



MICROBIOLOGY

TODAY

QUARTERLY MAGAZINE OF THE SOCIETY FOR GENERAL MICROBIOLOGY VOLUME 27 AUGUST 2000

Mycology today
Weird and wonderful fungi
Exploiting fungal metabolites
Brewing yeast selection
Yeast genomics
Fungal skin diseases
Biofilms

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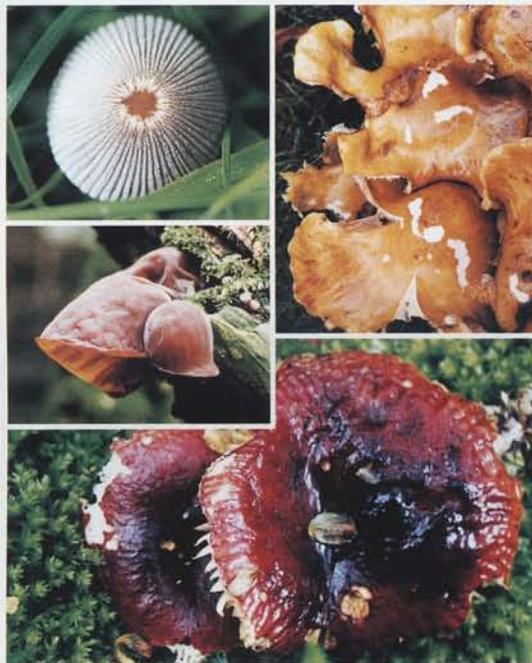
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Above: A selection of British fungi. Can you identify them?

Photos Ian Atherton

Vol. 27, Part 3, August 2000

Fungi provide the focus for this issue of *Microbiology Today*.

Tony Trinci, former President of the British Mycological Society, emphasizes the importance of fungi in our lives and ponders on the future of mycology (p. 115), whilst on p. 116 mushroom lover Elio Schaechter describes some of the weird and wonderful means by which fungi disperse their spores.

Classifying fungi was once believed to be straightforward, but rDNA sequencing data are revealing some unexpected relationships, as Roy Watling describes on p. 128. Developments in molecular biology are also enabling the decoding of entire yeast genomes. On p. 126 Alan Wheals explores the ensuing benefits for fundamental research and the potential applications of this knowledge.

Some yeasts may be used as model organisms, but down in the pub, their role in the production of alcoholic drinks is probably considered more important. Iain Campbell takes a look at beer and the selection of the yeasts used in brewing (p. 122). Fungi produce a whole range of useful secondary metabolites, such as antibiotics, as Geoffrey Turner describes on p. 118, but not all fungi are beneficial – some cause the horrible skin infections described in the article by Ruth Ashbee and Glyn Evans on p. 132.

Other topics included cover the ILT, the SGM Exeter meeting on biofilms and an account of the Society's participation the ASM 100th General Meeting.

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

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Institute for Learning & Teaching in Higher Education – Should you join?

Liz Sockett

Experienced university academics can currently apply for membership of the newly established Institute for Learning and Teaching in Higher Education (ILT). SGM Education Officer Liz Sockett outlines the nature of ILT and the application process so that SGM members can decide whether membership may be beneficial to them.

● What is the ILT?

The ILT is an organization for higher education professionals, recently established as a result of the Dearing Report into Higher Education, to promote and support excellence in learning and teaching in universities. Membership is intended for academics who can show evidence of innovating and developing their university teaching. ILT membership will provide them with further staff development opportunities and will give them formal recognition of their lecturing and teaching skills (which might be useful when seeking promotion.) It is possible that future QA audits of university teaching may also use membership figures as a positive indicator of a department's commitment to teaching quality.

● Applying to join

The conventional route for academics wishing to join the ILT is to successfully complete an accredited Postgraduate Certificate in Academic Practice (PGCAP) at their institution. As the ILT is a new organization, it also recognizes that existing experienced academics will already have the skills that such a PGCAP might provide to newer staff. Hence, until September 2001 ILT is accepting applications for membership from experienced staff without the PGCAP. Applicants are required to submit a CV with two references and to complete a form which asks them to comment on (and if appropriate supply a little photocopied 'evidence' of) their personal activities under six headings.

Teaching and the support of learning – Details of courses and types of teaching carried out, with examples of student feedback. Details of any teaching committee or leadership activities.

Design and planning of learning activities – Details of any teaching committee membership or any training or guidance given to others re teaching. Details of any resources developed for teaching.

Assessment and giving feedback to students – Details of the different types of assessment methods used, with any innovations or novel approaches highlighted. Explanation of how students with difficulties are helped.

Developing effective learning environments and student learning support systems – Details of student projects supervised in the lab, practical classes taught, library or web-based information tasks set or industrial placements or trips set up.

Reflective practice and personal development – Details of attendance at SGM Education Symposia and on any recent training courses on aspects of teaching or IT methodology.

Other information – Details of any mentoring done for new lecturers, any teaching done on university lecturing training courses, any presentations given on



the institute for learning and teaching
in higher education

education (e.g. at SGM meetings), how personal research is linked to teaching (including PhD supervision).

● Are the benefits of membership worth it?

There have been some fairly animated exchanges in the education pages of newspapers on the value of the ILT to the practising academic, and the monetary and time costs associated with applying.

Speaking from experience, it does take the best part of a weekend to complete the application and a little photocopying time to collate the 'evidence' (one or two pieces per section seems ample). As with other professional institutes there is a membership fee (£75 p.a.). Currently there is no pro-rata subscription for part-time staff, something that has been criticized. Several universities are offering to pay the fee on behalf of their academics, in the hope that it may improve the future TQA performance of the institution. As the ILT is relatively new, and only holding its first education conferences and symposia as we go to press, it is too early to evaluate the full benefits of membership. ILT will be publishing a refereed journal *Active Learning in Higher Education*; this may contain useful teaching ideas for science academics but only time will tell.

However, for those academics who have wished over the years that their contribution to teaching might be recognized or valued a bit more, ILT membership may be for you!

● Full details can be found on the ILT website <http://www.ilt.ac.uk/> or by writing to ILT, Genesis 3, Innovation Way, York Science Park, Heslington, York YO10 5DQ (Tel. 01904 434222).

Mycology today

Tony Trinci

Organisms commonly referred to as 'fungi' actually represent two distinct evolutionary lines, the true fungi (Kingdom *Eumycota*) and the algal-like fungi (Kingdom *Straminopila*); these groups contain about 70,000 and 750 species, respectively. The aquatic chytrids are the ancestors of the true fungi, whilst the algal-like fungi are related to the biflagellate algae. The algal-like fungi arose from a line which either never possessed chloroplasts or lost them. It follows that one of the most famous of all moulds, *Phytophthora infestans*, the cause of potato blight, is not a true fungus. Nevertheless, for practical reasons the two groups continue to be regarded as 'fungi' and as such are studied by mycologists.

Surprisingly, of the 1.5 million species of fungi thought to exist, only about 5% have been identified and classified. Where are the missing fungi? Many are thought to reside in the tropics, but the discovery of obligately anaerobic fungi in the rumen of herbivores indicates the need to seek missing species in more specialized habitats.

The formation of circular colonies is perhaps the most characteristic of all 'fungal' features. These colonies are observed as ringworms (*Trichophyton* spp.) on man and animals, and as fairy-rings (e.g. *Marasmius oreades*) in fields, as well as in conventional plate cultures. Since the highly polarized nature of fungal growth enables the hyphae of *Neurospora crassa* to extend at rates of up to $100 \mu\text{m min}^{-1}$, this fungus can colonize the surface of a 9 cm diameter culture plate in a matter of a few hours. Amazingly, fairy-rings can grow up to 200 m in diameter and some must be at least 500 years old. In Washington State, a clone of the basidiomycete *Armillaria ostoyae* was found throughout an area of over 1,500 acres and was estimated to be 400–1000 years old! Thus, fungal colonies can be long-lived and can grow to huge sizes. Remember this when you are next asked to name the largest living organism!

The importance of fungi to man is beyond doubt. The devastating effects they have on plants is well illustrated by the loss in the UK of some 30 million elm trees to the wilt fungus, *Ophiostoma novo-ulmi*, and the significant yield losses which still occur in agricultural crops. Until recently, few deaths in the UK were caused by fungal infections, but this has changed dramatically with the increase in the number of immunocompromised patients. Unfortunately, we lack effective treatments; the polyene amphotericin B, first discovered in 1955, is still the antimicrobial of choice for systemic human fungal infections, despite its very unpleasant side effects which include kidney damage. No wonder pharmaceutical companies worldwide are trying to develop new antifungal drugs.

Other examples illustrating the importance of fungi to man include:

- their role in lignocellulose turnover (surprisingly only fungi can degrade lignin, although some claims have been made for the streptomycetes)

- their symbiotic associations with higher plants (about 95% of vascular plants have mycorrhizal roots!)
- their use as sources of natural products (β -lactams, cyclosporin, etc.)
- their use as foods (mushrooms, truffles, Quorn™ myco-protein)
- their use as model organisms to study important biological problems (Beadle & Tatum used *Neurospora crassa* to establish the one gene: one enzyme hypothesis which led to their Nobel Prize in 1958).

Because of the significance of fungi in our lives, there is reason to be seriously concerned by the decline of mycology in the UK. Although there are reasonable numbers of geneticists and molecular biologists using fungi as model organisms, there are now few mycologists with a broad knowledge of fungi. Prior to the 1980s, nearly every Department of Botany had a mycologist (ironic, since we now know that fungi are more closely related to animals than to plants), but with the disappearance of these departments, few Schools of Biological Sciences feel the need to appoint mycologists to their staff. A similar fate has befallen mycologists in former Departments of Microbiology. Indeed, some microbiologists even refuse to recognize filamentous fungi as micro-organisms! Shame on them. Consequently, there has been a decrease in the number of mycologists in UK universities and an increase in the average age of those that remain. The exception is in medical mycology. To my knowledge, in the early 1980s there was only one clinically qualified medical mycologist in the UK. Today, the University of Manchester alone has three such staff, two of whom are professors. This change reflects the increasing importance of fungi as human pathogens.

I do not believe that the 'disappearing mycologists' problem will be solved by special pleading, but by increasing the quality of the research conducted by mycologists. This must encompass modern approaches, including molecular biology, genomics and bioinformatics. Second-rate research is of little value to anyone, even if carried out on a very important group of micro-organisms. One way to help to increase the quality of fungal research is by forging stronger links between UK societies with an interest in mycology (SGM, British Mycological Society, British Society for Plant Pathology, British Society for Mycopathology, etc.) and by liaising with societies in Europe. Without such an effort, the decline in UK mycology will continue. Indeed, perhaps it is already too late to reverse the present trend. I hope not.

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A thallus of an obligately anaerobic chytrid isolated from a water buffalo in Malaysia. This is a member of the true fungi. COURTESY TONY TRINCI

Weird and wonderful fungi

Elio Schaechter

Fungal spores are produced in prodigious numbers. Elio Schaechter describes some unusual mechanisms for their dispersal.

I happen to believe that all fungi are surprising and intriguing, and that many have stories to tell. From this extensive repertoire I have chosen a few examples to illustrate a particular point, how fungi appropriate or modify the structures and functions of their hosts to enhance spore dispersal.

If there is a theme that pervades the world of the fungi, it is an intense preoccupation with the widespread distribution of their spores. Fungi make prodigious numbers of spores and scatter them over large areas. A middle-sized mushroom, say one with a cap 10 cm across, may make as many as 100 million spores per hour. Giant puffballs may produce 20 trillion spores (a figure so large that laymen may grasp it only by comparison to the national debt of industrialized countries). Making so many spores is an example of conspicuous production. In this realm, lavishness is necessary: rare is the spore that germinates into successful fungal growth and helps the species spread in the environment. Such wastefulness, however, is not unlike the production of millions of unsuccessful sperm cells by the human male.

Not only are spores made prolifically, they are also dispersed in the environment by an impressive array of strategies. Frequently, spores are scattered about by mechanically intricate mechanisms. Thus, in the mushrooms, spores are forcefully discharged from the hymenial surface of a fruiting body. Being light, such spores are readily wafted aloft by breezes to be deposited at distant sites. This, however, is not good enough for certain fungi. For even more efficient dissemination, some species have developed cunning ways that involve modifying the behaviour or structure of their plant or animal hosts. As is often the case in biology, some of the most intriguing phenomena in this field involve the interaction between hosts and parasites.

● Fooling the pollinators

For tweaking the host into making a new and elaborate structure, the prize goes to a rust fungus, *Puccinia monoica*. This species infects wild plants of the mustard family (*Arabis* and others) and induces them to develop dense clusters of leaves at the tips of stems. These rosettes of leaves look like the petals of a real flower, all the more so because they become covered with fungal growth. The surface becomes sticky and sweet smelling. These pseudoflowers, as they are called, are of a beautiful yellow colour, different from that of the normal flowers of this plant but similar to those of other plants that grow in the same area. Insects arrive, with pollen on their agenda, and poke around the pseudoflower, collecting fungal spores instead of the desired pollen. And off they go, spreading spores to other plants. As seen in the photograph (Fig. 1), the impersonation is nearly faultless. The discoverer, Dr Barbara Roy of the Swiss Federal Institute of Technology, writes,



'The floral mimicry fools humans as well as insects: botany students at the Rocky Mountain Biological Laboratory have frequently collected pseudoflowers thinking they were flowers and, at a distance, many professional botanists have mistaken them for true flowers.'

● The urge to climb

Many ants that normally live on the forest floor drastically change their behaviour when infected by fungi. The kinds of fungi involved (often ascomycetes of the genus *Cordyceps*) do not develop rapidly, at least for some time. Because of this moderation, the infected ants stay alive and remain active, but alter their deportment: they acquire an urge to climb up the stalks of vegetation and trees. When reaching a certain height, they impale themselves with their mandibles and remain perched aloft for the rest of their life and thereafter. Such behaviour is seen in a number of other insect groups as well: infected grasshoppers, locusts, aphids and flies also exhibit this 'summit disease'. The fungi then grow and develop fruiting bodies replete with spores which can now be dispersed from on high, possibly to be carried over great distances (Fig. 2).

When the reason for the ants' urge to climb is sought, the answer depends on one's tolerance for teleology. 'Because it's there' won't do, but claiming that the fungus makes the insect climb for its own benefit is also seen with suspicion by some researchers. Clearly, remaining on the forest duff decreases the chances for aerial spore dispersal. However, getting off the forest floor means that infected insects are exposed to sunlight, therefore warming up to temperatures deleterious to the fungi. In the words of the entomologist R.A. Humber, *'this is a behavior quite analogous to your heading for a warm bed and constant supply of chicken soup when feeling sick'*.

In addition, the infected insect may climb for altruistic reasons, namely to avoid infecting other members of its

TOP:
Fig. 1. Pseudoflower caused by a rust fungus, *Puccinia monoica*, being visited by a *Polygonia* butterfly.

PHOTO B. A. ROY, REPRINTED WITH PERMISSION FROM *NATURE* 362, 56-58

FAR RIGHT:
Fig. 2. *Cordyceps curculionum* fruiting bodies arising from a weevil.
PHOTO JAMES BEACH

colony. This is suggested by the different behaviour of certain other insects when infected by fungi. Infected larvae of butterflies and moths do the opposite from the ants: they crawl into inaccessible spaces such as crevices or beneath tree bark, as if to get away from their kin. The fungus involved must develop a long stalk to make its fruiting body effective. Whatever the reason, the interplay of signals between the fungus and the insects seems extraordinary. Is there a mechanism that keeps the fungus from growing until the insect reaches a certain distance above the ground? What makes the insects develop the urge to climb up a tree? Who gains and who loses?

● People, voles and truffles

Human beings and other vertebrates are not immune to the commands of fungi either. Not only do people cultivate mushrooms, thus enhancing the fungi's reproductive potential, but they also hunt them in their natural state. If you need to be shown how human behaviour can be influenced by fungi, let me quote from Worthington Smith, who, in *Gardener's Chronicle*, reported on the first organized mushroom hunts held by the Woolhope Naturalists' Field Club, founded in 1851. He writes about Mordecai Cubitt Cooke, a leading light of that club and one of the fathers of British amateur mycology.

'Dr Cooke, furnished with a large leathery travelling trunk (in place of a hand basket or tin collecting case) was one of the first to arrive in the Forest. By 4 o'clock the Doctor's phenomenal portmanteau was full of funguses. Where one generally looks for a tooth-brush might be found a Phallus, in place of a sponge was a bloated Boletus, in lieu of writing paper, sheets of dry-rot. Shirts were shirked, and fungi both fresh and frouzy were in all the compartments of the valise. No one but an advanced fungologist could so treat a portmanteau.'

Whether such activities lead to enhanced spore dispersal is debatable, although nice specimens of ceps or chanterelle continue to shed spores in the collector's basket. Because such baskets are usually made from wicker or wooden slats, there is considerable opportunity for spores to escape. But it does not seem likely that this is an effective mechanism. More to the point is the fact that the spores of many fungi pass through the digestive tracts of vertebrates intact and are thus deposited wherever the animals go. Truffles, perhaps the most prized and certainly the most expensive fungi of all, grow underground. Humans, pigs and dogs are not the only animals that are attracted to truffles – so are small mammals and invertebrates, which play an essential role in the dispersal of the truffles. An example is a field vole that consumes the truffle from the Northwestern United States, *Tuber gibbosum*. These truffles do not compete with the famed ones of the Perigord or Piedmont, at least not

on the open market, but they constitute the main diet for the voles. People, of course, tend to cook the mushrooms they eat, something the fungi didn't count on in their evolution. A few mushrooms are eaten raw, as in a spinach and sliced *Agaricus* salad and I have wondered about the viability of such spores after passage through the human digestive tract! Granted, this may not be a burning problem for investigation. Attention should rather be paid to the other bewildering and engaging phenomena relating to fungi. There is no dearth of important questions left to be studied regarding their effects on animal and plant behaviour.

● *Elio (Moselio) Schaechter is an amateur mycologist and a retired microbiologist from Tufts University in Boston. In addition to his book on mushrooms, he has authored or edited several microbiological textbooks and treatises. He now lives in San Diego, where he is still looking for mushrooms.*
email mschaechter@sunstroke.sdsu.edu

Further reading

Cooke, M.C. (1892). *Vegetable Wasps And Plant Worms*. London: Society for Promoting Christian Knowledge. (A highly readable book on insects and fungi.)

Ingold, C.T. (1971). *Fungal Spores. Their Liberation and Dispersal*. Oxford: Clarendon Press. (Written by an erstwhile president of the British Mycological Society, this book not only systematizes the subject but also provides many cogent examples and illustrations.)

Schaechter, E. (1997). *In the Company of Mushrooms*. Harvard, MA: Harvard University Press. (For a broader view of the fungi.)



Exploitation of fungal secondary metabolites old and new

Geoffrey Turner

Fungal secondary metabolites have been exploited by scientists for many years. Geoffrey Turner describes some current applications and shows how increasing knowledge of fungal gene structure and metabolic pathways is paving the way for the development of new drugs.

The fungal kingdom offers enormous biodiversity, with around 70,000 known species, and an estimated 1.5 million species in total. Most of these are filamentous fungi, which differ from the yeasts not only in their more complex morphology and development (e.g. asexual and sexual structures), but also in their greater metabolic complexity. In particular, they are known for production of secreted enzymes and secondary metabolites, many of which have been exploited by Man. Genetic analysis of secondary metabolic pathways over the past 10 years has revealed some common themes and offered new approaches to the exploitation of natural products.

The best known fungal secondary metabolites in commercial production are the β -lactam antibiotics penicillins G and V and cephalosporin C, produced for over 50 years, with continuous strain and fermentation improvement programmes. During the past 15 years, most of the genes encoding the biosynthetic steps have been characterized, leading to a detailed understanding of the biochemistry and regulation of these pathways. Nevertheless, the long history of traditional strain improvement by mutagenesis and screening had already put into place many of the changes that an applied molecular biologist might have considered after isolating the genes. These include increased gene copy number and enhanced transcription, and limit the scope for further yield improvement. A more sophisticated approach, the engineering of a hybrid cephalosporin pathway in the penicillin producer *Penicillium chrysogenum*, was achieved as an alternative route to semi-synthetic cephalosporins, but its commercial advantage has yet to be established.

● Non-ribosomal peptide synthesis

One of the fascinating results of genetic analysis of β -lactam biosynthesis was the discovery that the first step, synthesis of the tripeptide δ -(L- α -amino adipyl)-L-cysteiny-D-valine (ACV) from precursor amino acids, was catalysed by a multifunctional enzyme closely related to those responsible for synthesis of the antibiotics gramicidin and tyrocidin by *Bacillus* species. While non-ribosomal peptide biosynthesis and its evolutionary significance had already been described by Fritz Lipmann 'before cloning', gene isolation and DNA sequencing have revealed a large and growing family of

Table 1. Some fungal peptides

Non-ribosomal peptide synthetase genes have been characterized for those shown in bold type.

ACV	<i>Aspergillus nidulans</i>
	<i>Penicillium chrysogenum</i>
	<i>Acremonium chrysogenum</i>
Ergotpeptides	<i>Claviceps purpurea</i>
Alamethicin	<i>Trichoderma viride</i>
Cyclopeptin	<i>Penicillium cyclopium</i>
HC-toxin	<i>Cochliobolus carbonum</i>
Tentoxin	<i>Alternaria alternata</i>
Ferrichrome	<i>Aspergillus quadricinctus</i>
Echinocandin	<i>Aspergillus nidulans</i>
Cyclosporin	<i>Tolypocladium inflatum</i>
Destruxin	<i>Metarhizium anisopliae</i>
Enniatin	<i>Fusarium oxysporum</i>
Beauvericin	<i>Beauveria bassiana</i>

peptide synthetases in fungi and bacteria. Although the peptide products show a wide range of biological activity, from antibiotics to pathogenicity factors (Table 1), the biosynthetic mechanism is conserved, and the genes responsible are instantly recognizable from their modular organization (Fig. 1). A module of some 600 amino acids is required for each amino acid incorporated into the peptide. Amino acids are recognized, adenylated, and covalently bound to a module via a 4'-phosphopantetheine cofactor, and less well conserved regions are probably involved in peptide bond formation. The final peptide is released as a linear or cyclic structure, depending on the system.

Cyclosporin A, a product of *Tolypocladium inflatum* (Fig. 2), was identified by screening in the 1970s as an antifungal and anti-lymphocytic compound, and exploited as an immunosuppressant, revolutionizing organ transplant surgery. Subsequent studies on its mode of action as an inhibitor of cyclophilin, a peptidyl prolyl isomerase involved in calcium signalling following antigen recognition by T-cells, opened up avenues for discovery of new immunosuppressants. Interestingly, the compound also has anti-*Plasmodium*

activity. Cyclosporin is an undecapeptide, assembled by a synthetase consisting of a single polypeptide with a molecular mass of some 1.7 million Da. Some of its 11 modules contain inserted domains responsible for N-methylation of the respective

Fig. 1. Modular arrangement in peptide synthetases

ACV synthetase



■ Adenylation

■ N-Methylation

| Thioester formation

Cyclosporin synthetase



amino acids (Fig. 1). This is one of the largest known enzyme polypeptides, incorporating 40 catalytic functions. While these enzymes appear to use a rather cumbersome way of assembling small peptides, their speciality is their ability to escape the bounds set by ribosomal peptide synthesis. In addition to incorporating valine and alanine, cyclosporin synthetase can *N*-methylate leucine, and incorporate 2-butenyl-4-methyl-L-threonine and α -aminobutyrate.

As medical conditions, including AIDS, resulting in a compromised immune system, have increased in recent years, systemic fungal infections have increased, stimulating a search for better antifungal drugs. The cyclic lipopeptide echinocandin, probably elaborated by a peptide synthetase, is produced by a number of fungi, including a sub-species of *Aspergillus nidulans*. Investigated for some time as an antifungal antibiotic, it interferes with fungal cell wall assembly by inhibiting the synthesis of β -1,3 glucan. Improved semi-synthetic derivatives produced by Eli Lilly and Merck are currently undergoing clinical trials as anti-*Candida* agents.

Ergot alkaloids produced by the plant pathogen *Claviceps purpurea* during infection of rye were responsible for outbreaks of St Antony's Fire, described as long ago as the 9th century. Victims suffered gangrene, convulsions and hallucinations after consuming contaminated rye bread. However, medical

applications, such as hastening labour or preventing post-partum bleeding, were recognized from the Middle Ages, and semi-synthetic derivatives such as dihydroergotamine were developed in the 1940s for treatment of blood pressure and migraine. Ergotamine and semi-synthetic derivatives are structural analogues of serotonin and interact with its receptors. Recent studies on the biochemistry and genetics of ergotamine biosynthesis have shown that lysergic acid, synthesized by the fungus, is converted to ergotamine via a three-module peptide synthetase which adds alanine, proline and phenylalanine (Fig. 3).

● Polyketide synthetases

Another major family of multifunctional enzymes responsible for biosynthesis of secondary metabolites are the polyketide synthetases, which are relatives of fatty acid synthetases. While these have been studied most intensively in the prokaryotic actinomycetes, they are also responsible for assembly of potent carcinogens, the aflatoxins of *Aspergillus parasiticus*, and the cholesterol biosynthesis inhibitor lovastatin, produced commercially by *Aspergillus terreus*. Lovastatin is an inhibitor of hydroxymethylglutaryl (HMG) CoA reductase, an early step in cholesterol biosynthesis, and was developed as a treatment for familial hypercholesterolaemia. Subsequently, it has been found to

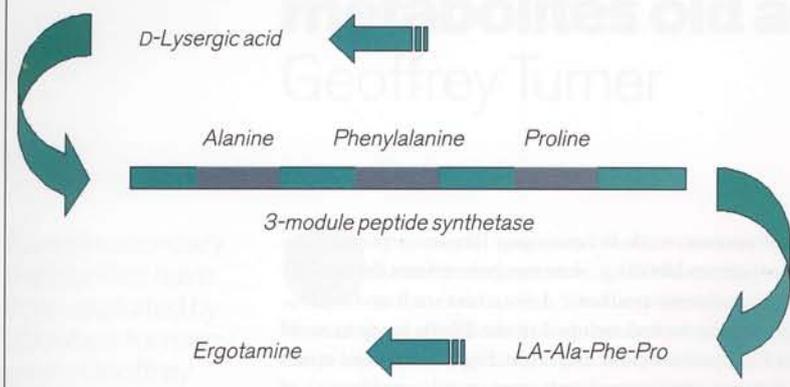
be effective at reducing cholesterol levels in individuals with dietary problems.

In the case of both polyketide (PKS) and non-ribosomal peptide synthetases (NRPS), in fungi and bacteria, these enzymes often form only part of a complex pathway involving many other genes for synthesis of precursors, or modification of products. Indeed, there are now some prokaryotic examples of PKS and NRPS modules co-operating to produce secondary metabolites, exemplified by rapamycin, a new immunosuppressant, and yersiniabactin, an iron-chelating siderophore and pathogenicity factor in plague. Elucidation of other pathway components is aided by the common observation that the PKS and NRPS genes are



LEFT:
Fig. 2. *Tolyposcladium inflatum*.
COURTESY BIOCHEMIE GMBH

Fig. 3. Ergotamine biosynthesis in *Claviceps purpurea*



Further reading

Lipmann, F. (1971).

Attempts to map a process evolution of peptide biosynthesis. *Science* 173, 875–884.

Kleinkauf, H. &

von Döhren, H. (1996). A nonribosomal system of peptide biosynthesis. *Eur J Biochem* 236, 335–351.

Penalva, M.A., Rowlands, R.T. & Turner, G. (1998).

The optimization of penicillin biosynthesis in fungi. *Trends Biotechnol* 16, 483–489.

Tudzynski, P. & others

(1999). Evidence for an ergot alkaloid gene cluster in *Claviceps purpurea*. *Mol Gen Genet* 261, 133–141.

Kennedy, J. & others (1999).

Modulation of polyketide synthase activity by accessory proteins during lovastatin biosynthesis. *Science* 284, 1368–1372.

McDaniel, R. & others

(1995). Rational design of aromatic polyketide natural products by recombinant assembly of enzymatic subunits. *Nature* 375, 549–554.

Stachelhaus, T., Schneider,

A. & Marahiel, M.A. (1995). Rational design of peptide antibiotics by targeted replacement of bacterial and fungal domains. *Science* 269, 69–72.

located within large gene clusters, which include genes for the other steps. Recent examples include the lovastatin and ergotamine gene clusters.

● Future drug discovery

While the examples of useful fungal secondary metabolites described above have been discovered via traditional natural product screening methods, the subsequent genetic analyses suggest alternative approaches based on the highly conserved and easily recognizable module, domain and motif structures of the biosynthetic enzymes. Either genomic data mining or PCR-based approaches could be used to discover new enzymes and secondary metabolic pathways, providing opportunities for product discovery where natural expression is low and the product cannot be easily detected in conventional screens. For example, the Canadian company TerraGen aims to use a gene-based approach to screen fungi which are difficult to culture, such as those found in lichens.

A common feature of commercially exploited fungal secondary metabolites is that natural products have been chemically modified to yield semi-synthetic derivatives. An attractive additional approach would be to redesign the biosynthetic pathways, including the multi-functional enzymes. This approach, using detailed knowledge of gene structure and pathway biochemistry, and taking advantage of the modular structure of the enzymes, has already led to promising progress in the case of polyketide synthetases of the prokaryotic actinomycetes, though success has been more limited so far for peptide synthetases, where a better understanding of enzyme structure and function is needed.

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Brewing yeast selection

Iain Campbell

RIGHT:

Fig. 1. Progress of a typical ale fermentation (top yeast), showing the best time (arrow) for 'skimming' the yeast head as inoculum for the next fermentation. The rapid fall in the number of yeast cells in suspension at the end of the period of active fermentation is caused by flocculation of the yeast.

● The brewing process

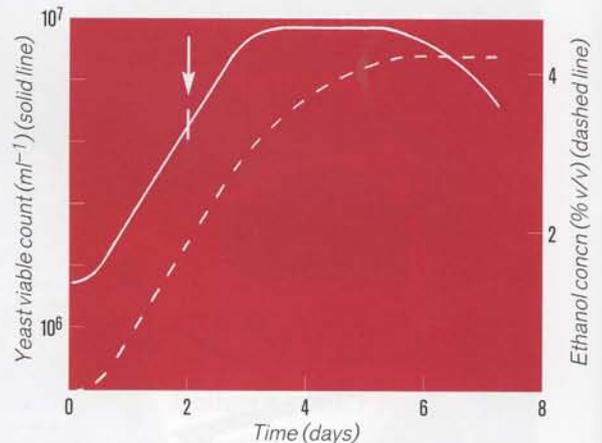
Perhaps it is best to start with a brief outline of the brewing process. The brewing yeast *Saccharomyces cerevisiae* is unable to utilize the starch of barley, so the grain is first germinated and the resulting malt is extracted with hot water to yield wort containing fermentable mono-, di- and trisaccharides and other yeast nutrients. The wort is boiled with hops or, in the past, other flavourings, cooled and inoculated with a suitable yeast culture. After a period of maturation and clarification the product should be a palatable beer.

● Selection in ancient times

Brewers have been selecting yeasts for thousands of years. The first beer fermentations must have been carried out by naturally occurring yeasts. That practice still survives in the production of Belgian lambic beer, for which airborne yeasts and bacteria and the resident microflora of the wooden wort cooler and fermentation vessels provide the inoculum. The ancient brewers must have noticed that some batches of naturally inoculated beer were better than others. They must also have realized that collecting the frothy head from the surface of the fermenting beer and adding it to the next batch of wort gave a much faster fermentation. Therefore, the first (unrecorded) instance of yeast selection was to combine these two observations and use the yeast head from a particularly good fermentation to repeat the favourable results with the next batch. Long before the requirements could have been expressed in microbiological terms, brewers instinctively recognized the characteristics of a good brewing yeast (Table 1).

● Flavour and flocculence

Another type of selection occurs during each fermentation. Yeast multiplies about 10-fold during a beer fermentation, so only about one-tenth of the yeast growth has to be collected from each fermentation to continue propagation indefinitely. Traditional brewing yeasts are unlikely to be pure cultures, so there is also the requirement to maintain a constant composition of the



mixture. Different strains of yeast vary slightly in their production of the numerous metabolites that contribute to beer flavour: at least 400, according to one estimate. It may not have been so important in the distant past, but now customers expect a particular brand of beer to have a consistent flavour. If the yeast head is collected at the same stage of each successive fermentation, the various strains which make up the yeast culture will be continued in approximately the same proportion, and therefore it is reasonable to expect consistent flavour production. Typically, one strain of the yeast population may accumulate in the head in the early stages of the fermentation, another strain rises later and a third strain predominates later still. Yeast head must be skimmed off several times during the fermentation to prevent it collapsing back into the beer and creating off-flavours, but only part of the recovered yeast is re-used for subsequent fermentations (selection!). After 48 h of fermentation (Fig. 1), using the second (middle) skimming from each successive fermentation gives the best chance of maintaining a constant balance of strains. Not only do yeasts vary in flavour production, there is also a variation in flocculence. Flocculation of yeast is the spontaneous aggregation into clumps which settle increasingly rapidly out of suspension (see Fig. 1). Too early flocculation brings the fermentation to a premature end; but non-flocculent yeasts remain in suspension and have to be removed by expensive centrifugation or filtration. Therefore the correct degree of flocculence developing late in fermentation is essential for economical production of bright beer.

● Probably the best yeast in the world? Lagers and ales

But, several hundred years earlier, perhaps the most important instance of yeast selection in the entire history of brewing was achieved in Bavaria. In Britain, enthusiasts become excited about the differences between 'ale' and 'lager'. In almost every other country of the world, the words 'beer' and 'lager' are synonymous. It is amazing that a speciality beer of an unknown Bavarian

Table 1. Essential properties of brewing yeast

a	Consistent production of flavour and aroma metabolites
b	Rapid fermentation
c	Efficient fermentation (maximum yield of ethanol, minimum production of new yeast biomass)
d	Tolerance to the inhibitory effects of wort and beer (osmotic stress of initial sugar, toxic effect of final alcohol and CO ₂)
e	Suitable flocculation and sedimentation properties at the end of fermentation (and for 'top fermentations', head formation)
f	High final viability for inoculating (pitching) the next fermentation
g	High genetic stability over successive fermentations

monastery has become the worldwide standard beer. Previously, beer had been fermented by 'top yeasts', harvested from the surface of the fermentation to propagate the next fermentation. The 'bottom yeast' of the lager fermentation did not form a true yeast head, only a foam which contained too little yeast to seed a subsequent fermentation. So settled yeast had to be recovered from the bottom of the vessel at the end of fermentation. The name lager came from the storage (*lagern* in German), really a secondary fermentation at low temperature, for improvement of flavour and CO₂ content. The other technical advantages of the production of lager are irrelevant to a discussion of yeast selection, but the fame of the initially local beer soon spread. First, the yeast was stolen by Czech brewers to begin brewing at Pilsen (which, perhaps unjustly, gave its name to that type of beer) and later by one of the Jorgensen family of the Carlsberg company. There, the pioneer yeast taxonomist E. C. Hansen, a contemporary of Pasteur, first isolated pure yeast cultures and recognized the 'top yeast' of the traditional beers of Belgium, Britain and Germany as a different species, *S. cerevisiae*, from the 'bottom yeasts' of the Bavarian and Czech beers which, in a shrewd career move, he named *Saccharomyces carlsbergensis*. Pure cultures of *S. carlsbergensis* were then exported, creating the worldwide production of the 'pilsener' type of beer.

● Current techniques for yeast selection

Much later, *S. carlsbergensis* was recognized as virtually indistinguishable from the wine yeast *S. uvarum*. So the original Bavarian isolate may have been a chance contamination from local wine production, and subsequently propagated because of its desirable flavour characteristics. Now, however, for improvement of a brewing strain the microbiologist must undertake some deliberate manipulation of the yeast. With its virtually unlimited possibilities, genetic engineering may spring to mind as the first means of selection. In fact, that would be the last choice, not least because of the potential impact on sales of beer made with such yeast. The techniques for genetic improvement of yeast are listed in the usual order of preference (Table 2).

Any type of genetic manipulation involves plating out the recovered hybrids or mutants, followed by trial small-scale fermentations with cultures from individual colonies. Therefore, it is sensible to start by screening the existing culture to discover if a strain of the desired properties is already present as part of the mixture. An important instance of this method was the selection of non-head-forming variants of the existing yeast at the time of change from traditional open rectangular tanks to modern enclosed cylindro-conical fermenters (Fig. 2). In the latter, not only is it technically impossible to use a skimming system for recovery of yeast, but the vigorous circulation by rising CO₂ and downward movement by

Table 2. Techniques for genetic manipulation of brewing yeast

- | | |
|---|---|
| a | Screening of existing culture and selection |
| b | Mutation (usually UV) and selection |
| c | Hybridization (crossing haploid mater cultures, or sphaeroplast fusion) and selection |
| d | Recombinant DNA technology and selection |

Table 3. Possible genetic improvements to industrial yeasts

Group 1: conferred by introduction of the appropriate gene

- | | |
|---|--|
| a | Hydrolysis of starch and dextrans |
| b | Hydrolysis of cereal β-glucan |
| c | Increased rate of fermentation |
| d | Optimal flocculation properties |
| e | Acetolactate decarboxylase |
| f | Hydrolysis of cellulose/cellobiose or lactose (not applicable to brewing yeast, but important for economical production of industrial alcohol) |

Group 2: economically important, but biochemical and genetic basis not yet defined

- | | |
|---|--|
| a | Reduced requirement for dissolved oxygen |
| b | Tolerance of high initial sugar concentration and high final ethanol concentration |
| c | Ability to ferment at higher temperature |

wall cooling creates even more head than in rectangular vessels. The amount of surface froth shown in Fig. 2 is typical of a non-head-forming yeast. If the traditional top yeast in the rectangular vessel at the top had been used in the large fermenter, at least half of its volume would have been wastefully filled with yeast head. A non-head-forming mutant of exactly the same flavour characteristics as the original yeast is preferable to the use of antifoam. It is true that lager yeasts could have been used, but these would have caused an obvious difference in flavour.

Mutagenesis, usually by irradiation, works by inactivating one or more genes. In any genetic manipulation it is essential to preserve the valuable existing properties of the brewing yeast and there is a distinct possibility that a mutation will delete some essential characteristic. Chemical treatment may be inadvisable because of the risk of residual mutagen, but UV irradiation has occasionally resulted in selection of an improved strain.

Successful results have been achieved by the chance deletion of a suppressor gene; alternatively, back-crossing the mutant with the original strain has added the desired improved characteristics. Certainly, there are possible improvements which require deliberate introduction of new genetic characters (Table 3).

In the life cycle of *S. cerevisiae*, discovered in 1935, the diploid nuclei of vegetative cells become haploid

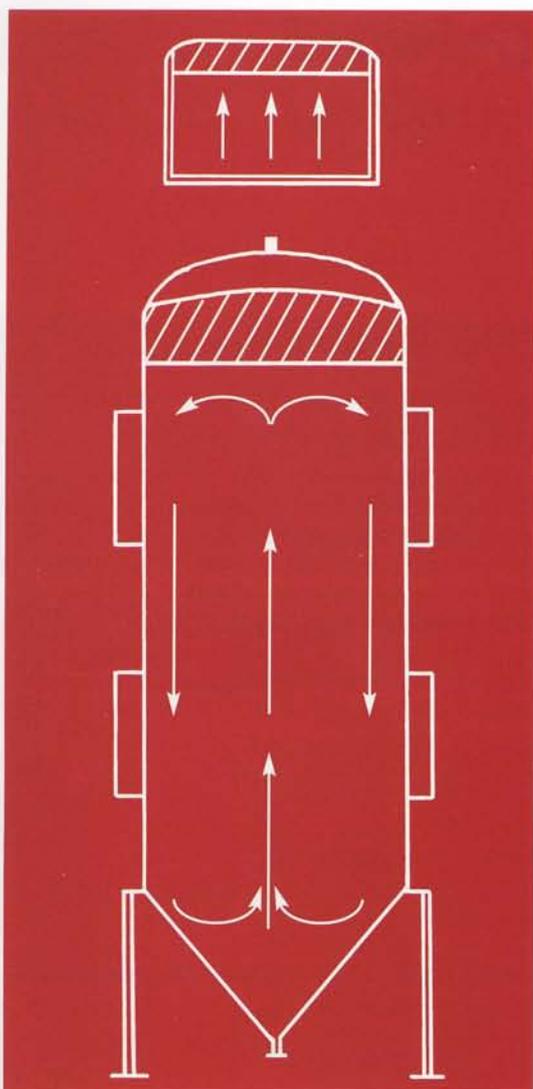


Fig. 2. Comparison of a traditional open rectangular vessel and a modern cylindro-conical fermentation vessel, drawn to the same scale. The shaded section represents head or froth above the fermenting beer; the arrows show the direction of currents within the fermenter.

Further reading

Priest, F.G. & Campbell, I. (editors) (1996). *Brewing Microbiology*, 2nd edn. London: Chapman & Hall.

Panchal, C.J. (editor) (1989). *Yeast Strain Selection*. New York: Dekker.

on sporulation; microdissection of spores and germination in the absence of the opposite mating type provide haploid mater cultures. This resulted in *S. cerevisiae* becoming a useful eukaryotic model for genetic research. Unfortunately, most brewing yeasts have lost the ability to form spores. Over centuries, or millennia, of propagation in a rich culture medium, spores were unnecessary; also, with the inevitable genetic exchange during such prolonged intensive cultivation these industrial yeasts are no longer diploid, but of complex ploidy which would inhibit sporulation even if all of the necessary genes were still present. However, sphaeroplast fusion does

not require maters and successful hybridizations have been achieved by that method.

Desirable genetic improvements

Introduction of the ability to ferment higher oligosaccharides than maltotriose has been achieved by methods (c) and (d) of Table 2. Since these dextrans constitute at least 20% of a normal wort, there is potential for additional alcohol yield from the same amount of malt, or production of 'light' or 'dry' beers after utilization of the dextrans.

Another potentially useful ability is hydrolysis of cereal β -glucan which, in excess, causes haze in the beer and by its viscosity, filtration problems. Improved filterability and destruction of glucan haze are valuable properties of that modified yeast. Only a single new gene would be required in each case, for either amylase or glucanase, but in most countries the same effect can be achieved legally and more easily by adding the appropriate enzyme to the beer. For some reason there is popular revulsion to genetically modified organisms but, except among the most dedicated beer enthusiasts, there seems to be little objection to the use of enzymic processing aids.

The economic benefits of faster fermentation are obvious and can be achieved by increased content of *MAL* genes for maltose transport and hydrolysis, although other methods may also be effective. Flocculation, the spontaneous aggregation of yeast cells,

is important for clarification of beer, but must be genetically programmed to occur only at the end of fermentation. Flocculation too early causes clumps of yeast cells to settle before fermentation is complete. Non-flocculent yeasts are also troublesome: they must be removed by centrifugation.

Introduction of acetolactate decarboxylase to brewing yeast reduces production of diacetyl, the buttery flavour which is generally regarded by professional brewers as an objectionable off-flavour, although at low levels it does not seem to annoy the general public. Acetolactate is a by-product of biosynthesis of isoleucine, leucine and valine, and if released from yeast cells is spontaneously oxidized to diacetyl. If acetolactate is no longer excreted there is no longer a diacetyl problem. Genetic manipulation to introduce appropriate *MAL*, *FLO* and *ILV* (isoleucine, leucine and valine) genes, therefore, has beneficial effects on beer quality.

S. cerevisiae is not a true facultative anaerobe like *Escherichia coli*. Although capable of fermentation, it is unable to grow indefinitely without oxygen. For flavour reasons, mainly related to diacetyl production, oxygen can be provided only in the early stages of fermentation. If other brewing qualities are acceptable, the best brewing yeasts have the lowest requirement for dissolved oxygen in the wort at the time of pitching.

Osmotic tolerance is important for the modern technique of high-gravity brewing, whereby plant capacity can be doubled by brewing double-strength wort, fermenting to double-strength beer and diluting to sales strength as the final stage of the process.

Ability to ferment at higher temperature is probably not relevant to beer production, but is important for distilled alcohol: the higher the fermentation temperature, the less energy is required for distillation. The ultimate goal would be distillation without any heat energy input, if the fermentation itself generated sufficiently high temperature that application of a partial vacuum would suffice.

All of the improvements listed in Table 3 are technically possible and many have already been incorporated into production strains of yeast. Using the others is dependent on public opinion rather than brewing technology, so it is impossible to predict how yeast selection will develop in the future.

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Yeast genetics and genomics

Alan Wheals

Research into yeast genetics has brought great insights into eukaryotic cell biology. Alan Wheals describes how yeast genomics is opening up even more exciting possibilities in microbiology.

There are two types of geneticists – those who attempt to understand the nature of inheritance and those who use genetics as a tool to understand biological problems. Yeasts are important in both of these areas of research. The genetics of baker's yeast, *Saccharomyces cerevisiae*, only took off in the second half of the 20th century, but it quickly proved essential for studying fundamental aspects of the inheritance of mitochondria and in the analysis of genetic recombination. In the early 1970s, many microbial geneticists turned their attention from prokaryotes to eukaryotes and looked for a suitable 'model' system. *Sac. cerevisiae* was already an obvious candidate and was described as the *Escherichia coli* of eukaryote genetics. The genetic system of the fission yeast, *Schizosaccharomyces pombe*, was also developed and it has complementary virtues. The genetics of both yeasts are now being supplemented by genomics, a new branch of science dealing with the entire genome of an organism.

has been successfully dissecting the complex association of proteins required to 'splice' RNA molecules before they leave the nucleus for translation. Hugh Pelham (Cambridge) has defined the signals on yeast proteins that target them to the right cellular compartments. Yeasts contain prion proteins, analogous to those found in BSE, and are being analysed by Mick Tuite (Kent). This cell biological knowledge is being used by pharmaceutical companies such as Glaxo-Wellcome and Zeneca to help discover and understand new drugs.

● *Saccharomyces cerevisiae* genomics

The most exciting new development is in the science of genomics. Steve Oliver (formerly UMIST and now Manchester) led a European consortium that sequenced the first eukaryotic chromosome (of *Sac. cerevisiae*) in 1992. This led to the creation of an even bigger multinational consortium, under the leadership of the Belgian scientist André Goffeau, which succeeded in decoding the entire genome sequence by April 1996 – the first eukaryote to be analysed. Having the sequence is one thing – understanding it is another. With reasonable confidence, it is possible to identify putative genes within the genome, so called open reading frames (ORFs). There are approximately 6,200 in *Sac. cerevisiae* of which the function of one-third could be described from either previous knowledge or because of a high degree of homology to genes of known function. Another third could not be unambiguously assigned but had features that at least gave some clues to their function. The most surprising discovery was that one-third of the genes were of totally unknown function. Since they belong to no known family, they are often called ORFan (orphan) genes. There is now a worldwide effort to understand the function of all the genes in *Sac. cerevisiae*. The European Functional Analysis Network (EUROFAN) project, headed once again by Steve Oliver, has systematically knocked out the function of approximately 850 genes one by one. Surprisingly, only one-sixth of the knockouts were lethal to the cell. The remainder are being analysed for a very wide range of phenotypes varying from recombination efficiency to the structure of the cell wall. Most knockouts do have a phenotype but often it does not give clear guidance to the underlying function of the gene – this will require further detailed analysis. However, the approach has proved sufficiently successful to have spawned the Yeast Deletion Project in which a European and N. American consortium will knock out all *Sac. cerevisiae* genes for a similar kind of analysis.

Other approaches, particularly in the USA, are being used to gain clues to the function of the genes. Transcriptome analysis has been designed to look simultaneously at the transcripts of 'all' the genes. A synthetic copy of each of the genes is spotted onto a slide in a high-density oligonucleotide array (a DNA

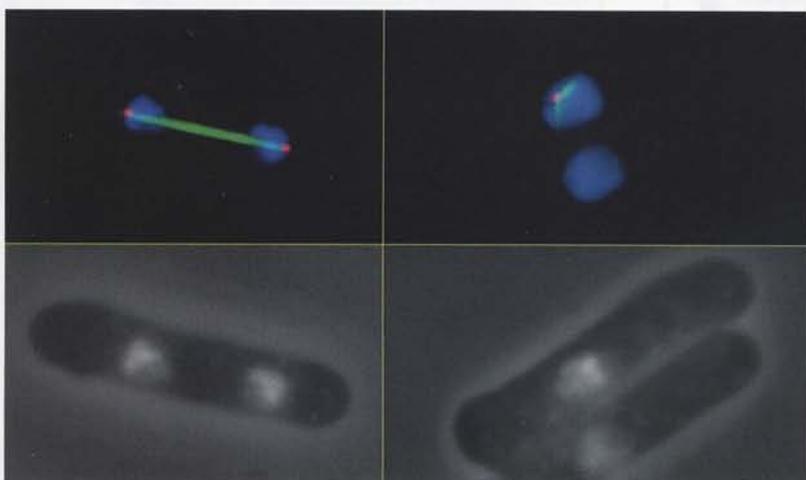


Fig. 1. Mitotic mutant of *Schizosaccharomyces pombe*. The cell outline and chromatin are shown (lower panels) for wild-type (left) and *cut7* mutant cells (right). Upper panel shows microtubules in green, spindle poles in red and chromatin in blue.

COURTESY DOUG DRUMMOND, MARIE CURIE INSTITUTE, OXFORD, AND IAIN HAGAN, UNIVERSITY OF MANCHESTER

● Significant findings in yeast genetics

What was described by one over-enthusiastic researcher as 'the awesome power of yeast genetics' has, in the hands of experts, provided many of the most important results in eukaryotic cell biology over the last 25 years. There is a very large community of yeast geneticists worldwide but the results can be illustrated with examples of work from some of more than 40 laboratories in the UK. Paul Nurse (ICRF, London) developed the fundamental concept of a universal mitotic control system and the importance of cyclin-dependent kinases. John Diffley (Clare Hall) and Lee Johnston (NIMR, London) have helped define the regulation of the initiation of DNA replication. 'Checkpoints' are required to assess whether a cell can safely proceed through the cell cycle and the molecular basis of this is being determined by Tony Carr (Sussex). Iain Hagan (Manchester) and Robin Allshire (Edinburgh) are analysing genes involved in the mechanism of mitosis (Fig. 1). Jean Beggs (Edinburgh)

chip or micro-array). Fluorescently labelled RNA taken from the cell under a particular set of conditions is hybridized to the DNA dots and the degree of fluorescence gives a measure of the amount of that RNA (Fig. 2). It is thus possible to find out which genes get turned on and off under the conditions of study. These changes in transcription do not reveal what the gene might be doing, but it at least focuses the attention of scientists on potentially important genes.

Some researchers are trying to see the amount and number of proteins present under different circumstances using two-dimensional electrophoresis coupled to mass spectrometry (proteome analysis). Others are looking at how every protein interacts inside the cell with every other protein – a task that, in principle, requires the study of something close to 18 million pairwise combinations. Resources to do these kinds of experiments (Cogeme) have just been established in the UK in Manchester and Aberdeen. This is the era of 'big science' in biology – not in the traditional sense of a big piece of apparatus but in the use of robots and automated machines to physically handle the materials and informatics to handle the analysis. However, it will ultimately require the laboratory expert to perform a crucial 'wet' experiment to confirm the speculation. It is a sobering thought that it is proving extremely hard even to determine the function of a modest number of genes in a convenient model organism. It will be orders of magnitude more difficult for the human genome project although comparisons between human and yeast genes are already proving informative.

● Other yeasts

The genomic approach to analyse *Sac. cerevisiae* provided the impetus for a similar genome sequencing project for *Sch. pombe* which is expected to be completed later this year. The second microbial eukaryote to be sequenced will provide important comparative information on these two brewing yeasts with a unicellular life form.

There are over 800 yeast species described in the latest taxonomic treatise but few have been studied genetically. Those that have possess interesting metabolic activities

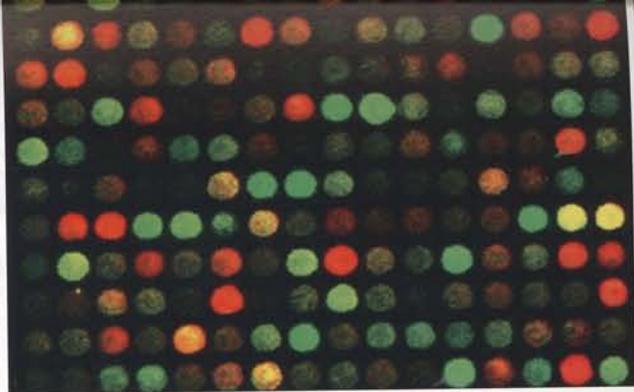
making them of potential economic importance. For example, *Kluyveromyces lactis* can utilize cheese whey, a waste product of the cheese industry, several *Pichia* species can grow on methanol, *Yarrowia lipolytica* and *Candida maltosa* can utilize hydrocarbons as carbon sources, *Debaryomyces (Schwanniomyces) occidentalis* can grow on starch, *Arxula adeninivorans* can utilize nitrate, and *Pichia guilliermondii* can over-synthesize riboflavin. Developing genetic systems – the ability to do crosses and have appropriate vectors (such as plasmids) to propagate genes independently of the chromosomes – is very time-consuming. However, genomics can provide an alternative route around these problems. Direct sequencing and making homology comparisons can identify genes of interest. Furthermore, it is often easy to express and analyse a gene from one organism in another, so-called 'surrogate' genetics. A good example is the naturally diploid yeast *Candida albicans* (Fig. 3). Neil Gow, Al Brown and Duncan Shaw have made Aberdeen a major international centre for the genetic and genomic analysis of this genetically intractable yeast. They form part of an international consortium that is sequencing the entire genome, due to be available next year. The results will undoubtedly provide valuable information to devise new strategies to attack this important human pathogen, which is a major killer of immunocompromised patients.

● The future

Although founded in the 19th century, genetics is essentially a 20th century science and genomics is its 21st century successor. *Sac. cerevisiae* and *Sch. pombe* will continue to remain model organisms for some time to come, but the full potential of yeasts has not yet been realized. The gene resources found in yeast species could be used for improvements in making bread, wine, beer and fuel ethanol, and in many other ways. However, public perception of the conjectured hazards of GMOs suggests that all microbiologists will need to work hard to convince consumers of the potential benefits of organisms we are now able to understand and exploit as never before.

● Dr Alan Wheals is Senior Lecturer in Genetics, Department of Biology and Biochemistry, University of Bath, Bath BA2 7AY. He has been working on yeast genetics at the University of Bath for nearly 25 years and has also done research in Germany and Brazil. He is currently screening the *Saccharomyces cerevisiae* genome for genes affecting stationary phase, analysing pectinase genes in several yeasts and designing species-specific PCR probes.

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ABOVE:
Fig. 2. Part of a *Saccharomyces cerevisiae* micro-array. The colour and intensity of the spots give information on the amount of RNA hybridized to the DNA spot. COURTESY PROFESSOR PATRICK BROWN, STANFORD UNIVERSITY, USA

LOWER LEFT:
Fig. 3. *Candida albicans*. Filamentous forms of this human pathogen containing an engineered green fluorescent protein gene glow brightly on infected murine kidney cells (red). COURTESY PROFESSOR NEIL GOW, UNIVERSITY OF ABERDEEN



Further reading

Botstein, D., Chervitz, S.A. & Cherry, J.M. (1997). Genetics – Yeast as a model organism. *Science* 277, 1259–1260.

Brown, P.O. & Botstein D. (1999). Exploring the New World of the genome with DNA microarrays. *Nature Genetics* 21, 33–37.

Wheals, A.E., Rose, A.H. & Harrison, J.S. (1995). *Yeast Genetics*. London: Academic Press.

Yeast Virtual Library website: <http://genome-www.stanford.edu/Saccharomyces/VL-yeast.html>

Now who would have thought it?

Roy Watling

The classification of fungi is turning out to be more complex than was once thought. Roy Watling considers the inter-relationships of fungi and the changing views of mycologists in the light of rDNA sequencing data.

A knowledge of fungal systematics is fundamental to searches for useful secondary metabolites, antibiotics and other compounds for industry, and for understanding lifestyles, pathogenic development, endophytic growth and exploitation of fungi for biocontrol. Now at last fungal taxonomy has a more scientific basis, with molecular techniques using nuclear 18S and 25S, and mitochondrial 12S rDNA sequences producing some startling revelations. Although species concepts have been consolidated, and some relationships not previously appreciated revealed, major areas of our classical classification have been thrown into turmoil.

Fungi separated from the main line of organisms in the early Phanerozoic; well over 500 million years ago, according to workers such as Pirozynski. They appear to have branched off from the plants, together with the animals, at an early stage in evolution. This of course contradicts our traditional teaching. Mycology has been taught, and still is, in university plant science departments and fungi are studied in botanic gardens, or in microbiology departments (although their inclusion is a rare event these days and mycology has rather tended to fall between the two stools). The relationship to microbiology is an uneasy one – perhaps because the larger fungi fit incongruously in the context of microscopic organisms – and the fungi are not related to the prokaryotes as put forward in the classical texts. But the edible mushrooms of the supermarkets spend much of their time hidden from view in the soil or woody substrates breaking down complex compounds, and the humble penny bun (*Boletus edulis*), so familiar to those who buy dried mushroom soup, undertakes a very sophisticated root association with trees called sheathing mycorrhiza,

before the 'micro-organism' forms its visible fructification: there are similarities in lifestyle between fungi and prokaryotes.

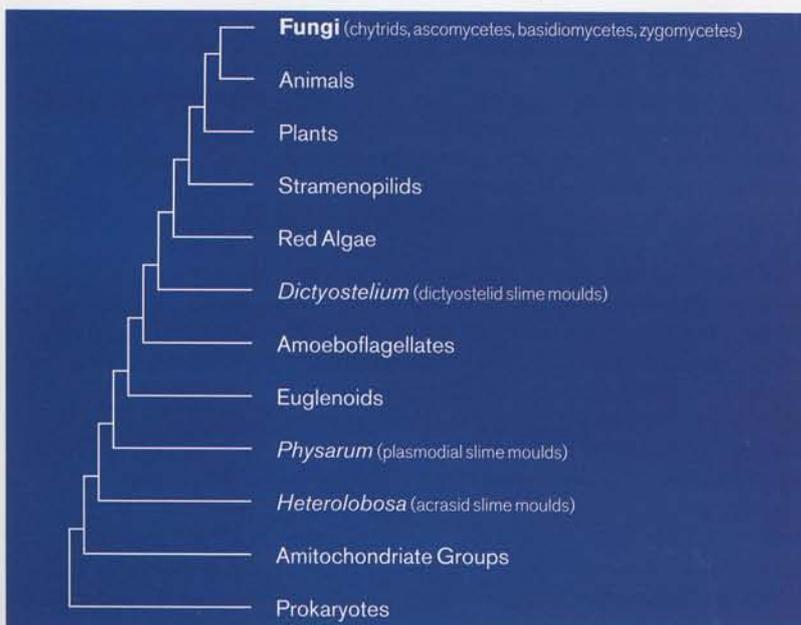
It now appears that the fungi are a mixture of disparate groups each with its own history. Based on small-subunit rDNA sequences, the majority of fungi, including our most familiar forms, can be distributed on four closely related branches (phyla) of the evolutionary tree, with the basidiomycetes and the ascomycetes closest to each other (see Fig. 1). Other organisms studied in the past under the umbrella term fungi can now be located in at least four other isolated groups, including three groups of slime moulds and one termed 'stramenopilids'. The latter, a kingdom in its own right, brings together the brown algae, diatoms and moulds related to the causal organism of potato blight, *Phytophthora infestans*. Thus the fungi can now be located in eight phyla, with some of the groups closer to animals than they are to other fungi. Nevertheless, it is still useful to maintain the old classical term fungi for a group of organisms which have similar modes of life and biological strategies.

The fossil record of fungi is rather sparse, although isolated spores attributable to this group of organisms have been found at a number of geological stages. Fossils of larger fungi are particularly rare, but some good examples have been located recently in ambers. Experimentalists such as Berbee and Taylor have suggested from 18S rDNA sequence comparisons that the origin of the basidiomycetous fungi was 400–300 million years ago and that mushroom ancestors appeared approximately 65 million years ago, as shown by the occurrence of clamp-connected hyphae in coal measures (Carboniferous). An early mushroom referable to the modern genus *Mycena* has been dated at between 15–20 million years and a *Marasmius* at 90–94 million years: both pre-date the separation of the ancient land mass Gondwanaland. These results suggest a rather long history perhaps as far back as the Cretaceous, the very period in which our now familiar flowering plants underwent rapid evolution.

Identification of the larger fungi, especially the mushrooms, toadstools and bracket fungi, has been fraught with difficulties over the years, differences between species being small and often based on subtleties in texture, taste and the like – all very subjective! Although these characters are underpinned by differences in secondary metabolites, anatomy and developmental features, identification of larger fungi has caused disbelief and frustration to those in neighbouring disciplines. Yet surprisingly, each new



BELOW:
Fig. 1. Phylogenetic tree, based on small-subunit rDNA sequence data and incorporating several eukaryotic taxa, showing the polyphyly of organisms known as the fungi.
DATA FROM VARIOUS SOURCES





SEVERN
BIOTECH
LTD

TOP LEFT:
Dictyophora (petticoat stinkhorn)
COURTESY R. WATLING

LOWER LEFT:
A mushroom market in northern
Italy.
COURTESY W. TAIT, EDINBURGH

various elements of the evolutionary pathway which have not become apparent from studying present-day fungi. But intriguingly, results keep emerging in each of the major groupings which suggest new relationships and challenge others. These results often appear in the most unexpected places, genera or even larger groupings of so-called fungi, and the value of features by which we identified a species in the field may have been almost entirely lost. Although for many mycologists, including the present author, the single taxon 'Gasteromycetes', which brought all these forms together in classification, was artificial and needed drastic sorting, in no way could it have been imagined just how fabricated it was!

True, some indication had already been given by developmental and micro-morphological studies which linked, for instance, the boletes with the false truffles. Bolete-like species, which have an intermediate morphology, had been placed in the genus *Gasteroboletus* and a morphological series proposed, but even this genus has been shown, by molecular studies, to be based on convergent evolution: the individual species should be assigned to a range of different, existing genera, as suggested also from morphological analysis. Recently, workers at Berkeley, California, using parallel methods have been able to date the supposed separation of one such gastroboletoid fungus from its proposed parent group.

There are some parallel examples in the secotioid fungi or tobacco pouches, e.g. *Weraroa*, which have been studied in the same way as *Gasteroboletus* and with similar results, various species being linked to a range of different mushroom families and genera. But these are not the core gasteromycetes. What of the birds nest fungi, the earth stars, the puffballs etc.? The brown-spored toadstool *Paxillus* has been associated by molecular techniques with the first group, but how different they are, one a mushroom and the other a small cup-like receptacle, the nest, containing capsules containing spores. Where is morphology now? Equally, the earth star, *Geastrum*, and cannon ball fungus, *Sphaerobolus*, are associated by molecular techniques with the fairy club fungus, *Ramaria*, and are separated from the puffballs despite the incredible resemblance, apart from the outer ray-like arms from which the common name 'earth star' derives. Puffballs (*Lycoperdon* and relatives) find themselves neatly parked amongst the parasol (*Macrolepiota*) and true mushrooms (*Agaricus*).

Using sequencing data the false truffle, *Melanogaster*, is now firmly within the boletes: this result is of great interest for over the years no true relationships have been proposed for this genus. This contrasts with some other false truffles which have each been associated with a family or genus of mushrooms based on anatomical similarities and which led to the term sequestrate being coined to delimit a morphotype and not a taxonomic entity. *Calsotoma*, a group of stalked puffballs with a



experimental technique has provided more support for the majority of species recognized on classical grounds. The recent application of molecular techniques has not discredited the use of field characters in species delimitation, but has thrown up relationships between species which few would have imagined only 10 years ago. Interestingly, so-called aberrant groupings within the larger fungi, especially those in the 'Gasteromycetes' or stomach fungi (such as the false truffles, puffballs and stinkhorns) have been brought into the fold. But relationships between what were at one time considered familiar and biologically sturdy groupings have been destroyed. So the species concept has been fairly well supported but our understanding of relationships within the macromycetes needs to go back to the drawing board.

With such a long history there are undoubtedly

Now who would have thought it? Roy Watling

stem of interwoven threads, gelatinized tissues and a suture-like apical hole from which the spores escape was also of unknown affinity. Recent work by Hughey and colleagues has shown, by using 12S, 18S and 25S rDNA analysis, that this genus can be also confidently inserted into the framework of the boletes. Horrors! The value of molecular methods is therefore demonstrated for not only does it throw up provocative data, but also it points to relationships in the absence of classical information. The bizarre-shaped and often evil-smelling stinkhorns (*Phallus* and its allies) now nestle amongst the agarics but at the moment the present author is at a loss to explain how the padi straw mushroom (*Volvariella*) sits with the split-gills (*Schizophyllum*), so frequently used in genetic experiments, and the beefsteak fungus (*Fistulina*).

Combining morphological information and molecular techniques allows objectives to be set, testing proposed positions and relationships, e.g. the presence of the phenolic hydroxy pigment pistillaridin found in certain club fungi should now be investigated in their newly proposed relatives. Such work would parallel the joint studies by Gill in Melbourne and the author who showed the use of anthraquinone production and pathways in helping to place the devil's club fungus (*Pisolithus*) in the boletes. Molecular support is required for the association of *Gyrophragmium*, a puffball-like fungus with *Agaricus*, demonstrated by the complex Schaeffer's test, which uses the reaction of aniline and nitric acid in the presence of the fungus tissues; also for the association of *Torrendia*, another puffball-like fungus, with *Amanita*, a genus which includes the death cap (*A. phalloides*), each pair only being previously linked through developmental similarities. Equally, on macro-morphology alone, *Podaxis* has been linked to the lawyer's wig, a fungus traditionally placed in *Coprinus* although in molecular terms even it is not closely related



TOP RIGHT:
Pleurotus ostreatus (oyster mushroom)
COURTESY R. WATLING

LOWER RIGHT:
Geastrum rufescens (earth star).
COURTESY R. WATLING

to most species presently placed in the genus.

The reassessment of relationships is happening in the three other phyla of fungi, viz. Ascomycota, Zygomycota and Chytridiomycota, with equally interesting results and from which I could have taken examples. The scene is set for an exciting start to the new millennium, the first task being to consolidate these new studies and bring them into the main structure of classification.

● Professor Roy Watling MBE FRSE was formerly Head of Mycology and Plant Pathology at the Royal Botanic Gardens Edinburgh before retiring in 1998. He is a former President of the British Mycological Society.
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Fungi and skin

H. Ruth Ashbee & E. Glyn V. Evans

Diseases of the skin, hair, nails and mucous membranes are the most common of fungal infections, with treatment costing millions of pounds each year in the UK.

Fungi are found on virtually all body surfaces but mainly on the skin and scalp. They are there either as commensals, transient flora or as the cause of disease. The commensal organisms are usually yeasts, whereas the pathogens are a mixture of moulds and yeasts.

● Fungi and healthy skin

The only fungi to live permanently on the skin as commensals belong to the yeast genus *Malassezia*. *Malassezia* species are dimorphic and most of the species in the genus have an absolute requirement for lipid to enable them to grow. Their lipophilic nature is responsible for defining the areas on the body where *Malassezia* occurs – namely those areas rich in sebaceous glands, such as the face, scalp, chest and back. The genus has recently been re-organized on the basis of molecular taxonomic studies and now includes six lipophilic species: *M. furfur*, *M. sympodialis*, *M. globosa*, *M. obtusa*, *M. restricta* and *M. slooffiae*. There is also a seventh member of the genus, *M. pachydermatis*, that does not require lipid for growth and is usually not found on human skin, but is often found associated with animals.

Population densities of *Malassezia* vary from person to person, as well as from site to site. However, on the chest and back as many as 10^4 organisms cm^{-2} have been recorded, whilst on the hands and feet there may be as few as <4 organisms cm^{-2} . The age at which colonization occurs is controversial, with some workers reporting it in children of only a few weeks of age and others finding no colonization until puberty. What is known is that maximal population densities occur in adults between late teens and early middle age, after which the number of organisms decreases as people get older.

Candida is found on the skin of some individuals, but it is not a true commensal and carriage is usually transient. The species found include *Candida albicans* and *Candida parapsilosis*. *Candida* may also be present on the mucous membranes of the mouth and vagina but here it does occur as a commensal. The percentage of people colonized and the level of colonization varies considerably between different groups in the population but around 10–20% of healthy individuals are thought to carry commensal *Candida*.

Both *Malassezia* and *Candida* are able to cause disease under certain circumstances.

● Fungi and skin disease

Diseases of the skin, hair, nail and mucous membranes are the most common of all fungal infections and they have a worldwide distribution.

Ringworm: Most of these infections are caused by a group of keratinophilic moulds known collectively as dermatophytes. They cause a complex of diseases, collectively known as ringworm (clinical name *Tinea*),



which affects the keratin in hair, nails and stratum corneum (top layer) of the skin. About 20 species of dermatophyte fungi from the genera *Trichophyton*, *Microsporum* and *Epidermophyton* are responsible. Most infections are caused by a single species, *Trichophyton rubrum*. Ringworms also occur in animals and these may spread to humans; transfer is commonest with *Microsporum canis*, the cause of ringworm in cats and dogs.

Ringworm lesions vary considerably in appearance, according to the site of the infection and the species of fungus involved. Sometimes there is only dry scaling or hyperkeratosis, but more commonly there is irritation, inflammation, swelling and vesicles. More inflammatory lesions with weeping vesicles, pustules and ulceration are usually caused by animal ringworm. The spreading, ring-like lesions with a raised, inflammatory border from which the disease name derives are seen on the body, face and scalp (Fig. 1). In infections of the scalp there is scaling and hair loss and sometimes a severe inflammatory response resulting in a raised boggy lesion called a kerion (Fig. 2) – this needs to be diagnosed and treated promptly otherwise there may be permanent hair loss. In nail infection, the nail becomes discoloured, thickened, raised and crumbly (Fig. 3).

Ringworm is the only truly contagious fungal infection and spreads through direct or indirect contact with an infected individual or animal. The infective particle is usually a fragment of keratin containing



BELOW:
Fig. 1. Body ringworm caused by *Trichophyton verrucosum* (cattle ringworm).
COURTESY E.G.V. EVANS

TOP RIGHT:
Fig. 2. Kerion lesion on the scalp due to *Microsporum canis*.
COURTESY E.G.V. EVANS

LOWER RIGHT:
Fig. 3. Nail infection due to *Trichophyton rubrum*.
COURTESY DR DAI ROBERTS,
SOUTHERN GENERAL HOSPITAL,
GLASGOW





viable fungus. Indirect transfer may occur via the floors of swimming pools and showers or on brushes, combs, towels and animal grooming implements. In industrialized countries, ringworm of the scalp, which occurs almost exclusively in children before puberty, accounts for only a small proportion of infection and is mostly caused by dermatophytes of animal origin, although scalp infections due to the human species, *Trichophyton tonsurans*, are on the increase in Europe. Foot ringworm (athlete's foot; Fig. 4), with its associated nail and groin infections is the commonest fungal disease and the increased use and availability of communal bathing facilities have brought this about.

These now comprise about 75% of all ringworm infections diagnosed in temperate zones. It is estimated that around 10–15% of the general population in the UK has foot ringworm and 5% nail disease. Currently, nothing is done to control the spread of these infections despite the fact that vast sums are spent treating them. The disinfectant foot-bath in swimming pools is worse than useless for controlling foot ringworm and is likely to contain a soup of skin scales, many of which contain fungus – jump over it!

Although dermatophytes are essentially disease-causing organisms, some believe in a carrier status. Dermatophytes can be isolated, for example, from the feet or scalp without there being any obvious sign of infection. Others dispute this and say that if you look hard enough you will find lesions.

Yeast infections: Infections due to *Candida* and *Malassezia* are generally endogenous in origin. *Candida* can cause infections at many sites on the body, commonly the folds, such as the armpits or beneath the breasts, where there is occlusion and increased moisture. The lesions appear as well demarcated, inflamed areas that may itch. The nappy area in babies, the groin and the skin between fingers (Fig. 5) and toes may also be affected.

Candida may also cause paronychia – inflammation around the cuticle of the nail, which may lead to swelling and production of pus (Fig. 6). It is common in kitchen workers and other people who frequently have their hands in water. *Candida* infection of the mouth and vagina is generally known as thrush because of the presence of white plaques of yeast on the surface of the mucous membrane (Fig. 7). Vaginal candidosis is very common and most women develop an infection at some point, frequently during pregnancy, and some suffer from recurrent infections. Oral infections are seen mainly in babies and the elderly. A number of predisposing factors are recognized for *Candida* infection, especially antibiotic therapy and immunosuppression, either drug- or disease-induced. For example, intractable chronic oropharyngeal candidosis is common in AIDS patients (<100%) and frequently there is associated oesophageal infection. The appearance of this infection often indicates the transition from HIV-positive to full-blown AIDS.

Malassezia is able to cause several skin conditions, including pityriasis versicolor, seborrhoeic dermatitis and folliculitis. It has also been known to cause systemic infection, including catheter related fungaemia in suitably predisposed individuals, such as newborn infants fed intravenously with high lipid feeds.

Pityriasis versicolor takes the form of scaly hypo- or hyper-pigmented lesions (Fig. 8) with minimal inflammation or itching. It occurs on the upper trunk, but may spread to include upper arms, legs and buttocks

TOP LEFT:

Fig. 4. Ringworm of the toe clefts (Athlete's foot) due to *Trichophyton rubrum*. COURTESY DR DAI ROBERTS, SOUTHERN GENERAL HOSPITAL, GLASGOW

MIDDLE LEFT:

Fig. 5. *Candida albicans* infection of hand (interdigital space). COURTESY E.G.V. EVANS

LOWER LEFT:

Fig. 6. *Candida* infection of the nail fold (paronychia). COURTESY E.G.V. EVANS



TOP & LOWER LEFT:
Fig. 7. *Candida* infection of the mouth showing white yeast plaques (top) and severe mouth infection in an AIDS patient (bottom).
 COURTESY E.G.V. EVANS

UPPER RIGHT:
Fig. 8. Pityriasis versicolor of skin with hyper pigmentation.
 COURTESY E.G.V. EVANS

temperature and humidity appear to be the most important. In hot climates it is often the most common fungal infection seen.

Seborrhoeic dermatitis presents as scaly lesions on the face, upper trunk and scalp which itch and are inflamed. Around 1–3% of the normal population are affected, but in HIV-positive patients the prevalence may be as high as 80%. Predisposing factors are not well characterized, but stress may be important. The condition is chronic and relapses are frequent. Diagnosis is largely based on clinical presentation.

Malassezia folliculitis consists of itchy acne-like spots and pustules on the trunk and upper arms. Antibiotic administration is the main predisposing factor, particularly in the immunocompromised, but overgrowth of *Malassezia* may be secondary to occlusion of the follicles.

Diagnosis: Ringworm and *Candida* infections may be reliably diagnosed in the laboratory by microscopical examination and culture of skin, hair, nail or material from mucous membranes.

Treatment: Ringworm generally responds well to topical creams, etc., except for nail and scalp infections, which require oral therapy. Topical agents include a number of azoles and terbinafine and amorolfine. Oral therapies include terbinafine and the triazoles

itraconazole and fluconazole, although terbinafine is the most potent anti-dermatophyte drug.

Candida infections and pityriasis versicolor respond well to the application of topical agents, although oral fluconazole and itraconazole are alternatives for severe or extensive cases. With pityriasis versicolor relapse is a major problem (reaching 60% within 1 year). Topical antifungals,

along with topical steroids, may also be used for treatment of seborrhoeic dermatitis.

● Future prospects

Current research into superficial fungal infections is focussing, for example, on molecular typing of dermatophyte strains to answer questions on epidemiology and pathogenesis; questions such as whether or not particular strains of dermatophyte species are more likely to cause nail (as opposed to skin) disease than others. There is an unaddressed need to develop measures to control foot and nail infections in communal bathing places. This would help reduce the expenditure on the treatment of these infections, especially as currently in the UK this costs circa £45.5 million.

Current treatments for superficial mycoses are generally satisfactory, although there is scope for improvement, particularly in nail disease where about 20% of patients fail treatment. A number of new antifungal agents, mainly azoles and cell wall inhibitors, are likely to become available over the next 1–3 years. Initially, it is probable that they will be used to treat systemic fungal infections but may be used later for superficial mycoses.

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Biofilms: united they stand, divided they fall

Peter Gilbert & Hilary Lappin-Scott



A preview of the topics to be discussed in the SGM Main Symposium *Community Structure and Co-operation in Biofilms* at the University of Exeter, 12–13 September 2000.

The introduction of the term 'biofilm' into general microbiology is relatively recent but the concepts that it embraces are not new. This umbrella term encapsulates the notion that bacteria, yeasts, moulds, and indeed some micro-fauna, co-exist in nature as spatially organized communities and that such communities can survive and exploit circumstances beyond their capabilities as individual microbes. Biofilms therefore epitomize the collective strength of the individual within a community structure and it is only when such interactions are studied that we can fully understand the way that microbes impinge upon all aspects of life.

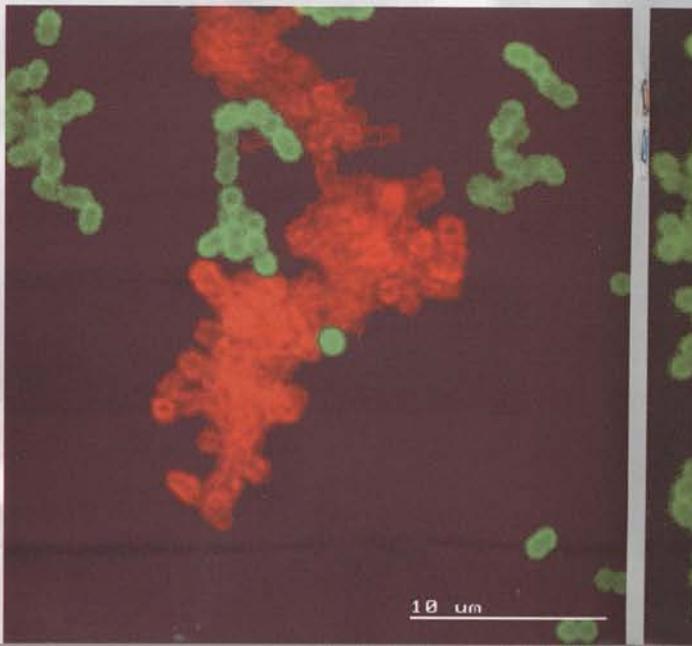
The keystone of biofilm study has been the general recognition that even single species of bacteria, when attached to surfaces and interfaces, express phenotypes that are not seen in liquid culture. For various genera whole cassettes of genes are repressed or de-repressed under the apparent control of touch receptors. Particularly, the 'sessile phenotype' more often displays a reduced susceptibility towards various antibacterial treatments and a more aggressive pathogenesis or corrosion potential than does the free-living planktonic cell. Part of the explanation for the unique properties of biofilm communities comes from the localized high cell densities that they facilitate through the synthesis of an extensive extracellular polymeric matrix. Such polymers not only cement the bacterial cells to the surface but also maintain a spatial arrangement of the different community members and are capable of entrapping many extracellular products and enzymes. Under such circumstances populations of cells become quorate and through the mediation and accumulation of cell–cell signals, such as the *N*-acyl-homoserine lactones in the case of Gram-negative bacteria, alter phenotypes at the

level of transcription. Cross-signalling between different species and genera allows complex, multi-functional consortia to become established. It is often only one of these properties, resistance, corrosion, degradation or biofouling potential, that renders them worthy of study by the industrial or medical microbiologist, and for consideration as therapeutic targets by medicinal chemists. In the Exeter symposium we seek to expose the commonality of process which links these disparate practical problems.

The formation and maintenance of a biofilm is a dynamic process involving a complex interaction of physical and biological processes. Irreversible attachment of planktonic cells to a surface is indicated by a loss of Brownian motion and within a few minutes a number of transcription events are initiated. These particularly concern not only the up-regulation of exopolymer biosynthesis and the deposition of the glycocalyx, but also the orchestration of many other physiological and biosynthetic events. In nature micro-organisms rarely encounter an uncolonized surface, yet much can be learnt about the transition from a planktonic to sessile mode of growth through studies where cleaned, sterile surfaces are exposed to growing suspensions of bacteria. This is of immediate practical importance to the colonization of an implanted medical device or prosthesis, setting the framework through which new materials may be designed to delay or prevent biofilm formation. The

ABOVE: Diagrammatic representation of morphological data from dozens of natural and *in vitro* biofilms, in the *x-z*-axis, showing the microcolonies and water channels that comprise these complex and highly structured communities. The sessile biofilm cells actually grow in matrix-enclosed microcolonies, of various shapes, and these microcolonies are often deformed by high shear forces to produce the streamers seen to project into the bulk fluid.

COURTESY DR. J. W. COSTERTON, MONTANA STATE UNIVERSITY, USA/ARTWORK PEG DIRCKX



precise nature of the colonizing species and its relationship with other bacteria determines the nature of the biofilm formed. In dental plaque such inter-relationships have been well characterized but similar processes are involved wherever surfaces are exposed to environmental micro-organisms.

The main symposium will be complemented by a second session entitled *Medical Implications of Biofilms*, organized by the Cells & Cell Surfaces and Microbial Infection Groups, examining aspects of biofilm physiology in the context of health and disease. There are also two evening workshops, one focusing on young researchers working in the areas of *Biofilm Formation and Control* and a second on *Teaching the Topic of Biofilms*. The latter will focus on three fundamental questions:

What elements of the biofilm story should be included in the undergraduate curriculum?

What properties of biofilm microbiology can be introduced into undergraduate practicals given the equipment constraints of the undergraduate laboratory?

What strategies of dissemination are most likely to be successful in getting information about biofilms to curriculum developers, textbook authors, planners of educational symposia and teachers?

We believe that the combined programme offers a superb opportunity for the novice and experienced 'biofilmologist' alike to gain a rounded insight into the impact that biofilms have on our lives and on the study



BACKGROUND:
A mixed community biofilm composed of bacteria and fungi.
COURTESY HILARY LAPPIN-SCOTT AND SARA ROBERTS

LEFT:
Confocal micrograph of a biofilm community with seven different species. The biofilm was fixed and embedded, and differentially labelled probes targeting *Pseudomonas putida* R1 (red), *Acinetobacter* sp. C6 (green) and all other eubacteria (blue) were added.
COURTESY PROFESSOR S. MOLIN, TECHNICAL UNIVERSITY OF DENMARK

BELOW:
SGM Symposium Volume 59.

of microbiology. We hope that those of you attending who have not already been bitten by the biofilm bug will be drawn to re-examine research in your area in the context of bacterial attachment and organization into communities.

Further details and a booking form appear in the enclosed programme booklet for the meeting. The symposium will be published as a book in the redesigned *SGM Symposium* series (vol. 59). A review of the book and an order form will appear in a future issue of *Microbiology Today*.

- Peter Gilbert, University of Manchester
- Hilary Lappin-Scott, University of Exeter

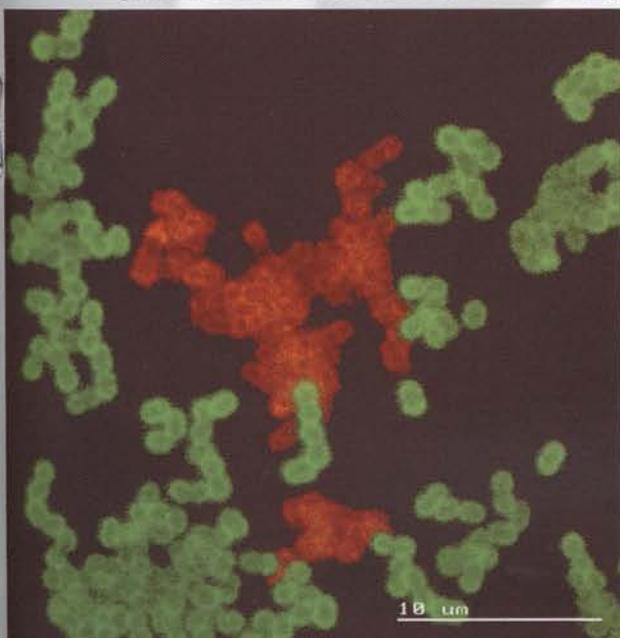
LEFT:
Representative CSLM images of a *Streptococcus gordonii* (green) and *Actinomyces naeslundii* (red) biofilm. Left panel: coadhesion of a single streptococcal cell (centre) bound to a clump of actinomyces and coadhesion of chains of streptococci to two different lobes of the clump of actinomyces (upper centre). Right panel: coadhesion of streptococci and actinomyces (upper centre) and bridging of adherent streptococci by a small clump of actinomyces (lower centre).
COURTESY DR P. KOLENBRANDER, NIH, BETHESDA, MD, USA

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**community structure
and co-operation in
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It's a jungle out there – L.A. in the 21st century

SGM at the ASM 100th General Meeting

Aidan Parte & Janet Hurst

We arrived in Los Angeles on Saturday afternoon: Janet Hurst, fresh from a week in Las Vegas, and Aidan Parte, stale from a week in Reading. The weather in the home of Hollywood, food fads, iced tea and Ice-T was an unseasonably warm 90 F, but over 100 F in the Valleys. Thank goodness for air conditioning! Our hotel was in Downtown L.A., not too far from the Conference Center.

After a sleepless night (for a jet-lagged Aidan, anyway), we went to the massive new L.A. Conference Center in Downtown, to set up our stand in the Publishers' Park section of the trade exhibition. Unlike last year, we decided to hire a stand from the ASM – this saves the aggravation of carting the famous blue wheelie-bin thousands of miles around the world. It was a great relief, though, that the seven boxes of journals, *Microbiology Today*, educational material, etc., had arrived safely at our allotted booth. What most conference-goers don't see is all the work behind the scenes. It is truly amazing! Fork-lift trucks zooming around, no carpets, cables and packing crates everywhere. Then when we came back in the morning, it was all transformed into a professional and smart-looking trade exhibition.

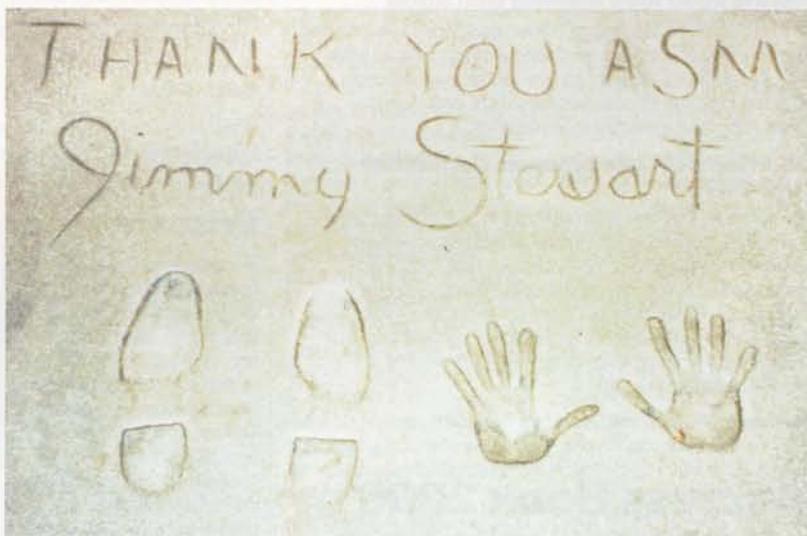
The conference opened on Monday 22 May and was immediately extremely busy, with nearly 8,000 scientific delegates registered for the 100th ASM Annual Meeting. The trade exhibition was in a hall that resembled an aircraft hangar and was arranged so that delegates had to go through it to get to the timed poster sessions. This resulted in a constant flow of people, with plenty of interest in the SGM's services, particularly membership (it is still staggering the number of people who think SGM is the British arm of the ASM!), *Microbiology Today*, posters, stickers and journals. It was surprising that there was not much interest in the online side of the journals operation, which we had available on a lap-top, probably because the novelty has worn off and it is now expected of us. This just shows how quickly things are moving in electronic publishing. It was also good to get plenty of positive feedback on our Symposium volumes. Many SGM members dropped by the stand – it was nice to see their friendly faces – and we were grateful to those who stopped to help for a while, enabling us to have a look round the 800 or so other 'booths'.

Liz Sockett, SGM Education Officer, made some useful contacts in the ASM Division W (their Education Group) and participated in a school-teachers' training day on microbiology, where she distributed packs of SGM resources. She also presented a poster on our educational activities for younger children which was very well received. All of the free handouts on the poster disappeared in a flash. Compared with most of the other educational material at the event, SGM products are of high quality and very innovative. The positive reaction of delegates was most welcome.

It was not all work, work, work at the conference. As you can see, we managed to get into the non-urban jungle, where we met a friendly lioness who even allowed us to have our picture taken with her! When it all ended on the Wednesday, most of our material had been taken and we only brought back our display copies of the Symposium volumes, and of course pens, chocolates and post-it pads that we had swiped from other stands!

We ate every night in the hotel. The reason we didn't go out is that Downtown L.A. is not very





nice! It certainly wasn't like the movies, except perhaps *Boyz 'n' the Hood*, and we heard every night on the TV about the latest tit-for-tat drive-by shooting not far from where we were staying. So that our dreams weren't completely shattered, in the free time before flying home we went on two coach trips. At Universal Studios we did a tour of the backlot – Bates Motel will give you a real welcome – and other special effects shows and rides including *Backdraft*, *E.T.* and *Back to the Future*. We also managed a whistle-stop tour of Venice Beach, Beverley Hills and stars' homes in Bel Air, and the Chinese Theater where we made our mark in the pavement!

All in all, it was a very successful conference and well worth the effort for raising the SGM's profile in the States.

- Aidan Parte, Managing Editor, *IJSEM*
- Janet Hurst, SGM Deputy Executive Secretary

FAR LEFT:
The skyline of Downtown L.A.

BOTTOM:
Universal Studios' backlot, Hollywood (Warner Brothers in the background).

CENTRE (UPPER):
The new L.A. Conference Center, Downtown L.A.

CENTRE (LOWER):
The SGM Stand in the L.A. Conference Center. From left to right: Aidan Parte (Managing Editor, *IJSEM*), Erko Stackebrandt (Editor, *IJSEM*), Janet Hurst (SGM Deputy Executive Secretary).

ABOVE (UPPER):
Janet Hurst and Aidan Parte with a friendly lioness in the non-urban jungle!
COURTESY APPLIED GRAPHICS TECHNOLOGIES

ABOVE (LOWER):
A 'thank you' from Hollywood legend James Stewart outside the Chinese Theater!

ALL PHOTOS AIDAN PARTE EXCEPT WHERE INDICATED

Society News

May Council Meeting

Honorary Members

● Council has conferred Honorary Membership on two distinguished microbiologists in recognition of their outstanding contributions over an extended period: **Professor John Guest** (Sheffield) for his work on bacterial physiology, and **Professor Sir John Pattison** (London), Director of Research and Development at the Department of Health for his work in medical microbiology.

Special Historical Perspectives Lecture

● Council agreed to the suggestion that an occasional lecture on the history of microbiology should be given at a Society meeting. The first talk will take place at Exeter in September.

Promega Prize Competition

● Council approved a recommendation from the Group Conveners that in future all winners from the 'Group stages' of the competition should be given a prize of £25 plus free membership of the Society for the following year.

Spring 2000 Joint Meeting with SfAM

● The Scientific Meetings Officer reported to Council that the meeting at Warwick had been very successful with over 1,000 delegates registered. The Symposium volume, entitled *Fighting Infection in the 21st Century*, was expected to be available in September.

SGM joins UK Life Sciences Committee (UKLSC)

● Professor Ritchie reported that the Society had been formally accepted as a member of this association of learned societies, which provides a forum for the co-ordination of opinions and policy in the biosciences community. Council sees this as a further step in our participation and support for the development of a respected common voice to represent the views of the biosciences community.

● Alan Vivian, General Secretary

Address Book 2000

A new edition of the Society's Address Book for members will be produced this year. Any member whose current address (as it appears on his/her mailing label) needs amendment, or whose telephone, fax or email details have changed since the last edition should inform the Membership Office at Marlborough House (email members@sgm.ac.uk) by **4 August**.

News of Members

Dr Bernard Dixon has been awarded an OBE for services to scientific journalism in the Queen's Birthday Honours List.

Dr Richard James, School of Biological Sciences, University of East Anglia, will take up the Chair of Microbiology in the School of Clinical Sciences, University of Nottingham, in September.

The Society notes with regret the deaths of **Dr C.Q. Darcel** (member since 1953) and **Dr S. Ramachandran** (member since 1989).

SGM Prize Lectures and Awards

Kathleen Barton-Wright Memorial Lecture

The 2000 Kathleen Barton-Wright Memorial Lecture has been awarded to **Dr Moira E. Bruce**, of the MRC Neuropathogenesis Unit, Edinburgh, for her outstanding contribution to research in the area of transmissible spongiform encephalopathies. Dr Bruce will deliver her prize lecture at the Society meeting at Heriot-Watt University in March 2001.

Undergraduate Microbiology Prizes

The prizes are intended to encourage excellence in the study of microbiology by undergraduate students and to promote scholarship in, and awareness of, microbiology in universities. The prizes are awarded annually to the undergraduate in each qualifying institution who performs best in microbiology in their penultimate year of study for a Bachelor's degree. Each winning student will receive £50, a certificate and a free year's undergraduate membership of the SGM. Invitations to nominate a student for the 2000 prizes have been sent to qualifying institutions. The closing date for receipt of completed application forms is **31 August 2000**. Further copies of the form and the full rules of the scheme are available on the SGM website.



Professor Sir David A. Hopwood

New SGM President

David Hopwood was born in Staffordshire in 1933. After grammar school education in Hampshire and Cheshire, he took a degree in Botany at Cambridge, followed by a PhD in genetics with Harold Whitehouse. He was an assistant lecturer in Botany at Cambridge for five years before moving to Guido Pontecorvo's Department of Genetics in the University of Glasgow in 1961. From 1968 he was John Innes Professor of Genetics in the University of East Anglia, Norwich, and head of the Genetics Department at the John Innes Centre; he is now an Emeritus member of both institutions.

Throughout his career he has studied the genetics of *Streptomyces coelicolor*, the 'model' member of the group of filamentous Gram-positive soil bacteria that are pre-eminent producers of antibiotics. His work – along with that of many others – led to the new field of 'combinatorial biosynthesis' of 'unnatural natural products', in other words the use of genetic engineering to produce 'hybrid' metabolites with potential applications as drugs, a topic with which he is still closely identified. A second strand of his current research is to co-ordinate the sequencing (at the Sanger Centre) of the chromosome of *S. coelicolor*, due to be completed by late 2000.

David has always been active in teaching, at both graduate and undergraduate levels, and in running practical courses at home and overseas. He is very much in sympathy with the aims of the Society, in training as well as in the support of microbiological research in all its exciting current aspects.

Annual General Meeting 2000

The Annual General Meeting of the Society for General Microbiology will be held on **Wednesday, 13 September 2000** at the Society meeting at the University of Exeter. Agenda papers, including reports from Officers and Group Conveners, and the accounts of the Society for 1999 are in the separate Annual Report booklet distributed to all members with this issue of *Microbiology Today*.

Staff News

Congratulations are due to **Susan Andrews**, former staff editor on JGV, on the birth of James (Jamie) Peter, who weighed in on 29 April at a healthy 7+ lbs. Baby was much admired on a recent visit to the office, but as he slept throughout, he cannot have been too impressed with Marlborough House!

Dr Meriel G. Jones

**New Editor of
*Microbiology
Today* from
November
2000**



When the SGM's members' magazine adopted its current incarnation as *Microbiology Today*, I started writing the 'Hot off the Press' section, which brings papers in the Society's scientific journals to a wider audience. I was surprised to be asked to be the next editor of *Microbiology Today*, and am certain that it will be a very interesting experience.

My scientific career started from a degree in biochemistry at the University of Bristol in 1976 and has led, via a doctorate in fungal chemotaxonomy at the University of London and postdocs at Essex, Rome and Dundee, to a lectureship at the University of Liverpool. My current research interests are in the rôles of flavour compounds in Alliums and gene regulation in fungi. I am also interested in ways of making science more accessible to the non-specialist.

Grants

International Research Fellowships

This newly established scheme allows scientists to travel from or to the UK/Republic of Ireland to carry out a defined piece of research in any field of microbiology. Applicants must be of postdoctoral level or above. The visits may be of up to 3 months duration. The awards cover the costs of return travel, a subsistence allowance and a contribution towards the costs of consumables in the host laboratory. FOUR copies of the completed application form (available on the website) and all supplementary documentation must be submitted to the SGM Grants Office for consideration. Full details of the scheme were published on p. 91 of the May issue of *Microbiology Today*. The closing dates for the two rounds of applications in 2000 are **31 July** and **30 November**.

International Development Fund

Members are reminded that Council has established an International Development Fund for competition this year. The purpose of the Fund is to make small grants available to help microbiologists in developing countries and Eastern Europe. Members may apply for funding to run training courses in laboratories in developing countries appropriate to the needs of those countries, or for any other small project to assist in technology transfer from Western Europe. Full details of the scheme were published on p. 92 of the May issue of *Microbiology Today*. The closing date for applications is **2 October 2000**.

Seminar Speakers Fund

The purpose of the Seminar Speakers Fund is to promote talks on microbiological topics in departmental seminar programmes. Applications are invited from Higher Education Institutions where microbiology is taught for grants of up to £200 towards the travel, and if necessary, accommodation, expenses of an invited speaker. Applications will be dealt with on a first come, first served basis during the academic year, which is defined as running from September 2000 to June 2001. Written submissions should be sent to the Grants Office for consideration. Details of the scheme were published on p. 92 of the May issue of *Microbiology Today*.

The Watanabe Book Fund

Members who are permanently resident in a developing country are reminded that they may apply for funding to acquire for their libraries books, or possibly journals, relating to microbiology. These annual awards are available as a result of a generous donation from Professor T. Watanabe of Japan. Full details of the scheme were published on p. 35 of the February issue of *Microbiology Today*. The closing date for the receipt of applications, which should be made to the Grants Office, is **6 October 2000**.

Details of all Society grant schemes are now on the website at <http://www.sgm.ac.uk>
Most application forms can be downloaded.

Requests for paper copies or any inquiries should be made to the Grants Office at SGM Headquarters (Tel: 01 18 988 1821; Fax: 01 18 988 5656; email: grants@sgm.ac.uk).

Vacation Studentships 2000

The vacation studentships enable undergraduates to work on microbiological projects during the summer vacation before their final year. They are intended to provide undergraduates with experience of research and to encourage them to consider a career in laboratory-based science. Support is provided at the rate of £135 per week, for a maximum period of 8 weeks. A small sum of up to £400 may also be awarded towards the cost of consumables. Students are required to submit a brief report of their research on the completion of the studentship, which in itself is a useful exercise. The scheme has proved to be very successful and popular. This year a record number of 54 applications was received. After careful scrutiny by referees and the Award Panel, studentships were offered to 35 applicants. A list of awardees is available from the SGM Grants Office on request.

Council has set aside a further sum to fund vacation studentships next year. Full details of the 2001 scheme will be announced in the next issue of *Microbiology Today*. The rules are available on the SGM website.

Education Development Fund

Members may apply for grants to support projects intended to lead to an improvement in the teaching of any aspect of microbiology relevant to education in the UK. Examples of work which might be funded include the provision of teaching materials (e.g. videos, slides, posters), the development of reliable, novel practical exercises, new approaches to teaching/learning familiar concepts (e.g. computer simulations or tutorials) or any other appropriate aspect. Grants are also now available to fund small projects to promote the public understanding of microbiology. These might include workshops, talks, demonstrations, posters, leaflets, broadcasts, activities at science festivals and AV or computer packages. The full rules of the scheme were published on p. 91 of the May issue of *Microbiology Today*.

Application forms are available on the SGM website. There is no closing date for applications, which will be considered on a first come, first served basis during the period **1 June 2000–31 May 2001**.

UNESCO-IUMS-MIRCENS-SGM Fellowships

The International Union of Microbiological Societies (IUMS) is a worldwide federation of national and international Societies and other organizations having a common interest in microbiological sciences.

The Microbial Resources Centres (MIRCENS) is an international network of academic and research Institutes spreading biotechnological and microbiological benefits especially to developing countries.

SGM, a member Society of the IUMS is making a separate contribution to this programme from its International Development Fund.

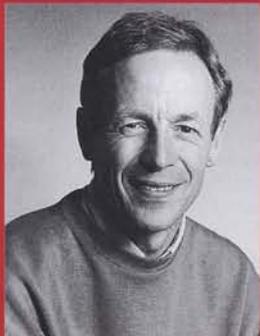
The UNESCO-IUMS-MIRCENS-SGM short-term fellowship is a co-operative scheme between the various listed organizations to provide an opportunity for young microbiologists from any developing country to pursue, or to complete, a part of an ongoing research programme in a laboratory in a newly industrialized or developed country. Microbiologists in developing countries actively pursuing research, often reach a facility *cul de sac* where research plans cannot be accomplished for want of materials, equipment or facilities. The UNESCO-IUMS-MIRCENS-SGM short-term fellowship is designed to ease these problems for deserving microbiologists from developing countries to enable them to overcome their research bottlenecks, and to strengthen the bonds of inter-regional scientific co-operation.

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

The award will be up to US\$4000 for travel and subsistence (room and board) to support the awardee for a maximum period of 3 months. Funds for salary and medical insurance will not be provided. Coverage for life and accident or health insurance is the personal and sole responsibility of the individual or the host organization.

Applications (four copies) must be submitted in English and should consist of a nominating letter from the head of the organization in which the applicant is working; the applicant's *curriculum vitae*; a letter of invitation or acceptance from the host organization describing facility support for the applicant; and two supporting letters addressing the applicant's achievements. Applications must be submitted to Prof. Dr W. N. Konings, Vice-president IUMS, Department of Microbiology, University of Groningen, Kerklaan 30, 9751 NN Haren, The Netherlands (Fax +31 50 3632154; email w.n.konings@biol.rug.nl).
Deadline: 1 December 2000.

Professor Chris Thomas New Editor-in-Chief of *Microbiology*



As a biochemistry student my interest in microbiology was fired by practical classes on bacteriophage T5 and a project on DNA replication in *Staphylococcus aureus*. I continued the latter for my DPhil in the Microbiology Unit, Department of Biochemistry, Oxford. I studied plasmids of Gram-negative bacteria with Donald Helinski in La Jolla and then joined

the Genetics Department in Birmingham in 1980, being promoted to a personal Chair in 1991. Broad host-range plasmids are still a major theme in my lab, justified by their role in bacterial adaptability and diversity – underpinning evolution of antibiotic resistance and biodegradative ability. Central to our research are the control circuits and partitioning mechanisms of plasmids and chromosomes because of their importance in the cell cycle and as potential drug targets. Research also extends to other applied areas such as polyketide biosynthesis. A connection between all these projects is the genus *Pseudomonas*.

My link with *Microbiology* goes back to 1989. After a short while as an MEB, I was an Editor from 1991 to 1997 and enjoyed being involved in the relaunch of JGM in its present form. It's a privilege to be taking over as Editor-in-Chief.

Glyn Hobbs New Group Convener Fermentation & Bioprocessing



I was originally introduced to microbiology by a sixth-form teacher. He had a PhD in the subject and an enthusiasm that fired my interest. These early experiences led me to my first degree in microbiology at University College Cardiff. The department provided a friendly, stimulating and entertaining environment for those who were lucky enough to have passed through its doors. It was the likes of David Lloyd, Terry Coakley, Julian Wimpenny and Ted Hill that focussed my interests towards microbial physiology. My next step was a PhD, funded by the Ministry of Defence, that allowed me to study the physiology of *Cladosporium resinae* under the watchful eye of Alan Griffiths. I then left Cardiff for Manchester in 1987 to take up a postdoctoral position with Stephen Oliver and John Cullum at UMIST. Further formative years followed when I learnt my fermenter trade and was introduced to the intricacies of *Streptomyces coelicolor*. I moved to Liverpool in 1992 to take up a lectureship in Applied Microbiology at Liverpool John Moores University. My current research interests are largely focussed on the physiology and metabolism of a range of actinomycetes.

Student Societies

SGM sponsored lecture scheme

Grants are available to support **two** lectures on microbiological topics per academic year at Student Society meetings.

A Student Society is eligible for support if:

- It is run mainly by and for students of life sciences, either postgraduates and/or undergraduates.
- It is based in the UK or Republic of Ireland

The invited speakers will be reimbursed directly for reasonable costs of travel and accommodation. However, please note:

- The maximum claim for each lecture is £150.
- One speaker may be invited from abroad or from Ireland, but there can be no increase in the maximum claim for the lecture.

The Society will be reimbursed for the costs of entertaining the speaker to dinner, including the expenses of **one** member of the committee.

Application forms are available on the website www.sgm.ac.uk or from The Grants Office at SGM HQ.
Tel. 0118 988 1821
Fax 0118 988 5656
email grants@sgm.ac.uk

- Contributions for Gradline from young SGM members are always welcome.

Life Science Careers 2000

Organized by:



UK
Life Sciences
Committee

www.lifesci.org

Are you graduating in 2001 or 2002 or a postgraduate student? Are you wondering what to do next with your life? To learn about the careers available for graduates in life science today, make sure that you attend the conference nearest to you. This year's events are being held at the following venues:

- **4 November 2000** University of Edinburgh
- **18 November 2000** UMIST, Manchester
- **2 December 2000** Queen Mary & Westfield College, London

Each event offers a wide range of talks on career choices and further training, plus guidance on job hunting and interviews. There are sessions on PhD studentships and postdoctoral opportunities. Time is available in the breaks for individual discussions with the speakers and with representatives of employers and higher education institutions. There is also an exhibition with plenty of literature to take away.

Sponsored by:



SCIENCE'S
next wave

uk.nextwave.org

Programme outline

- Introduction
- NextWave: the scientific careers website
- Research careers in large companies
- Coffee and individual discussions
- Clinical careers
- Publishing/science communication
- Lunch and individual discussions
- Split session: Further qualifications or postdoctoral positions
- Technology transfer/patent law/bioinformatics
- Tea and individual discussions
- Teaching in schools
- CVs, interviews and job hunting
- Summing up/general discussion

CV review service

To have your CV reviewed by a recruitment professional at the event, please send 3 copies to the address below before the closing date for bookings.

Cost

£7.00 (includes coffee, tea and lunch)

Bookings

See website for full details of programmes and to download a booking form:

www.sgm.ac.uk/meetings.htm

A booking form can also be found overleaf. All enquiries and completed application forms plus payment should be sent to:

Meetings Office
Society for General Microbiology
Marlborough House
Basingstoke Road
Spencers Wood
Reading RG7 1AG

Tel. 0118 988 1805
Fax 0118 988 5656
email meetings@sgm.ac.uk

Going Public

Microbiology in Schools Advisory Committee (MISAC)

Schools Competition 2000: Vaccination: Just a Shot in the Arm?

RIGHT (UPPER):
GCSE winner Kate Riley (back and front pages).

RIGHT (LOWER):
GCSE winner Natalie Gillam (front page).

BELOW (UPPER):
11-14 winner Laura Feaver (front page).

BELOW (LOWER):
11-14 winner Sam Piper (inside pages).

The aim of this year's competition was to encourage pupils' understanding that immunization enhances the body's natural defences. They were asked to create a public information leaflet, aimed at parents, which explained how immunization provides children with protection against disease. The leaflet had to describe vaccination and how it works, and to cover the vaccines that are available for children and the pros and cons of vaccination. Many of the pupils also included a brief history of vaccination and new developments in vaccines.

Over 170 schools took part in the competition, which was judged in two age groups, 11-14 and GCSE, and in excess of 2000 leaflets were submitted. For the first time two of the schools were from overseas, one in India and the other in Bangkok. There were also more entries from Scotland, Wales and both Northern and Southern Ireland than in previous years, which was pleasing. The large number of entries was probably due to the fact that the competition was linked closely to the UK National Curriculum and provided an excellent assessment opportunity for both Keystage 3 and GCSE pupils. This is highlighted by some of the comments sent in by teachers from participating schools:

- *Entering was a stimulating addition to recent KS3 work on Health and Disease.*
- *We've had OFSTED in and had the pamphlets on display for the inspectors...*
- *We have really enjoyed working towards this and thank you for giving us the opportunity.*
- *They were very keen to research the topic in the local library and doctors and all enjoyed the experience.*
- *All the pupils found this exercise to be both entertaining and educational. Please could you forward any other details of other such competitions that your committee is involved in.*
- *The chance to do the leaflets helped to enhance the theory taught in class.*
- *The competition has been a most valuable motivator...*

The quality of the entries was very high and it proved an extremely difficult process for MISAC members, under the chairmanship of John Grainger, to select the winners.

Presentations of cash prizes and certificates have taken place at the winning schools. In addition, a pack of microbiology teaching materials has been sent to every entering school and each student has received a certificate of participation in the competition. Further details of the winners are available on the SGM website.

A selection of the leaflets will be displayed at the Annual Meeting of the Association for Science Education at the University of Guildford in January 2001 as part of an international celebration of pupils' science work. It is also hoped that the Health Education Authority will be able to use the leaflets to promote vaccination.

MISAC wishes to express its sincere thanks to the sponsors of the competition: British Society for Immunology, Federation of European Microbiological Societies and Don Whitley Scientific.

● **Daniel Burdass, SGM**

WHY CHILDHOOD DISEASES STILL EXIST?

- Diphtheria
- Meningitis (infects your brain)
- Hepatitis B
- Measles
- Mumps
- Pertussis ("Whooping Cough")
- Polio
- Rubella ("German Measles")
- Tetanus ("Lockjaw")

WHY BOTHER WITH IMMUNIZATIONS?

- Unfortunately, some parents think that by allowing their children to get the disease, they will be able to produce the antibodies naturally. The best disease to illustrate this is all very serious. They can make children very sick. Some will die. Some will have long-term health problems and children in the days before immunization.
- Keeping children healthy and preventing these serious diseases and their complications are only two of the reasons for immunization. From a practical standpoint, children may not be allowed to enter day care, school or sport activities if they haven't been immunized.

ARE IMMUNIZATIONS SAFE?

- All medications can have some unwanted effects. This is true of vaccines as well. Most of the effects are mild - sometimes or

the injection site, occasionally a mild fever. For a very, very few children, however, more serious side effects are possible. The most common, but still of concerning the disease is far greater than the risk of suffering a serious side effect from the immunization.

- This is a classic case of varicella (Chicken pox) of the newborn.
- This child's leg has been damaged by polio.
- This newborn is not prepared - she died of liver cancer caused by hepatitis B virus infection.
- Small pox can now be eradicated by immunization.

The prize leaflets were selected because they displayed accurate knowledge which was attractively presented in a format suitable for the target audience of parents.

The first-prize winners in the 11-14 group were **Sam Piper** of Woodbridge School and **Laura Feaver** of St Margaret's School, Exeter, and in the GCSE range were **Kate Riley** of Stafford Grammar School and **Natalie Gillam** of the Royal High School, Bath.

Meetings

Meetings on the web

Up-to-date information on future Society meetings is available on the website: <http://www.sgm.ac.uk>

Meetings organization

The SGM meetings programmes are organized by the committees of the special interest groups, coordinated by the Scientific Meetings Officer, Dr Pat Goodwin. Suggestions for topics for future symposia are always welcome. See p. 156 for contact details of Group Conveners. Administration of meetings is carried out by Mrs Josiane Dunn of the Meetings Office at SGM Headquarters, Marlborough House, Basingstoke Road, Spencers Wood, Reading RG7 1AG Tel. 0118 988 1805 Fax 0118 988 5656 email meetings@sgm.ac.uk

Millennium meeting

University of Warwick
April 2000

Fighting Infection in the 21st Century
Symposium volume

This will be available later in the year from Blackwell Science. The price will be £65, with a 40% discount for members of SGM and SfAM. To receive an order form when the book is published, please complete the form on the meetings page of the SGM website, or contact the Events Administrator.

Autumn 2000

147th Ordinary Meeting

University of Exeter
12–15 September 2000

● Main Symposium (12–13 September) Community Structure and Co-operation in Biofilms

Organizers: P. Gilbert, P.M. Goodwin, H.M. Lappin-Scott and M. Wilson
Further information about the content of the symposium appears on pp. 136–137.

● PROGRAMME BOOKLET

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

● SYMPOSIUM VOLUME 59

The book of the Main Symposium will be on sale at the meeting. An order form for members will be published in the November issue of *Microbiology Today*.

● OFFERED POSTER PRESENTATIONS

Will delegates whose offered posters have been accepted please note that an area of 1 m x 1 m ONLY is available on the poster boards for their display.

● MICROSCENE NOTICEBOARD

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

● HISTORY OF MICROBIOLOGY LECTURE

1745 Tuesday, 12 September

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

Colin R. Howard (Royal Veterinary College, London)

In this first talk of a new series at SGM meetings, which aims to explore various historical perspectives of microbiology, Professor Howard will discuss his researches into why the UK public at large has an ingrained resistance to immunization and how this resistance has emerged. The lecture is based on material held in the Reece Collection at the London School of Hygiene and Tropical Medicine. Professor Howard is Vice-Principal for Research at the Royal Veterinary College. His own current researches focus on novel vaccines and post-exposure immunotherapy.

Offered Posters

Offered posters are welcome but each one should be associated with a Group. General Offered Posters will no longer be accepted. Titles and abstracts should be sent to the appropriate Convener, preferably by email. The subject content should be relevant to the remit of the Group (see website for details); it does not have to relate to the topic of the Group Symposium taking place at the particular meeting. Abstracts are required in a standard format – see website for details or contact the Events Administrator.

Promega Prize

- Are you
- a member of the SGM?
 - under 28 years of age?
 - a postgraduate or first postdoc?
 - thinking of presenting an offered paper or poster at an SGM meeting?

Why not enter for the Promega Prize Competition? You could win £200 in the SGM section of the competition and go on to compete for a further £2,000 in the *Young Life Scientist of the Year* event. Contact the Meetings Office or see website for details.

2000 Competition

Don't miss the 2000 final of the SGM round of the competition. It takes place at Exeter on **Wednesday 13 September**. Nine young members will make 10 minute oral presentations on their work. See enclosed programme booklet for details.

Future Meetings

SPRING 2001 – 148th Ordinary Meeting

Heriot-Watt University, Edinburgh
26–30 March 2001

● Main Symposium New Challenges to Health: the Threat of Virus Infection

Organizers: P.M. Goodwin, W.L. Irving, J. McCauley, D.J. Rowlands and G.L. Smith

Speakers:
C.J. PETERS (Atlanta) *Surveillance and detection of viruses*
B. GRENFELL (Cambridge) *Overview of the epidemiological impact of viruses*
R. ELLIOTT (Glasgow) *Hantavirus/bunyavirus*
B. RICHARDSON (Sydney) *Calicivirus*
A. HAY (NIMR) *Influenza virus*
S. LEMON (Texas) *Hepatitis virus*
R. WEISS (London) *HIV*
T. BARRETT (Pirbright) *Marbilliviruses*
C. WEISSMAN (London) *TSEs*
J.P. STOYE (NIMR) *Endogenous retrovirus/xenotransplantation*
C. BOSHOFF (London) *Gammaherpesviral infections in immunocompromised populations*
H.-D. KLENK (Marburg) *Ebola and Marburg viruses*
D. GUBLER (CDC, USA) *Dengue virus*
H. LUDWIG (Berlin) *Borna viruses*
G. DARBY (Stevenage) *Drug development and drug resistance*

New! Clinical Microbiology Group

The new Clinical Microbiology Group will be launched at this meeting. There will be a one-day symposium and a half-day session of offered papers. Offered posters will also be welcome. Contact the Group Convener, Stephen Gillespie (stepheng@rfc.ucl.ac.uk) for further details.

● Other Symposia, and Workshops

● Wall-less organisms Cells & Cell Surfaces Group

Organizers: I. Sutcliffe (iain.sutcliffe@sunderland.ac.uk) and M.J. Woodward (mwoodward@cvt.wood.gtnet.gov.uk)

● Monitoring and treatment of blood-borne viruses

Clinical Virology Group

Organizers: J. Connell (jeff.connell@ucd.ie) and C. McCaughey (cmccaughey@qub.ac.uk)

● Benchmarking in microbiology education

Education Group

Organizer: T. Cartledge (trevor.cartledge@ntr.ac.uk)

● Microbe-pollutant interactions: biodegradation and bioremediation

Environmental Microbiology Group

Organizer: K. Semple (k.semple@lancaster.ac.uk)

● Biotransformations Fermentation & Bioprocessing and Physiology, Biochemistry & Molecular Genetics Groups

Organizer: R. Hall (rmh3435@ggr.co.uk)

● New enzyme targets for anti-microbials

Microbial Infection Group with Biochemical Society

Organizer: L.J.V. Piddock. Please contact the Group Convener P. Andrew (pwa@le.ac.uk)

● Microbiology of nitric oxide

Physiology, Biochemistry and Molecular Genetics Group

Organizer: M. Larkin (m.larkin@qub.ac.uk)

● Post-transcriptional control of gene expression

Virus Group

Organizer: I. Brierley (ib103@mole.bio.cam.ac.uk)

● Special symposium: Genomics and their impact on bacterial systematics

Systematics & Evolution Group with the International Committee on Systematic Bacteriology

Contact G. Saddler (g.saddler@cabi.org) for details

● Evening workshop for young members: Genomics

Physiology, Biochemistry and Molecular Genetics Group

Organizer: M. Larkin (m.larkin@qub.ac.uk)

Offered posters are welcome. Please submit titles and abstracts to the appropriate symposium organizer or Group Convener by the deadline of **17 November 2000**.

AUTUMN 2001 – 149th Ordinary Meeting

University of East Anglia
11–13 September

● Main Symposium Mycobacteria: New Developments

Organizers: M. Goodfellow, P.M. Goodwin, H.M. Lappin-Scott, G. Saddler and D. Smith

Other symposia include: Microbial lifestyles/Research supervision – how to get it right/ Microbial interactions in aquatic environments/Monitoring and control of fermentation bioprocesses/Mobile elements in virulence/Clinical aspects of actinomycetes.

Irish Branch

Microbial Pathogens of the Respiratory Tract

National University of Ireland, Maynooth
7–8 September 2000

Speakers:
D. O'FLANAGAN (Ireland) *Epidemiology of tuberculosis in Ireland*
D. VAN SOOLINGEN (The Netherlands) *Use of DNA fingerprinting to examine the transmission of tuberculosis*
J. McFADDEN (University of Surrey) *Tuberculosis: identification, control and epidemiology*
M. CORMICAN (Galway) *Anti-bacterial drug resistance in lower respiratory tract infections*
J.P. LATGE (Institut Pasteur) *Molecular and cellular strategies to study the virulence of Aspergillus fumigatus*
D. DENNING (Manchester) *Diagnosis and management of invasive aspergillosis*
K. MILLS (Maynooth) *Mechanisms of immunity to Bordetella pertussis*

Offered oral and poster presentations welcome, especially from postgrads and postdocs who could win a prize. Deadline for receipt: **31 July 2000**.

For details contact the organizer Kevin Kavanagh (kkavanagh@may.ie)

Title t.b.c.

Waterford Institute of Technology
4–5 January 2001

Offered papers from postgraduates welcome.

Organizer: Catherine O'Reilly (coreilly@wit.ie)

Functional Genomics of Microbial Pathogens

Trinity College Dublin
22–23 March 2001

Organizer: A. Bell (abell@tcd.ie)

For details of Irish Branch activities contact the Convener, Martin Collins (m.collins@qub.ac.uk)

Other News

European Virology 2000

17–21 September 2000

Royal Concert Hall, Glasgow

Supported by a wide range of European virology organizations, including the SGM, the meeting aims to provide a forum for basic researchers and clinical virologists to exchange insights and information and enhance interactions. It is hoped that 1,200+ delegates will attend from around the world. Each day the plenary sessions will be followed by four workshops with a keynote speaker and offered papers and posters.

Plenary sessions include: Vaccines, Neurovirology, Hepatitis, Viruses & Cancer, Respiratory Viruses, Emerging/Disappearing Viruses, Viruses & the Immune System.

For further details and to register, see the website: www.euro-virology.com or contact: In Conference Ltd, 10B Broughton Street Lane, Edinburgh EH1 3LY (Tel. 0131 556 9245; email inconference@cablenet.co.uk).

● BURSARIES

Grants are available from the SGM for young members wishing to attend this meeting. Application forms can be downloaded from the website: www.sgm.ac.uk See the May issue of *Microbiology Today*, p. 93, for details.

● SGM STAND

SGM will have a stand in the trade exhibition. Please call in to learn about Society activities and publications and to meet the JGV editorial team.

New Meetings Officer

Howard Jenkinson



Howard graduated with a BSc in microbiology and virology at the University of Warwick (1975) and a PhD in applied biochemistry at the University of Nottingham in 1978. He then worked for 5 years as a postdoctoral research assistant with Joel Mandelstam at Oxford on the biochemistry and genetics of sporulation by *Bacillus subtilis*. He was appointed lecturer in Oral Biology at the University of Otago, New Zealand, in 1983, promoted to senior lecturer in 1987 and awarded a personal chair in 1996. During this period he was a Commonwealth Visiting Fellow at the Department of Biochemistry, University of Cambridge (1989–90) and at the Institute of Molecular Medicine, University of Oxford (1995–96). He was appointed to the Chair of Oral Microbiology at the University of Bristol in July 1997. Howard was Secretary, then President, of the New Zealand Section of the International Association for Dental Research (1987–94), Secretary of the New Zealand Microbiological Society (1991–94) and has been a member on the Cells & Cell Surfaces Committee since 1996. He is standing down from Convener of this Committee to take on the job of SGM Scientific Meetings Officer. Howard's primary research interests are concerned with the molecular characterization of microbial cell surfaces, in particular the adhesion and colonization determinants of bacteria, and their interactions with mammalian host cells and tissues.

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

THIS PAGE (RIGHT): During the development of *D. discoideum*, amoebae enter an aggregate by chemotaxis toward cAMP. This experiment shows that cells of a cheater mutant (labelled with green fluorescent protein) and those of the wild-type (detected by phase contrast) enter an aggregate with approximately equal efficiency. Each amoeba is 8–10 µm in diameter. See the following website for an animated view of aggregation: <http://cpmcnet.columbia.edu/dept/gsas/anatomy/Faculty/Kessin/index.html>

COURTESY DEE N. DAO (WHO THANKS MARY WU AND THERESA SWAYNE OF THE COLUMBIA UNIVERSITY CONFOCAL FACILITY FOR ASSISTANCE)

OPPOSITE PAGE (UPPER): Volcanoes National Park, Hawaii, from where the yeast *Pichia hawaiiensis* was isolated some 20 years ago.

COURTESY TRAVEL INK/GERAINT TELLEM

OPPOSITE PAGE (LOWER): Multiple resistance of transgenic tobacco plants. Plants were inoculated with TuMV (row 2) or TSWV (row 3) first, then those plants that did not show systemic symptoms after 34 days were inoculated with TSWV (row 2) or TuMV (row 3). Rows 1 and 4 were non-transgenic controls inoculated with TuMV and TSWV, respectively. The plants were photographed after 49 days.

COURTESY DENNIS GONSALVES, CORNELL UNIVERSITY, NY, USA

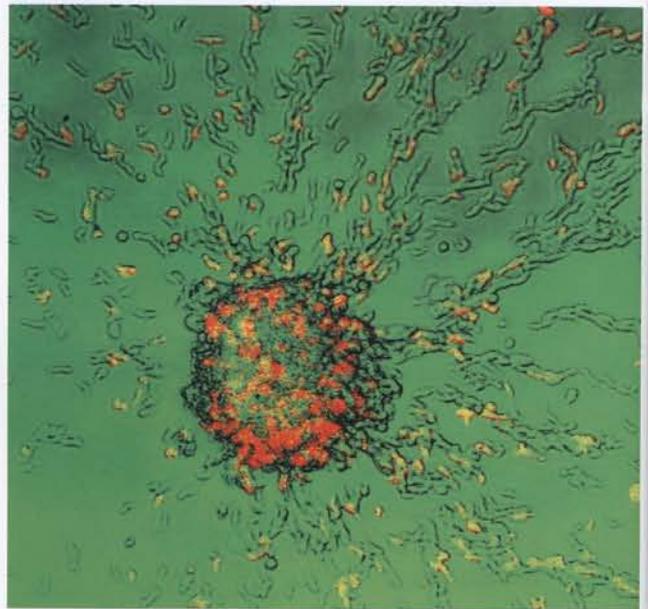
Recombination network

Molecular biology provides a new way of tracking epidemics, and can shed light on the origin of diseases. There is an epidemic of cotton leaf curl disease, which has spread through the major cotton-growing areas of Pakistan since 1985, caused by a novel series of forms of begomovirus. Begomoviruses cause many important plant diseases and typically carry all their genetic information on two circular single-stranded DNA molecules (DNA-A and DNA-B). The virus spreading through Punjab and Northern Sindh is unusual in apparently only containing DNA-A, along with a second very small circular strand of DNA that resembles part of the genome of a nanovirus and occasionally a third circle of DNA that is a defective piece of DNA-A. There are at least four types of this Pakistan cotton leaf curl virus (CLCuV-PK) DNA-A. All share sequences with a begomovirus that infects the vegetable okra, while the differences between some types are as much as between other begomovirus species.

The implication from this, and other, research was that CLCuV-PK in Pakistan was very prone to recombining its genetic information, with both itself and other begomoviruses. This requires plants to be infected with more than one begomovirus simultaneously. Researchers in Pakistan, Spain and the UK, led by Bryan Harrison and David Robinson from the Scottish Crop Research Institute, have been investigating exactly how many types of begomovirus can be found in leaves from cotton, okra and other plants in Pakistan. They have now reported a series of molecular biological experiments which identify substantial stretches of DNA-A from each type of CLCuV-PK very precisely, and pay particular attention to regions that seem prone to recombination.

Their results indicated that many plants in Pakistan were infected with more than one begomovirus. In one series of tests they found signs of two, or even three, types in 14 out of 43 plants. This happened in cotton, its relatives, and in totally unrelated plant species like tobacco and bottlegourd. Another test detected recombinant begomovirus sequences in 8 out of 18 plants. When the researchers examined begomoviruses extracted from plants growing outside the region of the cotton leaf curl epidemic, they could detect single infections with viruses that matched parts of CLCuV-PK, but not the whole of it. The relationships between the begomoviruses in Pakistan look like a network maintained by frequent recombination, a much more complex situation than reported in other parts of the world. New variants, like those causing the current epidemic of CLCuV-PK, can emerge and undergo further recombination, generating even more variants. The reasons for these constant genetic changes still await discovery.

Sanz, A. I., Fraile, A., García-Arenal, F., Zhou, X., Robinson, D. J., Khalid, S., Butt, T. & Harrison, B. D. (2000). Multiple infection, recombination and genome relationships among begomovirus isolates found in cotton and other plants in Pakistan. *J. Gen. Virol.* 81, 1839–1849.

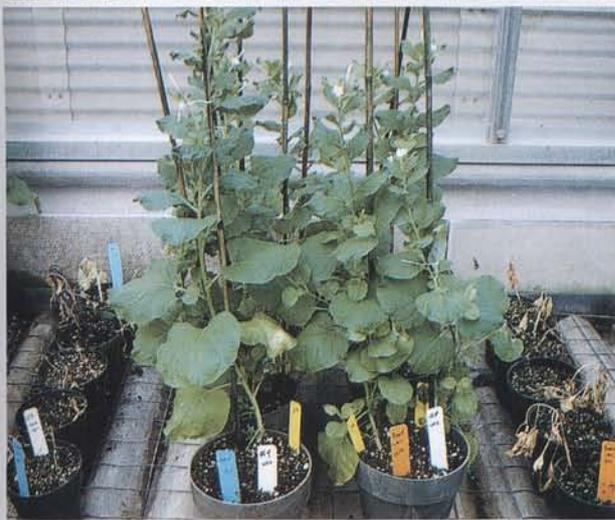


Developmental cheating

You always have the idea that microbes lead a lonely, single-celled life. However, individuals of some species can get together for a very definite purpose. The amoeba-like cells of the eukaryotic slime mould *Dictyostelium* normally live alone, engulfing their bacterial prey. When the supply of bacteria run out, they emit a chemical signal and 100,000 *Dictyostelium* individuals will come together and differentiate into a stalk with a mass of spores on top. Eighty percent of the cells make it into spores. The remainder will die, sacrificing themselves to shoot the spores away from the barren area and into the path of passing insects that will disperse the spores.

This type of mass suicide for the benefit of the species also happens in the myxobacteria, a group of prokaryotic microbes. These hunt as packs, secreting enzymes to digest other bacteria and then absorbing the resulting soup. When they run out of prey, they too aggregate and develop into a fruiting structure that unfortunately probably requires the death of most of the cells.

These microbes may provide insight into the evolution of the multicellular lifestyles adopted by most plants and animals. But they also interest scientists studying parasitism because of an unusual problem. Unlike most animals, the cells that get together are not genetically identical. Although differentiation may be good for the species, it is not necessarily good for each individual. Any *Dictyostelium* that finds itself in a stalk has come to a dead end. As Rich Kessin and his colleagues, Dee N. Dao and Herbert L. Ennis, at Columbia University, USA, point out, over evolutionary time, and given the genetic diversity in the wild, strains (called cheaters) should evolve that refuse to contribute to the stalk of *Dictyostelium* or the fruiting structures of myxobacteria. These strains would, in effect, be parasitic on their own species. The researchers predict that cheater strains of *Dictyostelium* should only form spores, and ignore signals



from other cells to participate in a stalk. They might even actively drive wild-type cells into becoming the stalk. One new difficulty for such strains might be an inability to form a fruiting body without wild-type cells.

But is there any evidence for cheater strains? There are strains of myxobacteria that are very bad at making spores on their own, but are efficient when paired with a normal partner. Myxobacterial spores are sticky and this may help cheaters to attach themselves to an exploitable strain. There is also suggestive evidence from some wild slime moulds, but the Columbia group now have direct evidence in the form of a cheater mutant (*chtA*). They isolated it by selecting cells of *Dictyostelium discoideum* that over many generations always ended up in spores. The *chtA* mutant cannot produce spores unless it is mixed with a few wild-type cells, which always form the stalk. The final signal for spore production comes from the stalk, so the *chtA* mutant relies on exploiting its law-abiding fellows. The mutation in the cheaters is in a protein that probably marks other proteins out for destruction. The targets are not known yet, but might include ones that regulate the final steps in spore production. The group is in hot pursuit of the target proteins.

This ability to make an unfair contribution to the next generation is not confined to microbes. In most animals, all cells apart from the gametes are genetically identical, and the cells that give rise to the gametes are themselves set apart early on in the embryo. Only they have any possibility to acquire an unfair share of the future. Despite this limited potential for cheating, a system called meiotic drive has developed that allows some gametes, particularly in *Drosophila* and in mice, to make unequal contributions to offspring. Cheating must be defeated somehow or else evolution would not occur.

Dao, D.N., Kessin, R.H. & Ennis, H.L. (2000). Developmental cheating and the evolutionary biology of *Dictyostelium* and *Myxococcus*. *Microbiology* 146, 1505–1512.

Gene silencing

When viruses infect plants, they take over the plant to make large amounts of the virus, rather than the normal components of a plant cell. Not surprisingly, many plants have developed ways to detect this abnormal activity and eliminate it. The plant's defences can act at the most fundamental level of gene activity and specifically destroy any instructions for making viral components as soon as they are synthesized. This process is called post-transcriptional gene silencing (PTGS).

Although the mechanism of PTGS is not fully understood, biotechnologists think it can be exploited to develop new varieties of virus-resistant plants and are exploring ways to do this. Tomato spotted wilt virus (TSWV) and turnip mosaic virus (TuMV) are, despite their names, among the 10 most important viruses that cause disease in vegetables. They both infect a much wider variety of plants than their names imply. Researchers at Cornell University, USA, have been investigating whether transgenic plants can be protected from both these diseases simultaneously by PTGS.

Several research groups have protected plants by adding whole viral genes to them. However, there are concerns that this might produce altered forms of virus. Dennis Gonsalves and his colleagues have now reported that only parts of a viral gene are required, provided they are attached to another gene that triggers PTGS. They have produced tobacco plants containing the gene for a TuMV protein joined onto a small part of a gene from TSWV. Some of these plants were resistant to both viral diseases. Interestingly, other plants were only resistant to TuMV and the researchers hope that these may help them discover which are the most effective gene segments for plant protection.

Jan, F.-J., Fagoaga, C., Pang, S.-Z. & Gonsalves, D. (2000). A single chimeric transgene derived from two distinct viruses confers multi-virus resistance in transgenic plants through homology-dependent gene silencing. *J Gen Virol* 81, 2103–2109.

The SGM publishes two monthly journals, **Microbiology** and **Journal of General Virology**.

The **International Journal of Systematic and Evolutionary Microbiology (IUSEM, formerly USB)** is published bimonthly on behalf of the IUMS in conjunction with the ICSB.

The three journals are now available online. For further information visit the journal website: <http://www.sgmjournals.org>

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Hawaii 2-0

The native trees of Hawaii have their own unique fungi, found nowhere else in the world. Cletus Kurtzman and his colleagues have now described one of them, the single-celled yeast *Pichia hawaiiensis*. It was found on rotting bark from *Charpentiera* trees in Volcanoes National Park on the island of Hawaii over 20 years ago, but its identity has always been uncertain. The traditional way of identifying yeasts is to test their ability to digest a large number of compounds. This can work very well, but runs into problems in some closely related species.

The American researchers have applied a new molecular biological method to sort out these difficulties. This relies on technical improvements so that large pieces of DNA can now be isolated and sequenced routinely. Earlier research by this group had shown that, in most ascomycete yeasts, one region of the gene for a structural component of ribosomes (26S rDNA) was sufficiently variable to distinguish one from another. When they applied this method to their Hawaiian isolates, it was obvious that they were different from all currently recognized species, although closely related to *Pichia populi* and *Williopsis californica populi*.

Phaff, H.J., Starmer, W.T. & Kurtzman, C.P. (2000). *Pichia hawaiiensis* sp. nov., occurring in decaying bark of *Charpentiera* trees in the Hawaiian archipelago. *Int J Syst Evol Microbiol* 50, 1683–1686.

OPPOSITE PAGE (FAR RIGHT): EPEC interacting with microvillus-like processes on HEp-2 cells. COURTESY ROBERT FITZHENRY, GADI FRANKEL, FABIENNE LAMOUREUX AND ALAN PHILLIPS

THIS PAGE (RIGHT): A scuba diver (Susanne Menger, Max Planck Institute for Marine Microbiology, Bremen, Germany) carrying out fine-scaled *in situ* measurements of temperature and pH at the hot water vent in Palaeochori Bay (Milos, Greece) in 8 m of water.

COURTESY WIEBKE ZIEBIS, MAX PLANCK INSTITUTE FOR MARINE MICROBIOLOGY, BREMEN, GERMANY

THIS PAGE (BELOW): Ultrathin section of cells of *Thiocapsa litoralis* BM5¹ from late-exponential growth phase showing a typical four-cell aggregate. The formation of thick cell septa and a mucous capsule keeps the cells together. Cells are approximately 1 µm in diameter.

PHOTO L.L. MITYUSHIMA
COURTESY JOHANNES F. IMHOFF,
INSTITUT FÜR MEERESKUNDE, KIEL,
GERMANY

Microbiology *Pseudomonas* special issue

Microbiology is publishing a special issue of the journal in October 2000, part of which will be devoted to pseudomonads. This issue will include peer-reviewed research papers from leading groups.

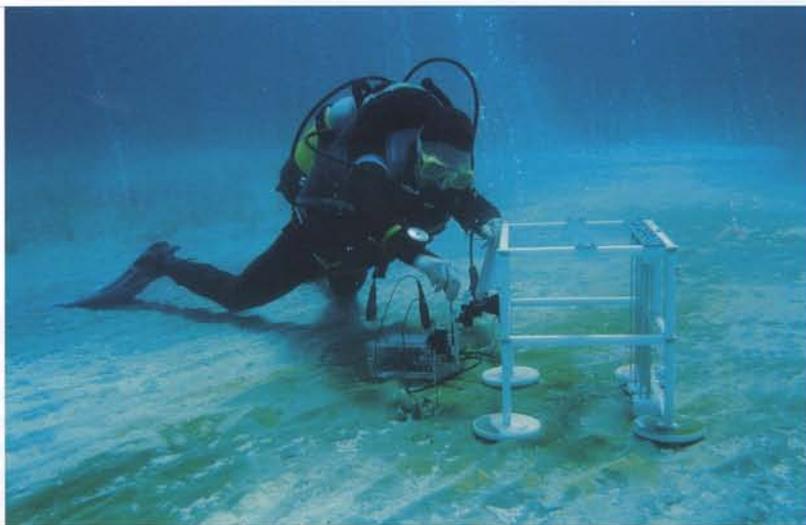
For further information and an order form see our website at:

http://www.sgm.ac.uk/mic_main

Purple haze

The beaches of the White Sea have shallow lagoons containing mats of microbial communities. Many of the microbes are photosynthetic, even ones that live on the surface of the sulphur-rich mud. They have special pigments to exploit the dim light effectively and use the sulphur compounds in place of water in reactions that convert light into a form of energy that is useful to a living cell. *Thiocapsa litoralis* is a newly discovered example of these bacteria. Its non-motile spherical cells stay together in small flat clusters, called platelets, surrounded by a thick capsule. The cells are pink to rose-red in colour and contain globules of elemental sulphur, formed as intermediates in metabolism.

Its identity, like that of all the *Thiocapsa*, is not determined by appearance alone. Another important feature is the sequence of part of a structural component of its ribosomes. These complex cell organelles synthesize proteins and can only tolerate limited alterations without suffering impaired function. By carefully choosing which areas to examine, taxonomists can see evolutionary changes to this molecule that translate



into the differences between species, genera or even whole kingdoms. As part of a collaborative project, researchers at the Institute of Microbiology in Moscow and Institut für Meereskunde at Kiel in Germany studied this feature in a newly isolated strain from the White Sea that looked like a *Thiocapsa*. The study confirmed that it certainly was a *Thiocapsa*, but sufficiently different from all known species of this genus to be a brand new species, *Thiocapsa litoralis*.

Puchkova, N.N., Imhoff, J.F. & Gorlenko, V.M. (2000).

Thiocapsa litoralis sp. nov., a new purple sulphur bacterium from microbial mats from the White Sea. *Int. J. Syst. Evol. Microbiol.* 50, 1441–1447.

If you can't stand the heat...

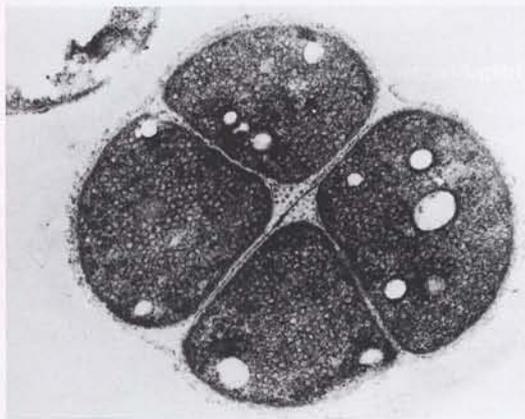
The prokaryotes now known as *Archaea* were originally detected as the only living cells in extreme habitats such as super-heated water or concentrated brine. Taxonomists have now classified prokaryotes into two domains, the *Archaea* and the *Bacteria*. It made a nice story that *Archaea*, which perhaps resembled the first life on Earth, only survived in undesirable places that more advanced organisms had abandoned. However, it is becoming apparent that this is far from the truth. It all depends on how you go looking for signs of life.

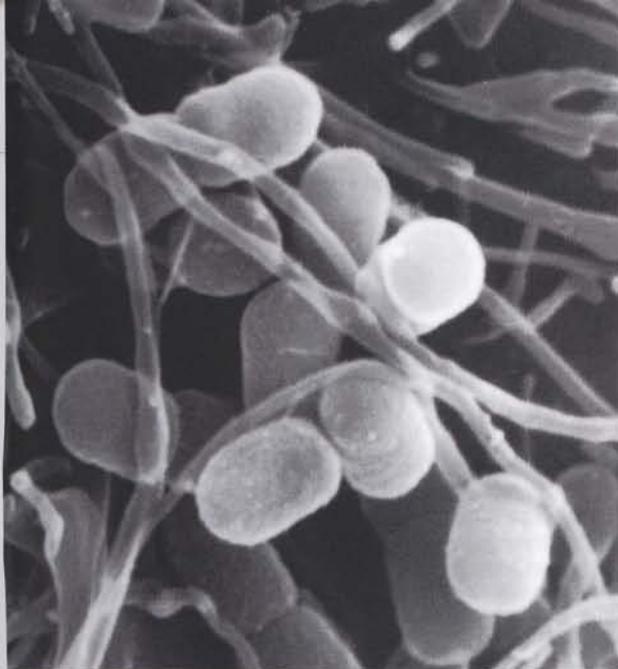
Microbiologists have known for a long time that if you search for bacteria by their ability to grow in the laboratory, you will miss ones that do not like the growth conditions on offer. So, they have a number of other ways to detect bacteria. One of these uses rRNA, which is part of the protein synthetic machinery of all cells. Cells need to make many proteins, so each has lots of rRNA molecules. Another useful feature of rRNA is that it contains conserved parts that evolve very slowly over geological time, as well as parts that evolve at a faster rate. Microbiologists can therefore use this information to identify bacteria at species, family and even kingdom level.

A group of researchers at the Max Planck Institute for Marine Microbiology in Bremen, Germany, have now reported their work on the bacteria living around a hydrothermal vent in a sandy bay off the island of Milos in Greece. This vent is another symptom of the geological processes that produce earthquakes and volcanoes in the region. Working in 8 m of water, scuba divers could collect sediment cores and simultaneously take their temperature. Back in Germany, the researchers sliced up the cores and extracted the rRNA. They then measured how much there was from either *Archaea* or *Bacteria* at different temperatures and depths.

The rRNA sampling showed that almost all the prokaryotic cells were in the top 2 cm of sediment, with much more near to the vent than in the cooler regions only 2 m away. The really surprising result was the proportion of *Archaea*. These were always a minor part of the microbial community, reaching only 11.9% in sediments at 82 °C. This matches some earlier reports from deep-sea vents and terrestrial hot springs, but is the first from a systematic study of the microbes living along a thermal gradient. However, the factors that allow *Bacteria* to dominate in a high temperature environment that was once believed to be the realm of *Archaea* remain elusive.

Sievert, S.M., Ziebis, W., Kuever, J. & Sahm, K. (2000). Relative abundance of *Archaea* and *Bacteria* along a thermal gradient of a shallow-water hydrothermal vent quantified by rRNA slot-blot hybridization. *Microbiology* 146, 1287–1293.





Bridging the gap

Diarrhoea is unpleasant at any age but strains of *Escherichia coli* called EPEC are a common cause of life-threatening diarrhoea in infants in the developing world. EPEC change the surface of intestinal cells. The microvilli, which normally absorb nutrients from food, are destroyed and bacteria become cradled in cup-shaped protrusions of the cell membrane. The EPEC strains force these changes onto the intestinal cells via the proteins they secrete. One of these, Tir, ends up in the intestinal cell membrane and another, intimin, can attach to Tir. EspA forms a structure on the surface of the EPEC cells that is needed to secrete EspB and Tir, as well as bridging the gap between the bacterial and intestinal cells. The importance of each of these, or other, proteins in the disease symptoms and exactly what they do are still unclear.

However, a collaborative project between Alan Phillips at the Royal Free Hospital in London and Jorgé Girón at Benemérita Universidad Autónoma de Puebla in Mexico, along with Gadi Frankel at Imperial College in London, have now pinned down a second role for intimin. They compared classic EPEC strains with others that lacked the ability to produce either intimin, Tir, EspA or EspB. The researchers grew layers of cells in culture and then put the bacterial cells onto them and took photographs over the next few hours with an electron microscope. Within an hour of adding EPEC bacteria, microvillus-like processes (MLP) had appeared as tubes on the surface of infected cells that grew to enmesh and anchor the bacteria. After another hour the MLP had degenerated to leave typical localized adhering clusters surrounded by cell debris. These had completely covered the cell surface after 6 hours. The scientists obtained similar results when they used their bacterial strains with samples of real intestine that had been removed from children, after the consent of parents and an ethical committee.

When they repeated their experiments with the strains that lacked individual proteins, one role of intimin became obvious. It was essential to trigger MLP production and elongation. Without intimin, the MLP were few and short and very few bacteria became attached to the cell layer. With it, MLP would even grow to envelop intimin-coated latex beads. This suggests that although Tir is one attachment point, there must be at least one other that is a normal part of intestinal cells. Additionally, proteins like Tir and EspB may be required for MLP degeneration, since much larger, cage-like structures appeared on cultured cells that were incubated with bacterial strains lacking them.

Phillips, A.D., Girón, J., Hicks, S., Dougan, G. & Frankel, G. (2000). Intimin from enteropathogenic *Escherichia coli* mediates remodelling of the eukaryotic cell surface. *Microbiology* 146, 1333–1344.

Announcing JGV Direct!

Journal of General Virology has a new web-based service. **JGV Direct** will publish selected JGV papers up to 3 months before they appear in print. The papers will be in HTML format, with all figures and tables. All papers published in **JGV Direct** will subsequently appear in the print journal of JGV. This site is freely available to all.

<http://www.sgm.ac.uk/>

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Antifungal toxin from fishery waste bacteria

The newest member of the genus *Paenibacillus* can produce an antifungal compound, the first member of its genus found to do so. Researchers in Korea isolated it among the bacteria that emerged from rice husk and fishery waste. They spread the diluted waste over laboratory media, with chitin as the sole source of nutrition. The reason for this restricted diet was that chitin is a major part of the cell wall of many fungi. Anything that could live on it alone might also be able to destroy fungi, and the bacteria were tested for this ability. One isolate was particularly impressive at inhibiting fungal growth, and it has turned out to be a *Paenibacillus*. Members of

this genus were already known for their production of enzymes that degrade natural polymers as well as antibacterial compounds, but none has shown antagonism to fungi before.

Paenibacillus have large rod-shaped cells that can sometimes switch to growth without any need for oxygen. Like all members of the family *Bacillaceae*, the cells can turn into survival structures called endospores in adverse environmental conditions. The distinguishing feature of *Paenibacillus* is the size and sequence of one region of its 16S rRNA molecule. When the researchers checked out their new strain, although it was definitely a member of *Paenibacillus*, it

was significantly different from the 24 other species. As well as differences in rRNA sequence, it had rather different nutritional requirements. The most interesting feature, however, was its ability to synthesize an antifungal toxin. This chemical was a small cyclic peptide from the iturin class. This means that *Paenibacillus koreensis*, as the new isolate has now been called, poisons fungi as well as taking their cell walls apart.

Chung, Y.R., Kim, C.H., Hwang, I. & Chun, J. (2000). *Paenibacillus koreensis* sp. nov., a new species that produces an iturin-like antifungal compound. *Int J Syst Evol Microbiol* 50, 1495–1500.

Reviews

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

Ingredients Handbook: Prebiotics and Probiotics

Edited by G. Gibson & F. Angus
Published by Leatherhead Food Research Association (2000)
LFRA Members £85.00/
Non-members £110.00, pp. 206
ISBN: 0-9057-48-824

While GM is currently harming most the public perception of science in relation to food, the up side is perhaps our potential ability to exploit micro-organisms in 'natural' ways to 'improve' the gut flora. Human preoccupation with bowel health invites science and faddism to meet, and enlarge the market for pre- and probiotics. This publication shows how. Editor Glenn Gibson's helpful introduction reminds the reader that 'pre' is nutrients, 'pro' is bugs. The nutrients, carbohydrates degradable only by bacteria, get most attention. Perhaps this reflects ignorance, in light of the incredible complexity of the gut flora, as to which ones are really beneficial. The material comes in a ring file, suggesting it might lie on the factory worktop for ready reference should one wish to stir in a tonne or two of inulin or lactulose. In that context I'm sure it will be valuable.

■ **Charles Penn**
University of Birmingham

Biofilms: The Good, The Bad and The Ugly

Edited by J. Wimpenny, P. Gilbert, J. Walker, M. Brading & R. Bayston
Published by BioLine for the Biofilm Club (1999)
Members: £22.00 (UK only)/
£23.00 (Europe)/£25.00 (ROW)
Non-members: £32.00 (UK only)/
£33.00 (Europe)/£35.00 (ROW)
pp. 371
ISBN: 0-9520432-6-2

Since the inaugural meeting in only 1993, the Biofilm Club has now become one of the primary arenas for researchers interested in this important area of microbiology, both in the UK and

around the world. This collection of over 40 articles includes previously unpublished data, as well as overviews of several key areas. The book, the fourth in the series of meetings, focuses on a range of themes from a diversity of backgrounds, including paper manufacturing, the food industry and medicine. The articles are laid out in a journalistic style so it is unlikely that the book could be read from cover to cover. However, it is well indexed and, as such, makes a good reference book. The book will be of particular interest to people who are already involved in biofilm research, especially when combined with the contributions from the previous three meetings.

■ **Jonathan Pratten**
Eastman Dental Institute, London

Dental Plaque Revisited. Oral Biofilms in Health and Disease

Edited by H.N. Newman & M. Wilson
Published by Bioline (1999)
Conference Delegates & Biofilm Club Members: £45.00 (UK)/
£50.00 (Europe)/£55.00 (ROW)
Others: £65.00 (UK)/£70.00 (Europe)/£75.00 (ROW)
pp. 599
ISBN: 0-9520432-7-0

The last time such a collection of papers dealing with dental plaques was published occurred some 30 years ago and so the appearance of this volume is certainly to be welcomed. The volume deals with bacterial biofilms – a really useful collection of up-to-date reviews on the topic in general; 'Oral bacterial biofilms', an accessible overview of the oral biofilm phenomenon; 'Plaque in health and disease', which tells you everything you hope will never go wrong with your mouth; 'Medical implications of oral biofilms', with an interesting paper on halitosis (perhaps a future 'citation classic' useful for those awkward conversations about oral hygiene!); and concludes with an overview of the treatment of

plaque-related diseases. This is a very useful overview of the topic although it is to be hoped we shall not have to wait quite as long for the next instalment of this fascinating story.

■ **Donald Reid**
The Robert Gordon University, Aberdeen

Monograph of the Oxytrichidae (Ciliophora, Hypotrichia)

By H. Berger
Published by Kluwer Academic Publishers (1999)
NLG880.00/US\$528.00/£308.00,
pp. 1,079
ISBN: 0-7923-5795-7

Oxytrichidae – a species-rich, well-known, yet highly confusing family of ciliates – has always attracted the interest of protozoologists working in the fields of ecology, taxonomy and cell biology. This up-to-date book provides comprehensive information on both historical and recent research, including a carefully defined synonymy list for each species, discussion (and corrections) of nomenclatural problems, detailed morphological and taxonomical descriptions with almost all published faunistic records, as well as tables providing complete morphometric data available. As another conspicuous feature, almost all ecological, physiological and faunistic information on each species scattered in the literature in the last 300 years is mentioned, which enables the user to determine species without referring back to the original literature. Thus, this book is not only a super field guide, but also a must-get reference book both for the novice and experienced taxonomists alike and should be on the shelves of every ciliatology laboratory.

■ **Weibo Song**
The Natural History Museum, London

Principles of Virology: Molecular Biology, Pathogenesis & Control

By S.J. Flint, L.W. Enquist, R.M. Krug, V.R. Racaniello & A.M. Skalka
Published by ASM Press (1999)
US\$89.95/£66.00, pp. 800
ISBN: 1-55581-127-2

This book very successfully achieves its aim in filling the gap between basic introductory texts and advanced reviews. Unlike many other virology texts, basic cell and molecular biology are described in detail, allowing a greater understanding of the ways in which viruses use and subvert the biochemical pathways of the host. The figures are clear and informative. In addition to the main body of text there are helpful inset boxes giving background information and detailed discussion of specific topics. Appendices giving concise details of viral structures, replication cycles and genome organization and expression are particularly useful. The book will be a valuable text for students as well as researchers who are new to a particular field. The book is detailed and yet very readable. The high price, however, is likely to restrict purchase of this book to institutions.

■ **Christopher Ring**
Glaxo Wellcome R&D, Stevenage

Carbohydrate Biotechnology Protocols. Methods in Biotechnology, Vol. 10

Edited by C. Bucke
Published by Humana Press (1999)
US\$89.50, pp. 337
ISBN: 0-89603-563-8

This relatively inexpensive volume represents a rather eclectic mix of topics ranging from microbial polysaccharides to maltodextrins and cyclodextrins, sugar nucleotides and enzymic transglycosylation. It brings together and provides more detail on methods which have appeared in the literature over the years. According to the Introduction it is aimed at newcomers to the field,

yet many will find the layout and descriptions daunting and even confusing. Each chapter follows a similar format but the result leads to a complex sequence of headings, often referring to material elsewhere, and a lack of clarity. Greater editorial control over the contributions might have achieved a simpler and more uniform style, improved diagrams and removed some of the grammatical errors such as 'is the bacteria' and factual errors such as the 'several million Daltons' mass ascribed to xanthan. There are now several excellent 'cookbooks' covering this general area and unfortunately there is no attempt to correlate the methods with those presented in *Glycobiology or Methods in Carbohydrate Chemistry*, etc.

■ **Ian Sutherland**
University of Edinburgh

Molecular Microbial Ecology of the Soil. Developments in Plant and Soil Sciences, Vol. 83
Edited by G. Hardarson & W.J. Broughton
Published by Kluwer Academic (1999)
£69.00/NLG195.00/US\$117.00, pp. 164
ISBN: 0-7923-5252-1

FAO/IEAE have carried out excellent work training scientists from developing countries. This volume covers work in soil microbial ecology, with a strong bias towards rhizobia nodulating *Phaseolus vulgaris*. These account for 14 of the 18 papers and form a useful and authoritative summary of recent work. However, the same papers, plus one on rhizobia as plant-growth-promoting bacteria, were published in *Plant and Soil* in 1998. So what is the point of this volume? There are introductory and concluding papers, and one on *rep*PCR fingerprinting of *Azospirillum*, but no index. Inevitably, the time between the original publication and the

present volume means that some of the material is out of date. It may be useful for the sponsors of the programme to have its output collected, but for anyone who has access to *Plant and Soil*, I can see no reason to spend a further £69 on this volume.

■ **Janet Sprent**
University of Dundee

Post-translational Processing: A Practical Approach No. 203
Edited by S.J. Higgins & B.D. Hames
Published by Oxford University Press (1999)
£31.95, pp. 352
ISBN: 0-19-963795-4

The *Practical Approach* books are well known for their descriptions of methodologies required to carry out specific assays and procedures in a variety of fields. It is sometimes difficult to know the nature of the readership at which these books are targeted. In this volume some protocols are too generalized (e.g. for that on phosphorylation of proteins *in vitro* one is tempted to ask, which proteins and which kinase?); conversely, other methods are highly specialized and will be of interest to only a few readers. There are some omissions, e.g. * no mention of the use of phosphorimager analysis for quantification of labelled phosphorylated proteins. An otherwise thorough chapter on protein degradation in mammalian cells has nothing on proteolysis in apoptotic cells or the caspase enzymes which mediate this. Nevertheless, this book is a valuable addition to the literature and should find its way on to several laboratory benches.

■ **Mike Clemens**
St George's Hospital Medical School, London

DNA Recombination and Repair. Frontiers in Molecular Biology, No. 22
Edited by P.J. Smith & C. Jones
Published by Oxford University Press (1999)
£31.95, pp. 224
ISBN: 0-19-963706-7

This book covers various aspects of DNA recombination in bacteria and lower and higher eukaryotes and will appeal to molecular biologists working in this field. Rather than dealing with basic mechanisms, the book, published in 1999, has eight diverse chapters, each dealing with a specific area of recombination in some detail. As the individual chapters are written by scientists currently researching in this area, there is a great deal of emphasis on an experimental approach to understanding the mechanisms involved. Research data is accompanied by diagrams (which would have benefited from colour) to clarify the principles involved. This book would be a good companion for the specialist but would not be as useful for the casual reader as the individual topics are covered in considerable depth and presuppose a good working knowledge of recombination. If this is your research area, it would be a useful addition to the laboratory library.

■ **Anne Glover**
University of Aberdeen

Current Clinical Topics in Infectious Diseases, Vol. 19
Edited by J.S. Remington & M.N. Swartz
Published by Blackwell Science (1999)
£59.50, pp. 360
ISBN: 0-632-04402-0

The 19th book in an established series represents an eclectic collection of reviews by expert authors. Most chapters are well written and helpful, in particular 'Emerging nosocomial infections and antimicrobial resistance' and 'Current concepts on animal bites'. Some titles are odd and less well focused, e.g. 'Sepsis in obstetric and gynaecologic patients' is

essentially an overview of sepsis in general and 'Pneumonia, tuberculosis and urinary tract infections of pregnancy' is as bizarre a title as I could find in the series. Reviews are often but not exclusively biased to a US perspective (e.g. 'Managed health care: outcomes and updates'), reflecting the authorship. In this context it is disappointing that, although a reasonable account is given, a US author has been chosen to write a chapter on prions (a UK subject if ever there was one!). The book is well priced and worthy of a place on library shelves as part of the *Current Clinical Topics* series.

■ **Mark Wilcox**
University of Leeds

Assessment and Control of Nonpoint Source Pollution of Aquatic Ecosystems: A Practical Approach. Man and the Biosphere Series, Vol. 23
Edited by J.A. Thornton, W. Rast, M.M. Holland, G. Jolankai & S.-O. Ryding
Published by The Parthenon Publishing Group (1999)
£52.00/US\$89.00, pp. 466
ISBN: 1-85070-384-1

Sometimes you can be put off by the title of a book, as I was with this, and I wasn't filled with the wildest enthusiasm when asked to read it, but I was very much mistaken. This book, part of the UNESCO *Man and the Biosphere* series, provides a very comprehensive coverage of nonpoint source of pollution of the aquatic environment. Nonpoint sources are defined as areas, such as the catchments, or on a smaller scale, urban developments or even fields rather than pipes or chimneys, from which a variety of pollutants enter aquatic ecosystems. The book describes types of pollution in great detail and it is well referenced. The chapters cover pollution measurement and monitoring, hydrological cycle and water quality, modelling,

control programmes and management systems. The aim of the book is to review current knowledge and experience and package it with a view to pollution management: it succeeds and forms a very useful reference book.

■ **Roger Pickup**
CEH-Windermere

Veterinary Virology, Third Edition
By F.A. Murphy, E.P.J. Gibbs, M.C. Horzinek & M.J. Studdert
Published by Academic Press (1999)
£56.95, pp. 629
ISBN: 0-12-511340-4

As one might expect from authors of this calibre, this is an impressive compilation of the full range of current knowledge on viruses and viral diseases of veterinary importance. I was particularly impressed by Part I, which deals with the principles of veterinary virology in a readable concise manner without losing any of the latest scientific information emanating from veterinary and other virological research. Both this and Part II (presented by individual virus families) are well illustrated with appropriate examples from veterinary and wider fields. The book will be of value to the veterinary clinician or pathologist who wants an approachable treatise on virology, and equally to the virology specialist who seeks insights into viruses and virus diseases beyond his/her own specialism. It will become an essential reference work for veterinary virologists and students, and should find a place in all veterinary libraries and local virology departmental collections.

■ **Steve Edwards**
Veterinary Laboratories Agency, New Haw, Addlestone

Induced Plant Defenses Against Pathogens and Herbivores: Biochemistry, Ecology, and Agriculture

Edited by A.A. Agrawal, S. Tuzun & E. Bent

Published by The American Phytopathological Society (1999)
US\$55.00, pp. 403
ISBN: 0-89054-242-2

This book provides an interface between the molecular world and the 'real world' of the whole organism in the environment. The book compiles information on a multitude of pests, catalogues the types of response they elicit, and discusses how these responses impact on plants' ability to survive attack in the field. Finally, accounts are presented of how these responses might be manipulated to improve crop fitness.

As a molecular biologist concerned with plant defence responses, I found the book very useful in the way in which these responses were correlated with performance. There are a few things which detract from the volume's impact, such as a seemingly random order for the chapters in each section and repetition of some information. Despite this, the text was up-to-date and broad-ranging in its coverage, and would be a useful point of reference for students or researchers in the area of plant defence.

■ **Mike Roberts**
University of York

DNA Virus Replication. Frontiers in Molecular Biology, Vol. 26

Edited by A.J. Cann
Published by Oxford University Press (2000)
£29.95, pp. 232
ISBN: 0-19-963712-1

The title of this book is rather misleading since it suggests that the contents would be an examination of the strategies which DNA viruses adopt to further their replication. Rather, it turns out to be a mixed bag of eight reviews covering specific aspects of the molecular biology

of some DNA viruses. However the contributions are very comprehensive (giving a total of over 1200 references) and do provide the reader with a fascinating insight into the molecular shenanigans of viruses as diverse as hepadna, papilloma and cytomegalovirus. To the non-specialist it is particularly revealing how much progress can be made without the facility of a permissive tissue culture system. Herpes viruses are well covered with 4 chapters on HSV, EBV and KSV as well as CMV. In all of these chapters, and especially the two on adenoviruses, the parallel unravelling of cellular and host regulatory mechanisms is a key feature. This book will be very useful for researchers who want to be well informed on both cellular and virus regulatory mechanisms associated with infection and latency.

■ **Willie Russell**
University of St Andrews

Prokaryotic Gene Expression: Frontiers in Molecular Biology, Vol. 21

Edited by S. Baumberg
Published by Oxford University Press (1999)
£32.95, pp. 346
ISBN: 0-19-963603-6

This book covers the main areas of its subject from a research perspective, with chapters written – sometimes elegantly – by experts in the field. It is a book that should be read and not merely used for reference. A problem with books called 'Frontiers in...' is that frontiers move in the time before publication. This is no exception, and for some chapters this time has been too long (from July 1995 in one case). The volume could have done with more rigorous editing: a chapter on DNA topology without a single explanatory diagram should not be permitted in a civilized society, and complex figures would have benefited from colour.

These are minor quibbles in an excellent book which will be compulsory reading for my graduate students. If you want to

understand the main mechanisms of bacterial gene regulation and to appreciate their history, breadth and detail, read this book.

■ **Nigel L. Brown**
University of Birmingham

Practical Statistics for Experimental Biologists. Second Edition

By A.C. Wardlaw
Published by John Wiley & Sons Limited (2000)
H/B £50.00; P/B £18.99, pp. 249
ISBN: H/B 0-471-98821-9;
P/B 0-471-98822-7

This book assumes it's not worth teaching students the mathematical principles of statistical tests (very true in my experience) and that the computer stats package MINITAB is very widely available (rather less so). With humour and patience, the reader is taken through the use of MINITAB to carry out the common statistical analyses of measurement, count and proportion data, plus correlation and dose-response, with emphasis on practical assumptions and limitations of the tests. The package doesn't do all of the tests properly, leading to some awkwardness in presentation, and no other stats package is usefully covered.

However, the examples and tests are nearly all relevant to microbiologists and the book could usefully be used as a self-learning statistics application course. Even without MINITAB, there's a lot that the uncertain user of statistics can easily learn from the very readable approach.

■ **Ron Bishop**
University of Ulster

Recent Advances in Carbohydrate Bioengineering

Edited by H.J. Gilbert, G.J. Davies, B. Henrissat & B. Svensson
Published by Royal Society of Chemistry (1999)
£69.50, pp. 312
ISBN: 0-85404-774-3

This is a book about enzymes, in particular carbohydrate-modifying enzymes. Despite the

title, this book covers all aspects of carbohydrate-modifying enzymes, 3D structures, mechanisms, domains (catalytic, binding, stability, etc.) phylogenetic classifications, site-directed mutagenesis and enzymes from extreme environments.

This book is a multi-author publication of the papers orally presented at the 3rd Carbohydrate Bioengineering meeting, April 1999. As such it is an accurate and up-to-date reflection of the research in this area. Some chapters are written as reviews, others as research papers. Microbiologists may find the catalytic chemistry of some chapters technically demanding, but throughout, the text is well presented and numerous diagrams aid the reader. I would recommend this book to anyone interested in carbohydrate-modifying enzymes and their potential in bioengineering, to postgraduate students, researchers and for institutional purchase. This book contains much of general interest but is too technically written for the general reader.

■ **Michael Stratford**
Unilever Research, Sharnbrook

Rotaviruses: Methods and Protocols. Methods in Molecular Medicine, Vol. 34

Edited by J. Gray & U. Desselberger
Published by Humana Press (1999)
US\$89.50, pp. 288
ISBN: 0-89603-736-3

This high quality compendium comprises 12 concise chapters, each presented in the same easy-to-follow layout. The protocols are step-by-step instructions and generally up-to-date. Highlights are a superbly illustrated review of rotavirus structure and the methods used (cryo-EM and X-ray crystallography); a description of two assays of virus entry, mechanisms of which are not fully characterized; and an excellently summary of the genetic analysis of rotavirus by

reassortment.

Also covered are pathogenesis, immunological methods, *in vitro* study of immunity, evaluation of vaccines and methods of typing/detection. Many of the techniques described, e.g. ELISA, immunostaining and RT-PCR, are generally applicable to other viruses and the rotavirologist might prefer to read specific research articles for details of the work. The book's focus on rotaviruses will attract only a very limited audience. Nevertheless, I think this book at \$89.50 is reasonable value and an essential reference for any laboratory undertaking rotavirus research.

■ **Ian N. Clarke**
Southampton

Human Virology: A text for students of medicine, dentistry and microbiology. Second Edition

By L. Collier & J. Oxford
Published by Oxford University Press (2000)
£24.95, pp. 224
ISBN: 0-19-262820-8

This book is a revised and updated version of the edition published in 1993 and its contents reflect the expansion in our knowledge since then. It serves as a very good introduction for those requiring a basic knowledge of medical virology. The book covers both the scientific and clinical aspects of the subject. The text is clear and concise. However, it is unfortunate that the term 'grown' appears in the book where 'replicate' would be far more accurate. Most of the figures are clear. Those showing genome organization and expression strategies, however, may well be confusing to those new to molecular biology and these figures would benefit from a greater use of colour. Unfortunately, the book lacks references to direct readers to more detailed texts. The purchase price is likely to make it very attractive to students, the target audience for this book.

■ **Christopher Ring**
Glaxo Wellcome R&D

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september 2000

SOCIETY FOR LOW TEMPERATURE BIOLOGY ANNUAL SCIENTIFIC MEETING. TIME TRAVEL FOR GENES (ORGANIZED JOINTLY WITH UK FEDERATION OF CULTURE COLLECTIONS)

Ambleside, Cumbria 1-2 September 2000

CONTACT: Dr Glyn Stacey, NIBSC, Blanche Lane, South Mimms, Herts EN8 3QG (email gstacey@nibsc.ac.uk)

ACINETOBACTER 2000. 5TH INTERNATIONAL SYMPOSIUM ON THE BIOLOGY OF ACINETOBACTER

Noordwijkerhout, The Netherlands 3-6 September 2000

CONTACT: Dr L. Dijkshoorn, Dept of Medical Microbiology, Leiden University Medical Center L4-P, 2300 RC Leiden, The Netherlands (Tel. +31 71 5263931; Fax +31 71 5248148; email dijkshoorn@rullf2.medfac.leidenuniv.nl)

EXTREMOPHILES 2000. 3RD INTERNATIONAL CONGRESS ON EXTREMOPHILES

Hamburg, Germany 3-7 September 2000

CONTACT: TUHH-Technologie GmbH, Ms. Gerlinde Loebkens, Schellerdamm 4, 21079 Hamburg, Germany (Tel. +49 40 76618012; Fax +49 40 76618018; email loebkens@tutech.de; http://extremophiles2000.de)

BIOTECHNOLOGY 2000. THE WORLD CONGRESS ON BIOTECHNOLOGY. 11TH INTERNATIONAL BIOTECHNOLOGY SYMPOSIUM AND EXHIBITION WITH 4TH CONGRESS ON MOLECULAR MEDICINE. 2ND EUROPEAN CONGRESS ON APPLIED GENOME RESEARCH. 1ST EUROPEAN CONGRESS ON AGRIBIOTECHNOLOGY AND 18TH DECHEMA ANNUAL MEETING ON BIOTECHNOLOGY

Berlin, Germany 3-8 September 2000

CONTACT: DECHEMA e.V., Congress Office, P.O.B. 15 01 04, 60061 Frankfurt am Main, Germany (Fax +49 69 7564 176; email biotechnology2000@dechema.de; http://dechema.de/biotechnology2000.htm)

MICROBIOLOGY TECHNIQUES - A TWO-DAY LABORATORY COURSE

Hatfield, Herts 4-5 September 2000

CONTACT: Dr Virginia Bugeja, Dept of Biosciences, University of Hertfordshire, College Lane, Hatfield, Herts AL10 9AB (Tel. 01707 284590; Fax 01707 286137; email v.bugeja@herts.ac.uk; http://www.herts.ac.uk/natsci/STC)

PROTEIN TECHNIQUES - A TWO-DAY LABORATORY COURSE

Hatfield, Herts 4-5 or 11-12 September 2000

CONTACT: Prof. John Walker, Dept of Biosciences, University of Hertfordshire, College Lane, Hatfield, Herts AL10 9AB (Tel. 01707 284546; Fax 01707 284510; email j.m.walker@herts.ac.uk; http://www.herts.ac.uk/natsci/STC)

SIXTH EUROPEAN WORKSHOP ON VIRUS EVOLUTION AND MOLECULAR EPIDEMIOLOGY

Leuven, Belgium 4-9 September 2000

CONTACT: Anne-Mieke Vandamme, Rega Institute and University Hospitals, AIDS Reference Laboratory, Minderbroedersstraat 10-12, B-3000 Leuven, Belgium (Tel. +32 16 332180; Fax +32 16 332131; email annemie.vandamme@uz.kuleuven.ac.be; http://www.kuleuven.ac.be/aidslab/veme.htm)

NUCLEIC ACID TECHNIQUES - A THREE-DAY LABORATORY COURSE

Hatfield, Herts 6-8 or 13-15 September 2000

CONTACT: Dr Virginia Bugeja (as above)

IMBEM 5 2000. 5TH INTERNATIONAL MEETING ON BACTERIAL EPIDEMIOLOGICAL MARKERS

Noordwijkerhout, The Netherlands 6-9 September 2000

CONTACT: Meeting Secretariat, Congress Care, Muntelbolwerk 1, 5201 AK's-Hertogenbosch, The Netherlands (Tel. +31 73 683 1238; Fax +31 73 690 1417; email info@congresscare.com)

ISOLATION AND IDENTIFICATION OF FUNGI FROM NATURAL HABITATS

CABI Bioscience UK Centre, Egham, 11-15 September 2000

CONTACT: Mrs Stephanie Groundwater, CABI Bioscience UK Centre, Bakeham Lane, Egham, Surrey TW20 9TY (tel. 01784 470111; Fax 01491 829100; email s.groundwater@cabi.org; http://www.cabi.org/bioscience/training.htm)

UNDERSTANDING THE USE OF MASS SPECTROMETRY IN PROTEOMICS - A ONE-DAY LECTURE WORKSHOP COURSE. IN CONJUNCTION WITH PROTEIN WORKS.

Hatfield, Herts 20 September 2000

CONTACT: Mrs Vera Jones, Science Training Centre, Univ. of Hertfordshire, College Lane, Hatfield, Herts AL10 9AB (Tel. 01707 284590; Fax 01707 286137; email v.g.jones@herts.ac.uk; http://www.herts.ac.uk/natsci/STC)

40TH ICAAC

Toronto, Canada 17-20 September 2000

CONTACT: ASM Meetings Department, 1752 N Street NW, Washington DC 20036, USA (Tel. +1 202 942 9248; Fax +1 202 942 9340; http://www.asmusa.org/mtgsrsrc/mtgs.htm)

INTERNATIONAL CONFERENCE ON MEASUREMENT, ANALYSIS AND CONTROL IN BIOPROCESS TECHNOLOGIES: CURRENT STATUS AND FUTURE PROSPECTS

Robinson College, Cambridge 24-26 September 2000

CONTACT: Society of Chemical Industry, 14/15 Belgrave Square, London SW1X 8PS (Tel. 020 7598 1500; Fax 020 7235 7743; email jacquim@chemind.demon.co.uk; http://sci.mond.org)

INTERNATIONAL CONFERENCE ON BACTERIAL AND VIRAL VIRULENCE FACTORS (ICBVVF)

Smolenice Castle, near Bratislava, Slovakia 24-28 September 2000

CONTACT: email uzaelabu@savba.sk; http://nic.savba.sk/sav/inst/uzae/ICB VVF_Site/intro_01.html

october 2000

BIOTEC' 2000. V IBERIAN CONGRESS, II IBERO-AMERICAN MEETING & I BRAZILIAN CONGRESS ON BIOTECHNOLOGY

Recife, Brazil 1-4 October 2000

CONTACT: Professor José Luiz de Lima Filho, BIOTEC' 2000 Secretariat, Universidade Federal de Pernambuco, Av. Professor Moraes Rego, S/N, Cidade Universitária CEP 50761-901, Recife, Pernambuco, Brazil (Tel. +55 81 2718484; Fax +55 81 2718485; email biotec2000@lika.ufpe.br; http://www.lika.ufpe.br/BIOTEC2000)

TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES

Alexandria, Virginia, USA 2-3 October 2000

CONTACT: Cambridge Healthtech Institute, 1037 Chestnut Street, Newton Upper Falls, MA 02464, USA (Tel. +1 617 630 1300; Fax +1 617 630 1325; http://www.healthtech.com)

BIOCONTAMINANTS AND BIOLOGICAL PRODUCTION ISSUES

Alexandria, Virginia, USA 3-4 October 2000

CONTACT: Cambridge Healthtech Institute (as above)

FRONTIERS OF CELLULAR MICROBIOLOGY AND CELL BIOLOGY: EUROCONFERENCE ON SIGNALING AND CYTOSKELETON PLASTICITY

Giens, Toulon, France 7-12 October 2000

CONTACT: Dr J. Hendekovic, European Science Foundation, 1 quai Lezay-Marnésia, 67080 Strasbourg Cedex, France (Tel. +33 388 76 71 35; Fax +33 388 36 69 87; email euresco@esf.org; http://www.esf.org/euresco)

CHARACTERISATION OF PLANT PATHOGENIC BACTERIA

CABI Bioscience UK Centre, Egham, 9-20 October 2000

CONTACT: Mrs Stephanie Groundwater (as above)

april 2001

METALS & CELLS. SEB AGM

Canterbury, 2-6 April 2001

CONTACT: Dr Pamela Robinson (email pamelarobinson@ncl.ac.uk; http://www.ncl.ac.uk/sbg/robinson/metalcell.html)

may 2001

10TH INTERNATIONAL CONGRESS OF HUMAN GENETICS

Vienna, Austria, 15-19 May 2001

CONTACT: ICHG Office, c/o Vienna Medical Academy, Alser Strasse 4, A-1090 Vienna, Austria (Tel. +43 1 405 13 83 33; Fax +43 1 407 82 74; email office@ichg2001.org)

june 2001

2ND EUROPEAN CELLS & MATERIALS MEETING

Davos, Switzerland 25-28 June 2001

CONTACT: Conference Secretary: Sonia Wahl (email sonia.wahl@ao-asif.ch; http://www.ao-asif.ch/events/other/ecm/index.html)

september 2001

ESCV '01 PROGRESS IN CLINICAL VIROLOGY VII

Lahti, Finland 2-5 September 2001

CONTACT: Organizing Secretariat & Congress Office, University of Helsinki, Lahti Research and Training Centre, Kirkkokatu 16, FIN-15140 Lahti, Finland (Tel. +358 3 892 20514; Fax +358 3 892 20219; email irmeli.paasikivi@helsinki.fi; antti.vaheri@helsinki.fi; virpi.tiilikainen@helsinki.fi)

Comment

Crossing the Great Divide: the academia/industry interface

Ten years ago I left behind a tenured lectureship and a well-funded research programme at Cambridge University and joined a fledgling biotechnology company operating from a glorified garage next to Cambridge airport with enough in the bank to pay me for 6 months at most. I'm relieved to say that things worked out. Cantab has prospered, with nearly 150 staff, partnerships with major pharmaceutical companies and several vaccine products in clinical trials.

It has been an amazing adventure and a remarkable learning experience. The major change for me was the need to focus single-mindedly on adding tangible value for our investors. Like most not-yet profitable biotech companies, we spend other people's money with the promise of a generous future financial return and we must do our best to deliver. This is a very different goal from academic research aimed at advancing knowledge. Yet for companies like mine, maintaining a close relationship with the academic community is of great importance.

The value comes in many forms. No matter how bright or large your own team, it is frankly naïve to think you can afford to ignore the vast repository of knowledge and experience in the academic community. Some of Cantab's product ideas were home-grown, but most came from elsewhere. We also benefit from academic expertise to provide important information relevant to our projects and to review our work independently.

I firmly believe, however, that it is a two-way street. Academic groups can benefit greatly from relationships with industry, and not just through cash, though this is important. Researchers can see their ideas turned into real products of benefit to the community and can learn about how industry works, which may prove valuable for them and for their institutions in future. Although the commercialization of science is not the job of the academic research community, all academics should encourage the application of their ideas and advances for ends useful to society. The whole justification for medical research is to improve human health and in practice this can't be done effectively without industry. The interface between academia and industry is therefore of crucial importance.

This interface is often represented as a kind of barrier which requires special measures to circumvent. In reality it simply boils down to personal interactions between academic and industrial scientists like you and me. Whether or not they work depends on individuals, not on the actions of technology transfer organizations, or on government initiatives. In my experience these interactions can be extremely effective, and I like to think that this view is shared by our academic partners. However, building good relationships isn't necessarily

easy, and requires real effort. So what are the ingredients for a successful partnership?

From the outset the two parties must understand and respect each other's needs. From the industrial viewpoint, it helps greatly if the academic is able to comprehend and accept the constraints that apply in industry, the need to deliver investor value, protect intellectual property and confidentiality, stick to an agreed work plan and provide proper documentation for future use. Suspicion of the profit motive is not helpful, since it is fundamental to business operations. On the other hand the industrial partner needs to understand that academic drivers are different, requiring freedom of action and communication, timely publication of results and understanding of the peculiar career situations of researchers on short-term contracts. These needs occasionally conflict, but with good will on both sides, a satisfactory compromise can usually be found.

Second, each party must care about and value the work that the other is doing. Relationships simply based on transfer of cash will not work nearly as well as those where there is genuine interest in the work being done and respect for the ability of those involved. Commonly, a collaboration may be established with every good intention, but priorities change along the way for one of the partners and unless both sides agree to a changed programme, frustration can result. At the outset, therefore, each side has to commit to a programme of work recognizing that it may not necessarily suit them down the line. That said, it is generally safer to avoid situations where one party is entirely dependent on the other to make progress.

Finally, communication is absolutely crucial. At the very least this means regular informal meetings between all parties, but time spent in each other's laboratories, regular email contact and occasional social events all help greatly. We have found it beneficial to invite our collaborators to join us for project reviews, not only to hear about progress, but also to learn about technical and commercial problems encountered, and contribute to finding solutions. This has proved an excellent way to provide mutual encouragement and create a real feeling of co-operation.

With these elements in place, the chances are that a productive partnership will be built and sustained. Success will lead to further and wider interactions, and will encourage others to participate. Multiply one successful collaboration by a hundred or a thousand and you have a recipe for success on a national and international scale.

● **Dr Stephen Inglis is Research Director at Cantab Pharmaceuticals, 310 Cambridge Science Park, Milton Road, Cambridge CB40WG.**

● Please note that views expressed in *Comment* do not necessarily reflect official policy of the SGM Council.