/ACT/manual/).

ACT may be simple in concept, but it has proved to be very powerful in application. This is most evident when comparing the growing number of genomes from closely related organisms. In this instance it is relatively straightforward to identify regions within each genome that have undergone insertion/deletion, frameshifts, inversions and translocation events. Regions such as these can be very telling when attempting to understand how organisms have evolved and what genomic strategy has been employed (e.g. reductionist or expansionist) for an organism to adapt to a new lifestyle.

Artemis and ACT can be freely downloaded from our web pages in several versions designed to run on different platforms (http://www.sanger.ac.uk/Software/Artemis/ or http://www.sanger.ac.uk/Software/ACT/). Like the organisms themselves, Artemis and ACT are undergoing continual evolution. These changes, some of which are a direct result of feedback from SGM workshops, filter quickly into the publicly available versions. Hence there is always a developmental as well as a 'tried-and-tested' version available on our website.

The running order for the workshops

The workshops themselves were split in two halves: the morning session began with an overview of whole-genome sequencing, followed by a practical session using Artemis. The afternoon followed a similar format but focused on comparative genomics. All the exercises were laid out in a comprehensive manual, written especially for these workshops, backed up by constant supervision (Fig. 4). The exercises were designed to not only demonstrate the functionality of the software, but also to highlight some of the more idiosyncratic and fascinating aspects of the bacterial genomes featured.

'Because of its multi-layered approach: seminar, learn-as-you-try, and one-to-one problem solving, the workshop inspired and educated newcomers and experienced users, alike.'

Dr Matthew Avison (University of Bristol)

Each of the guided exercises was written and championed by a demonstrator involved in the original analysis of that genome. Because many of the people on the courses were experts working on many of the genomes featured we were also able to pass on the baton to them and have some great discussions, undoubtedly one of the major highlights for us.

We realized that we could not make people 'power users' of Artemis and ACT in a day, but we could hopefully generate enough enthusiasm to overcome that initial activation energy that dogs us all when getting to grips with new software, video recorders, HSE rules..., etc., and we appear to have had success in this endeavour:

'Since the workshop we have used Artemis and ACT for the annotation of the Bacillus anthracis genome and its comparison with the genomes of other members of the genus Bacillus. In particular, we have used ACT for gross topological comparisons of gene organization and to generate comparative gene organization maps in relation to genes of specific interest.'

Professor Colin Harwood (University of Newcastle)

ABOVE:
Fig. 4. The exercises detailed in the workshop manual were backed up with a high level of supervision from a team of demonstrators involved in the original analysis of genomes featured.
COURTESY N. THOMSON

Location, location, location

Our task to find suitable locations for these workshops was not as simple as we initially anticipated. Whilst it is easy to find Unix-based computers in most UK universities, it is very difficult to find enough of them in the same room for a large-scale computer-based workshop. In the end we found some fantastic facilities at Newcastle, Bristol and Liverpool. We also played two home fixtures back here in Cambridge. We were all made very welcome by the event hosts (Colin Harwood, Anil Wipat, Matthew Avison and Peter Miller) who put in huge amounts of time making their events run very smoothly. As for the participants, they came from all strata of academia as well as some from industry. In addition to the local attendees some travelled great distances to get to these events. At the Cambridge workshop people flew in from Aberdeen and The Netherlands.

The title: 'Artemis: the Goddess of the Hunt'

Finally, to explain the title: Artemis, a character from Greek mythology, was hunter-in-chief to the gods. We felt this was an appropriate name for the genome analysis software, and consequently a banner for these workshops, because it can be used to search out the trends and minutiae hidden within a veritable forest of data. So come on, join in, the hunt is on!

Dr Nick Thomson is a Senior Computer Biologist at the the Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambs CB10 1SA, UK

If you want any more information on the SGM workshops see **www.sgm.ac.uk** or email us at **sgm@sanger.ac.uk**

More bioinformatics workshops will take place in 2003. See p. 35 for details.

The impact on public health of the 19th century anti-vaccination movement

Colin R. Howard

Today smallpox vaccination is an issue of public concern due to the threat of bioterrorism. Yet a different aspect of this topic was a cause of controversy more than a century ago, as Colin Howard describes.

Public confidence in vaccination is being eroded in the face of mounting criticism from lay people as well as a vocal minority of medical opinion. A current controversy centres on the safety of measles vaccine and MMR. Yet vaccination is among the most effective health care measures available to modern medicine. Despite the scientific evidence in its favour, scepticism as to its value lies deep within the British psyche. I believe the origins of doubt can be traced back to the early 1800s when Jenner's smallpox vaccine began to be widely used.

Late 18th century concepts of infectious disease

Towards the end of the 18th century medical explanations of disease tended towards the holistic, the result of a disturbance to the normal health-maintaining balance between the individual, the climate and environment. Smallpox was the exception. Physicians already understood the specific passage of contagious material by inoculation, the deliberate introduction of smallpox into the skin, as a means of protecting the susceptible against the ravages of disease, although many doctors opposed it. Market forces came into play, however, as the well-to-do insisted on protection for themselves and their families. The situation was quite different amongst ordinary people; as inoculation was usually carried out by amateurs and itinerant practitioners, and they could not afford the 2–3 week inoculation period away from work and subsequent long convalescence.

In Jenner's time, there was a lull in the arrival of new pathogens into Britain. Smallpox, however, erupted into epidemics at intervals. In the towns and cities it was essentially a childhood affliction, whereas in the countryside the risk groups were adolescents and adults and so the socio-economic impact of deaths from epidemics was much greater. Inoculation therefore gained greater acceptance in rural areas than in the rapidly expanding conurbations where smallpox was but one affliction to which an infant was exposed. It was not practised widely in towns until around 1790.

Jenner's discovery and medical practice

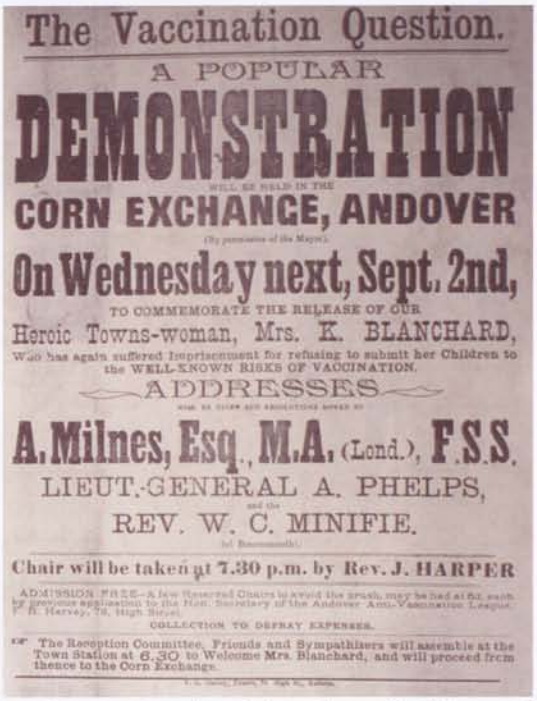
The medical profession was not prepared for the Jennerian approach. Unsympathetic to the contagion theory, it was difficult for the authorities of the day to accept, let alone understand, the significance of his findings. The implication was that, not only was the disease of smallpox specifically the result of contact with an infectious agent, but that a contagion of cattle was sufficiently similar to confer protection in humans. In the absence of knowledge of germ theory, the initial reaction of the educated and public alike was that transfer of animal matter may be necessary but was definitely undesirable. This is epitomized in Gillray's famous cartoon of the period.

The early 19th century saw a progressive decline in smallpox despite apathy among parents who often trusted in providence. The anti-vaccinationists (dubbed the 'anti-vacks' by Jenner) were isolated voices and failed to organize themselves into a coherent movement. In contrast, influential supporters of the Jennerian approach had come together to sign a supporting declaration as early as 1800. The public was content to accept their judgement, at least whilst the disease was under control. The Napoleonic Wars also undoubtedly diverted public attention away from any contention over vaccination.

In February 1806 the *Medical Observer* appeared, providing an effective mouthpiece for early anti-vaccinators such as Moseley and Birch. Jenner fully understood the power of the media, but he never used it to defend his work. Although worried, he was reluctant to get embroiled in publishing claim and counter-claim. In contrast, the anti-vaccination movement was quick to realize the value of the press. (Little has changed save that the power of the Victorian pamphlet has been replaced by the website. Entering the term 'vaccine' into any search engine invariably produces more links to anti-vaccination literature than to information as to the benefits of immunization!)

The *Medical Observer* gave publicity to the increasing number of smallpox cases presumed to be the result of vaccine failure and by 1808 pressure had mounted for a more rational explanation of these. Unfortunately for Jenner, the tools of epidemiology we use today were unavailable for the critical analysis of anecdotal cases of vaccine failure. The anti-vaccinationists capitalized

RIGHT:
A coloured print of a cartoon, thought to be by James Gillray, 1802, showing people developing bovine characteristics immediately after vaccination. The vaccinator may be Edward Jenner. Although this cartoon appears to be anti-vaccination, it may read as a satire on claims made by the opponents of vaccination.
COURTESY THE JENNER MUSEUM, BERKELEY, GLOUCESTERSHIRE


The Vaccination Question.

A POPULAR

DEMONSTRATION

WILL BE HELD IN THE

CORN EXCHANGE, ANDOVER

(By permission of the Mayor).

On Wednesday next, Sept. 2nd,

TO COMMEMORATE THE RELEASE OF OUR

Heroic Towns-woman, Mrs. K. BLANCHARD,

Who has again suffered Imprisonment for refusing to submit her Children to the WELL-KNOWN RISKS OF VACCINATION.

ADDRESSES

WILL BE GIVEN AND RESOLUTIONS MOVED BY

A. Milnes, Esq., M.A. (Lond.), F.S.S.

LIEUT.-GENERAL A. PHELPS,

and the

REV. W. C. MINIFIE.

(of Bournemouth).

Chair will be taken at 7.30 p.m. by Rev. J. HARPER

ADMISSION FREE—A few Reserved Chairs to avoid the crush, may be had at 6d. each by previous application to the Hon. Secretary of the Andover Anti-Vaccination League, F. R. Harvey, 78, High Street.

COLLECTION TO DEFRAY EXPENSES.

☞ The Reception Committee, Friends and Sympathisers will assemble at the Town Station at 6.30 to Welcome Mrs. Blanchard, and will proceed from thence to the Corn Exchange.

on this, arguing that if the safety and efficiency of vaccination with cowpox could not be proved, then it was best to stick with inoculation of smallpox virus, the drawbacks of which were well recognized.

Undoubtedly Jenner's unstinting belief that vaccination gave longevity of protection, combined with the total lack of quality control and standardization of the lymph used for vaccination, accounted for much of the confusion. A further disadvantage was that he diluted the lymph to ensure safety; this led to the need for a further dose in early adulthood. The supply of calf lymph was a major problem, even to the extent that Jenner had to resort to the inoculation of his own son with smallpox.

The introduction of compulsory vaccination

The founding of the National Vaccination Establishment in 1808 quickly led to the collapse of the voluntary organizations that promoted the benefits of vaccination. The next decades saw increasing distrust in vaccination with a significant number of failures and the increasing use of lymph of dubious origin. Attitudes to public health only changed with the arrival of cholera from Asia around 1830. Suddenly the country was in the grip of a disease, the nature of which had hitherto not been experienced. Smallpox and other infectious diseases remained endemic, but did not focus the public mind so vividly as cholera. The state was motivated to become actively involved with public health. Ultimately this led to compulsory legislation for smallpox vaccination, but it was not immediate. The government first introduced an Act in 1840 which enabled anyone to be vaccinated at public expense.

The demand for compulsory vaccination against smallpox came from the medical fraternity led by Dr Edward Seaton. Importantly, he convinced parliamentarians that vaccination was universally regarded as infallible. The Bill became law in August 1853, making vaccination compulsory for all infants under the age of 3 months.

This Act signalled the start of organized opposition to compulsory vaccination. John Gibbs, who is credited with initiating the nationwide movement, wrote that the Act '*invades the liberty of the subject, and the sanctity of the home ...(it) denies him possession of reason; outrages some of the finest feelings of the human heart...*' Such appeals to those in Government were to no avail. However, the Act was difficult to enforce and in 1867 it became a criminal offence for a parent to continually deny a child vaccination up to the age of 14 years.

The rise of the anti-vaccination movement

A powerful anti-vaccination lobby sprang up to defend the sanctity of the human body and to press the individual's right to chance their luck of becoming infected. Opposition was particularly well organized in Leicester, where the first imprisonment under the 1853 Act is recorded; William Johnson served 14 days after refusing to allow his child to be vaccinated. Supporters rewarded his intransigence with a silver watch. Other martyrs to the cause included Ann Supple, who received 25 summonses for refusing to have her child vaccinated, preferring to face gaol rather than '*be party to the poisoning of her baby*'.

Faith in vaccination was further dented with another extensive smallpox outbreak in 1870 affecting some 44,000 people. In 1871 another Act was passed which attempted to strengthen previous legislation by making it mandatory for local Poor Law Boards of Guardians to appoint vaccination officers. Fines of up to £1/5s were introduced for parents who refused to have their offspring vaccinated. The anti-vaccination protesters based their objections partly on individual freedom, partly on the political resistance to interference in the sanctity of the home and family, and on the more rational grounds that there were alternative means to limit and control smallpox. These distinctions were to become increasingly blurred, however, as the passion of the debate increased.

Leicester remained the epicentre of the anti-vaccination movement. Between 1869 and 1884, 61 people were imprisoned for non-compliance with the Smallpox Acts. On 23 March 1885 some 100,000 defaulters processed from the Temperance Hall to the Market Place where copies of the Vaccination Acts were burnt in full view of the Mayor and Chief Constable of Leicester. The cause, according to *The Times*, was '*...a widespread belief that death and disease have resulted from the operation of vaccination...*" The precipitating event was the failure of the Local Government Board to endorse the 'Leicester Method', which, in the eyes of the Board of Guardians, was proving so successful in controlling smallpox in the city. It called for strict quarantine of cases and all their contacts, coupled with a programme of disinfecting the infected person's dwelling and burning their bedding and clothing. It is likely, however, that this strategy owed as much to medical expediency as it did to pressure from local opinion leaders.

The Leicester Anti-Vaccination League came to have an influence out of all proportion to its size, largely thanks to the activities of J.T. Biggs, a local sanitation engineer. Local politicians and the MP for Leicester were all to come under his influence. Peter Taylor, the local MP, was eventually to become the President of the

LEFT:
A poster advertising a demonstration in Andover Town Hall in support of a Mrs Blanchard on her release from imprisonment for refusing to allow her children to be vaccinated (date unknown).
COURTESY THE JENNER MUSEUM, BERKELEY, GLOUCESTERSHIRE

London Society for the Abolition of Compulsory Vaccination, thus giving the Leicester perspective a national outlet. Although it is possible that the effect nationally of the anti-vaccination movement has been overestimated, we should note that it was highly organized and articulate, using the press and public debate to good effect.

Unquestionably, compulsory vaccination had failed to prevent the smallpox epidemics of 1857–59, 1863–65 and 1870–72. The anti-vaccinators' case became at times personal and critical of events that occurred many decades previously. Doctors were accused of spreading the disease in the 18th century by inoculation and Jenner remained the butt of criticism nearly 90 years after he published his inquiry in 1798. A further point focuses on the almost fetish preoccupation of the Victorian public health movement with cleanliness and sanitation, although improvements in water supply, sanitation and public works did not really take hold until the latter part of the century. Even so it was clear that the decline in incidence of smallpox, which began with the introduction of inoculation in the 18th century and which accelerated once vaccination was available, must have been specifically due to this active prevention because there was no corresponding reduction in other filth-borne diseases.

Evidence from 1880 onwards confirmed that protection induced by primary vaccination in childhood did not necessarily last into adulthood. Thus Jenner's contention that lifelong immunity followed vaccination was wrong. In Sheffield Borough Hospital during the 1887–88 outbreak none of the nurses and attendants who had been re-vaccinated got smallpox, whereas 6 cases ensued in those who had received only a single dose as a child. The outbreak still clearly showed the benefits to those who had been vaccinated but once and were subsequently exposed to the disease years later.

Anti-vaccinators began to argue that other diseases could be transmitted, such as infantile syphilis, but such fallacies were unnecessary as the movement achieved its immediate goal of decompulsion with the Vaccination Act of 1898. This introduced a 'conscience clause' whereby parents could opt out of vaccination by applying to local magistrates for an exemption certificate. This was not a soft option, however, as the lack of a vaccination certificate excluded Londoners from council housing and elsewhere non-vaccination meant that life insurance and employment were that much harder to come by.

In Leicester, home of resistance to vaccination, the decline was so steep that in 1890 only 3 % of babies were vaccinated in their first year. Nationally, the trend was little better. The number of vaccinated infants declined, from 96 % in England and Wales in 1875 to 78 % in 1889. This drop reflects at first sight parental apathy in the face of a disease that was steadily declining coupled with the Victorian strength of feeling that government should advise, persuade and provide rather than coerce both parents and local government into compliance.

With the tension over compulsion defused, the end of the 19th century saw a more rational and structured approach to application of vaccination policies. In 1903 Elizabeth Garrett Anderson wrote in *The Times* that the evidence strongly supported the '*protective power of vaccination*'. Experience during the London 1902 outbreak led to the inescapable necessity of re-vaccination at school age. Interestingly, Anderson promoted the concept of a more targeted approach to control, with rapid and effective isolation of index cases followed by rigorous re-vaccination of contacts, a central feature of the 'Leicester Method' which had evolved in the seat of the anti-vaccination movement.

This approach was used in 1968 in Nigeria and eventually proved to be the turning point in the WHO smallpox eradication programme, faced as it was with diminishing supplies of vaccine in West Africa. Vaccination became limited only to those persons who had contact with infected individuals, the victims being kept in strict isolation. This policy of surveillance and containment gradually became accepted universally from 1973 onwards, even to the extent of predominating over mass vaccination. It contributed significantly to the conquering of the disease some 180 years after Jenner's original discovery and has much to recommend it for the control of other infectious diseases.

The lessons from history

The application of any discovery is often fraught with public misconception, mistrust of scientific opinion, inadequate planning, and a failure to identify weaknesses in methodology. Despite the brilliance of Jenner's seminal observations, his publications were anecdotal and lacked conviction. His flawed insistence that immunity was lifelong did not help acceptance of his discovery. A centralized faith in public engineering as a reaction to cholera combined with difficulties in enforcing the vaccination acts turned opinion against vaccination, fuelled by the ascendancy of the press. The control of infectious disease requires great awareness of environmental and social issues, as recent outbreaks of infections in the national livestock industry have shown only too painfully. It took Victorian Britain over a century to grasp Jenner's original concept of vaccination and apply this in a socially acceptable manner. It teaches us much that is relevant today.

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Further reading

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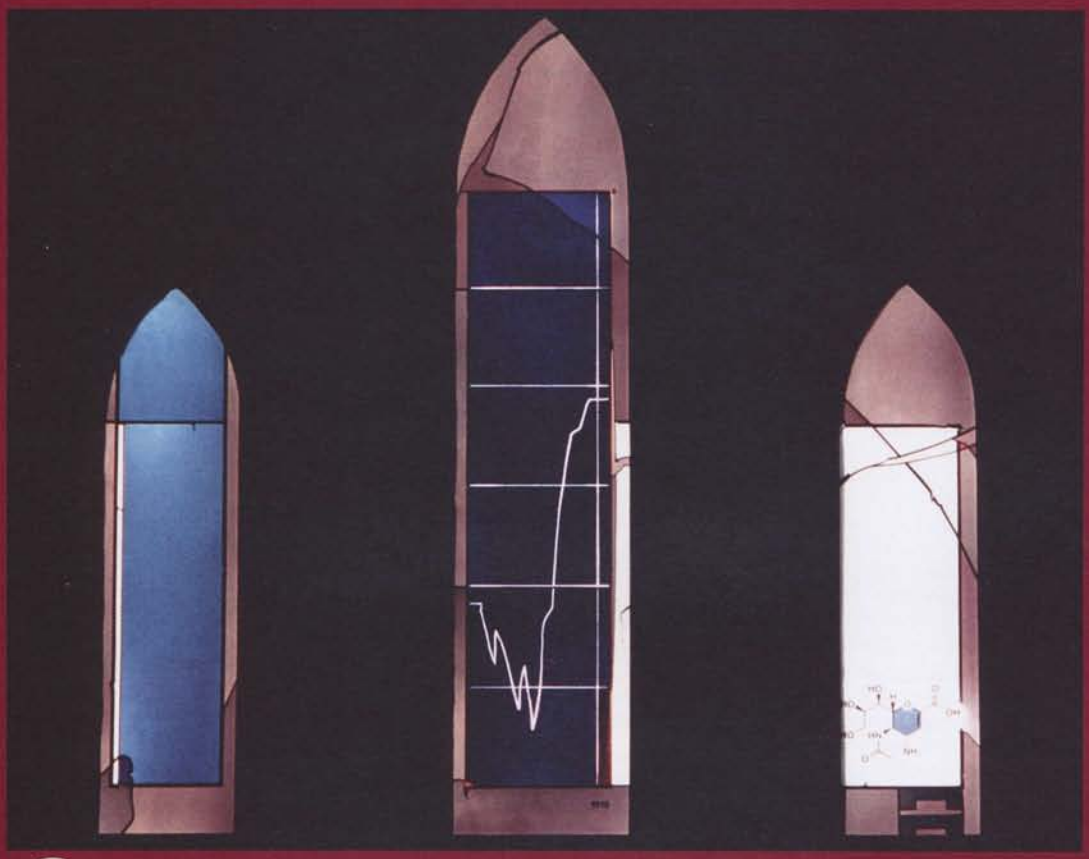
The influenza pandemic window – heroes and heroines of 1918–1919

John Oxford



LEFT:
The influenza pandemic window – heroes and heroines of 1918–1919.
COURTESY J. OXFORD

This window is the first memorial to those who died of influenza in the pandemic immediately after the Great War. No country escaped. In the UK, Germany and France there were more than 250,000 deaths in each country. 20 million Indians died and in some remote communities 80% of the population perished. It is estimated that there were 50 million deaths worldwide.

Every town and village in Britain has a memorial to the soldiers and sailors who died fighting, but this window offers the first remembrance to the casualties of the virus. The influenza pandemic has largely gone unrecorded. The window is intended not only to remedy this neglect but to suggest hope for the future. Nurses, soldiers, pathologists and scientists researching the disease died. There were also many acts of individual heroism as families and friends helped each other, while putting their own lives at risk. Perhaps as many conscious acts of heroism were carried out in ordinary homes as in the European battlefields of the preceding 4 years. No medals were issued at the time to those heroes and heroines. This window is a tribute to them.

The impact of the influenza virus has been incalculable and the virus remains one of the greatest killer diseases of mankind. Even in recent years the Royal London Hospital has been overwhelmed with influenza cases in the casualty and medical wards.

International glass artist Johannes Schreiter, who was commissioned by Professor John Oxford's virology group to create the window, has used blue to suggest the practical and medical help given by people during the pandemic and purple, which is the richly evocative colour of suffering, for both the sick and those who nursed them and subsequently died. Of this particular colour Schreiter has said '*I like it so much – there is something mystical and inwardly directed about the colour purple*'. The white area of glass in the right hand window acts as a 'healing field' and suggests the sense of optimism supported by the certainty that molecular science has the capacity to prevent these disasters. Careful research and public health planning for a new pandemic with full use of vaccines and anti-influenza drugs would certainly prevent a wave of deaths similar to that experienced in 1918.

The 1918 window was inaugurated at 11.00 am on 11 November (Armistice Day) by the Bishop of Birmingham, Dr John Sentamu, at the Medical School Library in Whitechapel. The library was formerly the church of St Augustine with St Philip. A memorial book has been opened and relatives of influenza victims are already sending in memoirs and photographs.

● *Professor John Oxford, The Queen Mary School of Medicine, London (email info@retroscreen.com)*

Society News

October Council Meeting

New Members of Council

● The President welcomed recently elected members, **Professors Peter Andrew** (Leicester), **Jeff Cole** (Birmingham), **Jeff Errington** (Oxford) and **Geoff Smith** (Oxford) to their first Council meeting. Members should note that there is no truth in the rumour that being called Jeff/Geoff is now a prerequisite for election to Council!

Education Officer

● Council learned with considerable regret that **Liz Sockett** had asked to step down from her post after 4 years to devote more time to her expanding research group. She will be greatly missed and her contributions to the promotion of the Society in the field of education have been innovative and highly successful. We wish her well in the future.

Journals

● Council approved the appointment of the Editor-in-Chief of *Journal of Medical Microbiology*, **Ian Poxton**, as a member of Council in that capacity and also the appointment of **Geoffrey Smith** as Editor-in-Chief of *Journal of General Virology* to succeed Stuart Siddell, who retired at the end of 2002. Stuart was thanked by Professor Hopwood on behalf of Council for his excellent work over recent years. A picture and biography of Professor Smith appeared in the November 2002 issue of *Microbiology Today* (p. 198).

Biosciences Federation

● Council spent a great deal of time discussing the details of the latest steps towards the setting up of a single body (to be called the Biosciences Federation) to represent UK Biology to government and other bodies. An interim committee of the proposed Federation had prepared draft Memorandum and Articles of Association and Council agreed in principle to join the Federation as a subscriber, subject to certain reservations to be resolved in due course. Since that time these issues have been resolved and Professor Geoff Smith has now signed the Memorandum and Articles on behalf of the Society, so that SGM is now one of the founding members (see p. 2).

New Prize

● Council has approved the award of a new prize to replace the *Promega Young Life Scientist of the Year* award, which Promega has discontinued in its present form. Details of the new Prize Award, which will be for postgraduates and early postdocs within 2 years of completing their PhD, appear in Gradline on p. 37.

Microbiology Awareness Campaign

● Council heard with pleasure about a recent initiative undertaken by the Professional Affairs Officer and other members of Council to raise awareness of microbiology and the exploratory meeting of Scottish microbiologists that had taken place at the Royal Society of Edinburgh. Council approved taking this initiative forward.

● *Alan Vivian, General Secretary*

Council News

Nominations for Members of Council

Two members, **Professor C.R. Howard** and **Professor D.J. Kelly** retire from Council in September 2003. Due to the appointment of **Professor G.L. Smith** to Editor-in-Chief of JGV, a further vacancy has arisen. Nominations are invited from Ordinary Members to fill these three vacancies. 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, Professor Alan Vivian, c/o SGM Headquarters to arrive no later than **30 April 2003**.

News of Members

The Society notes with regret the deaths of **Dr S.D. Cave** (Member since 1975), **Professor R.H. Cumming** (Member since 1976), **Dr A.C.R. Dean** (Member since 1955), **Dr D.C. Graham** (Member since 1964), **Dr G.A. Morrison** (Member since 1950), **Professor M. Moser** (Member since 1971, **Professor D. Ribbons** (Member since 1963), **Professor H. Veldkamp** (Member since 1957) and **Dr A.E. Wakefield** (Member since 1971).

An obituary of Professor Veldkamp, who was an Honorary Member of the Society, will appear in the next issue of *Microbiology Today*.

Staff News

In December we were pleased to welcome **Natalie Wilder** as a Staff Editor on *Journal of Medical Microbiology* and *International Journal of Systematic and Evolutionary Microbiology*. She will work alongside Managing Editor Aidan Parte. Natalie comes to the SGM from UCL where she has just completed her studies for a PhD.

SGM Website News

Abstracts on-line

Abstract submission is now available on-line (www.sgm.ac.uk/meetings). This will streamline the processing of abstracts for papers and posters at society meetings in the office, as well as making it easier for contributors to submit in the correct format. However, it will not affect deadlines, and potential contributors for the September 2003 meeting at UMIST are urged to submit their abstracts well in advance of the deadline of **9 May**. See the Meetings page for full details (p. 34).

www.biocareers.org.uk

A separate new website to promote careers and training in microbiology has been compiled by Jane Westwell. This is profiled in Gradline on p. 36. It can also be accessed through the SGM website.

Calling All Virologists!

The Learning and Teaching Support Network Centre for Bioscience has appointed a Discipline Consultant in Virology to disseminate good teaching practice within the discipline. If you are involved in teaching virology at any level Brian Martin would be interested to hear from you. The aim is to establish a network of colleagues who are interested in teaching-related issues and enhancing good practice.

If you would find such a network of value or interest to you or if you would merely like the opportunity to network with colleagues, do please e-mail him at **b.a.b.martin@bham.ac.uk**

Microbiology Technician Survey

As part of a general review, Council wishes to assess whether Society benefits meet the requirements of all microbiologists. They would particularly like to encourage microbiology technicians in universities and hospitals to become members, but first need to find out their views on the SGM. To this end, a questionnaire and information sheets have been distributed to departmental contacts.

If there is a technician in your department who can help us, please inform Jane Westwell (j.westwell@sgm.ac.uk) who will send them a questionnaire.

The Technicians' Meetings Taster Grant scheme is also continuing in 2003 (see p. 29 for full details). Please do promote this opportunity to sample an SGM meeting.

SGM and SfAM join forces

Representatives from the two societies have met twice now to discuss ways of collaborating to promote microbiology in the UK. The outcome has been extremely positive. In addition to ensuring that information is exchanged about relevant consultation papers and microbiological issues of political significance, an exciting new scheme is to be launched this year to sponsor joint regional one-day meetings. Prizes of £150 will also be awarded at the meetings for the best offered paper or poster by a microbiologist in the early stages of their career.

ABOVE: *From left to right:* Lynne Boshier & Margaret Patterson (SfAM), Janet Hurst, Hilary Lappin-Scott & Ron Fraser (SGM) and Hilary Dodson (SGM & SfAM) at their recent meeting at Marlborough House.

SfAM/SGM Microbiology in the Regions grants

Grants will be available to support two different kinds of one-day meetings.

Special Topic Meetings will focus on a particular field of microbiology and bring together local scientists working on or interested in this topic. They will normally take the form of a short symposium, with keynote speakers, offered papers and a poster session. Microbiologists in the early stages of their careers – postgraduate students, first postdocs and new lecturers – will be encouraged to make short oral presentations. Each meeting will be organized jointly by at least one local member of each society.

Local Microbiology Group Meetings will provide a forum for local microbiologists of all disciplines, irrespective of their employer, including postgraduate students. The format of events will be at the discretion of the organizers, but might take the form of keynote presentations followed by a workshop or roundtable. The meetings should aim to foster the exchange of information and encourage collaboration within the local area. Each event must be organized by at least one member of the sponsoring societies.

Grants of up to £2,000 are available and will cover invited speakers' expenses, room hire, etc. Applications will be judged by an award panel from the two societies.

The full rules of the scheme and an application form are available on the SfAM and SGM websites:

www.sfam.org.uk *or* **www.sgm.ac.uk**

SGM Membership Certificate Offer

Council is pleased to announce the availability of membership certificates for SGM members. These attractive certificates are suitable for framing. The cost is a nominal £5. For details and an application form, see the membership section of the SGM website.

Results of Industrial Member survey

As part of a general review of Society activities, SGM Council decided to assess whether the benefits and services meet the requirements of members based in industry. Last autumn staff in the External Relations Office sent out survey forms to all those members known to be working in the commercial sector and were delighted when a good proportion of the forms were returned. We have analysed the survey data and present a brief summary of the findings here.

Of the 128 members who responded to the survey over half described themselves as working in research or product development. SGM members also come from a wide range of employers with a significant number (41 %) of respondents employed in the pharmaceutical or medical industry. The next largest employment sector was biotechnology (24 %) with the remaining respondents mainly employed in food/drink, cosmetics, environmental, veterinary medicine and diagnostics companies. About half of the respondents joined as student members and the majority have been a member for between 5 and 20 years, although there are a few stalwarts with more than 30 years of Society membership.

We were pleased to see that *Microbiology Today* is read and enjoyed by 94 % of the respondents who do their bit to promote microbiology by passing the magazine on to co-workers. 57 % of respondents go to SGM meetings and do so mainly to attend symposia in their field and keep up to date with current research. Of those who do not attend meetings, a significant number cited lack of time as a reason. Legislation, new techniques and updating reviews on topical research themes were the most popular suggestions for future sessions at meetings.

We asked for feedback on SGM Corporate Membership and the comments have been very useful, resulting in a review of this membership category and the benefits it brings.

We are very grateful to those members who took the time to complete the survey form and we are pleased that the majority of them view their membership of the SGM positively. The results of the survey will be most helpful to us in the continued review of membership benefits and services.

On a final note, 60 % of survey respondents expressed an interest in the formation of a new group for industry-based members. New Groups are started in response to requests and this can only happen if members become actively involved. So, over to you...

■ ***Jane Westwell, External Relations Office***

SGM Prizes and Lectures

Colworth Prize Lecture

The 2003 Colworth Prize Lecture has been awarded to **Professor Tom Humphrey**, University of Bristol, in recognition of his distinguished contributions to the understanding of food-borne pathogens. The title of his lecture, which will take place at the Society meeting at University of Edinburgh on 9 April 2003, is *Oh for an 'ome of my own: Salmonella and Campylobacter as zoonotic pathogens.*

In March 2001 Tom was appointed to the Chair of Food Safety in the Department of Clinical Veterinary Science, University of Bristol. For 20 years before that the Public Health Laboratory Service (PHLS) employed him and for the last 5 years he was head of the PHLS Food Microbiology Research Unit. His initial training was as a meat technologist and he worked for the Animal Health Trust on enteric infections in food animals before reading for a BSc at the Hatfield Polytechnic and studying for a PhD at the University of East Anglia. His research interests include the epidemiology of *Salmonella* and *Campylobacter* spp. in poultry meat and egg production, bacterial stress responses and their impact on survival and virulence and sub-lethal injury in *Campylobacter* spp. His group has also undertaken work on the handling of high-risk foods in domestic kitchens and the persistence of *Salmonella*, *Campylobacter* and *Escherichia coli* following food preparation.

Fleming Lecture

The 2003 Fleming Lecture has been awarded to **Professor Chris Boshoff**, University College London in recognition of his groundbreaking work on viral oncology. The title of his lecture, which will be delivered at the Society meeting at University of Edinburgh on 10 April 2003, is *AIDS-associated cancer and KSHV/HHV-8.*

Chris trained in medical oncology at the Royal Free, Royal London and Royal Marsden Hospitals between 1993 and 1998 and did a PhD in viral oncology at the Institute of Cancer Research in the laboratories of Robin Weiss (1995–1998). He was the 1998 Dozor visiting Professor to Ben Gurion University, Israel, and was awarded the 1998 Glaxo Wellcome Prize Fellowship. From 1999 Chris was a Senior Lecturer at University College London (UCL) and in 2001 was appointed Professor of Cancer Medicine at UCL.

Chris' clinical research is focused on new molecular therapeutics for solid malignancies and his laboratory research focuses on mechanisms of AIDS-related cancer: in particular the sero-and molecular epidemiology of Kaposi's sarcoma-associated herpesvirus (KSHV) and functions of KSHV latent proteins. Chris was involved in some of the largest international serological surveys to describe the global seroprevalence of KSHV and he demonstrated mother-to-child transmission, characterized cell types in KSHV-related cancers infected by the virus, described functions of KSHV proteins like the viral MIPs, latent nuclear and membrane antigens and defined viral epitopes (with Frances Gotch, Imperial College) that elicit cellular and humoral immune responses. Chris also established large cohorts of KSHV infected individuals in London for prospective immunological studies.

Hot Topic Lecture

In the light of current concerns about the risks from bioterrorism **Professor Don Henderson** has accepted the Society's invitation to deliver a special lecture at the Edinburgh meeting on 8 April 2003. The title of his lecture is *Threat of bioterrorism – real or imagined?*

Don Henderson is Johns Hopkins University Distinguished Service Professor, and founding director (1998) of the Hopkins Center for Civilian Biodefense Strategies. He rejoined the Hopkins faculty

in June 1995 after 5 years of federal government service – initially as science adviser in the Executive Office of the President and later as Deputy Assistant Secretary in the Department of Health and Human Services. From 1977 to 1990 he was Dean of the Faculty of the School of Public Health. He directed the WHO global smallpox eradication campaign (1966–1977). He is a recipient of the presidential Medal of Freedom, the nation's highest civilian honor, the National Medal of Science, and the Japan Prize, as well as 14 honorary degrees and medals and awards from 15 different countries. Professor Henderson is a graduate of Oberlin College, the University of Rochester School of Medicine, and the John Hopkins School of Hygiene and Public Health.

Fred Griffith Review Lecture

The Fred Griffith Lecture has been awarded to **Professor Stan Cohen**, University of California, in recognition of his pioneering work on recombinant DNA and his many discoveries in bacterial and plasmid genetics. The prize lecture will be delivered at the Society meeting at UMIST in September 2003. Further details of the talk and a biography of Professor Cohen will appear in a future issue of *Microbiology Today.*

Peter Wildy Prize for Microbiology Education

The Peter Wildy Prize has been awarded to **Dr Dick Killington**, University of Leeds in recognition of his career-long contributions to microbiology education, especially virology. The prize lecture will be delivered at the Society meeting at UMIST in September 2003. Further details of the talk and a biography of Dr Killington will appear in a future issue of *Microbiology Today.*

SGM Local Representatives

Would you like to help the Society?

SGM Local Representatives in departments and organizations aid membership recruitment and ensure that news of all our meetings, publications, grants schemes and activities is widely publicized to their colleagues.

A Local Rep's 'kit' is provided, including membership application forms and information about the Society, and you will be sent updates, posters, etc., at intervals to display. It will only take a little of your time.

Why not volunteer today?

For further information, or to check if there is already a local rep in your department, contact Janet Hurst (Email: j.hurst@sgm.ac.uk)

Grants

President's Fund

The President's Fund offers financial support to younger members of the Society for the following:

1. Travelling to present a paper or a poster on a microbiological topic at a scientific meeting.
2. Attending a short course (up to two weeks).
3. Making a short research visit.

Larger awards are available for the short research visits and there are separate application forms for these.

1 & 2 Smaller Awards

Maximum grants are £125 for attendance at meetings or institutions/attending an approved course in the country of residence, £200 for travel to another European country and £300 for travel outside Europe.

3 Larger Awards

Up to £2,000 is available for making a short research visit of up to 2 months duration. The host institution may be overseas or in the applicant's country of residence.

All applicants must be resident and registered for a PhD or in a first postdoctoral position, in a country in the European Union. Only one application to the President's Fund may be made during the term of a postgraduate studentship or first postdoctoral position. The full rules of the scheme are published on the SGM website, from which application forms may be downloaded.

Postgraduate Student Meetings Grants

Postgraduate Student Members of the Society currently resident in the UK or another European Union country are eligible for a grant to cover the costs of accommodation and travel in attending one of the following SGM meetings:

University of Edinburgh, April 2003

UMIST, Manchester, September 2003

and any other Society Group or Branch meeting in 2003.

An application form giving full details of the scheme was sent to each European Student Member with their subscription invoice in October 2002, but a copy may be downloaded from the SGM website. Applications should be submitted well in advance of a meeting if members wish to ensure that their grant is received before making a booking.

Details of all Society grant schemes are available on the SGM website at **www.sgm.ac.uk**. Application forms for most schemes can be downloaded. Click on the 'Grants & Funding' button for details.

Any enquiries should be made to the Grants Office, SGM, Marlborough House, Basingstoke Road, Spencers Wood, Reading RG7 1AG (Tel: +44 (0)118 988 1821; Fax: +44 (0)118 988 5656; email: grants@sgm.ac.uk).

International Development Fund Awards 2002

The following awards have been made from the Society's International Development Fund. The Fund exists to provide training courses, publications and other assistance to microbiologists in developing countries. The rules for the 2003 Fund will be published in the May issue of *Microbiology Today*.

Dr Daniel O. Sordelli, representing the IUMS Fellowship Committee – US$6,000 each year for 3 years to support UNESCO-IUMS-SGM short-term fellowships.

Dr Peter N. Green, Chairman of Endangered Culture Collections Committee of WFCC – up to £4,390 for interim assistance to safeguard the culture collection housed at the Uzbekistan Academy of Sciences in Tashkent.

Professor Ralph Kirby, Department of Biochemistry & Microbiology, Rhodes University, South Africa – up to £4,500 to develop molecular microbial ecology in Nepal.

Dr R.I. Aminov, Gut Microbiology & Immunology Division, The Rowett Research Institute, Aberdeen – up to £4,800 to establish a genotyping centre in Armenia to diagnose and monitor multi-drug resistant *Salmonella* infections.

Dr Bambos Charalambous, **Professor S.H. Gillespie** & **Dr T.D. McHugh**, Dept of Medical Microbiology, Royal Free & University College Medical School, London – up to £6,000 to establish a technical co-ordinator for processing respiratory samples at the new reference and training centre for respiratory bacteriology in Tanzania.

Technician Meeting Taster Grants

- Are you a microbiology technician or an NHS-funded MLSO?
- Are you interested in attending an SGM scientific conference?
- Is lack of funding stopping you attending?

If so, this SGM scheme could be of interest.

The Society wishes to offer support to technical staff working in microbiology laboratories in universities, colleges, hospitals/PHLS, research institutes, etc., who are interested in joining the SGM and attending its meetings but consider the costs to be prohibitive. For a short period we are offering an opportunity for eligible technicians to sample an SGM meeting with expenses of up to £200 being met by the Society. The grant will cover travel, bed and breakfast for an agreed number of nights in university accommodation and a daily subsistence allowance. Non-member registration fees will be waived. Priority will be given to those who have not had the opportunity to attend a scientific meeting in the last 5 years.

In return, funded delegates will give their opinion of the meeting and make suggestions for benefits and membership services that SGM might offer to technical staff through completion of a detailed questionnaire.

Watanabe Book Fund

A generous donation to the Society by Professor T. Watanabe of Japan has enabled the Society to set up a fund to make annual awards for the benefit of members in developing countries. This is distinct from our own International Development Fund.

Members of the Society who are permanently resident in a developing country may apply. The purpose of the fund is to enable members involved in higher education and/or research to acquire for their libraries books or possibly journals relating to microbiology. Applications should include:

1. A list of the publications required together with an estimate of their cost (the total cost for any one application should not exceed £300 sterling).
2. A letter from the Head Librarian of the organization certifying the need for the books and the address to which the books should be sent, a statement on where the books will be kept and an outline of the loan arrangements for members of the organization.
3. A description of the member's organization and its involvement in microbiology, the number of staff and students and details of the nature of any courses in microbiology provided by the organization, i.e. BSc Microbiology, technical training, etc.
4. A *curriculum vitae* of the principal applicant.

None of these items (1–4 inclusive) should exceed one side of A4 paper each.

Applications (two copies) should be sent to the Grants Office at SGM HQ. The closing date is **3 October 2003.**

FEMS Congress, Ljubljana, Slovenia

29 June–3 July 2003

www.fems-microbiology.org/congress2003.htm

SGM Congress Grants

Grants to provide a contribution towards registration fees, accommodation and travel to the congress are available to eligible members of the Society. Full details of the rules and application forms are posted on the SGM website at **www.sgm.ac.uk**. The fund is aimed, in the first instance, at SGM members who are ineligible for a Royal Society Conference Grant, i.e. postgraduate students, research assistants, etc. (see **www.royalsoc.ac.uk** for details of their scheme). Ordinary Members applying to the SGM fund will have to provide evidence that their application to the Royal Society has been unsuccessful.

Any enquiries should be addressed to the SGM Grants Office (Tel. 0118 988 1821; email grants@sgm.ac.uk).

The closing date for applications is **28 March 2003**.

Vacation Studentships 2003

Awards are available by competition to enable undergraduates (in their penultimate year) to work on microbiological research projects during the summer vacation. The studentships provide support at a rate of £150 per week for up to 8 weeks; limited funding for consumables is also available. Applications are invited from members on behalf of named students. The full rules were published in the November 2002 issue of *Microbiology Today* (p. 199). The closing date for applications is **28 February 2003**.

UNESCO-IUMS-SGM Fellowships

The International Union of Microbiological Societies (IUMS), is a worldwide Federation of national and international societies and other organizations having a common interest in microbiological sciences. The Microbial Resources Centres (Mircens) is an international network of academic and research institutes spreading biotechnological and microbiological benefits to especially the developing countries. The SGM is making a separate contribution to this programme from its International Development Fund. The UNESCO-IUMS-SGM short-term fellowship is a co-operative scheme between the listed organizations to provide an opportunity to young microbiologists from any developing country to pursue, or to complete, a part of an ongoing research programme in a laboratory in a newly industrialized or developed country and/or to acquire theoretical or technical knowledge in their particular area of research. Microbiologists in developing countries aggressively pursuing research, often reach a facility *cul de sac* where research plans cannot be accomplished for want of materials, equipment or facilities and/or where essential theoretical or experimental knowledge is not available. The UNESCO-IUMS-SGM short-term fellowship is designed to ease these problems for deserving microbiologists from developing countries to enable them to overcome their research bottlenecks, and to strengthen the bonds of interregional scientific co-operation.

Fellowships can be awarded for (i) a research period of up to 3 months in a developed country and (ii) attendance at a workshop or specialized scientific meeting.

(i) The applicant from a developing country should be a permanent employee in the country of residence, must have adequate work experience, must have completed at least 5 years of postdoctoral training in any of the microbiological sciences and must provide specific evidence in the form of a proposal about the work which is intended to be performed at the host laboratory. Preference will be given to young women scientists and to scientists from Africa. Currently five fellowships are available every year of which two should be served in laboratories in the UK.

The award will be up to US$4,000 for travel and subsistence (room & board) to support the awardee for a maximum period of 3 months. Funds for salary and medical insurance will not be provided. Coverage for life and accident or health insurance is the personal and sole responsibility of the individual or the host organization.

(ii) The applicant from a developing country should be a graduate student in the final year of their PhD or a young postdoctoral fellow with less than 5 years postdoctoral training and intending to participate in a research workshop or specialized scientific meeting directly related to his or her current research activities. Specific evidence of these current research interests should be supplied in the form of progress reports, authorized by the head of the research institute and/or recent scientific publications. The award will be up to US$2,000 and cover the direct costs of travel to and accommodation at the meeting or workshop and the registration fee.

Applications (4 copies) must be submitted in English and should include a nominating letter from the head of the organization in which the applicant is working; the applicant's *curriculum vitae*; a letter of invitation or acceptance from the host organization describing facility support for the applicant or from the organizers of the workshop or scientific meeting; and two supporting letters listing the applicant's achievements.

Applications must be submitted to Prof. Dr Daniel O. Sordelli, Member at Large, IUMS, Departmento de Microbiologia, Facultad de Medicina, Universidad de Buenos Aires, Paraguay 2155-Piso 12, (1121) Buenos Aires, Argentina (Fax +54 11 4964 2554; email sordelli@fmed.uba.ar).

Deadlines

Research fellowships: **1 July 2003**
Meetings fellowships: **3 months before event**

2002 Fellowships

UNESCO-IUMS-Mircens-SGM fellowships were awarded to the following in 2002.

Dr R. Jeya Shakila, Department of Fish Processing Technology, Tamil Nadu Veterinary and Animal Sciences University, India

Dr Supawachee Ingsriswang, National Centre of Genetic Engineering and Biotechnology, Pathumthni, Thailand

Dr Christian Magni, Instituto de Biological Molecular y Celular de Rosario, Rosario University, Argentina

Dr Heba Rashed, Clinical Pathology Department, Assiut, Egypt

Dr G.S.N. Reddy, Centre for Cellular and Molecular Biology, Hyderabad, India.

FEMS Fellowship & Visiting Scientist Grants

For full details of these awards and how to apply, please visit the FEMS website: **www.fems-microbiology.org**. The deadline for applications is **15 June 2003**.

Nobel Prize Reception

ABOVE:
Left: Ian Gibson, MP, listens to the speech by Nobel Laureate Tim Hunt, assisted by his daughter! *Right*: Paul Nurse, Nobel Laureate, expounds on his prize as Ian Gibson, MP, looks on.

ALL PHOTOS RON FRASER, SGM

Winning a Nobel Prize must be just about as good an excuse as any for a party. The Prize for Physiology or Medicine for 2001 was awarded to two UK scientists, Paul Nurse and Tim Hunt, together with Lee Hartwell, USA. Paul and Tim are members of a number of learned societies, including variously the SGM, Biochemical Society, Genetics Society, British Society for Cell Biology and British Society for Developmental Biology. These five societies combined to organize a reception in the Terrace Pavilion of the House of Commons, on 8 October 2002, to celebrate the awards. Paul and Tim, together with some of their present and former colleagues, were joined by almost 200 representatives of the societies, parliamentarians and the scientific 'establishment'. The evening was hosted by Ian Gibson MP, Chairman of the influential House of Commons Select Committee on Science and Technology.

As befitted an informal occasion, the speeches were short but excellent. Ian spoke about the ongoing need to promote the qualities and importance of UK science. Paul said he would limit himself to three sentences, but admitted they were long ones! They included recognition of the unique contribution of learned societies to the cultural environment. Tim spoke of the importance of recognizing the unexpected in scientific discovery. He linked this with the challenging questions often asked by children about the world around them, carrying one of the sources of these questions (his daughter) as he spoke. Linda Partridge of the Genetics Society responded on behalf of the Presidents/Chairs of the five societies and congratulated Paul and Tim on their behalf.

It takes a long time to set up events like this, finding time in a number of busy diaries, and at a heavily booked venue. So the reception took place some time after the announcement of the 2001 prizes. But by serendipity, it occurred just the day after the announcement of the award of the Nobel Prize for Physiology or Medicine for 2002 to two other UK scientists, Sydney Brenner and John Sulston (together with Robert Horwitz, USA). Looks like an excuse for another party...

●*Ron Fraser, Executive Secretary*

ABOVE:
From left to right: Hilary Lappin-Scott, SGM Council, SfAM President Peter Silley and Alan Vivian, SGM General Secretary.

RIGHT:
Genetics Society President Linda Partridge welcomes the guests alongside Ian Gibson, MP.

LEFT TOP:
SGM Staff Jane Westwell, Janet Hurst and Ron Fraser with Chris Skidmore of the Biochemical Society (second from right).

LEFT BOTTOM:
From left to right: Alan Vivian, SGM, Geoffrey Schild, SGM Professional Affairs Officer, Sir William Stewart, Sir David Hopwood, SGM, Sir Paul Nurse, Hilary Lappin-Scott, SGM, and a rare sighting of SGM Council Member Dave Kelly wearing a tie!

Elections 2003 to Group Committees

A number of members of Group Committees retire in September 2003 at the end of their terms of office. Nominations are now required to fill the vacancies arising. Where the number of nominations to a Group Committee exceeds the number of vacancies, there will be an election by postal ballot. The current members of each Group Committee and number of vacancies are listed opposite. In making nominations, members are particularly asked to bear in mind the desirability of a breadth of scientific interest on each committee. Nominations, including up to five words describing the general area of interest of the nominee, should be sent to reach the appropriate Group Convener **no later than 22 April 2003** (contact details on p. 45).

(C) Convener
(CR) Council Representative
*Retiring 2003

Cells & Cell Surfaces (3 Vacancies)

C.D. O'Connor (C) (Univ. Southampton)	Stress adaptation, proteomics
J.I. Armstrong* (Univ. Sussex)	Yeast membrane trafficking, signal transduction
D.A. Devine (Univ. Leeds)	Antimicrobial peptides, anaerobes, stress
I. Henderson (Univ. Birmingham)	Protein secretion, autotransporter proteins
N.J. High* (Univ. Manchester)	LPS genetics and phase variation
B. Kenny (Univ. Bristol)	*Escherichia coli* pathogenesis, cellular microbiology
R. McNab* (GlaxoSmithKline, Weybridge)	Bacterial surfaces, adhesion
D.G.E. Smith (Univ. Edinburgh)	Adhesin-receptor interactions, intracellular bacteria, toxins
P.S. Handley (CR) (Univ. Manchester)	

Clinical Microbiology (2 Vacancies)

S.H. Gillespie (C) (Royal Free Hospital, London)	Tuberculosis, pneumococcal infections, antibiotic resistance
D. Ala'Aldeen (Univ. Nottingham)	Bacterial infections: pathogenesis and immunity
K.B. Bamford (Imperial College, London)	*Helicobacter*, chronic infection, host response
A.R.M. Coates* (St George's Hospital, London)	Tuberculosis, chaperonins, bacterial dormancy, novel pathogens
C.G. Gemmell (Univ. Glasgow)	Methicillin-resistant *Staphylococcus*, host–bacteria interactions
P. Hawkey (Univ. Leeds)	Mycobacteria, antibiotic resistance, molecular epidemiology
T.L. Pitt* (CPHL Colindale)	Nosocomial, respiratory and tropical infections, cystic fibrosis
B.G. Spratt (Imperial College, London)	Molecular epidemiology, bacterial population genetics, *Neisseria*
I.R. Poxton (CR) (Univ. Edinburgh)	

Clinical Virology (4 Vacancies)

T.G. Wreghitt (C) (Addenbrooke's Hospital, Cambridge)	Transplantation
S. Cameron* (Regional Virus Laboratory, Glasgow)	Hepatitis, HIV, clinical virology
B. Cohen* (CPHL Colindale)	Diagnostics, viral rashes, saliva testing
F. Irwin (National Virus Reference Lab., Dublin)	CMV, pathogenesis, molecular diagnosis, epidemiology
D. Paton (Institute of Animal Health, Pirbright)	Livestock viral diseases, exotic viruses vesicular and pest viruses
P. Simmonds (Univ. Edinburgh	Hepatitis viruses, molecular epidemiology, antivirals
D. Westmoreland* (Univ. Hospital of Wales, Cardiff)	Molecular diagnosis, hepatitis, congenital infections
P.M.B. White* (PHL, Norwich)	Public health, HLTV 1
A.A. Nash (CR) (Univ. Edinburgh)	

Education (No Vacancies)

J. Verran (C) (Manchester Metropolitan Univ.)	Applied microbiology, biofilms, group work
M.R. Adams (Univ. Surrey)	Food and beverage microbiology
S.J. Assinder (Univ. Wales, Bangor)	Mycology education, schools and public
R.J. Cooper (Univ. Manchester)	Medical virology, adenoviruses, herpesviruses
C. Jones (Manchester Metropolitan Univ.)	Biotechnology using www
B.A.B. Martin (Univ. Birmingham)	Molecular virology, gene therapy
J.D. Parry (Univ. Lancaster)	Free-living protozoa, freshwater biofilms
J. Perkins (Univ. Huddersfield)	Environmental microbiology
H. Sears (Univ. Leeds)	Supporting tertiary learning and teaching
Education Officer (CR)	

Environmental Microbiology (3 Vacancies)

K.T. Semple (C) (Univ. Lancaster)	Biodegradation, pollutants, ecotoxicology, bioremediation
G. Black* (Northumbria Univ. at Newcastle)	Bioremediation, plant–soil–microbe interaction, biomass utilization
G.M. Gadd (Univ. Dundee)	Metal–microbe interactions, sulphate reduction, fungi
F. de Leij* (Univ. Surrey)	Bioremediation, biological control, rhizosphere, sustainability
D.C. Naseby (Univ. Hertfordshire)	Microbial ecology, bioremediation, rhizosphere microbiology
S.L. Percival (Univ. Central Lancashire)	Biofilms, waterborne pathogens, biocorrosion
J.D. Porter (Univ. Exeter)	Microbial ecology, survival, culturability
I.P. Thompson* (NERC, Oxford)	Microbial diversity, pollution degradation and impact
M.G. Jones (CR) (Univ. Liverpool)	

Eukaryotic Microbiology (1 Vacancy)

C. Price (C) (Univ. Lancaster)	Fission and budding yeasts, cell cycle control
M.X. Caddick (Univ. Liverpool)	Filamentous fungi
A. Carr* (Univ. Sussex)	Fission yeast
A. Goldman (Univ. Sheffield)	*Saccharomyces cerevisiae*, meiosis, recombination
P. McKean (Univ. Lancaster)	Trypanosomes, cytoskeleton
A. Osbourn (Sainsbury Lab. Norwich)	Molecular phytopathology
S. Purton (Univ. College London)	Algae, chloroplasts, *Chlamydomonas*
P. Schaap (Univ. Dundee)	cAMP signalling, *Dictyostelium discoideum*
A.J.P. Brown (CR) (Univ. Aberdeen)	

Fermentation and Bioprocessing (1 Vacancy)

G. Hobbs (C) (Liverpool John Moores Univ.)	*Streptomyces* antibiotic production and morphology
R.R. England (Univ. Central Lancashire)	Bacterial slow growth, signalling
C. Hewitt (Univ. Birmingham)	Process monitoring, flow cytometry, *Escherichia coli*
F.W.J.M.M. Hoeks (Biotech Fine Chemicals, Lonza)	Biopharmaceuticals, integrated process optimization
P.A. Hoskisson (John Innes Centre, Norwich)	Chemostats, gene expression, development, actinomycetes
J. Miller (CBD Porton Down)	Recombinant proteins, protein purification, cell disruption
R. Swift (Evans Vaccines, Speke)	Fermentation, GMP, scale-up
A.M.E. Weiss* (Cobra Therapeutics, Keele)	Fermentation, lysis, vectors, expression
P.F. Stanbury (CR) (Univ. Hertfordshire)	

Food and Beverages (No Vacancies)

T. Humphrey (C) (Univ. Bristol)	Bacterial stress responses, zoonoses
M.L. Baillon (Waltham Pet Centre)	Microflora of companion animals
M.A. Collins (Queen's Univ. Belfast)	Lactic acid bacteria, food fermentations
G.R. Gibson (Univ. Reading)	Human gut microbiology, prebiotics, probiotics
M.W. Peck (IFR Norwich)	Food safety, *Clostridium botulinum*, physiology
R.A. Rastall (Univ. Reading)	Functional food ingredients, probiotics
A. Varnam (London Metropolitan Univ.)	Food-borne pathogens, probiotics, fermentation
J. Wells (IFR, Norwich)	Functional genomics, *Campylobacter*
K. Jones (CR) (Univ. Lancaster)	

Irish Branch (2 Vacancies)

C. O'Reilly (C) (Waterford Institute of Technology)	Microbial metabolism of cyanide and nitriles
C.V. Carroll* (Nat. Univ. Ireland Galway)	Physiological stress, gene expression, epidemiology
D.N. Dowling (Carlow Institute of Technology)	Rhizosphere microbiology, biodegradation
S.M. Doyle* (Nat. Univ. Ireland Maynooth)	Protein diagnostic/therapeutic agents
J.W. McGrath (Queen's Univ. Belfast)	Environmental bacteriology, pollution, biodegradation
J. Morgan (Univ. College Cork)	Mucosal virology/immunology, SRSV, rotavirus, astrovirus
M. O'Connell (Dublin City Univ.)	Bacterial iron acquisition
K.E. O'Connor (Univ. College Dublin)	Biocatalysis, green chemistry, oxygenation
A. Vivian (CR) (Univ. West of England)	

Microbial Infection (2 Vacancies)

P.C.F. Oyston (C) (DSTL, CBS Porton Down)	Bacterial pathogenicity, *Yersinia*, vaccines
N. Dorrell (London Sch. Hygiene Trop. Medicine)	Pathogenicity, *Helicobacter*, *Campylobacter*, microarrays
N. Fairweather (Imperial College, London)	Bacterial toxins, clostridia, surface antigens, vaccines
J. Fletcher (Univ. Bradford)	Enteropathogenic *Escherichia coli*, * signalling responses
P.R. Langford* (Imperial College, London)	Human/veterinary pathogens, proteomics, DNA arrays, meningitis
S. Patrick* (Queen's Univ. Belfast)	Anaerobic bacteriology, prosthetic joint infections
O. Sparagano (Univ. Newcastle)	Tick-borne pathogens, zoonoses, diagnostics
C. Winstanley (Univ. Liverpool	Cystic fibrosis pathogens, pathogenicity islands
P.W. Andrew (CR) (Univ. Leicester)	

Physiology, Biochemistry & Molecular Genetics (1 Vacancy)

G.P.C. Salmond (C) (Univ. Cambridge)	Quorum sensing, virulence, antibiotics, phages
B. Ashraf (Univ. Bradford)	Bacterial heat-shock proteins, molecular chaperones
J. Green (Univ. Sheffield)	Gene regulation, oxygen stress, toxins
J.C.D. Hinton (IFR Norwich)	Genomics, *Salmonella*, *Escherichia coli*, infection
N.P. Minton* (CAMR Porton Down)	Molecular genetics, industrial bacteria
M.K. Phillips-Jones (Univ. Leeds)	Signalling pathways, biochemistry, molecular genetics
M.C.M. Smith (Univ. Nottingham)	*Streptomyces*, bacteriophages, site-specific recombination
I. Stansfield (Univ. Aberdeen)	Translation, gene expression, yeast
J. Errington (CR) (Univ. Oxford)	

Systematics & Evolution (4 Vacancies)

G. Saddler (C) (SASA Edinburgh)	Systematics of plant-pathogenic bacteria
P. De Vos (Univ. Gent)	Pseudomonads, bacillae
T.M. Embley (Natural History Museum,) London	Eukaryotic evolution, hydrogenosomes, anaerobic organelles
R. Goodacre* (Univ. Wales, Aberystwyth)	Organism fingerprinting, molecular systematics, chemometrics
F.G. Priest* (Heriot-Watt Univ., Edinburgh)	Molecular systematics of Gram-positives
I.C. Sutcliffe* (Univ. of Sunderland)	Membrane-anchored molecules in Gram-positives
A.C. Ward* (Univ. Newcastle)	Data analysis in systematics and process control
R.A. Whiley (Bart's and London School of Medicine and Dentistry)	Streptococci, pathogenicity, diversity
H.M. Lappin-Scott (CR) (Univ. Exeter)	

Virus (4 Vacancies)

R.E. Randall (C) (Univ. St. Andrews)	Paramyxoviruses, interferon/immunity and vaccines
W.S. Barclay (Univ. Reading)	RNA virus replication, respiratory virus infections
J.P. Carr (Univ. Cambridge)	Resistance to plant virus infections
P.E. Digard (Univ. Cambridge)	Influenza, transcription, nuclear export, lipid raft, cytoskeleton
S. Efstathiou* (Univ. Cambridge)	Herpesviruses, pathogenesis, latency, viral vectors
K.N. Leppard* (Univ. Warwick)	Adenoviruses, gene expression, RNA nuclear export, cell cycle
S.A. MacFarlane (SCRI Dundee)	Plant-virus interactions
J. McLauchlan (Inst. Virology, Glasgow)	Hepatitis C virus, molecular biology
J.C. Neil* (Univ. Glasgow Veterinary School)	Retroviruses, cancer, immunodeficiency viruses/vaccines
M.D. Ryan (Univ. St Andrews)	Picornaviruses, polyproteins, virus proteinases
M.A. Skinner* (Inst. Animal Health, Compton)	Poxvirus, replication, morphogenesis, immunomodulation, vaccines
A.A. Nash (CR) (Univ. Edinburgh)	

Meetings

Meetings on the web

For up-to-date information on future Society meetings and to book on-line see: **www.sgm.ac.uk**

Meetings organization

The SGM meetings programmes are organized by the committees of the special interest groups, co-ordinated by the Scientific Meetings Officer, Professor Howard Jenkinson. Suggestions for topics for future symposia are always welcome. See p. 45 for contact details of Group Conveners.

Administration of meetings is carried out by Mrs Josiane Dunn at SGM Headquarters, Marlborough House, Basingstoke Road, Spencers Wood, Reading RG7 1AG (Tel. 0118 988 1805; Fax 0118 988 5656; email meetings@sgm.ac.uk).

Offered papers and posters

Many Groups organize sessions for the presentation of short oral papers or allow intercalated papers within their symposia. Offered posters are welcome at all Society meetings.

Offered posters

Each poster should be associated either with the Main Symposium topic or with a Group. The subject content of the latter should be relevant to the remit of a Group (see website for details); it does not have to relate to the topic of the Group Symposium taking place at a particular meeting. General Offered Posters will not be accepted.

Abstracts

Titles and abstracts for all presentations are required in a standard format and should be submitted through the SGM website. Each submission must be accompanied by a completed form also available on the website. Deadlines for submissions are published in *Microbiology Today* and on the web. For further information contact the Events Administrator.

Future Meetings

SPRING 2003 – 152nd Meeting

University of Edinburgh (7–11 April 2003)

● Main Symposium
Microbial subversion of host cells

Organizers: H.F. Jenkinson, D.G.E. Smith, C.D. O'Connor, A.R.M. Coates, P. Cossart, G.L. Smith & B. Kenny

●PROGRAMME BOOKLET

A booklet giving full details of the programme and a booking form is enclosed with this issue of *Microbiology Today*. Any changes will be posted on the SGM website.

●OFFERED POSTER PRESENTATIONS

Delegates whose offered posters have been accepted should note that an area of 1m × 1m only is available on the poster boards for their display.

●MICROSCENE NOTICEBOARD

At the meeting, a board will be set up with notices of jobs, postdoctoral positions, studentships, courses, conferences etc. Contributions are welcome and may be either brought to the meeting or sent beforehand to Janet Hurst at Marlborough House.

●SOCIAL EVENTS

A programme of evening social events has been arranged to entertain the delegates when they are not attending scientific sessions. These include:

Monday 7 April
Trade & Welcome Reception

Tuesday 8 April
Society Dinner, followed by a ceilidh

Wednesday 9 April
Tutored Whisky Tasting
Retro Disco

Thursday 10 April
Beverages Debate:
Beer vs wine vs whisky

Please support these events.

DNA50

On April 25th 1953 James Watson and Francis Crick described the structure of DNA in the journal *Nature*.

This momentous discovery, which was the culmination of research by Maurice Wilkins and Rosalind Franklin in London, and James Watson and Francis Crick in Cambridge, was one of the most significant landmarks of 20th century science. To mark the 50th anniversary the Medical Research Council, the Royal Society and *Nature* have joined forces to coordinate a programme of events in 2003 (see www.dna50.org.uk).

Research into the structure and role of DNA has been underpinned by studies on microbes and SGM is delighted to take part in the DNA50 programme. Contributions include the current issue of *Microbiology Today* and the whole of the 153rd Meeting at UMIST. The main symposium addresses a wide range of microbial genomics and genomics-related topics and will duly acknowledge the Watson and Crick anniversary, whilst the Group symposia cover various aspects of microbial molecular biology. Cambridge historian of molecular biology Soraya de Chadarevian, whose book is reviewed on p. 46, will also be delivering a public 'History of Microbiology' lecture on the DNA theme at UMIST.

AUTUMN 2003 – 153rd Meeting

UMIST, Manchester 8–12 September 2003

● Main Symposium
Exploiting genomes: bases to megabases in 50 years

Organizers: H.F. Jenkinson, D.J. Kelly, P.C.F. Oyston & J. Parkhill

● Speakers

G. WEINSTOCK (USA) *Genomes and beyond*

J. PARKHILL (Sanger Centre) *Comparative genomics of bacterial pathogens*

P. GHAZEL (Edinburgh) *Cytomegalovirus expression in human cells*

S. ANDERSSON (Sweden) *Genomics of Bartonella*

T. GAASTERLAND (New York) *Bioinformatics: making sense of megabases of data*

C. HUTCHISON (TIGR) *Minimal microbial genome*

P. KELLAM (UCL) *Global views of host/pathogen interactions; transcriptional changes in virally infected cells*

A. DAVISON (Glasgow) *Herpesvirus genomics*

D. USSERY (Denmark) *Prediction of highly expressed genes in sequenced prokaryotic genomes*

E. GARCIA (USA) *Comparative analysis of Yersinia*

P. BUTCHER (London) *Bacterial gene expression and infection: microbes, messengers and microarrays*

D. O'CONNOR (Southampton) *Proteomics*

B. WREN (London) *Genomics in Campylobacter jejuni pathogenesis*

P. RAINEY (Oxford) *The secret life of Pseudomonas fluorescens SBW25*

P. RATHOD (USA) *Identification of novel targets for anti-malarial drugs*

R. RAPPUOLI (Italy) *Vaccine antigen discovery in silico*

● Other symposia

● Microbial sensing and signalling
Cells & Cell Surfaces Group
11 September
Organizers: J. Armstrong (j.armstrong@sussex.ac.uk) & D. Devine (d.a.devine@leeds.ac.uk)

● Teaching bioinformatics: how and why?
Education & Training/ Systematics & Evolution Groups
10 September
Organizers: J. Verran (j.verran@mmu.ac.uk) & G. Saddler (gerry.saddler@sasa.gov.uk)

● Post genomics applied to processes: advances in eukaryotic microbiology
Eukaryotic Microbiology with British Mycological Society and British Society for Medical Mycology
10–11 September
Organizers: A.J.P. Brown (al.brown@abdn.ac.uk) & S. Purton (s.purton@ucl.ac.uk)

● Production of DNA and protein
Fermentation & Bioprocessing Group
10 September
Organizer: A. Weiss (amanda.weiss@cobrat.com)

● DNA-based detection methods
Food & Beverages/ Environmental Microbiology Groups
8–9 September
Organizers: G.R. Gibson (g.r.gibson@reading.ac.uk) & I.P. Thompson (ipt@ceh.ac.uk)

● Bacterial gene expression *in vivo*
Microbial Infection Group
10–11 September
Organizers: N. Dorrell (nick.dorrell@lshtm.ac.uk) & J. Hinds (j.hinds@sghms.ac.uk)

● DNA 1952–2003: from structure to function
Physiology, Biochemistry & Molecular Genetics Group
10 September
Organizers: J. Hinton (jay.hinton@bbsrc.ac.uk), C. Dorman (cjdorman@tcd.ie) & R. Dixon (ray.dixon@bbsrc.ac.uk)

Deadline for receipt of titles and abstracts for Offered Posters: **9 May 2003**.

● 'History of Microbiology' Lecture

1800 Wednesday 10 September

Speaker: Soraya de Chadarevian

SPRING 2004 – 154th Meeting

University of Bath

● Main Symposium

Microbe–vector interactions in vector-borne diseases

Irish Branch

Microbial diseases and the immuno-compromised patient

Maynooth
24–25 April 2003

Speakers:

P. LJUNGMAN (Stockholm) *CMV infection in transplant patients*

P.G. MURPHY (Dublin) *Burkholderia cepacia complex infection in cystic fibrosis*

N. GOW (Aberdeen) *Candida – host interactions at the site of infection: importance of the fungal cell wall*

W. MEIJER (Dublin) *Virulence mechanisms of Rhodococcus equi, an opportunistic pathogen of immunocompromised patients*

H. KAUFFMANN (The Netherlands) *Interaction of Aspergillus fumigatus with the innate and cognate defence system of the airways: significance for immune competent and immune compromised patients*

T. SCHULZ (Germany) *Clinical aspects and pathogenesis of KSHV/HHV8 infection*

Abstracts for oral and poster presentations should be emailed to the organizer Sean Doyle (sean.doyle@may.ie)

Biocatalysis

UCD, Autumn 2003

Joint with the Royal Society of Chemistry

Organizer: Kevin O'Connor (kevin.oconnor@ucd.ie)

Invited speakers: D. BOYD (Queens University Belfast), A. DOBSON (University College Cork), C. MURPHY (University College Dublin), F. HOEKS (Lonza AG, Visp, Switzerland), W. DUETZ (ETH Zurich and SME Enzyscreen) and C. KNOWLES (University of Oxford)

For details of Irish Branch activities contact the Convener, Catherine O'Reilly (coreilly@wit.ie)

Other News and Events

● Bioinformatics Workshops

Following the success of the workshops held jointly by the SGM and The Sanger Centre in 2002, as described by Nick Thomson on p. 19, the Society is delighted to announce that further events will be held this summer in Bristol, Ireland (provisional), Birmingham and Edinburgh (provisional).

Registration fees (to include lunch, refreshments and set of literature):

Company staff	£100
Academics (university & research institute)	£50
Postgrads/first postdocs	£20*

**Grants are available – see website*

Attendance is restricted to SGM members only.

Many members were disappointed last year because the available places filled so quickly. Register early to ensure your attendance. Full details of the workshops and a booking form will be available on the SGM website (www.sgm.ac.uk/meetings) as soon as dates are confirmed.

● SfAM/SGM One-day Regional Meetings

A joint initiative to sponsor one-day regional meetings in the UK and Ireland has been launched by the SGM and the Society for Applied Microbiology. See p. 27 for further information and the website of either society for the full rules and to download an application form.

● Group News

Food & Beverages Group Science Communication Prize

Sponsored by the Institute of Food Research

The Group is delighted to announce a new competition designed to encourage younger junior scientists (PhD students and those in their first postdoctoral or research appointment) to develop and demonstrate their skills in communication. Presenters in the early stages of a project will not be penalized by lack of results.

The prize of £100 and a certificate will be awarded to the oral presenter who in the view of the judges most clearly and concisely communicates the rationale for, and planned outputs of, the work they are presenting in a style that is suitable for scientists or technologists who, whilst not necessarily having expert knowledge of food microbiology, might have to make research management/financial/policy decisions based on the information given.

Judging will be by a panel from the Food & Beverages Group. The prize is offered for the best oral presentation at the Group symposium to be held at the SGM meeting at UMIST, 8–9 September 2003.

To enter the competition, please tick the appropriate box when completing your abstract submission form for the meeting.

● FEMS First Congress

29 June–3 July 2003
Ljubljana, Slovenia

For full details of the meeting see **www.fems-microbiology.org/congress 2003.htm**

Travel grants to attend the meeting are available to SGM members – see p. 30.

Gradline

If you have any stories or news for publication in Gradline, or if you would like to see any topics featured, please contact **mtoday@sgm.ac.uk**

Postgrads Matter

Questionnaire

In 2003 the SGM had nearly 900 Postgraduate Student Members. As microbiologists of the future you are very important to the Society and one of the recurring topics at Council's annual Strategy Group meetings is how best to meet your needs. Two Council members, Hilary Lappin-Scott and Dave Kelly, have been assigned special responsibility for postgraduate members, and they recently got together with Education Group Convener Jo Verran to produce a questionnaire to find out what you want from the SGM and what you think of the existing membership benefits. This was circulated to all Student Members in October and the responses have been analysed. They will be reported in detail in a future Gradline. Meanwhile, if you want to learn more about the findings you should attend the following event...

Successfully surviving your PhD

If you are attending the SGM meeting at Edinburgh University, don't miss this session being held by the Education and Training Group on Thursday 10 April. Aimed at improving the lot of postgraduate microbiology students, information on general PG topics will be supplemented by more subject-specific material from SGM members. There will also be an open forum.

Speakers include D. Green of the UK Council for Graduate Education on the 'changing postgraduate experience', T. Brown of the National Postgraduate Committee on 'rights, wrongs and expectations', Liz Sockett (former SGM Education Officer) on 'managing your supervisor', Jo Verran on 'PhD and what else?' which will explore the outcome of the questionnaire described above and finally Council member Hilary Lappin-Scott will explain about the 'SGM and you'.

This morning session will conclude with a free 'Pub Lunch' at the nearby Students' Union which will be available ONLY to people attending the talks! Tickets will be distributed at the event.

See enclosed programme booklet for full details.

Careers 'R' Us goes on...

Life Science Careers 2002

November 2002 saw External Relations Office staff turning out on cold Saturday mornings to participate in the Life Science Careers Conferences held in Glasgow, Sheffield and at King's College London. The conferences, now in their 15th year, followed the successful format of a range of presentations interspersed with generous breaks, where delegates were able to mingle with speakers and talk to exhibitors. In response to feedback from previous events, more coverage was given to careers outside the lab with topics including science communication and publishing, patent law and sales and marketing. The more traditional career pathways in industry, clinical science, teaching and academic research were also described. Around 20 different organizations, including companies and professional bodies, had stands at each conference. Delegates who submitted their CVs beforehand were able to have them reviewed by experts on the day.

The conferences were attended by a total of 680 undergraduate and postgraduate students from all branches of the biosciences and it was good to meet SGM Postgraduate Student Members who came to visit our stand during the refreshment breaks.

Our thanks are offered to staff of the Physiological Society whose turn it was to undertake much of the administrative work ably assisted by staff from the Biochemical Society, British Pharmacological Society and Society for Experimental Biology.

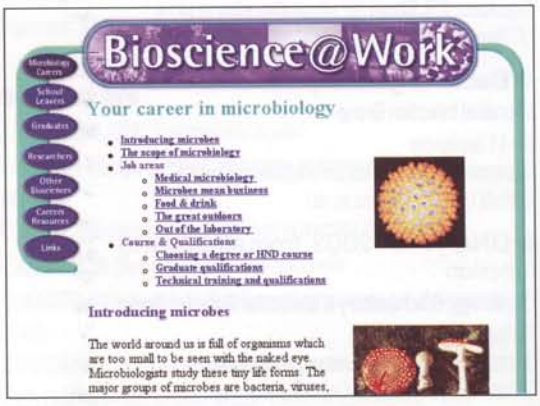
New careers website

www.biocareers.org.uk

The SGM careers resources and information service has recently undergone a major makeover and a new website separate from www.sgm.ac.uk has been launched. It focuses on training and opportunities for microbiologists at all stages of their careers. You will find answers to your questions about:

- Postdoctoral research
- Finding work outside the laboratory
- Successful job hunting
- Careers events

You can order our careers publications, including booklets and factsheets, online.



We want to develop the site further and would welcome suggestions for other topics that you would like to see included.

We plan to include a set of careers profiles on the website and it would be great to feature some PhD students and postdocs to inspire students at the beginning of their microbiology careers. If you are willing to be interviewed and profiled on the website, please contact Jane Westwell at SGM HQ (**j.westwell @sgm.ac.uk**). There will be CD gift vouchers for those who appear on the website.

Individual enquiries are still welcome and receive a personal reply. Simply email the External Relations Office on **careers@sgm.ac.uk**

Jane Westwell, Careers Administrator

SGM Microbiology Communication Prize

- **1st Prize...** *£500*
- **2nd Prize...** *£200*
- **3rd Prize...** *£100*

- *Are you a postgrad or postdoc who has gained their PhD in the last two years?*
- *Are you presenting a poster or offered paper at an SGM meeting?*

If so, you can enter your presentation for a communication prize competition which takes place at the SGM autumn meeting. Finalists in the competition make short oral presentations and the judges award cash prizes to the three best entries. All finalists receive a year's free Society membership. Their expenses for travel and one night's overnight accommodation at the meeting are met.

Selection for a place in the finals is through the sessions of the special interest Groups or at an Irish Branch meeting, so you must submit your abstract for consideration by the appropriate Convener. Details of Group scientific remits are available on the SGM website (www.sgm.ac.uk). Groups do not always hold sessions at every meeting and so you also need to check that the Group relevant to your work is going to be there. Information on future meetings programmes is available in *Microbiology Today* or on the website.

You must be a Society member, a postgraduate student or a postdoc within 2 years of gaining your PhD. In the case of a multi-author paper you must have contributed 60 % or more of the experimental work and been primarily responsible for the preparation and presentation of the poster/paper.

To enter all you need to do is tick the box on the abstracts submission form on the SGM website.

You will subsequently be informed when the judging session for the first round of the competition will be taking place.

For further information contact the Meetings Administrator (**meetings@sgm.ac.uk**).

ASM Biomedical Research Conference for Minority Students (ABRCMS)

■ *SGM Council sent along PhD student Saimon Malhotra to check out this annual event.*

November 2002 saw the gathering of the ABRCMS in New Orleans, Louisiana. This year was deemed special since it marked the 40th anniversary of the National Institute of General Medical Sciences (NIGMS) and the 30th anniversary of the Minority Access to Research Careers (MARC) and Minority Biomedical Research (MBRS) programmes. These bodies encourage students to pursue advanced training in the biomedical sciences and provide professional scientific support with resources for facilitating students' success. In return, students are given the opportunity to participate and present their achievements at a national conference, like this one.

I attended this conference to learn more about it by engaging with the students and the organizers. Like all other conferences I've attended, this one was enjoyable, informative and content-rich. It comprised scientific sessions, professional development workshops, student oral and poster presentations, as well as numerous exhibits. The programme also featured outstanding speakers, including two Nobel laureates.

However, this conference was designed for the minority groups in the United States, which are currently underrepresented across all aspects of the scientific field. The term 'minorities' as defined here, encompasses women and groups belonging to different ethnic backgrounds. The above-mentioned bodies are aware of the changing demographics in the country and are responding by running programmes designed to increase the number of minorities in biomedical research. These minority students, some of whom initially have no desire to pursue a career in science and others who want to but don't know how, are encouraged to undertake a period of research at local colleges. The rationale being that such programmes help to tap the talent of members within the targeted minority groups and make them realize how rewarding and satisfying a career in science could be.

The conference not only provides these students with the opportunity to present their work, but allows them to take advantage of the many educational opportunities available to help each student reach their full scientific potential. With this given opportunity in drawing underrepresented students into science to sample scientific research, the goals of the organizing bodies will only be fulfilled if participating students decide to stay on and further their development in science through education. In my opinion, this is a plausible scheme in introducing science to the underrepresented groups of a large population and may help to resolve the current minority issue. However, for a long-term solution, I believe investment of time, money and effort should be directed into schools to promote and encourage a career in science to minority groups who are currently underrepresented. By targeting these groups at an early age we may see the end of the need of such a conference.

■ ***Saimon Malhotra***
email s.malhotra@man.ac.uk

'Visions of Science' – seeking imagery in medicine

Can you take photographs that bring your work to life and help explain microbiology to a wider audience? If so, the 2003 Novartis and *The Daily Telegraph* 'Visions of Science Photographic Awards' are looking for entries that capture science in creative, surprising or thought-provoking ways.

The awards have some exciting new categories this year with a first prize of £1,000 and second prize of £400 in each one.

- **Action** for images that capture a scientific process or event in the natural world.
- **Close-up** for images that reveal the world in a way not seen with the naked eye.
- **People** for images that communicate the impact of science, medicine and technology on people's lives.
- **Concepts** for images that demonstrate or explain a scientific concept.
- **Art** for images that illustrate the beauty of science.

To celebrate the DNA Anniversary, the Medical Research Council is sponsoring a special DNA Award looking for the best image about DNA, the science of genetics, or its impact on people's lives, with a £500 prize. The *British Medical Journal* is sponsoring a special Healthcare Award, with a £500 prize, looking for the best image that shows the impact of science and medicine on people's lives.

NESTA, the National Endowment for Science, Technology and the Arts, is sponsoring The Novartis and *The Daily Telegraph* 'Visions of Science Photographic Awards'.

You have until **30 May** to send in your entries. If you want more information, visit the website **www.visions-of-science.co.uk** for an entry form, or telephone 0207 613 5577.

Winners will be notified in August. The Award ceremony will be held at The Royal Society in September.

SchoolZone

Schools Membership costs only £10 a year. For this, a named teacher representative will receive *Microbiology Today* each quarter, advance notification and copies of new microbiology teaching resources, and discounted fees for attendance on SGM training courses and workshops. Application forms are available at **www.sgm.ac.uk**

Over to you...

Contributions are welcome from teachers who have interesting microbiology material to share, such as novel investigations, useful tips or good sources of information. A copy of the post-16 resource *Practical Fermentation* (worth £15) will be sent to any school whose submission is published. The editors of *Microbiology Today* reserve the right to edit any material.

Enquiries:
education@sgm.ac.uk

Website:
www.microbiology online.org.uk

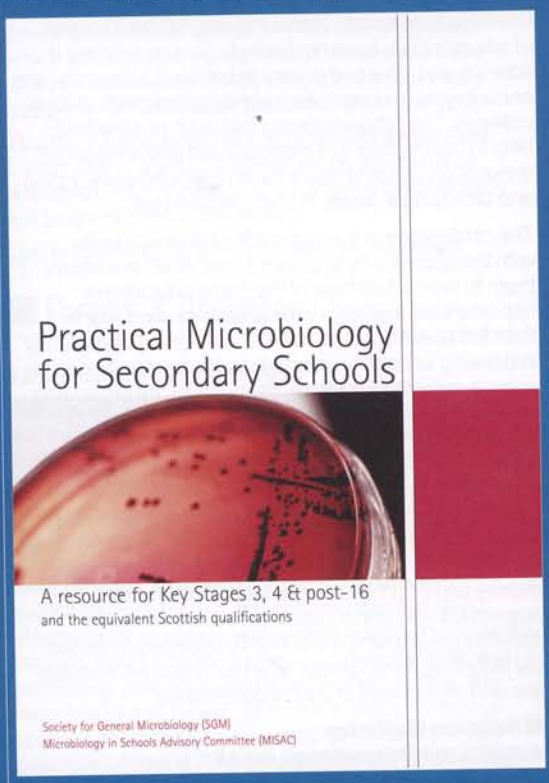
School Membership takes off

At the end of 2002 SGM had 320 School Members and the majority have already renewed for 2003. Feedback has been excellent and we have enjoyed meeting teachers from member schools at courses, the summer school and on our stand at the ASE annual meetings. Our various publications have been well received and continue to be distributed widely to schools throughout the UK and several overseas locations.

Practical Microbiology for Secondary Schools

This new resource for Key Stages 3, 4 and post-16 students, contains 21 safe, tried and tested practicals and includes two open-ended investigations. Many of the experiments can also be adapted for project work. The book, based on an earlier long out-of-print SGM teaching pack, but substantially updated and redesigned, was put together by a MISAC working party and edited by Janet Hurst (SGM) and John Grainger (MISAC).

Each investigation is in the form of a double-page spread, comprising a teacher guide and student worksheets which clearly set out the requirements for each activity and the procedure to be followed. The text is accompanied by helpful line drawings. The worksheets are arranged in four main themes: Life forms and processes; Microbes in the environment; Microbes and food; Health and hygiene, but each activity is stand-alone and offers students the opportunity to develop their investigative skills.



The book includes sections on good microbiological laboratory practice and practical techniques and tips plus details of further resources.

- Price: £10 (inclusive of postage and packing).

Contact Yvonne Taylor at SGM Headquarters to purchase a copy (email y.taylor@sgm.ac.uk); cheques should be payable to SGM.

A copy of *Basic Practical Microbiology: A Manual* (the detailed notes that accompany our training course) is supplied free with each order.

Basic Practical Microbiology Courses

Around 230 teachers and technicians have now received training in basic practical microbiology at the Society's one-day accredited courses delivered by Dr John Grainger (MISAC Chairman) and Dr John Schollar (NCBE Co-Director). Places are still available on the courses being held this summer

The two remaining courses this academic year are:

- Queen's University of Belfast — 11 June
- University of Exeter — 4 July

The course costs £40 (£30 to School Members), which covers course materials, certification, lunch and refreshments. Schools are offered a £100 flat sum per teacher per day to assist with supply cover.

Full details of the courses and a booking form are available on www.microbiologyonline.org.uk

Coming soon...

Tuberculosis: can the spread of this killer disease be halted?

Compiled by Dariel Burdass, this new factsheet covers the latest developments in the fight against TB, a disease which is rapidly making a comeback worldwide. Useful background information on TB in history, the organism that causes the disease, how the infection spreads and how the human body fights it precede descriptions of diagnosis methods and recent research into vaccines and drugs to control TB. The factsheet includes a glossary and a list of further resources. It is targeted at post-16 students, but will also be useful for those studying GCSE Applied Science.

MISAC Competition 2003

Your Body is a Fortress: a barrier to microbial invaders

Don't miss this excellent assessment opportunity for your Key Stage 3 and 4 students. The closing date for the competition, sponsored by the SGM, is 31 March.

Entrants should submit an eye-catching A3 annotated diagram of the human body, highlighting non-specific defences to infection by microbes. There are cash prizes for both schools and pupils. Each school that enters receives a pack of microbiology teaching resources and all students submitting entries which are scientifically correct are sent a certificate. See www.microbiologyonline.org.uk for full details and an entry form.

New Microbiology Code of Practice for Scottish Schools & Colleges

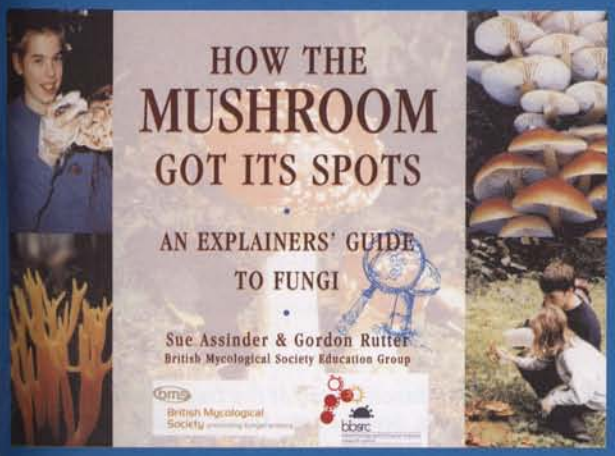
The Scottish Schools Equipment Research Centre has completely revised an earlier publication *Safety in Microbiology*. It covers microbiological work in Scottish schools right across the age range from primary to further education colleges. The code of practice offers a set of preventative and protective measures produced as a result of model risk assessments. To obtain a copy, contact SSERC (www.sserc.org.uk or email sts@sserc.org.uk).

Safety information for schools in England and Wales is available on the SGM education website www.microbiologyonline.org.uk

How the Mushroom Got its Spots

The new booklet from the British Mycological Society and the BBSRC provides an explainer's guide to fungi. It has been written by SGM member and BMS Education Secretary Sue Assinder and her colleague Gordon Rutter. It is aimed at anyone faced with talking about fungi to non-specialists, either in schools or to the public and includes some practical activities and quizzes plus information about organizing fungal forays as well as lots of fascinating facts about fungi. Safety issues are carefully considered.

Copies of the book are free from: The Librarian, British Mycological Society, Joseph Banks Building, Royal Botanic Gardens, Kew, Richmond, Surrey TW9 3AE (email v.barkham@rbgkew.org.uk).



Primary Poster Success

To mark Science Year, the SGM ran a popular competition for primary schools. Pupils had to create a poster entitled *Microbes: Friend or Foe?* which described the roles that different harmful and beneficial micro-organisms play in our lives (see *Microbiology Today* August 2002, p.139 for details).

The first prize of £150 for the school was won by 8-year old **Lauren Meader**, of the Abbey School, Reading. Recently Dariel Burdass, who runs SGM education activities, went along to the school to present the prize and to give Lauren her winner's certificate.

ABOVE:
Dariel Burdass presents a certificate to Lauren Meader, who won first prize in the SGM competition.
COURTESY *READING EVENING POST*

The school opted to use the money to help pay the Quantum Theatre Company's fee for performing its show *The Mysterious Disappearance of Mr Winchlever*, which brings alive scientific concepts using humour. They will also take Lauren's class on a trip to the Science Museum at SGM's expense.

A national network of science learning centres

The Wellcome Trust and the Department for Education and Skills are establishing a national network of centres where science teachers can enhance their professional skills by learning more about contemporary scientific ideas, undergoing training in effective teaching approaches and gaining experience in modern scientific techniques. The aim is to improve science teaching, to inspire pupils by providing them with a more exciting, intellectually stimulating and relevant science education and to raise morale in the teaching profession. £51 million is currently out to tender and bids are invited from single organizations or consortia that have the capability and capacity to develop and manage the proposed national centre and regional centres that will support its work. The announcement of the successful bidders is expected in October 2003. See www.dfes.gov.uk/sciencecpd/ for details.

Going Public

SGM Public Understanding of Science grants of up to £1,000 are available to members wishing to promote microbiology. See www.sgm.ac.uk for details and an application form.

The Underground Pulse

Royal Society Summer Exhibition 2002

This collaborative exhibit from Oxford University, Horticulture Research International and Cardiff University (http://www.sc1.ac.uk/discover/pulse.cfm) was based around the reporting of a new method for real-time *in vivo* imaging of the translocation of a 14C-labelled non-metabolized amino acid through the extensive mycelium of the woodland fungus *Phanerochaete velutina*. Earlier this year we had presented the first report of a pulsatile component of amino acid flow in mycelium, which we are currently investigating, funded by NERC. The new discovery was displayed in the exhibit and set in the context of fungal biology at different scales from ecosystem through organism down to cell and subcellular scale. The highly visual nature of the research made for an attractive exhibit, and generous sponsorship from SGM, as well as the British Mycological Society, Horticulture Research International, English Nature, Zeiss and St Hilda's College, Oxford, enabled us to produce an impressive exhibition stand and 1,000 leaflets to show visitors how fungi grow. An important aim was to show that fungi are individual, co-ordinated mycelial systems consisting of hyphae, that they exist as microbes, and that the more conspicuous mushrooms are just the spore-producing part, not the whole organism.

Fluorescent confocal imaging of living hyphae with double labelling of the dynamic vacuolar system and mitochondria was performed on the stand, while a video loop and backdrop explained fungal biology at ecosystem, organism and cell scale. Horticulture Research International staff Drs Kerry Burton and Dan Eastwood showed how mushrooms grow from mycelium, with free samples of spawn and instructions on how to grow your own, and Professor Lynne Boddy of Cardiff University showed live mycelium at work on a realistic woodland floor. Nearly 4,000 visitors attended, including about 2,000 school students, and VIPs from government, industry, the media and research funding bodies.

● ***Dr Sarah Watkinson works at the Department of Plant Sciences, South Parks Road, Oxford OX1 3RB, UK.***
email sarah.watkinson@plant-sciences.ox.ac.uk

TOP RIGHT:
Sarah Watkinson chats to a visitor at the Royal Society Summer Exhibition 2002.

RIGHT:
From left to right: Peter Darrah, Lynne Boddy, Mark Fricker and Sarah Watkinson at the Oxford University, HRI and Cardiff University exhibit.

BELOW:
The entrance to the exhibition at The Royal Society, London.

PHOTOS RUTH WATKINSON

Further reading

Tlalka, M., Darrah, P.R.D., Watkinson, S.C. & Fricker, M.D. (2002). Continuous imaging of amino-acid translocation in intact mycelia of *Phanerochaete velutina* reveals rapid, pulsatile fluxes. *New Phytol* 153, 173–184.

Dr Montville's double helix seaman scarf

June Oshiro has designed a knitting pattern for a double helix scarf. It was commissioned by Dr Thomas Montville, a professor at Rutgers University (and also the photo model) who kindly agreed to serve on June's doctoral thesis committee in return. The pattern is reproduced here by June's kind permission. We hope to see many readers of *Microbiology Today* sporting this scarf as an outward sign of their commemoration of the Watson and Crick anniversary.

Yarn

25 % Baby Alpaca, 25 % Merino, 50 % Tencel

Sport weight (~120 yds/50 g), White 4 hanks – includes enough yarn to make a 6″ × 4″ swatch (you'll have a little left over afterwards if your scarf has the same dimensions as mine).

Needles

US 4 (3·5 mm).

Gauge

12 stitches and 18 rows per 2 inches in seed stitch (see below).

Dimensions

Cabled region is ~23″ long and ~6″ wide, neck ribbing section is ~12″ long (ribbing will be slightly narrower than the rest of the scarf).

Seed stitch

On an even number of stitches:
Row 1: k1, p1, repeat till the end;
Row 2: p1, k1, repeat till the end.

Right twist mini-cable, aka Classic Mock Cable

Row 1 (right side): K2.
Rows 2 and 4 (wrong side): P2.
Row 3: Knit the second stitch (leave the 1st stitch on the needle and work around it), then knit the first stitch, slip both stitches off the needle.

Left twist mini-cable, aka Tamerna Stitch

Row 1 (right side): K2.
Rows 2 and 4 (wrong side): P2.
Row 3: Knit the second stitch through the back loop (leave the 1st stitch on the needle and work around it), then knit the first stitch through the front loop, slip both stitches off the needle.

DNA cable

See **http://noodle.pds.k12.nj.us/june/Helix3.pdf** for charted instructions.

Selvedge

Knit the last stitch of every row. Slip the first stitch of every row as if to purl.

Instructions

Cast on 40 stitches (includes 2 selvedge stitches). Instructions for the selvedge are given above and are not explicitly written out in the pattern.

Knit 8 rows of seed stitch.

Set up the scarf pattern: 5 stitches in seed stitch pattern, purl 2 stitches, 2 stitches in right twist mini-cable, 20 stitches in DNA cable, 2 stitches in left twist mini-cable, purl 2 stitches, 5 stitches in seed stitch pattern.

Following in the pattern as set, knit rows 1–38 of the DNA cable pattern. Repeat rows 3–38 of the DNA cable four more times (five repeats in all), ending the final repeat with rows 39–40 of the DNA cable.

Set up the back neck ribbing as follows: k5, (p4, k4) three times, p4, k5. Knit until ribbing is ~12″ long.

Set up the scarf pattern again as before, except switching the left and right twist cable positions. This will ensure that the cables twist outward from the center when the scarf is worn. Knit five repeats of the DNA cable (similar to the first half), then end with 8 rows of seed stitch and bind off.

Block by gently handwashing in lukewarm water, dry flat.

This pattern is freely available at **http://noodle.pds.k12.nj.us/june/HelixPattern.html**. It is not to be distributed, sold, or reproduced in any form without the author's explicit permission. The pattern is copyright 2002, by June Oshiro. For pattern support, contact **idlewild@rci.rutgers.edu**

● *June Oshiro, 1602 Sweet Briar Ct., Monmouth Junction, NJ 08852, USA.*

ABOVE LEFT:
Dr Montville models the double helix seaman scarf.

ABOVE:
Detail of the finished scarf.

PHOTOS JUNE OSHIRO

Hot off the Press

Microbiology Today Editor Meriel Jones takes a look at some papers in current issues of the Society's journals which highlight new and exciting developments in microbiological research.

What the eye can't see

For almost a century, microbiologists have relied on being able to grow bacteria from a habitat as one of their best strategies for identifying what is there. With the advent of molecular biology methods that rely on detecting minute traces of DNA, it has become apparent that this gives a very biased impression. For example, despite all the attention lavished on the inhabitants of the human gastrointestinal tract, most of the approximately one million million (10^{12}) cells in each gram of faeces represent bacteria that cannot yet be grown in the laboratory. Their interactions with each other, and their healthy host are equally poorly understood.

And although molecular methods provide a way to study these unculturable organisms, they raise new problems. There are many molecular methods and it is not obvious which is best for measuring the populations in a particular habitat. Researchers at Helsinki University in Finland have been working on this question by comparing three different methods to record the numbers of particular faecal bacteria. Their results show the value of the technique called real-time PCR. The polymerase chain reaction (PCR) is the basis of many molecular identification methods. It allows the presence of very small amounts of DNA with a specific sequence to be detected through adding reagents that make copies of the sequence, if it is present, until there is enough to be detected. These sequences can be unique to a species, or a genus. Real-time PCR records how the number of copies increases during the experiment, rather than simply checking at the end. Scientists think that this can be used to estimate of the number of bacteria that are present in the original sample, and the Finnish workers wanted to test whether this was correct for the faecal microflora.

They tested a series of reagents and experimental conditions for detecting *Bacteroides fragilis*, *Ruminococcus productus* and *Bifidobacterium longum*, representing groups of bacteria that are reported to be abundant in human faeces. As a contrast, they also tried to estimate numbers of *Escherichia coli* and *Lactobacillus acidophilus*, a minor part of the gut microflora, and of *Bifidobacterium lactis* which does not belong in the human gut but is increasingly used in dairy foods as a probiotic that may confer health benefits. The researchers could test how sensitively they could detect both purified DNA from these species, and DNA from these bacteria in authentic human faeces. Using real-time PCR the researchers could detect purified DNA from as few as 200–400 bacteria, or the presence of these species if they formed a mere 0·01 % of the bacterial population in a sample of faeces. When they measured their samples with an older, well-established method for studying faecal microbes, they could only detect bacteria that formed at least 3 % of the population.

Malinen, E., Kassinen, A., Rinttilä, T. & Palva, A. (2003). Comparison of real-time PCR with SYBR Green I or 5′-nuclease assays and dot-blot hybridization with rDNA-targeted oligonucleotide probes in quantification of selected faecal bacteria. *Microbiology* 149, 269–277.

Impact of meningococcal vaccine

Meningitis is a serious disease of children and young people, caused by the bacterium *Neisseria meningitidis*. Although prompt treatment with antibiotics is usually effective, the initial symptoms are not obvious, so medical attention may be delayed. Many people carry the bacterium within their nasal passages but remain healthy, and these carriers are essential to the spread of the disease. Several different varieties of bacterium circulate in this human reservoir, occasionally causing outbreaks of meningitis.

The Galicia region of north-west Spain has around half a million young people between the ages of 5 and 19 among its 2·7 million inhabitants. Meningitis is endemic, and by 1995/6 the incidence had risen to 11 cases per 100,000 in the population, caused by *N. meningitidis* serogroup C. After a review of all possible control measures, this situation was sufficiently serious for the Galician Regional Public Health Authorities to decide on a vaccination campaign, targeting everyone between 18 months and 19 years. Between December 1996 and January 1997 they vaccinated 472,465 children and young people using a vaccine that gave protection from serogroups A and C. By 1998, the incidence of meningococcal disease had declined to 4·3 cases per 100,000. The authorities decided to find out whether the number of healthy carriers had also decreased since these could be the source of any future disease.

The study examined children aged between 5 and 19 in two regions of Galicia that had different incidences of the disease before the vaccination campaign. The National Neisseria Reference Laboratory at Majadahonda, Madrid, tested about 14,500 nasal swabs, and worked out that the prevalence of carriers had decreased from 1·51 to 0·79 % after vaccination in the high-incidence area, and from 0·94 to 0·32 % in the low-incidence region. The tests allowed the researchers to check the serotypes of the bacteria, and they realized that only the decrease in serotype C carriers in the high-incidence region was significant. The number of carriers between 10 and 19 had decreased by over 70 %, but the number between 5 and 9, although small, had increased by 20 %. This fitted with earlier reports that the vaccine is less effective among the youngest children.

Interestingly, there was no increase in the carriage of serotype B one year after vaccination, which might indicate that this variety had failed to replace serotype C in the now-asymptomatic carriers. In addition, there had actually been a statistically significant rise in the carriage rates for serotypes other than B and C. Overall, the researchers are confident that despite these changes in the incidence of other serotypes, their data indicate the effectiveness of the 1996 vaccination campaign, especially since the incidence of disease caused by serotype C continued to decrease in 1997 and 1998.

Fernández, S., Arreaza, I., Santiago, I., Malvar, A., Berrón, S., Vazquez, J.A. & Hervada, X. (2003). Impact of meningococcal vaccination with combined serogroups A and C polysaccharide vaccine on carriage of *Neisseria meningitidis* C. *J Med Microbiol* 52, 75–77.

OPPOSITE PAGE:
E. coli cells viewed under the microscope. The green cells are viable gfp-labelled cells, while the red cells are non-viable cells stained with propidium iodide.
COURTESY S. TOZE, CSIRO CENTRE FOR ENVIRONMENT AND LIFE SCIENCES, WEMBLEY, AUSTRALIA

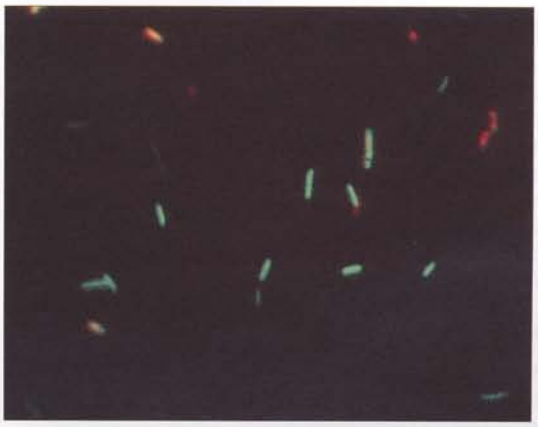
Persistent pathogens

Much of Australia has a low rainfall, and irrigation using recycled water is essential for agriculture. The water can be stored by injecting it into aquifers until it is needed. Bacteria in natural habitats often grow on surfaces in slimy layers called biofilms and during a pilot project in South Australia to store recycled sewage effluent, biofilms formed around the injection site. Researchers at CSIRO Land and Water and the University of Western Australia wondered whether this could lead to public health problems. The indigenous micro-organisms were unlikely to be a problem, but sewage water might contain pathogens. Tests for bacteria like *Escherichia coli*, a species found in faeces, are used as a way to check whether sewage has leaked into a water supply, but tests are sometimes positive without any obvious source of contamination. This has led researchers to think that pathogens can persist in the biofilms that sometimes coat the inside of water pipes. No-one knows whether the same happens in a natural environment like an aquifer.

Simon Toze and his colleagues decided to use a laboratory system designed to simulate porous rock to study the survival of both *E. coli* and *Pseudomonas aeruginosa*, a ubiquitous water-borne micro-organism and opportunistic pathogen. A very dilute nutrient solution flowed gently through a series of glass flasks containing microscope coverslips, and soon coated everything with patches of biofilm. Nitrogen gas was bubbled through the liquid to simulate the anaerobic conditions in an aquifer. To make the test bacteria easy to see, the researchers used strains that produced a green fluorescent protein. Then they simply had to retrieve a coverslip and check it for glowing green bacteria to see whether the test species had grown into the biofilm. If the bacteria did not join the biofilm, they should gradually be washed out of the flasks with the growth liquid.

The researchers managed to detect *E. coli* in the flasks long after it should have been washed away if it had not joined the biofilm, except when the liquid was recycled sewage effluent. Perhaps surprisingly, the *E. coli* cells died away more rapidly in this more nutritious medium. Earlier researchers have indicated that biofilms of indigenous river water bacteria can reduce the persistence of *E. coli*. The reason may be the presence of many more bacteria, all better adapted to this environment than *E. coli*. *P. aeruginosa* survived much better in the sewage effluent than the *E. coli* cells. These experiments indicate that although adding nutrient-rich effluent to an aquifer may stimulate the development of a biofilm, bacterial species will vary in their ability to survive within it. Pathogens like *E. coli* which are adapted to the human gut may not survive well, while others like *P. aeruginosa*, which are better adapted to a watery environment, may flourish.

Banning, N., Toze, S. & Mee, B.J. (2003). Persistence of biofilm-associated *Escherichia coli* and *Pseudomonas aeruginosa* in groundwater and treated effluent in a laboratory model system. *Microbiology* 149, 47–55.



Rabies alert in Australia

Until May 1996, everyone thought that Australia was free of rabies and rabies-like disease. Then, a virus with distinct similarity to the rabies virus was isolated from a juvenile black flying fox, and the situation became very murky. Since then this virus, named Australian bat lyssavirus (ABL), has been detected in all the common species of flying foxes in Australia, and also in the yellow-bellied sheath-tailed bat, which is insectivorous. Of additional concern is the fact that two people in Queensland have died from an illness with all the symptoms of rabies following contact with bats infected with ABL. Although vaccines against rabies are thought to provide protection against illness caused by ABL, more information was needed.

A collaboration between Australian scientists at the Queensland Department of Primary Industries, University of Queensland, and the Queensland Health Scientific Services and researchers at the University of Oxford in the UK, has investigated ABL to determine whether the virus is identical in all the infected bats, and to gauge the public health risk. ABL consists of a strand of nucleic acid encased in a protein shell surrounded by a lipid envelope. The lipid envelope is studded with glycoprotein spikes and the ABL researchers focused on the gene for this glycoprotein, as it is the first part of the virus to come into contact with a new host. Not only is it the major target for antibodies from the host's immune system, but it also has the function of allowing the virus to enter a host cell and so start an infection. Its structure is crucial in allowing ABL to infect a suitable host, such as a bat or person.

The researchers used samples of brain or salivary gland tissue collected from Queensland bats that had been caught after behaving abnormally – particularly if they had shown aggression towards humans or domestic animals. If the tissue tested positive for ABL with a fluorescent stain, the scientists attempted to extract the virus and analyse its genes. They analysed 22 isolates of ABL from both flying foxes and insectivorous bats, and compared them with other lyssaviruses from around the world, including rabies virus.

The ABL isolates divided into two groups, one from the fruit-eating flying foxes and the other from insectivorous bats. This is similar to the situation for bat lyssaviruses in other parts of the world, where bats with the same lifestyle harbour similar lyssavirus strains. In this study, ABL isolates collected from flying foxes caught 1,400 km apart were found to be virtually identical. Not only do flying foxes migrate over extensive distances, but thousands of them roost together during the day in trees. Under these circumstances, one strain of the virus therefore has a good opportunity to infect many bats. In contrast, the insectivorous bats travel much shorter distances, stay in groups of less than 30 and are unlikely to mix with flying foxes. The clear segregation between virus variants also suggests that ABL is rarely transmitted to other animals, but this is one aspect that the Australian scientists want to investigate further. While it has been suggested that the lack of variation between ABL isolates from the same bat species may be due to the virus becoming adapted to its most commonly encountered host, it has also been proposed that these viruses may have evolved to a point where they have become 'viral generalists' able to infect many different cell types such that they have a selective advantage when exposed to new host environments.

Guyatt, K.J., Twin, J., Davis, P., Holmes, E.C., Smith, G.A., Smith, I.L., Mackenzie, J.S. & Young, P.L. (2003). A molecular epidemiological study of Australian bat lyssavirus. *J Gen Virol* 84, 485–496.

Spore-forming Gram-negative bacterium

Four years ago Ryozo Iriye and Yukio Doi reported a rather strange bacterial species from activated sludge in a domestic wastewater treatment tank in Saku, Japan. The cells produced a red pigment, and contained structures called endospores. These are a characteristic of a few genera of bacteria that are within a larger grouping called the Gram-positive bacteria. When these species experience unfavourable conditions, such as a lack of nutrients, the interior of the cell transforms into a multi-layered structure around the bacterial DNA. This is the endospore, which can survive through adverse environments to grow again once conditions improve. The scientists, not unnaturally, assumed that they had found another species within this group, probably a member of the genus *Bacillus*, but were intrigued by some of its other features. They and their colleagues have now carried out a battery of tests on the organism and confirmed that it may be an example of something very interesting indeed.

Their tests show, without a shadow of a doubt, that the bacterium is a subspecies of *Serratia marcescens*. This is a member of the very large group of Gram-negative bacteria, none of which are known to produce endospores. However, their tests show equally clearly that pure cultures of the organism can produce structures very like the endospores of *Bacillus megaterium*, even down to the chemical dipicolinic acid that is only found in endospores. Cells containing these structures could survive a heat treatment of 62 °C for 15 minutes, while all the cells of an authentic strain of *S. marcescens* died at 60 °C. Authentic *Bacillus* endospores should have no difficulty in surviving these, and higher, temperatures. The researchers think that the most sensible explanation of their results is that they have isolated a strain of *S. marcescens* that has acquired the genes for endospore production from a *Bacillus* species within the environment of an activated sludge tank. If they are correct, an exciting example of natural gene transfer between two very distantly related organisms has been found.

Ajithkumar, B., Ajithkumar, V.P., Iriye, R., Doi, Y. & Sakai, T. (2003). Spore-forming *Serratia marcescens* subsp. *sakuensis* subsp. nov., isolated from a domestic wastewater treatment tank. *Int J Syst Evol Microbiol* 53, 253–258.

Chimeras raise their heads

One of the most effective molecular biological methods to discover what bacteria are present within an environment is to extract DNA from it and then use the polymerase chain reaction (PCR) to amplify one particular DNA sequence. This is the 16S rRNA gene sequence, which is an essential part of the cell's protein synthesis machinery. Decades of study of this molecule by hundreds of scientists have ensured that its characteristics are known in exquisite detail. Some parts of the 16S rRNA gene are invariant in all bacteria, while other regions are distinctive of particular groupings, or even individual species. By carefully choosing which sections to amplify, researchers can use PCR of the 16S rRNA gene to search for the bacteria of their choice, including new species.

However, Philip Hugenholtz and Thomas Huber from the Advanced Computational Modelling Centre at the University of Queensland have pointed out, in a recent issue of IJSEM, that this tool comes with a distinct drawback. It is possible to produce chimeric 16S rRNA gene sequences. These are artefacts of PCR that are caused by the amplification products of two separate 16S rRNA sequences becoming joined together. This results in a sequence with parts from two distinct organisms. If the researchers do not realize what has happened, their analysis will suggest the presence of a novel organism. However, this organism is actually non-existent, and the 16S rRNA gene sequence generated has the potential to confuse subsequent taxonomic studies. Scientists have been aware of this problem for over a decade, and attempt to both prevent chimeras forming and detect any that slip through. However, when Hugenholtz and Huber searched public databases of 16S rRNA gene sequences, they quickly found a number of chimeras. The authors suggest that these, and any more that come to light, should be removed from the databases, split into their component halves and then resubmitted. As an aid to identifying chimeras, they have created a program called BELLEROPHON (http://cassandra.visac.uq.edu.qu/perl/bellerophon.pl).

Hugenholtz, P. & Huber, T. (2003). Chimeric 16S rDNA sequences of diverse origin are accumulating in the public databases. *Int J Syst Evol Microbiol* 53, 289–293.

TB from the 18th century

Tuberculosis is caused by the bacterium *Mycobacterium tuberculosis*. It may have been responsible for a quarter of all deaths in Europe between the sixteenth and eighteenth centuries, and then spread worldwide. Researchers in the UK and Netherlands, working with staff at the Hungarian Natural History Museum, have been finding out about this ancient disease. The opportunity came following the chance discovery of a sealed crypt in the Dominican church at Vác in Hungary during repairs in 1994. It turned out to be the last resting place of members of prominent local families and clerics who had died between 1731 and 1838. Many of the bodies had become naturally mummified, and from examining the remains, as well as local family records, it seemed possible that many of the people were suffering from tuberculosis at the time of their death.

The unusually well-preserved state of the bodies allowed computer tomography to be used to confirm the symptoms of tuberculosis in one of them. Because the body tissues were so well preserved, the researchers sought permission to take some samples to carry out a detailed study of the mycobacterial DNA. Although mycobacterial DNA has been detected in old human remains, it is usually so fragmented that researchers can do little more than be confident that it is present. The complete sequences of several modern strains of *M. tuberculosis* and its relatives are now known and researchers want to understand how the bacterium has evolved. As well as purely scientific interest, this might indicate why it is such an effective pathogen.

The researchers took tissue samples from a mother, who died in December 1793 at the age of 55 and her two daughters. The younger daughter, aged 14, died in March 1795 and the older on Christmas day 1797, aged 28. To be confident about their findings, the researchers took very careful precautions against contaminating their samples. In addition, they obtained poorer results when they tested for longer sequences of DNA, which was an additional indication that they were really dealing with fragmented pieces of 200-year-old DNA, rather than a contaminant of fresh DNA that would be substantially intact.

One question that the researchers wanted to answer was whether the tuberculosis was in fact caused by *M. tuberculosis* or by its close relative *M. bovis*. This species infects cattle, but can infect people, particularly through dairy products. In the Europe of the past, when people lived closer to their domestic animals, many more people may have been infected with it than today. However, the researchers' tests found no evidence of *M. bovis* in the three bodies. Instead, several tests showed that the women were infected with *M. tuberculosis* similar to two modern strains. These included characteristics that are found across the globe today, which is consistent with the idea that the modern tuberculosis epidemic began in Europe in the 1700s and then moved to the New World and Africa.

Fletcher, H.A., Donoghue, H.D., Taylor, G.M., van der Zanden, A.G.M. & Spigelman, M. (2003). Molecular analysis of *Mycobacterium tuberculosis* DNA from a family of 18th century Hungarians. *Microbiology* 149, 143–151.

Reviews

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A classified compendium of book reviews from 1996 to the present is also available on the website.

A list of publisher's website addesses is given on p. 48.

Modern Microbial Genetics, Second Edition

Edited by U.N. Streips & R.E. Yasbin
Published by Wiley-Liss (2002)
£88.50, pp. 657
ISBN: 0-471-38665-0

A cross between a textbook and a collection of monographs, this retains the format and ethos of the first edition. It reviews our current understanding of genetic transactions in bacterial cells, demonstrating their elegance and variety, and explaining their complexity. Each chapter is independently authored and their length and style of coverage varies, but all provide a clear perspective, often laced with insight and enthusiasm. The experimental basis of the science is emphasized, and several chapters address how genetic technologies can be applied across the bacterial spectrum. Any microbiologist would find chapters to interest them, but it is expensive; it will make an excellent purchase for libraries and a source text for advanced undergraduate courses in bacterial genetics. Helping bridge the gap between textbooks and experimental research, it would also be an informative and very browsable addition to the lab bookshelf.

■ ***Anne Moir***
University of Sheffield

Designs for Life: Molecular Biology after World War II

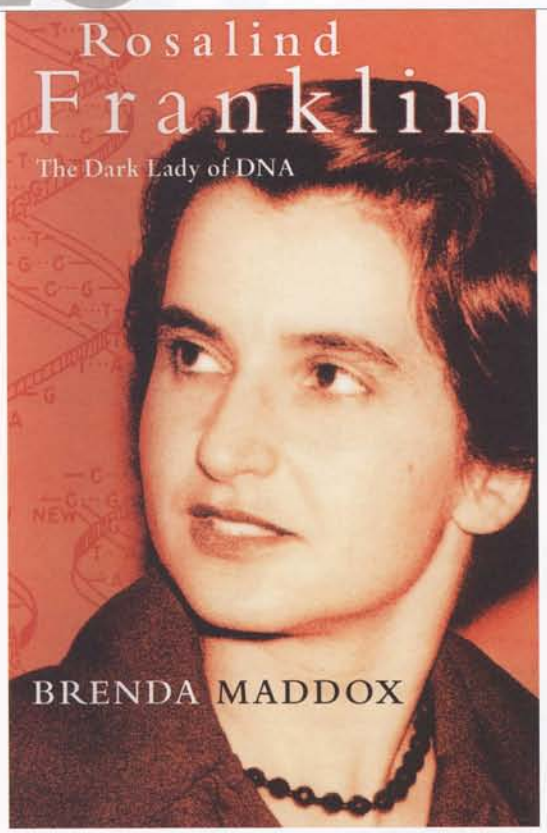
S. de Chadarevian
Cambridge University Press (2002)
£35.00/US$55.00, pp. 423
ISBN: 0-521-57078-6

Ask a microbiologist when molecular biology began and the answer will probably be: in 1953, with the announcement by Watson and Crick of the structure of DNA. Not necessarily so says Soraya de Chadarevian. True, the term was not generally used before 1953, but the seeds that grew into molecular biology as we now understand it had been sown much earlier, in the post-war rise of 'biophysics'. British scientists, some of whom had learned about science with practical objectives through their wartime activities, made a unique contribution to this development. The resulting groundbreaking work on protein crystallography at Cambridge by Kendrew and Perutz was a direct precursor of Watson and Crick's work in the unit that later became the world famous Laboratory of Molecular Biology. Dr de Chadarevian traces the making of molecular biology 'through the prism' of the LMB, its origins, ethos and role in shaping the growth and influence of the new field, including DNA sequencing, genomics and monoclonal antibodies. This is a scholarly work, drawing on innumerable interviews and unpublished letters, but it is also very readable, with many interesting photographs. The book is a 'must' for academics teaching molecular biology, and for anyone with even a passing interest in the history of what perhaps will be the most pervasive science of the 21st century. It provides a timely background to the worldwide celebrations that mark 2003 as the 50th anniversary of the double helix.

■ ***David Hopwood***
John Innes Centre, Norwich

Rosalind Franklin. The Dark Lady of DNA

By Brenda Maddox
Published by Harper Collins (2002)
£20.00, pp. 380
ISBN: 0-00-257149-8



Brenda Maddox' new biography aims to defend Rosalind Franklin, as much from the caricature-like presentation in Watson's book *The Double Helix*, as from her subsequent appropriation as feminist icon and to recover the full story of her life, from her up-bringing in a large, tightly-knit Jewish family in London to her premature death from cancer, at the time when she was heading a successful virus structure research group at Birkbeck College. A strong feature of Maddox' skilful narration are abstracts from Franklin's own vivid letters sent from an early age to family and friends. The nitty-gritty of science, although a central part of Franklin's daily life in the laboratory, finds less space in these letters and in Maddox' account, which clearly addresses a non-scientific readership. But this is hardly a drawback of the book as conceived. To the contested events surrounding Watson and Crick's presentation of the double-helical model of DNA Maddox brings an even-handed approach, although she leaves no doubt that Franklin was denied the credit she deserved. Fascinating to read, the book is destined to open rather than to close discussions on one of the most celebrated scientific events of the twentieth century.

■ ***Soraya de Chadarevian***
Cambridge University

The Genomic Revolution: Unveiling the Unity of Life

Edited by M. Yudell & R. DeSalle
Published by Joseph Henry Press (2002)
£19.95, pp. 250
ISBN: 0-309-07436-3

This is a written version of presentations at a conference entitled *Sequencing the Human Genome: New Frontiers in Science and Technology*, held in September 2000 at the American Museum of Natural History. The authors (all from the US) are eminent in their field. They cover sequencing technology, the Human Genome Project (though there is only passing reference to the input from outside America), applications of genomics, and the resulting social issues. According to the preface the book is intended for both lay and professional audiences, but to my mind it falls between the stools and will not satisfy either. There is too much unexplained jargon for the layman and the unattractive black and white diagrams are either very simplistic or over-complicated. The Editors admit that the book was 'long in the making'; this means it is out-of-date and therefore of limited interest to the professional.

■ ***Pat Goodwin***
The Wellcome Trust

Supercell. Making Sense of Science Children's Books Series

Series Editor F. Balkwill, Illustrated by M. Rolph
Published by Portland Press (2002)
£6.99/US$11.00, pp. 32
ISBN: 1-85578-093-3

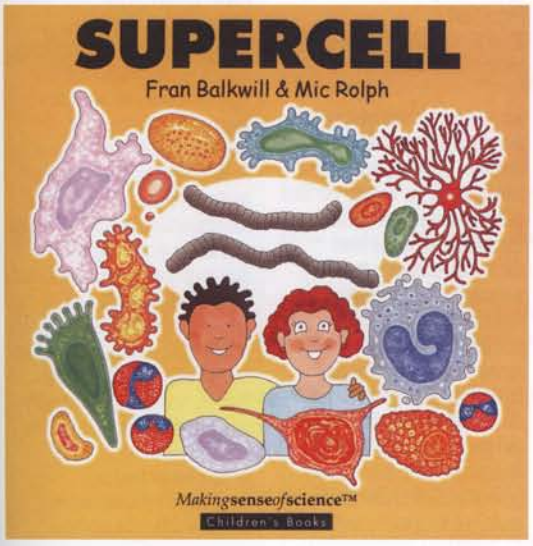
I shared this book with a group of Year 4 children as a non-fiction text rather than as a science book for an area of science we were covering. The children's knowledge of this subject was sketchy although they did know the terms 'cells' and recognized

this as a part of their bodily make-up. Some of the words within the text were difficult for them to understand – microscopic, colonize, etc. The children enjoyed the pictures and were able to explain their own thoughts and ideas, which were not completely accurate. On the whole top Year 4 children struggled to work with this book, finding the text too much and the concepts too difficult. Their own assessment of it was that they initially liked the layout, the text is written in a font they found easy to read, but the technical language was challenging and the concept difficult to fully understand.

■ ***M. Beeching***
Redlands Primary School, Reading

I shared this book with a couple of other Year 6's and we agreed that it is an interesting, funny, but still scientific, book about human DNA and cells. We believe that it would be suitable for most competent readers from Year 6 upwards. One Year 6 quoted "*I liked the page 'In the beginning' – it taught me lots of interesting things I didn't already know!*" I also found out many things from this book – mainly long names! My favourite was deoxyribonucleic acid! I think that this could make very interesting reading for someone planning a science lesson on the human body, but could make some children of the wrong age very confused! Overall I think it could be a very useful science tool.

■ ***Dexter Ryan and Krishan Sharma-McLachlan (Year 6)***
Redlands Primary School, Reading



Rabies

Edited by A.C. Jackson & W.H. Wunner
Published by Academic Press/Elsevier Science (2002)
US$125.00, pp. 493
ISBN: 0-12-379077-8

Rabies is a welcome summary of new discoveries, methods and techniques. The excellent chapter on molecular biology by Wunner distils the plethora of papers which have emerged over the last decade. Jean Smith reveals the detailed epidemiological information which is now derived from genetic typing of lyssaviruses. The chapter on the epidemiology of infection is dominated by data from North America. The immunology section concentrates on experiments in mice. The clinical features of human 'survivors' of rabies encephalitis is an apt addition by Jackson, whose review of human disease also includes rabies-related lyssavirus infections. His comprehensive balanced chapter on pathogenesis details the fragments of data which have yet to explain the intriguing neuronal transport and effects of rabies virus *in vivo*. Trimarchi & Smith's experienced evaluation of diagnostic techniques is a unique practical laboratory guide. This is a valuable view of rabies as seen from North America rather than a global survey.

■ ***Mary Warrell***
John Radcliffe Hospital, University of Oxford

Mobile DNA II

Edited by N.L. Craig, R. Craigie, M. Gellert & A.M. Lambowitz
Published by American Society for Microbiology (2002)
US$169.95, pp. 1,254
ISBN: 1-55581-209-0

This book focuses on genetic elements and processes that use non-homologous recombination to create new combinations of DNA. This includes, for example: transposable elements and integrating viruses; mobile introns and retrons; multimer resolution; antigenic variation in parasites and pathogens; antibody formation; and mating type conversion. Each chapter is written by specialists, so that style and focus vary widely. After an introductory section, the topics are primarily organized by the mechanism of recombination, but there is also a section on genomes and mobile DNAs which I personally will find the most useful for teaching. There is a good balance between prokaryotic and eukaryotic systems. The index is comprehensive and will facilitate its use as a reference work, an element which could be further strengthened in a future edition, but I noticed some errors in cross referencing. This is an excellent resource for a lab working in this area – graduate students will find it particularly useful to provide an overview of related topics. It is a must for libraries as a teaching resource for courses covering genomics of any sort.

■ ***Chris Thomas***
University of Birmingham

Management of Chronic Viral Hepatitis

By G.R. Foster & R.D. Goldin
Published by Martin Dunitz (2002)
£29.95, pp. 200
ISBN: 1-84184-088-2

The field of viral hepatitis is changing continually with major advances in the clinical management of infected individuals. This is an excellent and concise book, which provides easy access to current information, which is generally only accessible in larger textbooks. The format of the book with clearly defined chapters and subheadings in conjunction with well presented tables and diagrams makes the book very easy to read, and enables the reader to easily identify areas of interest. The yellow boxes, which highlight pertinent facts and the small question and answer section at the back of each chapter help to reinforce the most important facts of each chapter. The sections of the management of HCV and HBV are very well presented and include up-to-date recommendations. In particular the algorithms for both testing and anti-viral treatment are very well presented and would be very useful for reference for clinical virologists.

■ ***Jeff Connell***
University College Dublin

Advances in Microbial Physiology, Vol. 44

Edited by R.K. Poole
Published by Academic Press (2001)
US$129.95, pp. 277
ISBN: 0-12-027744-1

This six-chapter volume on 'stress' joins the microbial physiology series under Robert Poole's expert Editorship. Green *et al.* provide an expertly narrated tour of CRP-FNR function and Hecker and Volker describe general bacterial stress responses. Lund sketches the physiological functions of molecular chaperones, followed by Coote's review of environmental cue sensing in *Bordetella*. Robinson and colleagues describe microbial metallothioneins, outlining advances in our understanding of the physiological mechanisms involved in the 'metal bashing' economy of microbes. Finally, Rowbury fashions an interesting, provocative chapter on generation and detection of physico-chemical cues used as molecular harbingers of imminent physiological stress. This volume, appropriate for advanced undergraduates, postgraduates and other researchers, has varying chapter presentational styles – but is accessible throughout. It is an essential purchase for any departmental microbiology library. I found it extremely useful as an information source on multiple topics covering advanced teaching areas in molecular microbiology.

■ ***George Salmond***
University of Cambridge

Food Shelf Life Stability: Chemical, Biochemical, and Microbiological Changes

Edited by N.A.M. Eskin & D.S. Robinson
Published by CRC Press (2001)
US$109.95/£76.99, pp. 370
ISBN: 0-8493-8976-3

This book comprises 10 chapters in 370 pages. The authors are primarily from Canada, but there are also contributions from scientists in Mexico, Israel and the UK. If one was to go by the title alone, one would expect a significant portion of the book to involve discussions on the effects of food components, packaging and shelf life on the numbers and types of micro-organisms in foodstuffs. In fact, very little of the book is devoted to microbiology with most discussion being concerned with changes in either the physical or chemical characteristics of raw and processed foods. Thus this book is probably not a very useful addition

to the library of SGM members. It would, however, be a quite useful publication for students in food science and food technology. I would imagine that its target audiences are undergraduate and early postgraduate students and people in the food industry with a professional interest in food quality. In general the book is well written and, because there is a tendency not to over complicate issues, a quite easy read. Tables are clearly presented and generally easy to follow, although a number of the diagrams are of poor quality. That having been said, the book is not an expensive one for a collected work of this kind particularly as many of the authors have international reputations in their subject areas. It is in my view that this book would allow food scientists to get a good understanding of the factors affecting shelf life.

■ ***Tom Humphrey***
University of Bristol

Cells, Gels and the Engines of Life: A New Unifying Approach to Cell Function

By G.H. Pollack
Published by Ebner and Sons (2001)
US$27.95, pp. 305
ISBN: 0-9626895-2-1

The publisher's hype on the covers of this book would appear to make criticism by mere mortals seem perverse! It is written in a style that either entertains or annoys, depending on the reader's preferences or even mood. Personally, I find the cartoons and occasional 'Disney' layout annoying. Do not, however, be put off by these criticisms. Most modern biology books are prescribed by our current excessive-peer reviewed mentality; this book breaks free and challenges many of the sacred cows of cell biology. The author treats the cell as a gel and believes that our current thinking on living systems is over complex. To my mind though, the chapter on the origin of life, like most of its kind, is less than convincing. Buy a copy, ignore the style and see if, as suggested by one of the cover reviewers, it becomes your 'scientific bible'. Perhaps not, but it certainly makes a challenging read.

■ ***Milton Wainwright***
University of Sheffield

The Mechanisms of Neuronal Damage in Virus Infections of the Nervous System. Current Topics in Microbiology and Immunology, Vol. 253

Edited by G. Gosztonyi
Published by Springer (2001)
€126.00/SFr232.19/£93.00/US$135.00, pp. 278
ISBN: 3-540-67617-1

The subject of neurovirological pathogenesis is not an easy one. The twelve reviews compiled into a single volume on different aspects of how viruses actually do it, is no exception. It is not the sort of book that medical students would use for cramming before an exam, nor does it fall into the category of lofty tomes used for reference. It is rather a book for academics who have a personal interest in the field and after having perused the different chapters would either feel happy because the author agrees with their hypothesis, or irate because something glaringly obvious was missed. My only personal disappointment was that there was not enough said on the fascinating topic of how viral proteins interfere with neurotransmitters, which may result in excitotoxic neuronal death or chronic degeneration.

■ ***Ras Smit***
Public Health Laboratory, Birmingham

Antibiotic Development and Resistance

Edited by D. Hughes & D.I. Anderson
Published by Taylor & Francis (2001)
£65.00, pp. 264
ISBN: 0-415-27217-3

I was quite prepared to not like this book, as there have been very few recent good reviews of antibiotic resistance, which have been informative and useful and almost none on antibiotic development. However, I started to change my mind from the first chapter and would highly recommend anyone who is interested in any aspect of antibiotic resistance and the development of new antibiotics to have access to this book. The chapters cover the mechanisms and genetics of antibiotic resistance that we need to know about today, no lists, and discuss how new antibiotics might be discovered. This is a novel approach and one that works very well. It is unfair to single out specific chapters but I particularly liked the chapters on integrons and gene cassettes and efflux mechanisms and multi-drug resistance. No UK contributors though: shame!

■ ***Hilary Richards***
University College London

Techniques in Mycorrhizal Studies

Edited by K.G. Mukerji, C. Manoharachary & B.P. Chamola
Published by Kluwer Academic (2002)
€220.00/US$202.00/£138.50, pp. 554
ISBN: 1-4020-0532-6

This book aims to describe the various techniques used to study mycorrhizal biology. Despite the title, a number of more general techniques are also covered, including general microbiological isolations, rhizosphere biology and soil analyses. Ten chapters focus on arbuscular research, three on ectomycorrhizas and four on ericoid, orchidoid and monotropoid mycorrhizas. A wide variety of useful methods are covered, and sometimes explicit instructions are provided. Unfortunately, some chapter references are not always up-to-date and the opportunity has been missed to include more recent field and laboratory functional techniques. Detailed consideration of the problems associated with implementing or interpreting data has often been omitted. Also, undersized, monochrome (no colour) photographs and numerous typographical errors lessen the impact. Nonetheless, this volume is a valuable methodological source.

■ ***Lynne Boddy & Damian Donnelly***
Cardiff University

Genomic Technologies: Present and Future. Functional Genomics Series, Vol. 1

Edited by D.J. Galas & S.J. McCormack
Published by Caister Academic Press (2002)
£90.00/US$180.00, pp. 418
ISBN: 0-9542464-2-X

The chapters in this book reflect the range of technical advances that have, and are presently, transforming the way we perform genomic analyses in the lab. Topics covered range from the role of robotics in the automation/transformation of certain molecular biology procedures (e.g. DNA sequencing) to new imaging methods available that permit chromosome structure analysis and gene function elucidation. Topics covered in this book are generally covered well and clearly explained, plus each chapter contains a helpful further reading section. This book covers a broad subject matter, but would be of general interest to anyone working within the genomic technology field. However, given the retail price and the number of typographical errors contained within, on the whole I was slightly disappointed with this book.

■ ***Kerstin Williams***
Arrow Therapeutics

Science and Technology Ethics

Edited by R.E. Spier
Published by Routledge (2002)
£15.99, pp. 247
ISBN: 0-415-14813-8

This book is part of an excellent series on Professional Ethics, under the general editorship of Ruth Chadwick. However, this particular volume may be less widely cited than it deserves. The main reason for this is that it attempts to cover too much. Of its 11 chapters, one is an introductory overview, one looks at how science is done, one looks at computers and society, one at science and the military, three at fundamental aspects of ethics, two at engineering ethics, one at bioethics and one at ethical issues associated with nuclear power. The chapters also vary considerably in their level. Michael Atiyah provides a very readable and non-referenced chapter on science and the military which would not be out of place in a good Sunday newspaper. At the other extreme, several of the authors produce academic analyses about the foundations of ethics. My favourite chapters were those by Brad Hooker, who provides a particularly useful discussion of consequentialism, Andrew Reeve, who writes extremely well about the existence of a social contract, Vivian Weil, who looks with great clarity at the roles and responsibilities of engineers, and Susan Hodgson and Slobodan Perdan, who provide an excellent analysis of engineering and the environment.

■ ***Michael Reiss***
Institute of Education, University of London

Publishers' website addresses

Academic Press	www.academicpress.com
ASM Press	www.asmusa.org
Caister Academic Press	www.caister.com
Cambridge University Press	uk.cambridge.org
CRC Press	www.crcpress.com
Ebner and Sons	www.ebnerandsons.com
Harper Collins	www.harpercollins.com
Joseph Henry Press	www.nap.edu
Kluwer Academic	www.wkap.nl
Martin Dunitz	www.dunitz.co.uk
Portland Press	www.portlandpress.com
Routledge	www.tandf.co.uk
Springer	www.springer.de
Taylor & Francis	www.tandf.co.uk
Wiley	www.wileyeurope.com

Comment

The significance of European Bat Lyssavirus infection in Great Britain

A bat conservationist in Scotland died recently from a form of rabies after being bitten by an infected animal. This caused much media attention, but how much of a risk does bat lyssavirus pose to human health in the UK?

Bat rabies is enzootic in the UK. The first bat found to have European Bat Lyssavirus (EBL) infection, in Newhaven in 1996, was assumed to have been imported, but a further bat isolation from Lancashire in 2002 and the human death in Scotland, have confirmed that the virus is indigenous. This discovery reveals unexpected dangers and creates opportunities for misunderstanding and inappropriate responses.

Bat rabies has occurred in continental Europe for at least 50 years, but only four human deaths from infection have been reported. On the continent, where there has been a greater danger of fox rabies, EBL infection is regarded as an insoluble problem which causes little concern, and the only costs are increased need for post-exposure treatment and the prolonged anxiety of recipient patients. Since the UK has been free of rabies for a century, should we be more concerned?

The distribution of the four EBLs seem well defined, so far as is known. Lyssavirus genotype 5 is EBL type 1, and genotype 6 is EBL type 2, both have subtypes a and b. EBL type 1a, the most common, occurs across Northern and Central Europe to Russia. EBL type 1b is in some Western coastal countries down to Spain. EBL type 2 has very rarely been identified: 2a in the Netherlands and the three UK isolates, and 2b in Switzerland. Both infected English bats were Daubentons' (*Myotis daubentonii*), whereas the few Dutch EBL 2a isolates came from *Myotis dasycneme*. Both genotypes of EBLs cause similar rabies-like encephalitis in man, but differences in their glycoproteins may influence pathogenesis. There is very little known about natural infection with EBL 2.

European insectivorous bats are protected species and population control would be inappropriate and impossible. Although oral vaccination has dramatically controlled the fox rabies epizootic, bats are inaccessible to vaccine treatment.

What are the risks of EBL infection in the UK? Human disease has always been associated with known contact with a bat (unlike the majority of human infections from bats in the USA, where the virus is rabies genotype 1). Bats which appear sick or behave abnormally are more likely to be rabid. However, apparently healthy bats may be infectious before symptoms of their illness show. European bats can recover from infection, become seropositive, and survive for years. Virus RNA has been detected by PCR in the brain or saliva of healthy looking Spanish bats, without evidence of active viral replication. Re-emergence of infectious virus may be possible.

The chance of EBL infecting other animals is small but finite. It is striking that four of the five EBLs identified in terrestrial animals to date have been isolated from Danish sheep. The fifth was from a stone marten in Germany recently. Detailed typing of rabies isolates has not been routine in Europe, but is increasingly performed. Although there has been no known transmission of EBL from a terrestrial mammal to man, the possibility exists. Should domestic animals dying from undiagnosed acute neurological diseases in the UK now be tested for rabies?

The slightest physical contact with a bat now requires immediate post-exposure treatment. The first-aid procedure of scrubbing the wound with soap or detergent and water, should be widely disseminated. Anyone who plans to handle bats should have pre-exposure prophylaxis, but who pays for the expensive vaccine?

Current rabies vaccines, all containing genotype 1 antigens, have had variable effects against EBLs in different experiments. Protection may be less efficient against some EBLs than against most terrestrial virus strains. As there is no alternative treatment, the urgency of post-exposure treatment is paramount. Furthermore, the enhanced secondary immune response provided by pre-exposure vaccination is even more important here.

The UK now joins France, Denmark, Belgium, The Netherlands and Spain in being enzootic for EBL in the absence of rabies genotype 1 virus. Australia harbours its own rabies-related virus, genotype 7, Australian Bat Lyssavirus, in colonies of flying foxes (*Pteropus* sp., fruit bats). According to the WHO definition, in the absence of terrestrial rabies, all these countries remain officially rabies-free!

EBL has probably existed in the UK for many years, and it cannot be compared to some other potential virus infections, for example West Nile virus, which has spread uncontrollably across the USA in three years. Although mosquito-transmitted, the virus survives winter temperatures and avian vectors cover great distances. There is no treatment and no vaccine or other specific prevention against West Nile virus infection. The whole population is at risk and other animals can be infected. Transfer of the virus to the UK is not inconceivable and perhaps the discovery of EBL here will alert people to the importance of keeping foreign animals out of Britain. The 'pet-passport' scheme, allowing pets to travel abroad, has already introduced parasitic infections not previously seen here.

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Further reading

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