Making money from microbes
Patent strategies
Material issues
Spinning out and starting up
Getting into biobusiness
Biotechnology YES – being entrepreneurial
Uninvited participants in whisky fermentation
The future of scientific journals
**Contents**

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**Articles**

- **Making money from microbes** David Onions
- **Money matters** Simon Browning
- **Patent strategies for biotechnology companies** Sandy Primrose & Richard Gillard
- **Materials Transfer Agreements—"material" issues** Claudia Riordan
- **Making money from microbes—case studies**
- **Getting into biobusiness** Faye Jones
- **Biotechnology** YES John Peberdy & Gavin Thomas
- **Lactic acid bacteria—the uninitiated but generally welcome participants in malt whisky fermentation** Fergus G. Prest
- **Open access publishing—is it the future for scientific journals?** Ron Fraser

**Regular Features**

- **Society News**
  - November Council Meeting & Council News
  - News of Members & Staff News
  - SGM Membership Certificate Offer
  - SGM Prizes & Lectures
  - More back issues of SGM journals online
- **Grants**
- **IUMS Congresses 2005**
- **Health matters**
- **Elections to Group Committees 2004**
- **Meetings**
- **Public Affairs**
- **Gradline**
- **Diary**
- **SchoolZone**
- **Reviews**
- **Health matters**
- **Meetings**
- **Public Affairs**

**Other Items**

- **A new year resolution from the SGM President** Hugh Pennington
- **Communicating microbiology workshop**
- **A strange episode in the history of antibiotics** Michael Cattle
- **Unearthing your 'Vision of Science'**
- **Obituary: Dr John Smith**
- **International Research Fellowship report**
- **Involvement of quorum sensing in regulating pyoverdine synthesis in Pseudomonas aeruginosa lain Larnot**
- **Education Development Fund report**

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**Erratum**
In the article "Does West Nile Virus pose a threat to the UK?" by Ernest Gould (Vol. 30, 160-161), the sentence starting 'Since its emergence 20 years ago...' should read 'Since its emergence 2000 years ago...'

The views expressed by contributors are not necessarily those of the Society; nor can the claims of advertisers be guaranteed.
2003 opened with SARS in China teeing up for its transmission to Hong Kong, Singapore, Vietnam and Canada in the spring and the summer. It closed with a case of BSE in the United States, and the Secretary of the US Department of Agriculture saying that she would be eating beef for Christmas. Shades of John Gummer and a succession of English Chief Medical Officers addicted to eating it ‘with confidence’! As ever, the objects of our professional attention have been showing their teeth, reminding us that we share the world with them, that there is much unfinished business, and that we ignore them at our peril. Even if influenza virus continues to be relatively quiet, noroviruses have continued to make life miserable for passengers on cruise liners and for patients in hospitals. The best that could be said about those dangerous institutions is that to get projectile vomiting from a virus there is generally a better deal than being infected with another well-ensconced hospital resident, MRSA.

A major outcome of all these events has been their political impact. Senior Chinese officials were sacked because of SARS. Just one case of BSE immediately became an emergency to be handled at the top level of the US administration. Yet another government initiative to control MRSA was announced in Westminster at the end of the year. So it is reasonable to conclude that politicians need microbiologists as never before. Many relationships could be fostered, but it is you, the members, who will do the work. Go to it!

The one-day training workshop will take place on 29 April at SGM Headquarters in Reading. It will be run by Myc Riggulsford, a professional facilitator with extensive experience of science journalism. Each participant will work with Myc to produce, by the end of the day, a one-page article in a readable style that communicates the key points about a piece of their research and its relevance to the wider community. The articles will be co-ordinated by SGM staff who will also edit and design the publication and get it into print. Key points from the workshop will be summarized and the resultant factsheet posted on the SGM website for the benefit of all members.

As scientists we fully understand the importance of carrying out microbiological studies, but the public, which tends just to hear about controversial issues such as GM foods and MMR vaccination, representing only a tiny fraction of UK research, may have a very negative view of science. Millions of pounds are spent each year on research involving micro-organisms and yet the public often perceive it as esoteric and unlikely to impact significantly on their lives. What can we do to change their minds and alert them to some of the amazing discoveries being made?

Scientists have a responsibility to explain their findings to the world outside of academia. Indeed, this is now required by many funding bodies. SGM, which has always striven to improve the public understanding of microbiology, announces an exciting initiative to help its members communicate their research and disseminate it to the wider community.

The intention is to produce a research-focused promotional publication. This will have an attractive, glossy format and take a case study approach. It will be distributed free of charge to schools, at careers fairs and at science events for the public, but it will also be a useful tool in influencing policymakers involved in research funding. The obvious approach would be to commission the articles from SGM scientists who are already good at writing for the public. Instead the Society is taking the opportunity to offer training to scientists who have less experience in this area, but wish to develop their science communication skills.

Each participant will get an expenses-paid day out at Marlborough House, professional development in communication skills and positive publicity for themselves and their institutions. They will also fulfil the promises made in their grant applications to disseminate their research findings to the public. Copyright for the articles will rest with SGM.

Interested in taking part?

Each participant will get an expenses-paid day out at Marlborough House, professional development in communication skills and positive publicity for themselves and their institutions. They will also fulfil the promises made in their grant applications to disseminate their research findings to the public. Copyright for the articles will rest with SGM.

There will be places on the course for 10–12 microbiologists of final year postgraduate level or above. The objective is to cover a broad range of topics in the publication. If you wish to be considered for a place, please email Faye Jones (fjones@sgm.ac.uk) giving full contact details, a brief CV and a summary of your research topic. The deadline for applications is 12 March 2004.
Making money from microbes

David Onions

Making money out of microbiology is not new. It has been suggested that the origins of the earliest fermented beers range back as far as 5,000 years. Like the other staples arising from microorganisms, bread, wine and cheese, beer played an important part in early economies. In the last century, microbiology underwent two revolutions and in both cases the scientific developments and social benefits were dependent on interaction between scientists and new industries. Now in the midst of the second revolution, recombinant DNA, some of the features that have led to successful commercialization of scientific ideas are becoming apparent. These have included:

● The availability of venture capital
● Flexible employment contracts permitting staff of academic institutions to play a leading role in the formation of companies
● A scientifically driven and flexible regulatory environment
● A culture of enterprise.

It is no accident that the biotechnology revolution started in the USA and particularly in California where all of these elements have combined with outstanding success. In other countries where one or more of these elements has been lacking, progress has been delayed, despite the presence of world-class academic research. In Germany the 'gene laws' and rigid academic contracts inhibited biotechnology company development until the second half of the 1990s. In 1996 the German government initiated a programme to create one of the world's leading biotech sectors by 2000. While this policy resulted in a burst of company formation, rising from 225 in 1999 to 370 by 2001, the hasty creation of so many companies has inevitably led to failure of some and by 2002 the number had fallen to 360.

In the UK, the availability of start-up venture capital was certainly a problem in the 1980s and until recently entrepreneurial activities were viewed with some distrust by the academic community. Nevertheless, the UK now has a thriving biotech industry with two primary centres in the London, Cambridge, Oxford triangle and a second one based around the biomedical universities in Scotland. A notable feature of the Scottish development has been the involvement of Enterprise Scotland, a government agency that has assisted in the creation of a receptive environment for biotechnology. One of the innovations in Scotland has been the establishment of Intermediary Technology Institutes aimed at fostering the transfer of academic activities into new industries.

Biotechnology is becoming one of the leading industries of the first half of this century. In the US biotechnology already generates annual revenues of 26 billion Euros and employs 142,000 people, many of them with backgrounds in microbiology. Europe lags behind, but revenues increased by 10% in 2002 to 7-6 billion Euros while employment slipped a little to 33,000. While the focus of microbiology remains on the healthcare and food industries, new microbiological applications are emerging. Microbiology has been playing an increasing part in environmental remediation and the first steps have been made in applying the science to nanotechnology. Despite the setbacks that have been encountered, gene therapy will evolve as an adjunct therapeutic modality for cancer treatment and as a treatment for some genetic diseases.

In this edition of Microbiology Today, the experiences of microbiologists who have had the courage to start new companies and the experiences of scientists involved in public policy and science have made a valuable insight into the commercialization of microbiology. Microbiology has claims to be one of the major beneficial influences on societies in the last century. Technological change is often the driving force of social change and in this century microbiology will continue to transform lives in ways yet to be imagined. Continued success will depend upon public understanding and acceptance of our discipline, and upon synergistic and equitable arrangements between academia and industry.

● David Onions is Professor of Veterinary Virology at the University of Glasgow and was a founder of O-One Biotech which was recently acquired by BioReliance. Tel. 0141 946 9999 email d.onions@bioreliance.com

Further reading


Coming up with a great discovery is one thing, but financing its development is another matter. Simon Browning sheds some light on ways to fund a new biotechnology venture.

Hidden in the laboratories of the world's best research organizations and universities are discoveries and inventions capable of creating significant wealth. But unlike in industry, those who have made discoveries and inventions are only infrequently motivated by the possibility of exploiting a profit opportunity. After all, why go into academia if you want to be an entrepreneur?

Starting a business can be a life-changing experience. The cultural change from grant-based research to investment-based sales and production requires a major shift in mindset - it's certainly not for everyone, but with the right support scientists can choose to enter the new venture full time, or may remain within academia as a technical consultant. Few academic researchers are cut out to be CEOs of high-growth businesses.

Traditional funding routes for biotech companies have included a number of financing rounds, starting with proof of concept and seed funding before larger amounts are invested as 'Series A' and 'Series B' rounds. A tougher investment environment has led to a reduction in the number of funding rounds and pressure on businesses to produce revenue more quickly.

**Case studies**

1. **Syntopix Ltd**
   Founded by two members of Leeds University’s Skin Research Centre, Syntopix has adopted a strategy geared towards the rapid discovery of effective topical alternatives to antibiotics for clinically and economically important dermatological diseases. The first of these will be Staphylococcus aureus infections, including methicillin-resistant S. aureus (MRSA), followed by acne.

   Researchers Anne Eady and Jon Cove have received £500,000 through the Wellcome Trust’s technology transfer division (formerly Catalyst Biomedica) for a pre-clinical research programme, and Syntopix will employ four scientists to assist the process.

   New anti-staphylococcal drugs are urgently required to prevent the spread of both methicillin-susceptible S. aureus and MRSA within and outside hospitals. Fears are growing that MRSA is emerging as a significant community pathogen.

   ‘The novelty of our approach lies in the combination of tried and tested agents in new ways that harness both their antimicrobial and pharmacological effects,’ says Dr Cove. ‘Syntopix has developed a specific and efficient screening process that should facilitate the prediction of in vivo efficacy. Our goal is to remove the need for antibiotics for all but the most serious staphylococcal infections.’

   The Wellcome Trust’s business analyst, Dr Angela Lohli said, ‘In making a funding decision, we look at the healthcare need, the potential of the technology to meet this need, and we look at the strength of the team. With this project, we were impressed with all of these factors. The innovative approach to development means that the time to market for potential drugs should be relatively short, and the focus on MRSA in particular addresses an important and growing area of healthcare.’

   CEO of Syntopix, Bryan Greener, said, ‘Despite the difficult market, we found investors very approachable.

2. **Photopharmica**

   Photopharmica has recently raised second-round funding of £3.5 million to sustain its business, enabling the testing of putative medicines in patients in several therapeutic areas, and the development of its pipeline through the Centre for Photobiology and Photodynamic Therapy at the University of Leeds. The company also makes photosensitizers for purpose and contracts with industrial partners to meet specific needs.

   The company was originally funded by the White Rose Technology Seedcorn Fund. The fund is owned by the universities of Leeds, Sheffield and York and can provide finance to companies based on their research.

   This platform technology, known as photodynamics, can produce drug candidates for a number of therapeutic indications within oncology and infectious disease with large markets and unmet medical need. The company has contracted with a major player in the photodynamic therapy (PDT) market to develop its leading anti-infective compound.

   The company is aware that early revenue streams are essential to mitigate financial risk, as well as short-term enhancement of share valuation through an accelerated route to the clinic. The company has commenced industrial negotiations to co-develop intellectual property outside of its core business. The early conclusion of such a deal should result in an early revenue stream.

   CEO of Photopharmica, John Lyon, said, ‘Despite the difficult market, we found investors very approachable.'
and they were impressed by our solid technology and our management team which has a good mix of academic and commercial experience.

What help is available?
Several organizations provide support to new ventures. Most universities have dedicated technology transfer officers who can help academics to take an idea through to a viable business. Many parts of the UK have set up bioscience clusters led by regional development agencies and these will have relevant programmes. These cluster groups will have information on seed financing funds available regionally.

My own organization, Connect Yorkshire, runs a series of seminars to help new ventures become investment-ready, and holds investment conferences where early-stage companies present to potential investors.

Finding investment may not be easy, but help is at hand and the best ideas will be funded. Persistence and dogged determination are vital attributes and will also indicate the quality of the management team.

Simon Browning is the Managing Director of Connect Yorkshire, a support organization for early-stage technology businesses. He has a background in Electronic Engineering and spent 10 years as managing director of an international electronics and software company based in Bradford.

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If you haven’t already entered the Oxoid Food & Brewing Awards then make sure you enter soon - the closing date is 28 February 2004. The winner of the Oxoid Technician of the Year will receive £1000 plus a trip to the 2004 International Association of Food Protection Meeting in Phoenix, Arizona, USA. 1st prize winners of the Oxoid Contract Laboratory of the Year, Oxoid In-House Laboratory of the Year and the Oxoid Award for Laboratory Education and Training will each win £500. 1st prize in the Oxoid Award for Beer Quality and Brewery Hygiene is £1000. The Awards are easy to enter so don’t leave it until the last minute. Contact Val Kane on 01256 841144 or email Awards@oxoid.com for full details and entry guidelines and you could be one of our 2003/2004 winners!
Patent strategies for biotechnology companies
Sandy Primrose & Richard Gillard

There are three key financial issues for any new biotechnology company: value, funding and cash flow. Intellectual property rights (IPRs) such as patents, designs and trade marks have an impact on all three of these issues. For most early-stage biotechnology companies patents have the greatest importance. To understand why, it is important to remember that patents are exclusive rights to practise an invention which are granted by the state for a limited time (usually 20 years). Thus a patent does not provide any rights to put a product on the market or to use a process. Instead, patents are used to prevent competitors from putting a competing product or process on the market. However, a company which has the technology to open up a particular market needs patents to prevent their competitors moving into that market, thereby improving market share and profit margins. As well as being a barrier to competition, patents can provide revenue through sale of the patent or through royalties from licensing agreements, usually with larger companies. Patents also provide opportunities for co-operation with other companies through cross-licensing agreements.

When to file
Having identified potentially patentable inventions, consideration needs to be given to whether a patent application should be filed and, if so, when. Usually the answers to these questions are 'yes' and 'as soon as possible'. However, it is worth mentioning that sometimes filing a patent application is not the best course of action, e.g. where the company only needs freedom of use or where it would be very difficult to detect infringement and a patent application would only give away information to competitors which would be better kept as a trade secret. As a general rule a patent application should be filed if an invention is patentable and commercially relevant.

Deciding the right time to file a patent application requires careful consideration. Late filing allows the company to carry out more R&D and should permit a broader and stronger patent. However, the company risks prior publication of relevant prior art anticipating their patent. Early filing minimizes the risk of publication, but ultimately there is often some sacrifice in terms of scope of protection and strength of the patent. Thus early filing versus late filing must be weighed up on a case by case basis. In a competitive field early filing will be essential. In a new field, where the company is establishing disruptive technology, later filing may be more appropriate. For safety, it is often sensible to file early and then abandon and re-file if appropriate. This strategy allows applicants to regenerate their priority date if they are not yet in a position to file further (e.g. foreign) applications. The advantages of this approach are that it is cheap and allows for flexibility. The disadvantage is that the applicant risks prior publication of relevant prior art anticipating their patent.

In considering when to file, it should also be borne in mind that the patent term of 20 years runs from the filing date so the timing of the filing affects the patent term. This will be less relevant in fast moving technologies, but an important consideration where the full patent term is important, e.g. pharmaceuticals. Also, publication of the application occurs at 18 months from the priority date and so early filing leads to early publication. Publication of the application can be a useful source of information for competitors. The corollary is that publication is also a useful source of information on your competitors.

Anticipating the costs of patent filings
Once a decision to file a patent application is made, the costs are predictable with what may seem to many a surprising degree of precision. Such information is of particular use to finance directors or those in a similar position. Before setting out the likely costs, however, it is
necessary to provide some background to the different patent filing strategies.

For a patent to be valid, the invention must be new. By filing a patent application, the company establishes a priority date. Provided the company can keep their priority date, nothing disclosed after that date can prejudice the validity of the patent (there is an exception for earlier filed patent applications published after the priority date). The priority date is also valid in most countries in the world, provided foreign patent applications are filed within 12 months of the priority date.

Foreign patent applications may be filed directly with the different countries within the 12 month period mentioned above. For example, three separate applications may be filed in Europe, the US and Japan. Alternatively, a single international (PCT) application may be filed which must eventually be split into separate applications in, say, Europe, the US and Japan. These two filing strategies are shown schematically in Fig. 1 and cumulative costs are shown in the bar chart in Fig. 2.

The appropriate patent filing strategy will depend on commercial strategy and cash flow. A balance must be struck between cost and potential reward. Early grant of patents is good for obtaining funding and licensing. Deferring costs may assist cash flow. In addition, deferring weak patent applications will make decisions difficult for competitors who will not be sure whether or not a patent will eventually be granted.

It should be pointed out that there are some patent costs which are less predictable, such as litigation costs, oppositions and opinions given by attorneys. A view can be taken, however, on the possible risks of litigation, oppositions, etc., depending on the area of the market in which the company is operating. As a rough guide, only about 7% of granted European patents are opposed and of these, about one-third of the decisions go to appeal.

**Conclusion**

In conclusion, companies involved in the biotechnology sector should appreciate that patents are vital for increasing the value of the company by keeping competitors out of the market and by providing revenue through royalties from licensing agreements. Patents are a key factor in obtaining funding from investors. The costs for procuring patents and the timing of such costs are predictable with a high degree of precision allowing control over cash flow. Filing strategies may also be tailored to the needs of each company. A proper patent strategy requires professional advice.

**Resources**

The UK Patent Office produces a number of useful booklets on different aspects of intellectual property and details can be found at www.patent.gov.uk

A full list of UK patent attorneys can be found at www.cipa.org.uk

Readers wishing to access issued patents can download these from either the US Patent and Trademark Office website (http://patft.uspto.gov) or the European Patent Office website (http://gb.espacenet.com).
Materials Transfer Agreements – ‘material’ issues
Claudia Riordan

Scientists in different research organizations have traditionally shared materials and reagents, but an increasing awareness of the legal and commercial issues involved – not least the potential value of intellectual property rights arising from any research – has led to a proliferation in the use of Materials Transfer Agreements (MTAs) to put such sharing on a controlled, contractual basis. Many organizations, both commercial and academic, now routinely use their own ‘standard’ MTAs. It is important, however, that such routine use does not lead to complacency. Ultimately, both parties to the agreement will be bound by its terms, and they should therefore ensure that they understand the agreement, are satisfied that it is appropriate for the circumstances, and are able to comply with its requirements.

Understanding the agreement
One fundamental issue, which can be surprisingly complex, is understanding precisely which materials are covered by the agreement. This requires analysis from both legal and scientific perspectives.

Legal analysis
If the materials in question are biological in nature, four categories can potentially be included in an MTA.

1. The transferred materials themselves
2. Unmodified derivatives of the transferred materials. This category would include, for example, the descendants or progeny of transferred materials capable of replication, monoclonal antibodies secreted by a transferred hybridoma cell line, or proteins expressed by transferred DNA.
3. Modified derivatives (or modifications) of the transferred material. These are substances created from the transferred material which contain or incorporate some or all of the transferred material (or its unmodified derivatives). Examples might be recombinant strains derived from cells or organisms received from the provider, or any genetically modified organism containing a gene or genes originating in the transferred material.
4. Substances which are created by the recipient through use of the transferred materials, but which do not fall within categories (2) or (3). An antibody produced as a result of research using a transferred antigen would be such a substance.

Scientific analysis
The legal analysis clarifies in theoretical terms what restrictions the MTA will impose on the recipient. But it is important to think about the actual planned research project and the specific nature of the products that are likely to result from it. Is it clear from the definition(s) in the proposed agreement which category each of these falls into, and therefore whether (and how) each is affected by the agreement?

The answer may not always be straightforward. Suppose, for example, a recipient organization receives an adult stem cell line from the provider and carries out research resulting in a stable, differentiated cell line. The genetic content of the new cell line is unchanged, so it could be viewed as direct progeny of the original cells, i.e. an unmodified derivative. Alternatively, it could be argued that because the new cell line exhibits properties different from those of the transferred materials, it must be a modified derivative. If modified derivatives and unmodified derivatives are treated differently in the agreement, it would be essential to resolve this uncertainty.

If a dispute should arise which eventually comes to court, the judge is likely to have serious difficulty in interpreting scientific definitions which the scientists themselves find ambiguous.

Assessing the implications of entering into the agreement
A proper legal and scientific analysis will clarify precisely how the proposed research will be affected by the MTA, and which group of scientists will be restricted by its terms. Armed with that knowledge, the recipient organization can explore the legal, commercial and practical limitations on the area and type of permitted research, on their transfer to other research groups or on their disposal when the agreement terminates. As regards intellectual property rights, the agreement might restrict publication of research results, require all intellectual property rights arising from the research to be assigned to the provider, or give the provider the right to be granted a royalty-free licence to use this intellectual property.
Legal questions to consider include:
- Are there any pre-existing or proposed contractual arrangements which restrict a recipient's freedom to comply with the terms of the MTA? There might be existing MTAs relating to other materials essential for the research, or agreements covering research grants, fellowships, funding, etc. In the latter case it is important to identify all the individuals who are likely to be involved in the project, and to check any independent funding agreements.
- If the provider is to receive intellectual property rights in inventions arising from the research, does the recipient organization have the necessary agreements in place with all research staff to enable it to assign any intellectual property rights in this way?
- Commercial implications include potential restrictions on future revenue. Not only might the MTA limit the commercial exploitation of the research to which it relates, but also the restrictions which it imposes could jeopardize the chances of receiving future funding covering projects in which the relevant materials will be used.
- Practical considerations require an assessment of whether and how the restrictions imposed by the MTA can be implemented, e.g.
  - To comply with the terms of the agreement, all staff involved in the research project will need to be aware of which substances are subject to the MTA. Are there systems in place which can clearly identify these products and control their location?
  - If the project involves collaboration between different groups or teams, how will any appropriate permission requirements be dealt with in relation to the transfer of materials to third parties?

No doubt it is frustrating for the individual research scientist, keen to obtain materials essential to his research, to be forced to participate in this sort of analysis before he can proceed. However, the identification of potential problem issues at an early stage is essential to minimize the risk of future costly disputes.

Dr Claudia Riordan, formerly a research biochemist, is in the final year of her training contract with Mills & Reeve, a leading law firm. She works in their Cambridge office at Francis House, 112 Hills Road, Cambridge CB2 1PH, UK. Tel. 01223 222558

A strange episode in the history of antibiotics
Michael Carlile

Clevendon is a small seaside resort on the Bristol Channel, a few miles upstream from Weston-Super-Mare. It was the site of the Medical Research Council's Antibiotics Research Station from 1949 to 1961. I visited it in the late 1950s at the invitation of Dr Codner, who told me about its origin.

During the Second World War, the therapeutic value of penicillin was demonstrated by a group at Oxford, an achievement for which two members of the group, Howard Florey and Ernst Chain, shared the Nobel Prize with the original discoverer, Alexander Fleming. For several years there was a desperate shortage of penicillin, so the Royal Navy thought that it should get in on the act and produce some for itself. The Navy acquired a large old house at Clevendon and got to work. At that time the antibiotic was produced by the fungus Penicillium notatum in surface culture in any handy vessels - bedpans for example. Such vessels could not be moved after fungal growth had begun, otherwise the necessary surface mat would be liable to sink. So storing vessels for easy access without excessive disturbance was a problem. The navy had its unique solution. A long, narrow and very high room, perhaps once a corridor, had shelving installed to the ceiling along one wall. Culture vessels with sterile medium were placed on the shelves and inoculated with Penicillium. The young ladies that accomplished this task were raised to the necessary level in a bosun's chair, of dimensions adequate to accommodate the rear of an elephant, and suspended from a steel beam that could have supported a battleship! On my visit I saw some relics of the Royal Navy's culture facility.

After the war the building was taken over by the MRC for antibiotic research, with a director who was not a biochemist or microbiologist, but a statistician. I was told by Ernst Chain that this strange appointment was due to the influence of Howard Florey, who was convinced that fungi (Von Haller's 'mutable and treacherous tribe') were so variable in their behaviour that a statistician was needed for planning and interpreting experiments. The MRC decided to close the research station in 1961. This of course occurred almost simultaneously with the isolation by station staff of a strain of the fungus Cephalosporium giving high yields of the antibiotic cephalosporin, the best-selling of all antibiotics.

Dr M. J. Carlile is a retired microbiologist living at 42 Durleigh Road, Bridgwater TA6 7HU, UK. Tel. 01278 447033 email mjcarlile@mjcarlile.plus.com

Since receiving this article much interesting information has come to light about the history of the research station and some of its staff. This will be published in a future issue of Microbiology Today.

Any further recollections are welcome. Please email Janet Hurst (jhurst@sgm.ac.uk).
Making money from microbes – case studies

Spinning out

Jeff Errington

The traditional approach to antibiotic discovery was to screen chemicals or natural products (e.g. microbial culture filtrates) for the ability to inhibit the growth of bacteria. This was spectacularly successful in the golden age of antibiotic discovery—the 1940s and 1950s. However, from the 1960s onwards, the discovery of new antibiotic classes began to dry up. Most new compounds that killed bacteria also killed mammalian cells or belonged to one of the known classes of antibiotic. In the early 1990s the pharmaceutical industry hit on a new model for drug discovery, based on genomics; the so-called ‘target-led’ approach. Good targets are proteins that are essential for bacterial viability and are conserved across a broad range of bacteria, but with no counterpart in mammalian cells. Chemical inhibitors that work on such targets should be selectively toxic for bacteria and active across a broad range of pathogens. Genomics promised to provide a plethora of new targets and therefore rejuvenate the search for novel antibiotics.

Over the years, most pharmaceutical companies had accumulated large collections of chemicals—‘compound libraries’—that could be screened for specific kinds of activity. Active molecules would then be modified to optimize their potency and pharmacological properties, so as to produce new drugs. The challenge for the pharmaceutical industry was to develop good screening assays for compounds acting on the desired targets. A major bottleneck arose here because this usually required a deep understanding of the biological function of the target. This specialist basic knowledge is usually available only in academic labs that have focused their energy and intellect on the subject area over many years. I realized that the skills and expertise that my lab possessed in the molecular genetics of cell cycle processes in bacteria might be applicable to the new target-led screening.

On the advice of a friend, I drafted, and the university filed, several patents describing ideas that I had on various screening assay methods. We tried to interest a number of companies to take out licences on the patents. Unfortunately, this proved to be difficult. The main problem was that our assays were based on the use of live bacterial cells containing reporter genes, whereas the screening departments in industry were geared up to do assays on purified proteins, and so were run by biochemists rather than microbiologists. It soon became clear that we needed to demonstrate that the assay principle worked in a high-throughput format, rather than at lab scale. The challenges of developing robust high-throughput screening assays, and ‘marketing’ these to the pharmaceutical industry seemed achievable only through a spin-out company.

Aided by the University of Oxford’s superb technology transfer resource, Isis Innovation Ltd, and after a huge amount of time and effort, Prolysis was finally launched in June 1998. The early days were particularly difficult. For an academic with no knowledge of the commercial environment, I was on a very steep learning curve. We had to recruit the right staff, including a mixture of scientific and commercial people. We had to find premises, and organize the refurbishment and equipping of them. Most problematic of all, the administrative tools and facilities needed for a proper business had to be set up, including health and safety, employment, a library and a minefield of legal and commercial documentation. Most academics have no concept of these issues because they are usually taken care of by central administration in a university department.

Prolysis currently employs 15 full-time staff, including 13 graduate or doctoral scientists, and we have now gone far beyond the proof of principle stage. We complement advanced compound screening approaches with a range of molecular genetic and digital imaging technologies, and have several ongoing compound development programmes running in parallel. We play to our strengths on the biological side and access top-class chemistry through a collaboration with an Oxford-based company, Evotech OAI, where we fund a team of seven full-time medicinal chemists. We have established our own library of >100,000 different chemical compounds, with drug-like characteristics. These are screened for potential antibiotic activities using the cell-based assays mentioned above. Promising active compounds are then put into a development pipeline. Although the costs escalate the further into the pipeline compounds go, the company could profit hugely from compounds that make it into the clinic and beyond.

The main difficulty Prolysis and most other biotech companies face is that huge costs are incurred before any financial return is possible, and the only way to raise funds in the early years of the company is through venture capital. Fund-raising can be a draining and demoralizing process. An investment round can take 9 months or more from start to cheque and can involve scores of presentations to potential investors. Even when the decision to fund has been taken, there are lengthy negotiations, incredible legal costs and huge legal documents to read. Nevertheless, Prolysis is now a vibrant, well established biotechnology company with a bright future. Provided that the economic outlook continues to improve, the prospects for further growth into a fully fledged drug development company look good. The last 5 years has been an exciting adventure into the world of commerce for me, and I look forward optimistically to the day when Prolysis announces its first drug.

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Starting up

Duncan Maskell

Founding a start-up company is the beginning of a long and arduous journey that encompasses many potential pitfalls along the way. It would be nice to think that having the innovative idea required to get a company off the ground was the hard bit, and that as long as the science was good enough, somehow, as if by magic, loads of money would come rolling in. If only life were that simple!

Most start-ups are specifically designed to do clever basic research and to bring it closer to an applied outcome. Inevitably therefore, the attrition rate is high, with many companies failing at an early stage. This may be because it becomes obvious that the original ideas are not going to work after all, or because the investors cannot see sufficient increased future value and will not put in the funds to support the company beyond the life of the initial (usually minimal) seed funding. Even if the company gets beyond this stage and starts to build a profile and pipeline, it is often at the expense of tension between the initial scientific ideas and the agenda that is set by investors in terms of where they see the best business opportunities coming from. Companies that walk this tightrope for any length of time and succeed in achieving an initial public offering (IPO) on the stock market, or in being bought out for a large sum of money in a trade sale, often look very different from when they were founded and indeed often end up working in areas that did not form part of the initial business plan.

When I founded Arrow Therapeutics Ltd in 1998 with Ian Charles, Alastair Hawkins, David Stammers, Jeremy Stables and Ken Powell, I had the naif belief that because our ideas for antimicrobial drug discovery were strong, then there was little or no reason why we should not succeed in bringing products to the market in the near future. To a large extent this confidence was justified, and we delivered some excellent research that led to the identification of several candidate chemical series and the development of at least one of these nearly into a pre-clinical programme. This level of success was enough to keep our initial 'investment angels' very happy and to ramp up the valuation of the company considerably when we landed our first really big chunk of investment. The company grew rapidly and was very successful. However, as is all too common in research, some of our programmes did not progress beyond certain checkpoints and the normal attrition rate set in to our research pipeline. This was disappointing and not entirely unexpected, but it certainly made me grow up quickly and realize that being able to cash in my founder shares to make a significant profit in the short term was becoming somewhat unlikely.

This fantasy was further shattered on 11 September 2001, when the markets collapsed as a consequence of the terrorist attack on the USA. The market conditions in the aftermath of that kind of world event are inevitably very poor for flotation, or indeed any business transactions. Consequently, the company, which had by then grown to an appreciable size, employing about 70 or 80 people, had to make moves to go out for another large tranche of venture capital finance. Even this was going to be difficult in the market conditions, as the attitude to risk of the people with the money had hardened enormously. A requirement to have potential near-market projects was now the common message from all of the potential funders. Fortunately, Arrow Therapeutics had re-focused a little, bringing some of its projects forward to replace some of the earlier ones that had run their course. One of these was successful antiviral research that had identified lead compounds that could be moved quickly into a Phase 1 clinical trial. This is a clear example of how a company's research portfolio has to evolve and how projects that were not at the front of the queue when the company was founded can move up in the pecking order and rapidly become its central activity. This doesn't always please all the people involved from the start in a small company, but in the real, hard world out there, this is often simply what has to be done to survive. In our case, the team running the company was able to secure substantial funding, despite the hostile investment environment, that should see Arrow survive and prosper for quite some time, albeit with a scientific agenda that, though basically the same, is different in detail from that at foundation over 5 years ago.

In all of this roller-coaster ride, inevitably, my share in the company has diminished. It is unlikely that I will get rich in the short term, but longer term, if it does float successfully on the stock market, or goes through some similar kind of exit strategy, I may still be in for a handsome pay day. I have already made some money out of the exercise through being paid a consultancy fee, but it still doesn't bring my combined earnings up to even a fraction of those of the various other professionals with whom we have interacted during the life of the company!

Making money out of the start-up was only one aspect of why we did it. It has enabled us to do some fantastic science with much more resource and much less hassle (amazing but true) than would have been the case if we had tried to do this work with public money. It has brought over 80 new jobs into existence and has engendered antimicrobial drug programmes that may soon result in completely novel therapeutic drugs for some serious medical conditions. I think that, all-in-all, I am happy with this outcome. Maybe we'll make even more money out of our next start-up!
Getting into biobusiness
Faye Jones

Finding help and advice to transform a great concept into money-making reality can be daunting. Yet there are many websites and other resources with information and guidance for aspiring entrepreneurs. Government-run information services cover everything from protecting intellectual property and financing the venture to new and updated guidelines and laws. Faye Jones gives a brief overview of just some of the resources that support innovation and promote enterprise in the UK.

● GENERAL BUSINESS RESOURCES

UK
Department for Trade and Industry – DTI for Business
www.dti.gov.uk/for_business.html
The DTI is involved in many initiatives to encourage successful start-ups and the DTI for Business website is the best initial port of call for finding out about setting up a new enterprise. It also provides links to numerous other relevant websites.

Other useful DTI-linked sites:
Business Link
www.businesslink.gov.uk/blogin/action/home
Through this site, the DTI provides useful information and practical help for small and new businesses, including how investment and skills can benefit businesses; improving business performance; expanding a business; making technology work; and help with regulations, environmental and European matters.

Small Business Service
www.sbs.gov.uk
The Small Business Service is one of the key driving forces taking forward the Government Action Plan for Small Business published in January 2004. The plan is structured around seven strategic themes.

Scotland, Wales and Northern Ireland
The administrations in Scotland, Wales and Northern Ireland work with DTI to support firms in their respective countries. They also operate individual initiatives to help businesses.

Scotland
Scottish Executive
www.scotland.gov.uk/Topics/?pageID=120
Scottish Enterprise
www.scottish-enterprise.com/sig-biotechnology
Business Gateway
www.bgateway.com
Intermediary Technology Institutes Scotland
www.itscotland.com

Wales
Welsh Development Agency
www.wda.co.uk/index.cfm/wda_home/index/en2
Business Eye
www.businesseye.org.uk
Wales for Innovation (technology brokerage service to support the transfer of new technologies)
www.walesinnovation.com/default.asp

Northern Ireland
Invest Northern Ireland (formerly Local Economic Development Unit for Northern Ireland)
www.investni.com
IRTU - Industrial Research and Technology Unit
www.nics.gov.uk/irtu

England
Government Offices in the English regions
www.government-offices.gov.uk/GO/default.asp
Regional Development Agencies (RDAs)
www.rdauk.org/rdauk
RDAs aim to promote economic development and regeneration in the regions. They operate as non-departmental public bodies. They provide funding towards regional regeneration activities in conjunction with other regional partners. Each RDA has its own website which can be reached through the main RDA website (address above). The nine RDAs are One NorthEast, Advantage West Midlands, South East England Development Agency, North West Development Agency, South West of England RDA, Yorkshire Forward, East Midlands Development Agency, East of England Development Agency and London Development Agency.

● BIOTECHNOLOGY

i-bio UK
www.i-bio.co.uk
The website gives easy access to a wealth of information about UK biotechnology. It provides links to DTI programmes such as BIO-WISE; grants for research and development; an overview of relevant activities in industry, academia and medicine; information about regulatory issues; and a summary of the latest biotech-related news.

Information includes establishing industry partnerships and navigating the complex regulatory system, current investment opportunities, the latest technical developments and initiatives from across the research community, support available from UK Government and the Research Councils.

The Biotechnology Regulatory Atlas is a rapid retrieval system providing a guide to the regulatory architecture of biotechnology, which signposts laws, offers official guidance and provides details of how to comply with UK regulations, as well as an overview of the EU and US frameworks.

BioIndustry Association
www.bioindustry.org
The trade association for innovative enterprises in the UK's bioscience sector exists to encourage and promote a thriving, financially sound sector of the UK economy, built upon developments across the biosciences.

● TECHNOLOGY TRANSFER

University Units
UK Universities have support networks to help academic researchers through the commercialization process. Many have dedicated technology transfer offices, where academics can find out about and get help with intellectual property rights, sourcing funding and starting a spin-out company, etc. Information is available on individual university websites.

Unico
www.unico.org.uk/members.htm
Unico represents the technology exploitation companies of UK Universities. It provides a forum for exchange and development of best practice. Member companies transfer
technology and expertise through the formation of spin-out companies, licensing, consultancy, training, design and development projects, contract research, testing and evaluation, and problem solving.

Office of Science and Technology (OST)
www.ost.gov.uk/enterprise/knowledge/index.htm
Includes information about knowledge/technology transfer and how the Government supports it.

OST Science Enterprise Challenge
www.ost.gov.uk/enterprise/knowledge/sec.htm
The Challenge forms part of the Government’s strategy to introduce a ‘third mission’ for higher education, alongside teaching and research, to encourage transfer of science and technology innovation to the business sector. £25.6 million has been allocated to a challenge competition, leading to the establishment of 12 Science Enterprise Centres in universities around the UK. OUST Office Challenge

University Challenge enables universities to establish seed funds, which will assist the successful transformation of good research into business. This early funding is the riskiest stage of the venture process. Seed funding helps the commercialization process in a number of ways:

- financing access to managerial skills by securing or enhancing intellectual property
- by supporting additional R&D
- construction of a prototype
- preparation of a business plan
- covering legal costs, etc.

Faraday Partnerships
www.faradaypartnerships.org.uk/index.html
Faraday Partnerships are dedicated to improving the competitiveness of UK industry through more effective interaction between the science and technology base and industry. Each Faraday Partnership employs a number of technology translators — people with broad experience of knowledge transfer — who can facilitate projects between Partnership members.

Faraday Partnerships aim to:

- be widely recognized for their technical expertise and be UK industry’s first choice for help with new product and process development
- provide better ways of exploiting R&D to create new products and processes
- provide more effective and coherent uptake of the various support mechanisms available, e.g., LINK, CASE awards, SMART, European Union Framework Programmes.

There are 24 Faraday Partnerships, some of which have interests linked to microbiology.

Technology Transfer and Innovation Limited
www.tti-ltd.com

- FUNDING

Research Councils
Research Councils UK support the further development of research ideas and technology transfer. Many have dedicated sections on their websites containing valuable information on knowledge/technology transfer, intellectual property and funding schemes.

Knowledge Transfer Partnerships
www.ktponline.org.uk
These are supported by the Research Councils.

LINK scheme
www.ost.gov.uk/link/info.html
BBSRC and NERC also support this Government scheme.

Medical Research Council
www.mrctechnology.org
The MRC has its own dedicated technology transfer unit, Medical Research Council Technology (MRCT). MRCT files patents and negotiates licensing arrangements on behalf of MRC, as well as assisting in starting up new companies.

Wellcome Trust
www.wellcome.ac.uk/en/1/biotrd.html
The Wellcome Trust provides translation funding and technology transfer. The service superseded Catalyst BioMedica Ltd in March 2003, which had supported early stage projects with potential healthcare applications.

NESTA
www.nesta.org.uk/insidenesta/hrw_invent_inno.html
NESTA’s Invention and Innovation programme aims to turn ground-breaking ideas into innovative products, services or techniques with commercial or social potential. NESTA is the UK’s biggest single source of early-stage seed funding, enabling the development of projects that might otherwise not get off the ground. They also prepare promising projects for further investment elsewhere.

Prince’s Trust and Livewire
www.princes-trust.org.uk
www.shell-livewire.org
Young people wanting to set up a business can find advice and sometimes finance from these bodies.

- INTELLECTUAL PROPERTY

UK Intellectual Property
www.intellectual-property.gov.uk
A government-backed site dealing with all aspects of intellectual property including copyright, designs, patents and trademarks.

IP2IPO Group Plc
www.ip2ipo.com/introduction/introduction_a.htm
Forms partnerships with universities to invest in their intellectual property.
Biotechnology YES: Being entrepreneurial – hard work, but it can be fun
John Peberdy

Exploiting microbes can be highly lucrative. John Peberdy describes a scheme to teach young scientists some of the necessary skills to become an entrepreneur.

PhD and post-doctoral scientists can learn how to make money out of microbes by participating in the Biotechnology Young Entrepreneur's Scheme (YES). If you are unaware of this Scheme, then you are one of a decreasing minority. It is in its seventh year and its popularity grows with 'age'. So what is Biotechnology YES? Simply it is a competition, but more importantly a learning experience, for PhD students and post-doctoral bioscientists to gain an understanding of the processes involved in the commercialization of the biosciences and biotechnology. It is of interest therefore to microbiologists from all aspects of the subject.

Biotechnology YES was launched in 1996 and involves a partnership of the University of Nottingham and the BBSRC, with the support of several other sponsors. Participants are required to develop an idea, based on real science and technology, for an imaginary business, and to show the start and development of the business through the presentation of a business plan.

Working teams of four or five students are formed in schools, departments or laboratories in universities throughout the country, and there is competition for the places for 36 teams.

Getting trained
So how is the learning experience delivered? The Scheme begins with a briefing session held several weeks in advance of the workshops where participants are advised of the initial work required before the competition starts. Three regional workshops follow at which practitioners share their knowledge and experience with the participants. Each workshop runs over 3 days during October and November. On the first day a programme of talks introduces the key issues, intellectual property rights, an understanding of the market(s) for new technologies, strategies for technology development and commercialization, sources of and the staging of finance to achieve commercialization, the operation of biotech companies and relevant case studies of biotech enterprises at different stages of development.

The knowledge gained from these presentations provides the basis for the true YES learning experience. The serious work for the participants begins when they adjourn to their assigned syndicate rooms and start developing their plan. Help is on hand from expert mentors to see them through. The plan is very much the work of the participants as mentors often raise questions that require serious thought or suggest different approaches to a problem calling for difficult decisions to be made by the team. The learning is truly experiential! This is reflected in a comment by one of the participants in the 2002 competition - 'I still remember it weeks later, whereas after my exams the information was lost'.

The climax of the workshop on the final day involves presentations by the participants to panels of hypothetical investors - these panels are again made up of the range of practitioners that one would meet in presentations to venture capitalists. Two winning teams emerge from each workshop and go through to a final held in London in December. At this event the overall winning team receives a prize of £1,000.

Success stories
Whilst our mission is to provide the learning experience described in this article, it is not surprising that participation in Biotechnology YES awakens the entrepreneurial spirit in some of the participants to the extent that they go ahead and start a business. Dr Tim Hart, the Managing Director of Cybersense Systems based in Oxford, is one such example. Tim's business has a microbiological connection in that the underlying technology of the company involves the measurement of...
of bioluminescence emitted from soil bacteria. He is now a stalwart of the Scheme and a frequent speaker, and says of YES Research Institutes and Universities across the UK are simply oozing with creative, energetic young scientists and it only takes a few of these to discover their hidden talents and awaken their passion for entrepreneurship through the YES scheme. Other companies that participants have developed are in the disease diagnostic field and in plant biotechnology. For many other participants, taking part in YES provides awareness of career opportunities outside of the lab. It is interesting to learn that many practitioners in intellectual property, venture capital, marketing, and business development have a background in the biosciences. Polly Todd of Oakland Ventures told us 'the competition not only gave me a good grounding in a variety of skills that were necessary for getting into the biotechnology business, such as an introduction to intellectual property and patents, but also the confidence to feel that I could get out there and do something myself'.

You can learn more about Biotechnology YES and see some of the ideas that past teams have presented at our website (www.biotechnologyyes.co.uk). Registration for the 2004 competition will open in April; however, expressions of interest can be sent now to tracey@biotechnologyyes.co.uk

The author thanks Simon Mosey and Tracey Hassall-Jones for their advice and helpful comments. Other sponsors of the Scheme are MRC, NERC, Gatsby Foundation, Cancer Research UK, Syngenta, Eric Potter Clarkson and Cyberscience Systems.

Professor John Peberdy MBE was Professor of Microbial Biotechnology in the School of Life and Environmental Sciences at Nottingham University. Since 1999 he was also Director of Curriculum Development at the University of Nottingham Institute for Enterprise and Innovation (UNIIE). He is now retired and is Emeritus Professor in Residence at UNIIE.

Microbiology Today Editor Gavin Thomas interviewed the winners of the 2002 Biotechnology YES scheme from the University of York. The imaginary company the team created, Aviaclean, specialized in using bacteria to clean up bird waste from monuments, buildings and public spaces. The team comprised five second year PhD students in the Biology Department: Jemma Jowett, Julie Richards (JR), Graeme Park (GP), Simon Chandler (SC) and Alex Venn.

The members of the team had heard about the scheme from flyers and lab colleagues who had entered previously. They decided it would be a good chance to experience what went on in a biotechnology company.

'It looked like being fun – and will look good on our CVs!' GP

The first thing the team needed to do was to come up with an idea, which was inspired by working in York. The large bird population living on the lake results in serious deposition of guano on the campus.

'There were products on the market to kill fungi and also to clean up bird waste, and we were looking to combine the two.' JR

Once they had the idea, they chose their roles within the team, which were managing director, marketing director, R&D director, strategy director and financial director.

The team attended the briefing workshop, which proved to be very useful, and then started developing their idea for the regional workshop. They researched on the internet and spoke to existing companies, academics within the Biology Department and experts from the university involved directly in bio-enterprise. At the regional workshop they were glad they had their full complement of five team members as there were specific talks for each aspect of the company and each person could focus on their individual role. The expert help available was important in developing the product and influenced their business plan.

'What we came up with before got completely changed!' SC

Being realistic about the process was an important factor and the group found themselves scaling down their ideas to a few key products.

The competition was judged by the team's presentation on the final day and the team had done some extra preparation for this even before coming to the workshop. With money from the Biology Graduate School they paid for a short animation to be made illustrating how their products could be used in the marketplace and also designed a logo and produced company name badges. They split the 20-minute talk among the members of the team.

'The structure was that Simon started as the MD, then Jemma talked about the research, Alex talked about marketing, Julie about strategy, Graham on finance and then finally Simon to summarize.' SC

Presenting their ideas to the judges was quite daunting as they asked very difficult questions, but the team felt they had done well and were selected to go forward to the finals.

They used the time before the finals to hone their presentation and increase their background knowledge before heading down to the DTI in London to present their case to a panel of three venture capitalists and head of BBSRC, Julia Goodfellow. The judges were very critical and uncompromising, and focused on weaknesses they thought existed in each team and how much the team really believed in their idea. However, the York students managed to hold together as a team during the questioning.

'It was quite shocking quite how nasty some of the questions were. Some totally undermined people's projects.' GP

After surviving the panel, the team was named winner and collected the trophy and prize of £1,000. Reflecting on the scheme, they were convinced that using a microbiologically based project was important.

'I think one of the reasons we did so well with microbiology was that a lot of the teams chose to market something medical. The judges liked the simplicity of our idea and the fact that it would deliver returns in a few years rather than having to wait for clinical trials.' GP

The team was unanimous that it was a worthwhile and fun experience and has changed the way they think about bio-enterprise. They enjoyed the teamwork aspect and having the opportunity to speak to people who had actually started their own companies. Also, the fact that they did so well was a bonus.

'Winning was my favourite part of the process.' JR
How does malt whisky acquire its unique flavour? Fergus Priest explains how lactobacilli can play a crucial role.

Scotch whisky – a multimillion pound industry

The production of Scotch malt whisky is governed by The Scotch Whisky Act (1988) which limits the ingredients to water, malted barley, whole grains of other cereals, yeast and caramel for colour adjustment. Interestingly, no mention is made of bacteria, yet we are beginning to think that lactic acid bacteria help refine the flavour of malt whisky in important ways. But first, a little background to the Scotch whisky industry.

The production of Scotch whisky employs around 41,000 Scottish residents and 65,000 people throughout the UK, generating about £1.3 billion of income for UK households. Sales of Scotch whisky topped £2.3 billion in 2002 and reached more than 200 countries, making it the largest matured spirit market in the world. Apart from the quality of the product, two related developments led to this phenomenal dominance of Scotch whisky. By the end of the 19th century the continuous still, patented by Aenas Coffey in 1827, enabled the prodigious production of grain whisky on a scale that could never be emulated in traditional pot stills. Second, this grain whisky provided the lighter base for blending with malt whisky to provide the consistency and quality of blended whisky. Blended whisky, which today often involves 30–40 individual whiskies, is the major component of the modern Scotch whisky market.

Malted barley is prepared from a mash of malted barley which is fermented, distilled in traditional copper pot stills and matured in oak casks for not less than 1 year and generally a lot longer. Malt whisky is increasing in market share with a buoyant demand for ‘boutique’ products. However, despite increased export volume last year (by 9.3% to £268 million), malt whisky still represents only a little over 10% of the export market. About 85 malt distilleries operate today in Scotland, but their production is dwarfed by the dozen or so grain distilleries. Grain spirit is prepared from unmalted cereals as a source of starch, saccharified with malt enzymes, fermented and distilled in a continuous or Coffey still. Like malt whisky, it must be matured for a minimum of 3 years. Grain whisky is the base of the standard blends such as Famous Grouse, Teachers, and Johnnie Walker which will contain between 15 and 30% malt whisky.

Both products use a similar process, but here we will focus on malt whisky. Malted barley is milled, infused in water at about 64°C for some 30 minutes to 1 hour and the wort is drained off into a fermenter or washback. The grain bed is rinsed with a second water at a higher temperature (typically about 70°C) to remove residual nutrients from the fermentation. Finally, it is rinsed with a third water at about 80°C which is used as the mashing water for the next mash. The spent grains are removed for cattle feed. You will note that the wort is not boiled as it is in a brewery. This is to permit the enzymes from the malted barley to continue to operate during the fermentation and to ensure complete hydrolysis of starch into glucose, maltose and other fermentable sugars. Two types of yeast are generally used: a pure-culture distiller’s yeast obtained from a commercial yeast supplier and spent brewer’s yeast. The practice of adding brewer’s yeast is increasingly rare, but it is thought by some to impart important positive flavour characteristics to the spirit. Interestingly, Scotch whisky distillers are not so possessive of their yeasts as brewers and do not develop and maintain their own yeast strains with particular fermentation and flavour properties. Instead, they rely on the distillation process to govern the flavour profile of the finished product. The fermentation is conducted in wooden or stainless steel washbacks and is not attempered. Consequently, the temperature can rise to over 30°C and the fermentation is complete within 2 days, reaching a little under 10% alcohol by volume (abv). The wash, as it is known, is first distilled in the wash still to 21% abv. It is then distilled a second time in the spirit still to over 70% abv. Finally, it is reduced to 60% abv for maturation in used (generally ex sherry or bourbon) oak casks.

Lactic acid bacteria

Malted barley carries a varied microbial load with a predominance of lactic acid bacteria. These Gram-positive bacteria are strictly fermentative organisms that cannot respire using an exogenous electron acceptor. They produce either lactate (homofermentative) or a mixture of lactate, acetate and carbon dioxide (hetero-fermentative) from glucose catabolism. Consequently,
they do not require oxygen for growth and flourish at relatively low pH (pH 6 to about 3.5). This fits them well for growth in alcoholic beverages in which they have both beneficial (e.g. the malolactic fermentation of wine) and spoilage effects.

While most of these bacteria from malted barley will be killed by the mashing process, some will survive to enter the fermentation (Fig. 1a). Many will also colonize the pipework, heat exchangers and other parts of the distillery plant. If too many occur at the early stage of the fermentation (generally more than 10^6 per ml of wash) they will grow strongly in the fermentation, inhibit the yeast and reduce the alcohol yield. This early lactic fermentation is to be avoided since it reduces the distillery efficiency; these are unwelcome participants in the fermentation. Attention to plant cleanliness is generally sufficient to avoid the early lactic fermentation. In a well-maintained distillery, the numbers of bacteria entering the fermentation are relatively few and bacterial growth is hardly evident during the initial ethanol fermentation stage (Fig. 2). Then, as the yeast dies, after about 36 hours, the bacteria proliferate, growing at the expense of yeast autolysis products, malt-oligosaccharides and pentose sugars (Fig. 1b). Finally, after about 80 hours even the bacteria begin to die (Fig. 1c). The wash is normally distilled after about 60–80 hours, and everything is discharged to the still, wash, yeast and bacteria.

For many years it was thought that the lactic acid bacteria grew homogeneously throughout the fermentation. However, recent studies using denaturing gradient gel electrophoresis (DGGE) have revealed changes in the population as the fermentation proceeds. Initially, a mixed flora of various cocci and rods enters the fermentation. This is followed by a reduction in diversity resulting in Lactobacillus fermentum and Lactobacillus paracasei as commonly dominant species by about 40 hours. During the final stages when the yeast is dying, a homofermentative bacterium related to Lactobacillus acidophilus often proliferates and produces large amounts of lactic acid.

**Effects of lactobacilli on the flavour of malt whisky**

The bacteria can affect the flavour of the spirit in two ways. First, they will reduce the pH of the fermentation through the production of acetic and lactic acids. This will lead to a general increase in esters following distillation, a positive feature that has traditionally been associated with the late lactic fermentation. This general effect is apparent in the data presented in Fig. 3 in which the concentrations of various esters are increased in non-matured (new-make) spirits from laboratory-scale fermentation/distillations with and without lactobacilli. However, lactobacilli might also produce specific flavour compounds that contribute in a unique way to the flavour of the spirit. We have investigated these effects
**Table 1. Effects of some *Lactobacillus* strains on the organoleptic qualities of new-make spirit evaluated by sensory analysis**

<table>
<thead>
<tr>
<th>Species</th>
<th>Strain</th>
<th>Sensory evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>L. acidophilus</em></td>
<td>1</td>
<td>Estery + Fatty - Fruity + Leafy + Other Green</td>
</tr>
<tr>
<td><em>L. brevis</em></td>
<td>1</td>
<td>Estery + Fatty - Fruity + Leafy + Other Strong character</td>
</tr>
<tr>
<td><em>L. casei</em></td>
<td>2</td>
<td>Estery + Fatty - Fruity + Leafy + Other Cereal</td>
</tr>
<tr>
<td><em>L. fermentum</em></td>
<td>1</td>
<td>Estery + Fatty - Fruity + Leafy + Other Cereal</td>
</tr>
<tr>
<td><em>L. pentosus</em></td>
<td>1</td>
<td>Estery + Fatty - Fruity + Leafy + Other Daracetyl-like</td>
</tr>
<tr>
<td><em>L. plantarum</em></td>
<td>2</td>
<td>Estery + Fatty - Fruity + Leafy + Other Husky</td>
</tr>
</tbody>
</table>

by preparing laboratory-scale fermentations with different bacterial strains present and analysing the new-make spirit by gas chromatography-mass spectrometry (GC-MS). The presence of bacteria increased the concentrations of damascenone in the new-make spirit from 24 (peak area) in the control to 41–72 (peak areas) in *Lactobacillus*-containing fermentations with *Lactobacillus acidophilus* having the greatest effect. Damascenone has a floral, herbal, tobacco-like aroma and has been reported to be an important flavour component of whisky. Exactly how the lactobacilli effect these changes are unknown.

However, the flavour changes are introduced, they are noticeable in the spirit as it emerges from the still. This new-make spirit from a series of laboratory fermentations containing various *Lactobacillus* strains isolated from malt whisky fermentations was analysed by a sensory panel. The flavour notes associated with various bacteria are described in Table 1 where it is evident that characteristics like estery, fruity and leafy are among the positive attributes.

**Conclusions**
Malt whisky flavour involves an enormously complex chemistry derived from the raw materials, the yeast, the distillation process and the oak cask in which the spirit is matured. That lactic acid bacteria can play a minimal role in this process has been appreciated for generations, but the organisms involved and their contributions are only now being discovered. Some American Bourbon distillers embraced this many decades ago by adding their own mixtures of lactic acid bacteria to their fermentations to provide consistency of flavour. Perhaps it is time for Scotch distillers to appreciate their uninvited guests and consider a similar practice.
The 2004 Marjory Stephenson Prize Lecture has been awarded to Professor Stanley Falkow, Stanford University, California. Professor Falkow is a world-renowned expert in the genetic and molecular basis of microbial pathogenicity. He currently studies the aetiology of infectious diseases via the genomes of pathogens in endemic and epidemic settings, and previously made fundamental contributions to plasmid and transposon biology. In a career spanning 40 years, he has worked on every bacterial pathogen of significance.

Professor Falkow will deliver his prize lecture at the Society meeting at Trinity College Dublin in September 2004.

Further details of the talk and a biography of Professor Falkow will appear in a future issue of Microbiology Today.

The Fleming Lecture is awarded annually for outstanding research in any branch of microbiology by a young microbiologist in the early stages of his/her career. The award is £1,000.

The 2004 Fleming Lecture has been awarded to Dr Mark Paget, University of Sussex, in recognition of his work developing expression and promoter-probe vectors for use in streptomycetes and analysis of the roles of auxiliary RNA polymerase sigma factors in redox-sensing in bacteria.

The title of his lecture, which will be delivered at the Society meeting at University of Bath on Tuesday 30 March 2004, is Managing redox stress in bacteria. The Streptomyces bacteria, best known as major producers of antibiotics and other pharmacologically active compounds, have dominated Mark’s research career. His research group currently focuses on the regulatory mechanisms that allow Streptomyces and other bacteria to sense and respond to redox-related stresses such as oxidative stress and oxygen deprivation.

Mark received his first degree from Liverpool John Moores University, and then undertook a PhD in Streptomycetes genetics at UMIST in the laboratory of Dr Colin Smith. In 1994 Mark took up a postdoctoral position with Dr Mark Buttner in the Department of Molecular Microbiology at the John Innes Centre. He remained in Norwich until 2000, when he took up a lectureship in the Department of Biochemistry at the University of Sussex.

Anthrax kills many animal species, and was used to prove Koch's Postulates in 1876. Soon afterwards, the classical bacterial toxins from other species were produced in vitro, but until 1950 a lethal toxin had not been demonstrated in either anthrax bacillus or culture filtrates. The cause of death had been an enigma for 70 years. During the 1950s, a toxin was recognized by examining bacteria and their products obtained from guinea pigs dying of anthrax. The toxin was in their plasma and was shown to contain two components. It was then produced in vitro and a third component recognized. This work reawakened interest in bacterial toxins and showed that toxins could be multicomponent. It demonstrated for the first time that previously unknown determinants of bacterial pathogenicity could be discovered by examining organisms grown in vivo, now a vogue subject in microbiology.

Professor Smith was trained as a chemist. In 1947 he joined the Microbiological Research Establishment at Porton and worked on anthrax, plague and brucellosis until 1965, when he was appointed Head of the Department of Microbiology at the University of Birmingham. He retired in 1988 but has continued active research. He is an internationally recognized leader in studies of the molecular basis of microbial pathogenicity. He was President of the SGM from 1975 to 1978, elected FRS in 1979 and received a CBE in 1993.

The Peter Wildy Prize for Microbiology Education has been awarded to Dr Nick Thomson, The Wellcome Trust Sanger Centre, in recognition of his distinguished contribution to bioinformatics teaching. The prize lecture will be delivered at the Society meeting at Trinity College Dublin in September 2004. Further details of the talk and a biography of Dr Thomson will appear in a future issue of Microbiology Today.
A mycologist at Westminster

Gareth Wyn Griffith

In December 2003 I was fortunate to participate in an MP-Scientist Pairing Scheme funded by the Royal Society as part of their Science in Society programme. This scheme involves 22 scientists from different UK universities and MPs representing their local areas. The aim of the scheme, which has run since 2001, is to provide scientists with an opportunity to learn about the workings of government and for MPs to learn what the job of a university-based scientist involves. My pair was Simon Thomas, the Plaid Cymru MP for Ceredigion. Most MPs (Simon included) are not scientists (only 34 out of 659 have any significant scientific qualification, compared to 75 lawyers), so I was keen to find out how they assess scientific evidence presented to them, particularly when some of the issues under consideration are complex and may involve conflicting evidence. Scientists in general are poor at conveying their views to Parliamentarians, so I was also curious to find out how this was done.

Perhaps unsurprisingly, there were no specific mycological issues under discussion at Westminster during my shadowing period. By chance, however, there were several events which were relevant to my job as a university lecturer and to my research interests. The first of these was a meeting of the Select Committee on Science and Technology (SCST) at which the senior staff of the Biotechnology and Biological Sciences Research Council (BBSRC), an important funder of my research, and many microbiologists, were being questioned. A similar meeting of this committee with the Medical Research Council (MRC) led to a highly critical report, and another one of the people who interviewed me for my present job was Professor Chris Pollock, director of our local BBSRC station (IGER - Institute of Grassland and Environmental Research), who chaired the Scientific Steering Committee which oversaw the trials. Chris was one of the people who interviewed me for my present job and someone who has been very helpful in guiding my research. However, he is no slouch as an inquisitor, so it was a strange experience to see him in the hot seat, Other witnesses were representatives of English Nature and the Department for Environment, Food and Rural Affairs (DEFRA) and by the end of the meeting there appeared to be a consensus that the trials were more useful in highlighting the damaging effects on biodiversity of modern agricultural practices (e.g. silage vs. haymaking) rather than GM crops per se.

Again the level of debate was of a high standard and at times quite scientific (e.g. the testing of null hypotheses) and by the end of the meeting there appeared to be a consensus that the trials were more useful in highlighting the damaging effects on biodiversity of modern agricultural practices (e.g. silage vs. haymaking) rather than GM crops per se.

On the Wednesday morning Central Lobby was filled with students from all over the UK (apart from Aberystwyth - train delays had caused them to miss a connection) who arrived to lobby their MPs after the highlight of the Parliamentary week, Prime Minister’s Questions. ‘Grammar school boy’ Michael Howard and ‘public school boy’ Tony Blair held an entertaining but unenlightening shouting match on the subject of university top-up fees in front of a full chamber. This was followed by a debate on the same subject as part of the Queen’s Speech debate (with only about 50 MPs staying for this), though again this consisted mainly of repetition of party policy. There was little
discussion of the key issues [e.g., should Governments set targets (or caps) on student numbers; what will be the effect of variable top-up fees on student numbers; courses such as microbiology which can be expensive to run, but do not guarantee a high income (in my experience) for graduates?]. The very nature of the Commons chamber is not conducive to reasoned discussion and I was far more impressed with the Select Committee meetings where the party politics is far less apparent.

My week in Westminster was a thoroughly enjoyable and educational experience. Meeting up with the other paired scientists was also very interesting, not just to talk shop, but also to compare experiences. These ranged from attending a dinner at the Korean embassy to appearing on TV in Kilroy. The reciprocal visit (mine will be in January 2004) also allows the MPs to gain some insight into the daily life of their scientist pairs. I am very grateful to the Royal Society for organizing this scheme and would recommend future pairing schemes most highly. There is even talk of extending the scheme to MEPs and shadowing in Brussels. Further details can be found at http://www.royalsoc.ac.uk/scienceinsociety/data/parliament/index.html.

Gareth Wyn Griffith is a lecturer in mycology at the Institute of Biological Sciences, University of Wales Aberystwyth, SY23 3DD, UK. Tel. 01970 22325; email gwg@aber.ac.uk

Further reading


Science and the Scottish Parliament 2003

12 November 2003, Signet Library, Edinburgh

This annual event, run by the Royal Society of Chemistry, aims to raise awareness of science issues to MSPs and civil servants working in the Scottish Parliament. This year it focused on the environment as matters such as waste management, GM crops, energy and pollution dominate much of the work of MSPs.

The event was attended by 20 MSPs, three Government Ministers, a host of senior public and civil servants and over 180 scientists from all over Scotland. Experts from SGM were amongst the scientists there to explain how microbiologists can help to solve many of our most difficult environmental problems, including cleaning up land and water contaminated by waste from industrial processes, wiping out harmful bacteria like E. coli0157 in farm animals and the food chain, keeping farmed fish healthy without polluting the sea or harming the well-being of humans and using microbes to make novel fuels to cut down greenhouse gas emissions.

Deputy First Minister and Science Minister, Jim Wallace MSP, gave the keynote speech and later visited the SGM stand to find out about some microbiology research.

Sir Harry Kroto, President of the RSC, gave the opening address saying that 'UK science is in the balance' and that there are three crises – in public understanding of science, in loss of qualified experts, and in science education in schools. Sarah Boyack MSP, Convener of the Parliament's Environment and Rural Affairs Committee, then focused on the real need for dialogue between scientists and politicians, as scientific information is vital on a day-to-day basis for making policies and legislation in Government. Professor James Curran, from the Scottish Environment Protection Agency, addressed the issue of public understanding of science, pointing out that, because of human rights implications, environmental concerns are no longer straightforward.

Eleanor Scott MSP, Green Party Spokesperson on the Environment, talked about the need for scientists to pause and reflect on their discoveries before rushing to apply them, as there is no bad science, just bad applications. Finally, Maff Smith from the Scottish Renewables Forum, elaborated on the need in the UK to supply funds for new ideas for energy sources.

Faye Jones, Public Affairs Administrator

BELOW TOP: The SGM stand. From left to right: Peter Catgrewre (Save British Science). Faye Jones (SGM), Janet Hurst (SGM), Jim Wallace (Deputy First Minister, Scottish Parliament). PHOTO ROYAL SOCIETY OF CHEMISTRY

BELOW BOTTOM: SGM experts at the event. From left to right: Willie Russell, Geoffrey Schild, Brian Austin, James Reil. PHOTO RON FRASER, SGM

Further reading


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A job in... The Civil Service Fast Stream

Profile

Name: Stuart Wainwright
Age: 25
Present Occupation: Department of Trade and Industry (DTI), Women and Equality Unit
Previous Employment: DTI, Bioscience Unit
Numerous part-time summer jobs
Education: PhD, University of Sheffield, Iron acquisition in the gastric pathogen Helicobacter Pylori
BSc, University of Sheffield, Genetics

Q: Why did you decide to leave bench science?
A: Although I enjoyed bench science, I didn't think I was particularly good at it! Felt my strengths lay in other areas so I decided to try my hand at something different.

Q: What is the Civil Service Fast Stream?
A: It is a graduate entry programme which concentrates on developing the skills and experience needed for rapid advancement within the Civil Service. It provides exposure to a wide variety of jobs and roles in a relatively short period of time. Fast Streamers typically spend around 4 years taking on short (6-12 month) postings that offer challenging, high-profile work. A great deal is expected of Fast Streamers and they are often thrown in at the deep-end to work in important and exciting areas.

The Civil Service recruits around 200 graduates per year to the Fast Stream programme. A large proportion of successful candidates have postgraduate work experience or qualifications (a surprisingly large number of biology PhD students are on the scheme!), but it is not too uncommon for recent graduates to be selected.

Q: Please describe a typical day.
A: There are no typical days on the Fast Stream. The variety and scope of work means you never get bored. In my last post I was charged with helping to produce a report entitled Bioscience 2015. Days could vary: perhaps drafting sections of the report or running large brainstorming sessions. I also visited several biotechnology companies.

Q: How do you see your future?
A: I'll probably remain on the Fast Stream for another 3-4 years. After this I hope to win promotion to full managerial level. Although I am currently working in the Women and Equality Unit of DTI, my heart still lies with science. I'm sure that I'll be drawn back to work in areas of Government that influence science policy. I'd also like to experience life in the private sector so shall probably move out of Government at some point in the future. However, I don't think you can plan too far ahead, since you never know what opportunities lie round the corner.

Q: What advice can you offer people planning to apply to the Fast Stream?
A: Go for it - definitely. I have enjoyed myself immensely. Being thrown in at the deep end allows you to develop in ways that you didn't think you could.

Selection process for the Fast Stream is pretty tough. If you get the opportunity, attending a GRADschool provides experience similar to the assessment centre exercises. Also, emphasize your background in science - the Civil Service really does value people with an analytical mind.

Further information

Civil Service Fast Stream (www.faststream.gov.uk) gives information about the opportunities available on the Fast Stream and outlines the application and selection process.

UK GRAD website (www.grad.ac.uk) provides information about the range of GRADschools, course dates and venues. The SGM offers grants to support GRADschool attendance by Postgraduate Members who are not eligible to obtain sponsorship from their funding bodies. Information and application forms are available from www.sgm.ac.uk/grants/pl.cfm

Career Development Workshop – 1 April, University of Bath

Brush up your presentation skills and gather some useful tips on career planning at our evening workshop PhD and Beyond at the Spring meeting in Bath. The session will close with a buffet and drinks.

A CV clinic will be running during the preceding afternoon. More details will be provided when you register for the meeting.

For more information contact Jane Westwell (j.westwell@sgm.ac.uk).

Calling all food microbiology postgrads

Don't miss the opportunity to present your work to other postgrads and academics at The Royal Society of Chemistry Food Group Post-Graduate Meeting, 15-16 July 2004, at University of Reading.

The meeting is open to postgraduates in all disciplines of food science and the organizers would particularly like to encourage more microbiologists to attend this year. Whether your research lies in the area of food safety, production, molecular methods, food biotechnology or development you are welcome to register for the meeting and submit an abstract (closing date 7 May 2004). Some delegates will have the chance to make oral presentations; others will present posters.

The meeting costs £20 including meals and accommodation for one night. You can even take your supervisor along for a mere £50. More details are available from Dr Bob Rastall (r.rastall@rlg.ac.uk).
Open access publishing – is it the future for scientific journals?

Ron Fraser

In the ‘traditional’ model of scientific publishing, authors submit a paper to a journal, and if it survives the rigours of peer review, is copy-edited, typeset, printed and distributed in the next available issue to individual and institutional subscribers. The publisher’s income from subscription sales covers the costs of review, production and distribution. This model translated into the electronic age: access to the online version of the journal is restricted to subscribers. However, there have been two main criticisms of the model: one, financial, and one technological.

In a study of US periodicals, subscription prices rose by an average of 9.5% annually over the past 16 years, compared with an average rate of inflation of 3.1%. Some of this has been justified by page number increases and the additional costs of online publication. However, the university library budgets have not increased by anything like 9.5% a year. This has led to the so-called ‘serials crisis’, in which subscriptions have been cancelled, and publishers have put up their prices even more to compensate for the lost income: a vicious circle that reduces the availability of articles to the average reader.

In considering pricing, it is important to distinguish between journals produced by the not-for-profit sector – learned societies and many university presses – and the for-profit commercial publishers. Many of the latter operate with very high profit margins in their journals businesses, much of which is channelled to shareholders and out of the research and educational sector. A small survey of microbiological journals showed that those produced by commercial publishing houses cost between 3 and 5 times as much per printed page as those published by learned societies such as SGM.

Of course many learned society publishers do make a profit (tastefully called a ‘surplus’ in the not-for-profit sector) on their journals; for many it is a major source of income alongside membership fees, investment income and meetings registration charges. In SGM’s case, the journals surplus funds the Society’s charitable activities, such as student grants, support of meetings, educational and public affairs work and so on, and is recycled to the benefit of the academic community.

The technological objection to the traditional subscription model is that it perpetuates 19th century methods; surely the advent of the internet offers new opportunities to making the scientific literature as freely available as possible. This thought, together with a growing backlash in the academic community to rising journal costs, has led to the development of ‘open access’ experiments. These range from online publication of papers on individual or university websites, to free online journals such as Public Library of Science PLoS Biology, or the BioMedCentral (BMC) journals on PubMed Central.

Such journals have production and maintenance costs which have to be recovered, generally by an ‘author-pays’ mechanism, in which the author (or the institution) pays a fee for publication. Different free access publishers are trying different models: some charge a flat fee per published article, others charge a submission fee for all articles, including those eventually rejected, as well as a publication fee. At the most complex, one publisher is proposing to charge both of these fees, plus extras per word, figure and table! No one knows at present whether these models will be economically viable in the long term, and acceptable to authors. PLoS charges $1,600 per article, but this appears to be subsidized from a $9M start-up grant from a charitable foundation. BMC charges $500 per article, said to be well below the economic costs of production. Several learned society publishers have calculated the true costs of publication, including a small element of surplus; most come up with an average fee of around $2,000–3,000 per article.

The subscription and author pays models are the extremes of a spectrum, and there is actually a lot of overlap in the middle. Many traditional journals have had page charges for years; many charge extra for colour illustrations. These are examples of author-pays within the subscription model. SGM has traditionally been against page charges, and offers free colour where scientifically justified.

Many subscription journals make back content freely accessible, such as articles more than 12 months old in SGM’s Microbiology and JGV at HighWire. The 346 journals online at HighWire have made a total of 666,000 articles freely available. This contrasts with a total of 30 research articles currently on open access in PLoS Biology.

In a hybrid experimental model the basic subscription system remains, but authors can choose to pay a fee to have their article free online from the time of publication. Again, the fees seem far below the true costs of publication: will this approach yield robust conclusions about its value for migrating from a subscription to an open access model?

SGM will obviously be monitoring the situation as the different business models develop, and considering whether SGM should change its procedures. The strategy will need to balance the different objectives in publishing: attracting authors to submit their best work; keeping the support of scientific editors and referees; securing wide dissemination to readers; maintaining scientific and production quality standards; ensuring archival permanence and accessibility of work published online, and retaining economic viability. The subscription model has achieved all of these objectives short of completely open access; the author-pays models still have to prove themselves.

In the meantime there are many intriguing questions. Will open access journals attract a significant flow of quality papers and build up respectable impact factors, or will the author payments relegate many of them to the level of vanity publishing? Will there be a transfer of budgets from librarians to authors, and a redefinition of the role of librarians? How will commercial publishers react? If author self-publishing on personal or university websites becomes commonplace, will there be an erosion of the quality standards that the established journals have built up? Recent discussions with other publishers have made it clear that there is no single industry view of how things will develop, but most people expect the landscape to be different or at least more varied in future.

More reports from the Marlborough House crystal ball will follow. Views from members would be welcomed.

- Ron Fraser is SGM Executive Secretary.

email r.fraser@sgm.ac.uk
Concerns about recruiting microbiology undergraduates are grave; universities are losing courses and replacing them with more popular subjects such as forensic science or sports studies. Yet there has never been a greater need for microbiologists. What can SGM members do? One successful approach is to interact with local schools and enthuse the pupils about microbiology. Microbes are fascinating and affect all of us daily. Kids relate particularly well to young scientists telling them about the subject as it knocks on the head their perceptions of boffins in white coats! Here we describe some ways to promote microbiology in schools.

### Honours projects with a difference

**University of Sheffield**

The Department offers school-based projects as an alternative to the conventional final year laboratory investigation. In the 2 years that we have run these, 19 students (out of around 200) have taken the school option. Of the ten students who carried out school projects in 2002/2003, five are now training to be teachers.

Early indications suggest that a similar number will enter schoolteacher training from the current cohort.

We have mainly dealt with primary schools, but this year we included one secondary school. Almost all the projects have been based on microbiology, because it became clear in initial discussions with schools that this was an area that they found difficult to teach and where the resources of the university could be used to most effect. The SGM World of Microbes booklet has been used as the basis of the teaching sessions, but in all cases the students were required to produce their own material.

Students and the academic staff involved had a session with the LEA Science Advisor to discuss the National Curriculum (NC) science requirements for primary school pupils before pairs of students were assigned a school.

Further discussions followed with the class teacher and then the students were required to prepare a minimum of three full afternoon lessons for their class. Students also attended lessons before and after their allotted slots.

The teacher was present at all times, which avoids any problems with the students not having been vetted.

Assessment of the projects is as follows:

(a) the final teaching session is observed by a member of university staff and with comments from the class teacher constitutes 15% of the mark

(b) the students prepare a presentation to their peers and staff (5%)

(c) the students write a 5,000-8,000-word report, which must include the background of the NC, all methods used in class experiments, all worksheets used, the outcome of the lessons and a discussion of whether their aims and objectives were met and what would they do differently if running the lessons again. The students also submit a laboratory book which details the development of their teaching sessions by making contemporaneous notes (80%).

**Jim Gilmour, Department of Molecular Biology and Biotechnology, Krebs Institute, University of Sheffield, Sheffield S10 2TN, UK (j.gilmour@sheffield.ac.uk).**

The students’ views

Emily Stringer (Ecclesall Junior) – Biochemistry; Sarah Thompson (Dore Primary) – Genetics; Anna York (Dore Primary) – Genetics/ Microbiology; Emma

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**Farley (Netherthorpe Primary) – Genetics and Leanne Sunter (Chaucers Secondary School) – Biochemistry/ Microbiology gave their opinions of the scheme.**

**Why choose a school-based project?**

Three of the students were considering becoming teachers anyway, and thought it would be useful experience. The others were not so keen on lab work and valued the opportunity to try something different. As Sarah said, ‘I am interested in several non-lab-based careers, including teaching, and thought that this project would allow me to develop skills required for these careers as well as have an insight to a teacher’s everyday tasks’.

**The type of school and age range taught**

Emily and her partner were allocated a class of 30 year 5 children (aged 9–10), whilst Sarah and Anna taught a year 4 (aged 8–9) class. The school decided this would be the best class for us to work with, as the Year 6 class were busy revising for SATS tests. Emma was based at a primary school with eight students of mixed ethnic and social backgrounds, aged 10. Leanne was the only student to work in a secondary school. If I did go into teaching I would want to teach secondary, so this gave me the most relevant experience.

At secondary level, as well as the NC, teachers have to meet examining bodies’ specifications for GCSE and post-16 courses. Leanne used these to design an investigation for Year 10 which had to give them access to high marks in all four areas of coursework assessment. For Year 8, I used NC guidelines as a basis. Information on food and digestion was very easy to find, but the Year 10 exam information was more problematic.'
Project objectives

At primary level the basic learning objectives were to introduce the idea that microbes are small living organisms that come in many forms; some are beneficial and others are harmful. Emily also had to complete a scientific investigation and to produce an activity book, which proved to be very popular with the children. She felt that the objectives were met. Sarah and Anna could not cover all the topics in Unit 5B due to time constraints, but they also taught about hygiene and how disease microbes are passed from person to person. They had pupils of widely differing abilities to cope with, leading to three bands (levels) of work being produced.

Emma felt that the main objectives were achieved successfully and that the children understood the importance of micro-organisms in our world. They were able to answer questions correctly and to fill in worksheets!

Leanne had slightly different objectives, personally, to gain a real life experience of working in a school. As part of my university project, to make science more interesting for the children, I think the objectives were achieved.

Student reactions

All of the students felt that the children really enjoyed the lessons. ‘They appreciated doing some practical work, were very interested in the photos of microbes and loved the opportunity to ask real scientists who wear white coats (their words) lots of questions about microbes, particularly regarding illness and food’ (Emily). Sarah and Anna agreed and noted that pupils also liked the interactive quiz and the microscope work. Emma felt that they enjoyed learning something new, although some of the information seemed a little beyond their understanding. Leanne found that enthusiasm waned as the pupils got older; ‘Year 8 definitely enjoyed it and I think Year 10 did, but they didn’t want to do coursework.’

Would the students do anything differently?

Emily felt that she needed more experience in developing effective worksheets, whereas Sarah would prepare work at different levels according to ability. They all agreed that extra time would be useful to cover more topics and activities. Leanne would try harder to make it fun and more exciting for the children.

Teaching Microbiology to Year 1 Primary School

Year 1 children are aged 5–6. Microbiology is not part of their key stage (KS1) curriculum, but I decided that a microbiology practical experiment could contribute towards the goals. The KS2 section on micro-organisms, although aimed at children aged 9–10, gave me a starting point for my lesson. Other information on teaching microbiology to KS1/2 pupils was quite difficult to find and my list of references was not extensive. The internet proved to be quite useful, and the SGM www.microbiologyonline.org.uk website was very handy and perhaps one of my best sources.

In planning my lesson it was essential to find out what children already knew about micro-organisms and also what they were capable of in the classroom. I attended science classes weekly for about 3 months and observed the children, talked to them and conducted mini-experiments with one or two. I was on a steep learning curve. For example, that they did not know what ‘thousands of times smaller’ actually meant when describing a microbe, and that it was easier to describe them as ‘a lot, lot smaller than an ant’! I also found out that some children did have rudimentary knowledge of the processes of decay. Microbes were abstract concepts to them, and I began to realize that they really did need to take form in the children’s minds. This gave me the idea for the microscope puppets.

My final lesson plan aimed (1) to aid children in understanding that micro-organisms are very small creatures that are all around us and (ii) that we can magnify objects otherwise invisible to us. I first engaged the pupils with the moving arms microscope puppet I had made, before they (1) looked at some fungi/dead flies/spider legs under a microscope and drew them, (2) used an ICT programme Mad about Microbes I had devised, (3) used an Intel

The students had to research and deliver a class either to year 1 students or to year 5. John Lindley (see below) stuck to the theme of good and bad microbes for the year 1 children. One student doing the key stage 2 project chose soil microbes and the children made mould gardens to look at decay. The other did vaccination and had the students playing an infection game using coloured stickers to understand how disease microbes stop disease. The children all enjoyed the lessons and as part of the project the students went back to see how much the pupils had retained - in all cases the response was pretty good.

The teachers were as interested in the lessons as the children and this year the students are being asked to produce a set of teacher’s notes as these will be of long-term use to the school.

Cath Rees, School of Biosciences, University of Nottingham, Sutton Bonnington Campus, Loughborough LE12 5RD, UK (Cath.Rees@nottingham.ac.uk).

University of Nottingham

I have been into my children’s school several times to talk about microbiology and this gave me the idea of offering a school-based project to final year BSc microbiology students as an alternative to the lab. The science curriculum coordinator have permission and last year was the first time we ran the projects. As they were so successful we are doing them again in 2004.

Mad about Microbes, the fun, interactive ICT package that John Lindley devised, with animation and sound, describes the activities of some good and bad micro-organisms. It includes a quiz to test children’s knowledge.

This will be available on www.microbiologyonline.org.uk soon.
microscope attached to a computer to find very small words printed on a piece of paper and (4) made moving arm microbe puppets.

I think I definitely achieved my objective regarding magnification, which the children found fantastic. However, they were mainly interested in the insect legs and not so much in the fungi!

Several children seemed to grasp that there are good and bad micro-organisms and gave examples to the class. However, children may also need experimental proof that micro-organisms exist; this lesson did not tackle the issue. I feel that after the lesson the children probably knew more about microbes than a large percentage of the country's adult population.

I enjoyed the project immensely. In fact, I sometimes felt a bit guilty listening to other students complaining about experiments in the lab going awry and people pinching their solutions. Some also seemed to think that I was getting an easy ride. This was definitely not the case. The title gave scope to put into the project what you wanted to get out, and I decided to maximize the benefits both for me and the children. My literature review involved looking at pedagogic theory, the importance of ICT and the teaching skills needed for primary school. I enjoyed learning how to use Macromedia Flash and also how to communicate with children. I also liked the primary school classroom environment and feel that this is a career that I might like to move into. At the moment I'm teaching English as a foreign language in Spain and I'm hoping to work with children in this field too.

As for the children, I'm sure that the majority enjoyed the lesson as there was a good buzz around the classroom. Feedback from the teacher was positive. The teacher did not have much idea about microbes before we started working together, but she too enjoyed conducting the lesson and was fascinated by the topics we covered. Her help and the good working relationship we developed were invaluable.

John Lindley (johnlindley_uk@hotmail.com)

Resources for School Members enclosed with this issue:

- Cold Wars factfile
- Microbiology – a subject for life CD-ROM

Coming soon:

- Malaria factfile

Researchers in Residence

This scheme, supported by Research Councils UK and the Wellcome Trust, encourages young research scientists (postgrads and postdocs) to contribute towards making school science more relevant and exciting for secondary school students. Researchers in Residence are allocated a local school where they plan activities such as a talk or practical with the appropriate teacher. They spend around 24 hours in the school. A day's briefing is provided before the first school visit.

The scheme is run by the Centre for Science Education at Sheffield Hallam University. Contact Laura Doleman (Tel. 0114 225 3785; email ljdoleman@shu.ac.uk).

Partnership Grants: Linking schools with scientists and engineers

The Royal Society, with Exxon Mobil and the Mercers Company, has set up a grant scheme to support partnerships between practising scientists and UK teachers. The students involved must be aged 5–16. Applications must be made in conjunction with the partner, but grants (£250–2,500) are paid to the school. For full details and an application form see www.royalsoc.ac.uk/education

Nuffield Science Bursaries

Instead of scientists going into schools, this scheme gets post-16 school students into labs to experience science in the real world. Students take part in science-based projects in university, industry, hospitals or research institutions during the summer holidays. Students can find their own placement or apply for project placements organized by Nuffield Regional Co-ordinators. 600 bursaries are awarded each year. Project providers are urgently needed. Can your lab help? See www.nuffieldfoundation.org/grants/scibsc

SGM Public Understanding of Science Grants

Grants of up to £1,000 are available to SGM members for science promotion activities. Past awards have supported microbiology workshops and training courses for school students which members have run in their university labs. The SGM will supply packs of teaching resources and has plenty of suggestions for suitable investigations to carry out. Application forms are available on the SGM website.
Post-16 Microbiology Summer School

Following the success of the event held in 2002, SGM will be running a residential summer school for post-16 biology teachers at the University of Leeds from 12 to 16 July this year. The programme has been carefully planned to reflect the microbiology content of the current post-16 examining body specifications, including the new pilot specification from Salters/Nuffield. The microbiological issues studied throughout the week will be set in the context of real life applications, making the content both relevant and stimulating. The latest research findings in each topic will also be addressed.

There will be a mixture of talks by experts who are also proven communicators, workshops, practical sessions and a visit to the Thackray Museum.

The Summer School will begin with an introduction to microbiology, followed by a session on science communication, led by a professional science writer. On Tuesday and Thursday mornings four microbiological themes (medically important diseases, molecular microbiology, environmental microbiology and biotechnology) will be explored by in-depth talks.

Practical sessions will take place on Monday, Tuesday and Thursday afternoons, including an investigation into the antibacterial properties of Tea Tree oil, DNA finger-printing, PCR, data logging and the use of microscopes. All practicals will adhere strictly to current schools safety guidelines. On Wednesday there will be a half-day visit to the Thackray Museum, which through its collections, galleries and interactive displays brings to life the history of health and disease, treatments and cures and medical discoveries. The afternoon will be spent in the university library, working in groups, to produce a scientific poster that will be presented later that evening to a panel of science communication experts. The Summer School will conclude with a questions session and an overview of Science in the 21st Century.

Exciting social events will provide light relief after an intensive day’s study, including an evening cruise down the River Ouse with supper and a Gala dinner at University House.

The Summer School costs £100 for SGM members and £130 for non-members, to include all course materials, lunch, refreshments, accommodation, visits and social events. Due to the limited number of places available only one teacher per school will be eligible to attend and priority booking will be given to SGM members.

Contact Daniel Burdass (d.burdass@sgm.ac.uk) for information.

Unearth your ‘Vision of Science’

A vision of science is an attention-grabbing image that gives new insight into the world of science and the workings of nature. It may show something never seen before, it may explain a scientific phenomenon, it may illustrate scientific data or it may simply be an image that shows the beauty of science.

Now is the time to start planning your 2004 entries to win £1,000 first prize or £400 second prize in the main entry categories, or enter the special awards, with prize money of £500. The categories are:

- **Action** - Images that capture the scientific process or event as it happens in the natural world.
- **Close-up** - Images that are beyond the naked eye.
- **People** - Images that communicate the impact of science, medicine and technology on peoples’ lives.
- **Concepts** - Images that demonstrate or explain a scientific concept.
- **Art** - This ever popular category is for images that illustrate the beauty of science.

There are also three special awards:

- **Scientists at Work** sponsored by NESTA - images that challenge the perceptions of how and where scientists carry out research.
- **Medicine and Life** sponsored by the British Medical Journal - images that portray disease, diagnostic techniques and treatment.
- **Young Photographer** sponsored by NESTA Learning Programme and Kodak

The panel of judges will include scientists, photographers and picture editors.

Information on how to enter and an entry form is on the web at www.visions-of-science.co.uk or call 020 7613 5577. The closing date for entries is 7 May 2004. Photographs taken on or after 1 January 2000 are eligible for entry and up to 6 images may be entered in each category or special award.

Organized by Novartis Pharmaceuticals in association with The Daily Telegraph as part of the company’s ongoing support for science education in the UK. The category prize money of £7,000 and additional support comes from the Science Photo Library.
John Smith, a pioneer in the field of nucleic acid research, helped to establish the structure of RNA and to discover the methylation of the bases in bacterial DNA. The information about the structure of RNA was crucial to the double-stranded model of DNA proposed by Watson and Crick. Later, he helped to unravel protein synthesis by establishing key properties of transfer-RNA molecules.

John Derek Smith, the only child of an insurance inspector, was born in Southampton on 8 December 1924. His early life was unhappy, being marked by the death of both parents in a flu epidemic when he was 5 years old. He was brought up in Wetherby by an aunt, and he spent holiday periods in Worthing with another aunt. He attended, first, The Convent High School in Wetherby and then King James' Grammar School in Knaresborough. In both schools he was head boy. In 1942 he went up to Clare College, Cambridge, to study Botany. After graduation, he joined the Agricultural Research Council's virus research unit at the Molteno Institute. Here, he and Roy Markham worked out how to separate by paper electrophoresis single nucleotides and small oligonucleotides, obtained from the RNA genomes of plant and animal viruses. They showed that under the influence of a high voltage, the ribonucleotides and oligoribonucleotides migrate across the moist paper with mobilities that decrease with increasing size.

Much later, the procedure became developed into the separation of nucleic acid fragments by gel electrophoresis for sequencing both RNA and DNA. Smith and Markham shared their results with colleagues with common interests in the Chemistry Department, and, by 1952, thanks to their joint efforts, the chemical structure of RNA had been established. In the same year, Watson and Crick, also in Cambridge, and with knowledge of the chemical analysis of RNA, built the iconic double helical model of DNA.

Smith continued his work at the Molteno Institute where, with David Dunn, he discovered the unexpected methylation of DNA bases in bacteria. At the time, the biological significance of this finding was not understood, but it is now known that bacteria methylate their DNA bases as part of a defence mechanism to allow the DNA of invading viruses to be recognized and digested selectively by bacterial restriction endonucleases.

In the late 1950s Smith went to work first at Berkeley and then at Caltech (California Institute of Technology) where he demonstrated that polyoma is a DNA virus. In 1962 he was recruited back to Cambridge as a permanent member of staff of the newly founded Laboratory of Molecular Biology, joining Francis Crick and Sydney Brenner in the Division of Molecular Genetics, where he remained until his retirement in 1988.

In the 1960s Smith took part in research to understand the process of how information encoded in DNA is used to make specific proteins. In the late 1950s Francis Crick had proposed that transfer of information from DNA is mediated by adaptor RNA molecules (later called transfer- or tRNAs) carrying specific amino acids, which would then be arranged in the correct order specified in the sequence of the messenger RNA. In 1964 Sydney Brenner found that a mutation in one tRNA overcame nonsense codons in the messenger RNA. Instead of terminating, the protein chain continued to elongate, and apparently, the mutation had changed the genetic code of the organism. Smith and his colleagues demonstrated that each tRNA has an anti-codon region complementary to the corresponding codon in the message, and that mutations of the anti-codon of one particular tRNA alter its properties making it complementary to a codon that was not recognized usually, allowing it to be read as a specific amino acid.

Smith was elected a Fellow of the Royal Society in 1976. He was a member of the Society for General Microbiology from 1941 and one of the Society's longest standing members.

John Smith was self-effacing, kind and humane. He was generous with his time and ideas, given freely without any expectation of personal benefit. He influenced and was respected by a wide range of young scientists, many of them now distinguished across different areas of molecular biology. He loved to converse, often with a cigarette in one hand and pint of beer in the other, about diverse topics, including science, the history of scientific discoveries and politics.

His marriage to Ruth Aney was dissolved in 1968.

Professor Sir John Walker, The Medical Research Council Dunn Human Nutrition Unit, Cambridge, UK.
Rapid identification of TB
Tuberculosis is an increasing public health problem in many countries. The World Health Organization estimates that there are 20 million cases of TB worldwide, with 8 million new cases and 3 million deaths each year. The speedy identification of patients is essential for TB control. Kits can identify the presence of DNA from the Mycobacterium tuberculosis complex (MTBC), but growth of cells in culture is still needed both to confirm the presence of a live infection and to test the antibiotic susceptibility of the strain. Considerable effort is therefore going into developing systems with improved sensitivity for dividing Mycobacterium cells. The BACTEC 460 TB system from Becton Dickinson Ltd takes 4–8 days to give a result, requiring the BACTEC NAP enzyme assay and a DNA test for confirmation. Researchers at the Central Tuberculosis Laboratory of Singapore General Hospital have been comparing it with the BD ProbeTec ET system from the same company. This system can give a result in a day, and the researchers wanted to know if it matched the BACTEC NAP system for sensitivity and specificity.

A total of 145 clinical specimens were used, and these were obtained from fluids such as blood, pus and urine, as well as from patients' lungs and other tissues. Conventional procedures were used to select for MTBC organisms, ending up with a BACTEC 12B culture vial. The researchers then used the manufacturer's recommended methods to test for MTBC using both the BACTEC NAP and BD ProbeTec ET systems. The test systems were capable of detecting the presence of MTBC and determining whether the organism was actually a closely related species incapable of causing TB.

The researchers worked out that 89 of the specimens contained MTBC, while the other 56 contained other Mycobacterium species. The BD ProbeTec ET system correctly identified 87 out of the 89 MTBC isolates, and all of the others. Three of the non-tuberculous mycobacteria were initially mis-identified by BACTEC NAP, but came up correctly when the researchers altered the growth conditions slightly. It was concluded that the BD ProbeTec ET system is reliable for identification of MTBC isolates, and that its speed, and the fact that the test reagents can be stored at room temperature, offers distinct advantages.


The importance of biofilms in plague
It would be good to know exactly what makes some bacteria into pathogens, and which features of their host they exploit. That would help with the design of new medical treatments as well as strategies to prevent infections. However, many experiments infecting mammalian cell cultures or animals with bacteria would be needed to find out this information. Apart from ethical and financial reasons for wanting to minimize the number of these experiments, it would be easier to understand the outcome of them in genetically simpler systems. Scientists are therefore investigating alternatives, and researchers at the London School of Hygiene and Tropical Medicine have been seeing what can be learnt from infecting nematode worms with plague bacteria.

Researchers have studied the 1 mm long nematode worm Caenorhabditis elegans in incredible detail. They know the fate of each of its 1,030 cells and have an extraordinary collection of mutants. It was the first animal to have its entire genome sequenced. As a consequence, the researchers can test strains of worms with traits that might be important in allowing or preventing infections.

The bacterial genus Yersinia contains a number of species. The most notorious is Y. pestis, which causes bubonic and pneumonic plague. Other species, such as Y. pseudotuberculosis, cause very unpleasant food-borne diseases of the digestive tract. Some scientists think that Y. pestis evolved from Y. pseudotuberculosis between 1,500 and 20,000 years ago. All the tools of molecular biology can be applied to these bacteria, as well as collections of isolates from many parts of the world.

The researchers already knew that some strains of Yersinia could infect the nematode by forming a layer of bacteria over its head, preventing it from feeding. This layer is called a biofilm, and occurs in several bacterial diseases. The researchers therefore focused on trying to understand what genes in the bacteria were essential for forming a biofilm on nematodes. They tested 41 strains of Y. pseudotuberculosis, and discovered that most strains could not infect the nematodes. There was also no obvious similarity among the six bacterial strains that caused severe infections of the nematodes. However, the researchers were able to identify several genes within the nematodes that help them resist the formation of bacterial biofilms and are now investigating the exact role of these genes.

Further evidence for simian origin of HIV

The origin of the AIDS epidemic in humans is likely to have started in the first half of the twentieth century by transmission of an immunodeficiency virus from African non-human primates to humans. Researchers have identified many simian immunodeficiency virus (SIV) viruses in monkeys and apes, confirming that these infections are more common than was thought a few years ago. There is a lot of variation among the viruses, adding weight to the idea that they have an ancient relationship with African non-human primates. It is commonly accepted that a SIV called SIVcpz, which has a low prevalence in wild chimpanzees, is the ancestor of HIV-1 while a second virus from sooty mangabeys has evolved into HIV-2. These viruses often cause no detectable illness in their animal hosts but may pose a real risk of providing further immunodeficiency viruses to infect members of the human population, who encounter the animals as pets or bushmeat. Researchers are therefore interested to know how many other immunodeficiency viruses occur naturally in African monkeys and great apes.

While researchers in the Netherlands were screening serum samples from various non-human primates for antibodies against SIV, they spotted an unusual result in a sample from a local zoo taken from a Schmidt's guenon, a subspecies of the red-tailed guenon. The results of further tests indicated that what this was a distinct variant of SIV, which the researchers called SIVschm. The most closely related virus to it, SIVgsn, had been isolated from greater spot-nosed monkeys, but the two were not particularly similar. However, the most exciting feature was that the genome of SIVgsn contains a gene that was thought to be unique to HIV and the SIV viruses from chimpanzees. The identification of another virus with this gene provides more information about the origin of the human immunodeficiency virus HIV-1.


The SGM publishes four journals, Microbiology, Journal of General Virology (JGV), International Journal of Systemic and Evolutionary Microbiology (IJSEM) and Journal of Medical Microbiology (JMM).

They are all available online with full-text HTML and other features such as CiteTrack, Email-a-Friend and Most-cited/Most-read listings. For further information visit the journal website: www.sgmjournals.org

Members may purchase SGM journals at concessionary rates. See p. 1 or contact the Membership Office for details. Information on commercial subscriptions is available from the Journals Sales Office.

The ‘crypton’ factor

Transposable elements (TEs) are an important part of most genomes. For example, almost half the human genome consists of various types of TEs. They are regions of DNA that once had, and sometimes still have, the ability to move around the genome. Researchers are still learning about this type of mobile DNA, particularly how and why it moves. Tim Goodwin and his colleagues Margaret Butler and Russell Pouliier at the University of Otago in New Zealand have recently discovered a new type of TE that they have named crypton. They had detected an enzyme in higher organisms that carries out the essential step of re-integrating mobile DNA into the genome, and was already known in bacteria. The Ngaro 1 and DIRIS 1 groups of retrotransposons both contain the gene, and other researchers have identified it in the ciliate Euplotes crassus. The researchers’ recent studies have now revealed more about TEs with this type of tyrosine recombinase enzyme.

The researchers have been studying pathogenic fungi such as Coccidioides posadasi, Cryptococcus neoformans and Histoplasma capsulatum that can infect the respiratory tract and also act as a threatening opportunistic pathogens, especially to immunocompromised individuals.

The genomes of these fungi have been sequenced, and the researchers searched for matches to the characteristics of cryptons. The fungi contained several copies, with the number differing between strains of the same species. The usual explanation for this is that the TE was active comparatively recently. As the researchers discovered more about cryptons and their tyrosine recombinase genes, they became convinced that these were part of a new and very different sort of transposable element.

One unusual feature in C. neoformans was that the gene for the tyrosine recombinase contained introns. These regions of the DNA sequence are removed as the cell gets the gene transcript ready for translation into a protein. Introns are present in eukaryotic genes, but are rarely found in bacterial ones. The fungi in which the researchers detected cryptons belong to different major divisions that have evolved separately for over 400 million years. All the evidence indicates that cryptons existed prior to this separation.

The genome of two strains of H. capsulatum has been sequenced. The researchers detected 35–40 cryptons in one, and about 10 in the other, all in different locations. This suggests that they have moved around the genome since these two strains diverged from their common ancestor. Movement of a TE can be bad news, since if it lands inside a gene it will affect its normal function. Some fungi have a system that puts mutations into any DNA sequence that appears multiple times in a genome, since such sequences would not be normal genes and mutations should inactivate them. The researchers spotted evidence that some fungi have been trying to stop the cryptons moving. There were many mutations within the H. capsulatum and C. posadasi cryptons, typical of this defence process.

The researchers also found a tantalizing suggestion of what else an organism might do to a crypton when they looked at the genome of Candida albicans, the fungus that causes thrush. There was the sequence for a protein that looked as if it started as a tyrosine recombinase, but had now developed into something else. C. albicans might have managed to exploit the crypton for its own ends. This new class of TE, as well as giving an insight into the way that DNA can recombine, may also provide ideas about evolution.

Is there life on Mars?

Scientists, and science fiction writers, have speculated about this for centuries. It would be unfortunate if any of the unmanned space probes sent to the red planet were accidentally accompanied by life from Earth. spacecraft are therefore cleaned of microbial contamination while they are being prepared for launch. Myron La Duc and his colleagues, Masataka Satomi and Kashiuri Venkateswaran, working at the Spacecraft Assembly and Encapsulation Facility II in the Kennedy Space Center in the USA, have recently reported that a very small number of organisms were left on the surface of the Mars Odyssey spacecraft as it was readyed for launch in April 2001. In February they counted around 30 organisms per 25 cm², far below the number on most terrestrial surfaces. Standard tests showed that most were bacteria belonging to many different genera, including Acinetobacter, Curtobacterium, Rolstonia and Bacillus, but there was also one species of fungus, Aureobasidium pullulans.

The researchers focused on the Bacillus isolates because this genus is well known for producing spores that are very resistant to destruction. One strain had unusual and distinctive spherical spores composed of a series of layers around a core. The outermost rather loose layer might have been responsible for adhering efficiently to the spacecraft surfaces. A series of biochemical tests, and examination of a region of a gene that is characteristic in many bacterial species, indicated a close relationship with several Bacillus species, but no exact match. Therefore, the researchers became convinced they had a new species, which they named Bacillus odysseyi, after the spacecraft.

Mars Odyssey has been orbiting Mars since October 2001, with no intention of landing. The big question is whether B. odysseyi, or other microbes that have resisted all human attempts to remove them, could survive the highly oxidative UV and gamma radiation-rich environments they would encounter in space and the surface of Mars. If any did, this could be a problem for assuring that any apparently extraterrestrial life is truly alien. The researchers therefore tested how well the spores resisted the lethal effects of hydrogen peroxide, UV light, desiccation and gamma radiation from a radioactive cobalt source. Although all, except desiccation, killed many of the spores, a surprisingly large number survived. Compared with a standard reference Bacillus strain, the spores of B. odysseyi survived between 3 and 10 times better. Whether this would be sufficient to survive a trip to Mars, only more experiments will tell.


Animal origins of human T cell leukaemia virus

Primate T lymphotropic virus type I virus causes a very aggressive form of leukaemia or lymphoma. It includes different strains that affect either humans and/or non-human primates (monkeys and apes) of the old world. The strains of this virus that infect people, human T cell leukaemia virus type I (HTLV-I), show remarkable genetic stability. There are four major geographic subtypes and researchers have strongly suggested that some of them originated when the virus was transmitted from monkeys or apes to humans. The evidence comes especially from identifying African strains of simian T cell leukaemia virus type I (STLV-I) in wild-caught chimpanzees and mandrills that are similar to some types of HTLV-I that infect humans. However, most strains of STLV-I have been isolated from captive animals in Europe, North America and Asia, making both the origin of their viral infections, and the relationship with HTLV-I, less easy to ascertain.

A collaboration between researchers at the Centre Pasteur in Yaoundé in Cameroon, and colleagues at the Institut Pasteur in Paris has now surveyed over 61 wild-caught gorillas and chimpanzees in Cameroon for the virus. Most of the animals had been kept as pets after hunters had killed their mothers; and any infections were probably transmitted from the animals' mothers. The animals had either been confiscated by the Ministry of Environment and Forestry, or taken directly to a zoo or an animal sanctuary. The researchers tested for antibodies characteristic of virus infection and found signs in two animals, a young female gorilla and chimpanzee. To find out how similar these viruses were to other strains of HTLV-I and STLV-I, the researchers sequenced two fragments of the genome: the complete long terminal repeat, which is quite variable, and the gp21 env gene. The virus infecting the chimpanzee turned out to be more similar to HTLV-I than any isolate STLV-I from other chimpanzees. Both viral isolates matched the B subgroup of HTLV-I, most isolates of which come from humans in central Africa.

The researchers point out that only a proper survey of primates in the wild, examining, for example, the viral content of faeces, will reveal the true prevalence, geographic and subspecies distribution of the STLV-I viruses. However, the close relationship between the STLV-I isolates identified in this study, and the HTLV-I strains characteristic of infections of the human inhabitants of the same region, reinforces the idea that STLV-I has been transmitted from animals to humans.

Benefits of retrovirus infection?

Retroviruses have the unique ability to integrate their genome into the DNA of the host cells. As a consequence, any host cells that survive a retroviral attack can contain viral genes. It is therefore not entirely surprising that projects to sequence genomes, like the Human Genome Project, have found retroviruses, although the amount has been surprising. There are estimates that 8% of each human's DNA consists of retroviral genes. As a consequence, scientists wonder if these so-called endogenous retroviruses (ERVs) actually confer a benefit on their hosts.

Ideas that ERVs could protect their host from infection by exogenous (e.g., horizontally transmitted) retroviruses have developed, and also a hypothesis that ERVs are essential in the development and function of the placenta. Researchers in the 1990s realized that two ERVs were always switched on in the human placenta during pregnancy. Proteins produced by one bore a remarkable similarity to proteins that could suppress the immune response, while the other affected cell shape. Could it really be possible that remains of an ancient retrovirus help the foetus invade its mother's tissues and fend off her immune response?

Massimo Palmarini and his colleagues in the USA have been studying a retroviral disease transmitted from sheep to sheep, and come up with more facts to add to this debate. Jaagsiekte sheep retrovirus (JSRV) causes a major infectious disease resulting in lung cancer. However, every sheep already has about 20 copies of a very similar retrovirus (enJSRV) nestled among their genes. The researchers discovered they are switched on in several tissues and that at least one had all the instructions to make virus particles, but with two very small changes. These differences made laboratory cultures of cells expressing a particular enJSRV less susceptible to release JSRV viral particles. This could be a good example of an ERV providing protection from a viral disease, but more experiments convinced the researchers that enJSRV may also be important in sheep reproduction.

During the second week after fertilization, the outermost layers of an embryonic sheep attach to the endometrium lining the uterus of its mother. The next step starts the development of the placenta, which will nourish the embryo, remove its waste products, defend it from its mother's immune system and provide it with oxygen until it is time to be born. The complexity of these roles, and its necessity for successful reproduction, is another of the puzzles of evolution. How can adaptation allow the evolution of an organ with so many complicated and essential functions? A closer look at placental development and enJSRV is giving researchers hints towards an answer.

During embryo implantation, unusual multinucleated cells are formed in the placenta. Once formed, these multinucleated trophoblast cells expand and invade the mother's endometrium to get closer to blood vessels. In the endometrium of the uterus, enJSRVs respond to levels of the pregnancy hormone progesterone and are particularly abundant in the endometrium during the time when an embryo begins to implant. Further, the enJSRVs are specifically expressed in the multinucleated trophoblast cells of the placenta. The researchers felt that the fact that they could see enJSRV proteins on the surface of the endometrium and in the multinucleated cells of the placenta at this key moment in pregnancy could not be a coincidence. They wondered if an interaction between the enJSRV proteins on the mother's endometrium and other proteins on the embryo helped implantation and formation of the placenta. After all, the invasive behaviour at the start of placental development was reminiscent of some cancerous cells, and wild JSRV causes cancer.

An organ to act as a placenta has evolved repeatedly, in fish, reptiles and amphibians, as well as mammals. Even the structure of placentas within the mammals varies widely, indicating that it has evolved several times. enJSRVs are present in the genomes of sheep and goats, and two of them look as if they were present before these groups diverged approximately 4–10 million years ago. There are even vague similarities in the genomes of cattle that diverged 18 or 19 million years ago. The complexity of the placenta has also changed, supporting the idea that enJSRVs assist in creating the elaborate invasive tissues of the embryo. Further research could not only indicate whether a virus really has an essential role in mammalian reproduction, but would also provide greater understanding of how retroviruses and immune tolerance works.

**Reviews**

**Cytokines and Chemokines in Infectious Diseases Handbook, Infectious Disease Series**
Edited by M. Koth & T. Calandra
Published by Humana Press (2003) US$145.00, pp. 458
ISBN: 0-89603-939-0

This is a timely publication. Understanding the role of cytokines in infectious diseases has increased dramatically in recent years. We now have a much better understanding of the role that cytokines play in host defense and the way that they may also contribute to pathology when produced in excess or when there is inappropriate cytokine production during infection. This is leading to the development of therapies for some infectious diseases (e.g. sepsis) based on anti-cytokine strategies. ‘Handbook’, however, is the key word in the title. This is not a text that makes easy bedtime reading! An understanding of immunology, cytokine nomenclature, and cytokine biology and associated jargon is a pre-requisite for tackling the very detailed text presented. This handbook will be of most use as a reference for academics teaching aspects of microbial immunity/pathogenetics at an advanced level and for those actively pursuing research in the field. 

**Eileen Ingham
University of Leeds**

**Bioremediation: A Critical Review**
Edited by L.M. Heid, I. Singleton & M.G. Milnor
Published by Horizon Scientific Press (2003)
£50.00/US$180.00, pp. 301
ISBN: 1-898486-36-0

This book is the result of what must have been an enormous achievement and is the result of what must have been an incredible amount of painstaking work. Even with its extent of 702 pages, the guide

**Biotechnology for the Environment: Soil Remediation. Focus on Biotechnology**
Edited by S.N. Agathos & W. Reineke
Published by Kluwer Academic (2002)
Euro/US$68.00/£47.00, pp. 140

This book is a compilation of multidisciplinary research works on soil remediation. It successfully integrates the depth of the scientific principles with the breadth of application of biotechnology in treating contaminated soil. This book can be approached on two levels: as a useful reference and a research treatise on bioremediation. The introduction chapter gives a clear overview of the current trends in bioremediation; the chapters on humification of nitroaromatics and phytoremediation are recommended reading for any practitioner interested in bioremediating polluted sites, including those contaminated by munitions. At a more advanced level, this book describes state-of-the-art research in clean-up technologies such as slurry-based methods and life-cycle assessment, which will be pertinent to researchers and academics in the field of bioremediation. This is an invaluable source book for soil professionals who are interested in the environmental application of biotechnology. 

**Diane Purchase
Middlesex University**

Edited by S.-Y. Ying
Published by Humana Press (2003)
US$99.50, pp. 330

As one who constructs and handles many cDNA libraries, I was looking forward to receiving this book. With chapters detailing diverse methods for cDNA library construction, normalization and subtraction, as well as applications in RACE, SAGE and 2-hybrid systems, this promised to be a useful volume. I must admit, however, that I was slightly disappointed. Don’t get me wrong; it does contain some very detailed annotated protocols that have been written by experts and are at the cutting edge of this field. My overall impression though was that the book was disjointed. With minimal introduction and little for the inexperienced it is basically a collection of useful protocols in a particularly logical order, with some material either repeated or spread ever several chapters when it should be together. As a result this book will be both useful and of interest to some, but will be inaccessible to others.

**Michael A. Oxen
Wellcome Trust Sanger Institute, Hinxton**

**The Freshwater Algal Flora of the British Isles: An Identification Guide to Freshwater and Terrestrial Algae**
Edited by D.M. Jahn, B.A. Whitton & A.J. Break
Published by Cambridge University Press in collaboration with The Natural History Museum and The British Phycological Society (2002)
£75.00/US$125.00, pp. 702
ISBN: 0-521-77051-3

This reference work represents an enormous achievement and is the result of what must have been an incredible amount of painstaking work. Even with its extent of 702 pages, the guide
Plant Biotechnology: The Genetic Manipulation of Plants
Edited by A. Slater, N.W. Scott & M.R. Fowler
Published by Oxford University Press (2003)
£19.99, pp. 368

Quite simply this is a superb book and a valuable resource for all those with an interest in the genetic modification of plants, either as students of the science or potential consumers of the produce. Although primarily directed towards undergraduates, the authors, all from The Norman Borlaug Institute for Plant Science Research, De Montfort University, have produced a text that deserves a much wider circulation. The layout is logical with a number of introductory chapters outlining the basic technology, before giving more in depth treatments of herbicide, pest and disease resistance, stress tolerance, yield enhancement, molecular 'pharming', the regulatory set-up and possible future directions. The coverage is well-structured, balanced and good use is made of examples, chapter summaries, suggested further reading and a companion website. The latter contains a number of case studies to work through, and I defy anyone not to be drawn to the one on the development of the flatulence-free baked bean! In short a great book, well worth the money.

Project Biotechnology
Edited by M.A. Andrade
Published by American Society for Microbiology (2003)
US$169.95, pp. 232

These two volumes provide a comprehensive overview of all aspects of clinical microbiology, covering not only pathogenic microorganisms, but also other topics such as laboratory design, management, information technology and infection control. There is also the now obligatory chapter on agents of bioterrorism. The particular strength of this book is the vast wealth of detail contained in each of the many chapters on individual bacterial, viral, fungal and parasitic pathogens. The chapters are supplemented with useful tables and figures (some in colour) and up-to-date lists of references. The book is also well indexed which facilitates the retrieval of information. One slight drawback for the non-American reader, however, is the bias towards systems used in American laboratories, which is particularly marked, for example, in the section on susceptibility testing. The price of two volumes will probably deter individuals from buying. They should, however, definitely ensure that their library gets a copy.

Stress Tolerance: Yield Enhancement
Edited by A. Slater, N.W. Scott & M.R. Fowler
Published by Oxford University Press (2003)
£19.99, pp. 368

From this book I expected an update on the mechanisms of action and resistance mechanisms of the fluoroquinolones as well as...
their use as therapeutic agents. I was not disappointed, although at times the going was heavy. There is a lot of data in the early chapters describing structure, activity, resistance and pharmacokinetics, which means that this is not a book to pick up and read in total. The chapters stand alone which inevitably means that there is some overlap, but most are comprehensive. If you want a well referenced review describing the evidence base for the use of fluoroquinolones in the treatment of UTI, STI, gastrointestinal infections, including travellers diarrhoea, all aspects of respiratory infections, soft skin and bone infections or neutropenic patients, then this is the book for you. It may also make you think about how to prevent further problems of resistance.

Imperial College, London.

**Rumen Microbiology**

By B.A. Doherty

Published by Nottingham University Press (2002)

£40.00, pp. 322


This is the first complete book on rumen microbiology since Hungate’s *The Rumen and its Microbes* (1968). This is an exceptionally well written and well arranged book that will be of great value to rumen and anaemic microbiologists alike. The format of the book is different from that used by Hungate, focusing on the microbiology. The opening chapters describe the evolution and physiology of the ruminant stomach, which provides a sound understanding of the digestive system of the ruminant. The protozoa, bacteria and fungi are segregated into their own chapters and are well described. The bacteria are conveniently grouped into those that ferment cellulose, hemi cellulose, pectin and starch, as well as the facultative anaerobes. The appendix contains a very useful set of possible experiments for students of rumen microbiology. Several notable omissions concerning the detection of oxygen in rumen fluid and the respiration of ruminant protozoa are apparent. It would be useful to have at least one glossy page of photographs representing the major groups of protozoa.

**The Other End of the Microscope: The Bacteria Tell Their Own Story**

A Fantasy by Elmer W. Koneman

Published by American Society for Microbiology (2002)

US$29.95, pp. 200


This is an extremely entertaining book that looks at life from the standpoint of bacteria. The black and white sketches that are scattered through the book are particularly amusing. The scene is set with the microbes gathered at an imaginary ‘First Congress of the Prokaryotes’ chaired by E. coli. At this congress various bacteria, some of them notorious and others not so well known, compare notes on their structure and function, niches and habitats, modes of survival, human infections and antibiotic resistance. Throughout the text the bacteria discuss the way humans have changed their names often and stand alone which inevitably means there is some overlap, but most are comprehensive. If you want a well referenced review describing the evidence base for the use of fluoroquinolones in the treatment of UTI, STI, gastrointestinal infections, including travellers diarrhoea, all aspects of respiratory infections, soft skin and bone infections or neutropenic patients, then this is the book for you. It may also make you think about how to prevent further problems of resistance.

**Non-Conventional Yeasts in Genetics, Biochemistry and Biotechnology: Practical Protocols**

Edited by K. Wolf, K. Brenig & G. Barth

Published by Springer (2003)

Euro99.95/CHF166.00/US$119.00, pp. 494

ISBN: 3-540-44215-4

Non-conventional yeasts are really those yeasts other than *Saccharomyces cerevisiae* and *Schizosaccharomyces pombe* which now represent the best understood eukaryotes. In addition to these model budding and fission yeasts, several species are now being studied using molecular genetic tools and are being exploited as hosts for heterologous gene expression. They include *Candida*, *Dactylylomyces*, *Kasnanaus*, *Kluyveromyces*, *Pichia*, *Schautaomyces*, *Zygosaccharomyces* and *Zgypsaccharomyces* species. This book, which is a follow-up of the 1990 text *Non-Conventional Yeasts in Biotechnology*, edited by K. Wolf, is a laboratory handbook which outlines experimental protocols on physiology and molecular biology of 15 non-conventional yeast species. The protocols cover such techniques as molecular characterization, foreign gene expression, lipid/vitamin/enzyme/pigment/ethanol/organic acid production, and classical genetic approaches. The experiments have been tried and tested and many should be applicable to yeasts in general. As such, this text would prove useful in yeast research labs. I doubt, however, if it would be of much use for undergraduate teaching purposes.

**Microbes: An Invisible Universe**

By H. Gest

Published by American Society for Microbiology (2003)

US$39.95, pp. 234


This book aims to offer an insight into why microbiology is one of the most exciting areas of modern science. It has the unusual feature of incorporating extracts from historical documents detailing groundbreaking experiments. Although sometimes over-long, these give the reader an interesting perspective on the emergence of microbiology as an independent discipline. The content is interesting and the style readable, although the structure is a little unbalanced. Some basic material in early chapters would arguably sit better in an Appendix, whereas the section on microbial bioterrorism is of sufficient topicality to warrant a higher profile. The author is frank about concentrating on bacteria, but I couldn’t help feeling that the fungi were somewhat short-changed. Those with a knowledge of microbiology are unlikely to learn much from the book, but may appreciate the unusual historical plant. The non-specialist would probably find it an enjoyable read, albeit somewhat expensive for a slim volume.

**Lentiviral Vector Systems for Gene Transfer. Medical Intelligence Unit 31**

Edited by Gary L. Buchschacher, Jr

Published by Kluwer Academic/Plenum (2003)

US$240, pp. 372


This is the first complete book on lentiviral vector systems for gene transfer since the whole field has been segregated into their own chapters and subjects. The opening chapters describe members of the lentivirus family and discussing the advantages and disadvantages of each virus in terms of their use as vectors. I would recommend the book to anyone who is considering using such vectors; however, it is probably too expensive for individual researchers.
My answer is not yet available.
About 15 years ago, the scientific community started to realize that it no longer enjoyed the unmitigated support of the wider public. For decades, science and technology had been seen as the great engines of a better world, delivering such wonders as electric light and plastic containers that kept food fresh. It is hard for many of us now to remember the days before antibiotics, when common illnesses were often deadly. But not everything had been rosy. Thalidomide and DDT had caused as many problems as they had solved, with devastating consequences for some people. As we realized that public support was no longer as strong as it had been, scientists took action. We formed a committee, awarded each other grants and went on training courses. We started giving talks to the Women's Institute, visiting schools and talking to journalists. In large part, these efforts have been successful. There are more science programmes on television than ever before, ever more 'popular science' books are published. Some science programmes, such as Walking with Dinosaurs, attract more viewers than even the most popular soap operas, and when asked to choose the 'Greatest Briton', the public voted Darwin, Brunel and Newton into the top ten, while only one writer (Shakespeare) and no sportsmen made it onto the list.

And, partly due to this activity, British people know more basic scientific facts than the people of other industrialized nations. They also have a better understanding of some of the fundamental principles of the scientific method. A higher proportion of people in Britain understand the need for a control group in a drug trial than in almost any other country. But when the average citizen is asked whether he or she is enthusiastic about scientific and technological advances, the British are far more sceptical than their counterparts in other European countries. Many people see this as a problem, claiming that our society is ripe with anti-science sentiment and that the great British public is determined to be backward-looking.

I suspect, however, that British scepticism is in part a reflection of our greater understanding and a testament to the success of the scientific community in engaging with the public. When non-scientists have a basic understanding of how science works, they can ask the right sort of probing questions, rather than accepting that scientists know more than them and must always be believed.

By opening up the scientific process, we have revealed its great strength. Science is not about certainty; it is about picking a route through uncertainty. And it is on the uncertain issues - BSE, the safety of mobile phones, the environmental effects of genetically modified crops - that we need more public engagement. While the scientists, pressure groups, media and the wider public have developed a rigorous, wide-ranging and often frustrating debate about these issues, there is one group that seems to remain semi-detached, unsure whether it should take sides in any argument, or whether it should stand back and just listen, or try to mediate.

The world of politics still takes the view that science should be dealt with by a small group of specialists. Individual parliamentarians may bluster about a particular subject (mobile phones if they have a mast in their constituency, BSE if they represent an abattoir), but in the main, they hide behind 'scientific advice' rather than making up their own minds. The demands of short-termism and the need for 100% certainty sometimes seem to make science and politics inherently incompatible.

In many ways, the scientists who invented the movement for the public understanding of science were extremely prescient. The wider public is much more sceptical than it was, partly because of social changes that mean we are (in general) much less deferent to authority, partly because technological changes have made information easier to find and partly because science is not, and never was, a great panacea to cure all ills.

If we do not develop new lines of defence, the era of killer bacteria will be back. The 'superbug' MRSA may just be the first in a long line of microbes that are resistant to existing drugs. It has arrived just as we start to understand more about prions, disease-causing agents that were virtually unstudied just a few years ago, and as we have a much greater appreciation of the role that viruses may play in diseases that were traditionally attributed to other causes.

It is more important than ever, in microbiology as in all areas of science, not only that the scientific community continues to engage with the public at large - including sceptics and critics - but also that we force the political world to listen to us, to engage with us more, and to take science more seriously.

Dr Peter Cotgreave is Director of the pressure group Save British Science (email peter@savebritishscience.org.uk). His most recent publication is 'Science for Survival: Scientific Research and the Public Interest' (ISBN: 0 7123 0891 1).