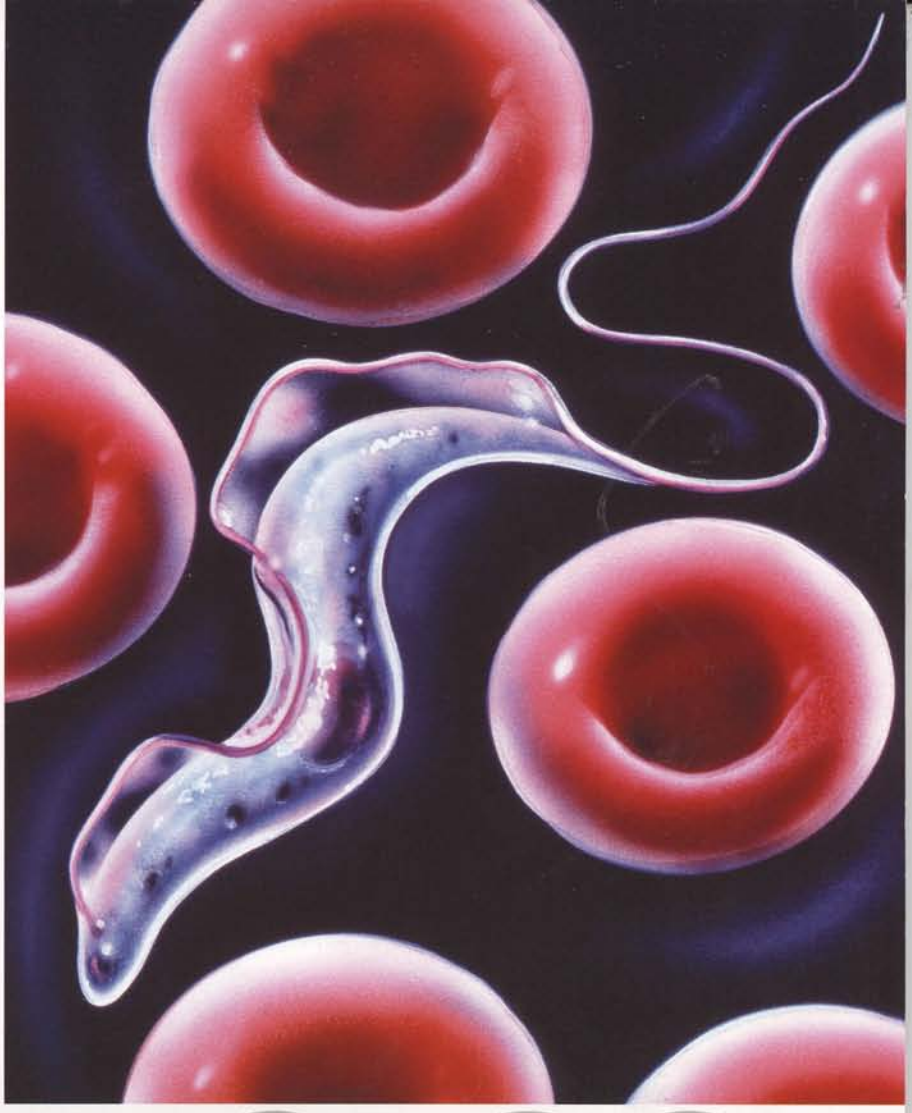

MICROBIOLOGY TODAY

QUARTERLY MAGAZINE OF THE SOCIETY FOR GENERAL MICROBIOLOGY VOLUME 29 AUGUST 2002

Eukaryotic microbes: something for everyone

Fungal pathogens – the devil is in the detail

DNA damage responses

Going green: the evolution of photosynthetic eukaryotes

New hope for the neglected diseases

What's for dinner – how do fungi choose what to eat?

Survival by cAMP in social amoebae

Badgers and bovine TB

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Above: *Trypanosoma brucei*, the sleeping sickness parasite, moving past human red blood cells. *John Bavosi/ Science Photo Library.*

Vol. 29, Part 3, August 2002

In this issue we celebrate the formation of a new SGM special interest group which aims to support the study of eukaryotic microbiology. It will provide a forum for the discussion of the molecular, cellular and organismal biology of eukaryotic microbes such as filamentous fungi, yeasts, slime moulds, protozoa and microalgae, as new convener Clive Price describes on p. 119.

Compared with bacterial pathogens, only a few fungi cause life-threatening infections in humans. As Al Brown explains, these mycoses are becoming more prevalent, are harder to treat and are often diagnosed too late (pp. 120–122). One of the reasons fungi can exploit so many niches is they can metabolize a wide range of compounds. Mark Caddick explores how, given a choice, they select what they eat (pp. 132–134).

The DNA in every living cell is constantly subjected to damaging events. Fiona Benson and Tony Carr (pp. 123–125) describe how the integrity of genes is maintained.

The chloroplast is the site of photosynthesis in plant and algal cells. Saul Purton explains (pp. 126–128) how this important organelle evolved from a photosynthetic bacterium. Remarkably, certain parasitic protists also have plastids which indicate photosynthetic ancestors. These may be a possible target for the drugs which are desperately needed in the fight against protozoan diseases, as Paul McKean describes (pp. 129–131).

The social amoeba is a fascinating organism which uses the cAMP signalling system to control the dissemination of its spores, as Pauline Schaap explains on pp. 136–138.

Equal opportunities are important for people who take a career break, or who have disabilities. Education Officer Liz Sockett lists some of the schemes now available and describes new legislation that will affect all universities (pp. 140–141).

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

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Letters

Letters to the Editor are welcome and should be emailed to **mtoday@sgm.ac.uk** or sent to SGM HQ. SGM reserves the right to edit letters prior to publication.

Bioremediation inspiration

Dear Editor

The articles on 'putting microbes to work' in the May issue of *Microbiology Today* and in particular those that focussed on bioremediation were nice to see and gave some good introductions to parts of the bioremediation world. However, they also gave a somewhat roseate impression of the importance and potential need for microbiology and bioremediation in dealing with our historic pollution.

If bioremediation is to grow in importance it is vital that we understand the extent of the problems that are faced. Expressions of the amount of land where contaminants are present are always impressive. But much of this land may not need to be treated. Certainly, in the UK the legislation only requires action on land contamination if it can be demonstrated that the contaminants may, or do, cause significant harm or if they pollute a controlled water. Sites where this can be said of a metal may be few and far between; rather it is normally organic contaminants that drive the risks associated with land contamination.

Beware also of underestimating chemical or engineering solutions on contaminated sites since many of the problems (and thus the costs) of implementing these will also apply to active (micro)biological methods.

Jonathan Lloyd is right that for bioremediation to prosper there must be a true multidisciplinary approach. It is important then that microbiologists understand not only their own discipline, but also the regulatory context and the other disciplines involved. The establishment of the FIRST Faraday Partnership for remediation plus the DTI LINK Programme on Bioremediation both give excellent vehicles for bioremediation to develop in the UK. The latter needs good proposals from microbiologists and others.

Lastly, the remediation of all contamination is unaffordable. Microbiology must therefore play a key role in understanding the environmental capacity for natural attenuation of contaminants. This should provide a huge driver for the better understanding of fundamental microbial ecology of soil and the subsurface so that regulators can understand when intervention is needed and when not.

● ***Dr Alwyn Hart, Programme and Information Manager, National Groundwater and Contaminated Land Centre, Environment Agency. Tel. 0121 711 5879; Fax 0121 711 5925***

Boiling muds and scalding soils

Professor John Postgate has pointed out an inaccuracy in my article published in the last issue of *Microbiology Today* (May 2002, p. 64). The black smoker ecosystems are not completely independent of solar energy input; although there is no sunlight in the abyssal depths, downwelling oxygen, used in the sulphur oxidation reactions, is photosynthetically generated in surface waters. So is there any ecosystem that is truly independent of solar energy?

● ***Professor David Lloyd, Microbiology, Cardiff University, PO Box 915, Cardiff CF10 3TL, UK. Tel. 029 20874772; Fax 029 20874305 email lloydd@cardiff.ac.uk***

Reaction to anthrax 'Comment' article – Professor Titball replies

Dear Editor

Dr Hambleton has kindly copied his letter of 1 March, concerning anthrax vaccine, to me (see May issue of *Microbiology Today*, p. 62). I am pleased that Dr Hambleton found this article enjoyable. With respect to his specific points:

1. The data sheet provided with older batches of the anthrax vaccine reads: '*When Anthrax vaccine (Alum precipitated Anthrax Antigens) is for the active immunization of man against the various forms of anthrax, four doses of 0·5 ml should be given intramuscularly. The three doses should be given at intervals of 3 weeks, followed by a fourth dose at an interval of 6 months. Reinforcing doses of 0·5 ml intramuscularly should be given annually.*'

The data sheet provided with the latest batch of anthrax vaccine that we have received at Dstl reads: '*The primary (first) course of four single injections is followed by a booster dose given once a year. For each dose your doctor will inject 0·5 ml of the vaccine into a muscle.*' The accompanying table shows:

Injection	When will the injection be given?
First injection (0.5 ml)	First visit
Second injection (0.5 ml)	3 weeks after first injection
Third injection (0.5 ml)	3 weeks after second injection
Fourth injection (0.5 ml)	6 months after third injection
Booster	Once a year

The data sheet associated with the older batches of vaccine does state that the vaccine is produced at CAMR Porton Down, but this information is not provided with the new data sheets.

2. The UK anthrax vaccine is stated to contain '*significant but varying amounts of contaminating lethal factor and oedema factor*' (1). If the amounts vary and are not controlled, then one cannot be certain that some batches (or some past batches) will not contain these antigens. The text reads '*may*' because the additional toxin components 'may' impart side effects.

3. Nowhere in this article do I state that PA is the only protective antigen, merely that it is the active component of the vaccine. We are actively searching for additional vaccine antigens at Dstl Porton Down. Of the articles cited which identifies additional antigens, two were published after this commentary was written, and neither of these articles identify any additional antigens – they do suggest that additional vaccine antigens exist. The third (Price *et al.*, 2001) refers to protection against anthrax toxin, not protection against anthrax.

● ***Professor Richard W. Titball, Dstl, Porton Down, Salisbury, Wiltshire, UK.***

1. Brachman, P.S. & Friedlander, A.M. (1999). Anthrax. In *Vaccines*, 3rd edn. Philadelphia: W.B. Saunders.

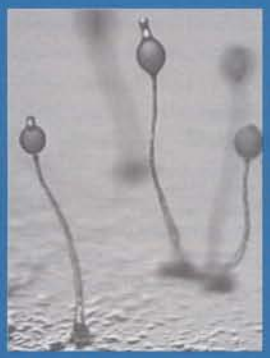
Eukaryotic microbes: something for everyone

Clive Price

The types of eukaryotic micro-organisms are many and broad-ranging. Clive Price, Convener of the new SGM Group set up to promote this field, describes their significance and what the group hopes to achieve.

Eukaryotic microbes are of major economic importance to the modern world. On the positive side we have vast food and beverage industries founded the world over on the properties of humble yeasts; bread and alcohol, nothing could be more fundamental to human life. Filamentous fungi are widely used in the production of food additives and medicines, in the form of antibiotics. More antagonistically fungi represent increasingly important human pathogens and have long been recognized as the most serious crop plant pathogens. Other eukaryotic microbes are the culprits in several major forms of human and animal infectious disease, including malaria (*Plasmodium*), sleeping sickness (*Trypanosoma brucei*), Chagas disease (*Trypanosoma cruzi*) and leishmaniasis.

In addition most, if not all these organisms serve as important models employed in basic research into the genetics, biochemistry and cell biology of eukaryotes. This clearly constitutes a very broad church that has led to difficulties in terms of promotion and representation of common interests, both scientific and professional, and which is reflected in the number of very successful, but relatively small and often ad hoc societies or interest groups. Many members of the SGM working with microbial eukaryotic systems felt that their interests had been poorly served within the SGM for a considerable time, whilst believing that the SGM could and should provide an appropriate home for them. These concerns were accepted by Council and duly led to the creation of a new group in September 2001. It is not the intention that the SGM should subsume other smaller groups, rather that it is well placed to provide a strong voice in professional matters, ranging from concerns over funding in research and education to recruitment and career structure. The main remit of the Eukaryotic Microbiology Group will be to organize meetings of general interest to that constituency. However, it will be important to identify areas of interest with other groupings within the Society which will emphasize biological commonalities between prokaryotes and eukaryotes. Several immediately suggest themselves: DNA metabolism, the evolution and function of organelles (mitochondria and chloroplasts), fundamentals of quorum sensing and signal transduction. Another area of broad interest is the cytoskeleton which forms the grist for the first SGM eukaryotic symposium, *The Cytoskeleton as an Integrator of Cell Function* to be held on 19–20 September 2002 at the University of Loughborough. There is an exciting list of international speakers covering a wide range of topics and organisms, from bacteria to man. We hope to see many people there to launch the new enterprise (see the enclosed programme booklet for details and a booking form).



Another important role for the group will be to forge links with Societies and interest groups outside of the SGM. A start has already been made in this direction as the second group symposium for UMIST 2003 is being organized by Al Brown and Saul Purton in conjunction with the British Mycological Society and the British Society for Medical Mycology. This meeting will cover four broad biological areas (a) genome organization/sex; (b) pathogenicity; (c) cell signalling; and (d) regulatory mechanisms. In particular it will focus on the insights garnered from post-genomic approaches to these problems (transcript/profiling/proteomics/metabolomics). Discussions are already under way for a meeting covering epigenetic inheritance to be held at Trinity College, Dublin, in 2004 and in due course all of the areas discussed above will be covered. It is important that members recognize that the committee is always open to suggestions of suitable topics for future meetings.

The articles assembled in this edition of *Microbiology Today* provide a flavour of some of the subject areas within eukaryotic microbiology. How do pathogens arise and what differentiates them from their benign relatives? How do fungi respond to nutrient availability and their environment at the level of gene expression? Why are blood-borne pathogens so persistent and difficult to treat? What are the evolutionary relationships between organelles in protists and signalling systems in slime moulds? Why and how do prokaryotes and eukaryotes respond to the presence of DNA damage? These articles will provide general answers to these important questions and serve as primers for those readers whose imagination is captured.

The accompanying illustrations depict various eukaryotic microbes discussed above on the basis that it is a good idea to be able to recognize your neighbour, both friend and foe alike. For the future, we would like to see this group expanded and for its voice to be more strongly represented both within and without the SGM.

● *Clive Price is Convener of the Eukaryotic Microbiology Group. He may be contacted at Biological Sciences, Institute of Environmental and Natural Sciences, Lancaster University, Bailrigg, Lancaster LA1 4YQ, UK.*
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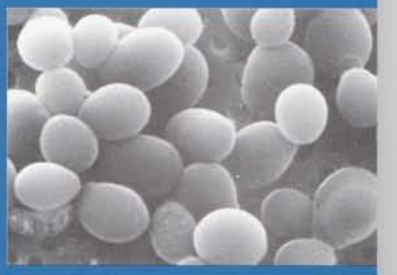
LEFT:
Dictyostelium discoideum.
PAULINE SCHAAP

BELOW:
Candida sp. (upper) and *Saccharomyces cerevisiae* (lower).
PHOTO SGM (UPPER); JAMES BOYNE AND CLIVE PRICE (LOWER)

FAR LEFT BOTTOM:
Trypanosoma brucei.
PHOTO FLAVIA MOREIRA LEITE AND KEITH GULL



Fungal pathogens – the devil is in the detail

Alistair J. P. Brown

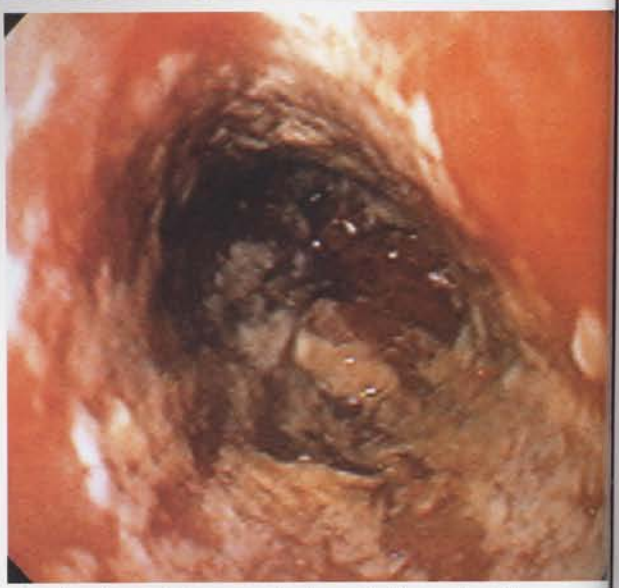
Compared with bacterial pathogens, a relatively small number of fungal species cause life-threatening infections in humans. However, these fungal infections are becoming more prevalent, they are harder to treat, and they are often diagnosed too late.

Fungi are eukaryotes, and are more closely related to humans than bacteria. Some protein components of fungal and human cells are even functionally interchangeable. For example, human proteins with fundamental roles in the cell division cycle, stress responses, gene regulation, protein localization, metabolism and in energy generation, can functionally replace the corresponding proteins in the budding yeast, *Saccharomyces cerevisiae*. An important consequence of this is that it is harder to identify the significant differences between fungal and human cells that might make useful targets for antifungal therapies. Relatively few antibiotics are available to fight fungal infections. These include azoles, polyenes, flucytosine and echinocandins, which block ergosterol biosynthesis, interfere with fungal membrane permeability, block nucleic acid biosynthesis and inhibit cell wall β-glucans, respectively. The cell wall is different in fungal and human cells, and hence fungal cell wall biogenesis is a major target for the development of new antifungal drugs.

Fungal opportunists

Microbial pathogens can be divided into those that cause disease in healthy individuals (primary pathogens), and those that only tend to do so in enfeebled hosts (opportunistic pathogens). Many of the major bacterial pathogens are primary pathogens. For example, *Bacillus anthracis*, *Escherichia coli*, *Listeria monocytogenes*, *Salmonella typhimurium*, *Shigella flexneri* and *Yersinia pestis* invade and colonize healthy individuals. In contrast, relatively few fungal species are primary pathogens. They include *Histoplasma capsulatum*, *Coccidioides immitis*, *Paracoccidioides brasiliensis*, *Blastomyces dermatitidis* and the dermatophytes (i.e. those fungi that infect the skin). Other major fungal pathogens such as *Candida* species (e.g. *C. albicans*, *C. glabrata*, *C. tropicalis*, *C. dubliniensis*), *Aspergillus fumigatus*, *Penicillium marnefei*, *Pneumocystis carinii*, *Rhizopus oryzae* and *Fusarium solani* are opportunistic pathogens. These fungi only tend to cause life-threatening systemic infections in patients with severely compromised immune systems. *Cryptococcus neoformans* can cause community-acquired infections, but mostly infects immunocompromised patients. Hence, this fungus appears to lie somewhere between the extremes of opportunism and primary pathogenicity.

Histoplasma capsulatum infections are widespread in tropical and temperate regions around the world, whereas *Paracoccidioides brasiliensis* infections are limited to Latin America. In the Americas, *Coccidioides immitis* infections are mostly restricted to hot, dusty climes. These geographical distributions appear to be related to the environmental niches that these fungal pathogens occupy outwith their human hosts. *Histoplasma capsulatum* grows in bat or bird droppings, whereas



Coccidioides immitis grows in dry alkaline soils. The environmental source of *Paracoccidioides brasiliensis* is not clear, but it is known that most people in endemic regions are exposed to the fungus before they reach 20 years old. *Histoplasma capsulatum*, *Coccidioides immitis* and probably *Paracoccidioides brasiliensis* infects people by the inhalation of dust containing high concentrations of this fungus. They colonize the lung, initially causing pulmonary infections, but then they can spread to other internal organs. *Aspergillus fumigatus* is also widespread in the environment (Fig. 1). Again, its primary route of infection is via inhalation into the lung where it can grow rapidly to form large boluses of fungal cells in the immunocompromised patient. *Pneumocystis carinii* also infects via inhalation of spores, germination and invasion of lung tissue. This unusual fungus was originally classified as a protozoan parasite, until recently when DNA sequencing revealed an evolutionary relationship to ascomycetous yeasts. All of these fungal infections can prove fatal.

TOP RIGHT:
Fig. 1. Conidia producing the infective spores of *Aspergillus fumigatus*.
PHOTO E.GUEHO, CNRI/ SCIENCE PHOTO LIBRARY

BOTTOM RIGHT:
Fig. 2. White patches of *Candida albicans* growing on a patient's oesophagus.
PHOTO DAVID M. MARTIN MD/ SCIENCE PHOTO LIBRARY

OPPOSITE PAGE:
Fig. 3. *Cryptococcus neoformans* forms a thick protective polysaccharide coat *in vivo*.
PHOTO ALFRED PASIEKA/ SCIENCE PHOTO LIBRARY

Candida albicans is the most common cause of systemic fungal disease. This fungus is found in warm-blooded mammals, but a clear niche for *Candida albicans* has not been identified in the environment outside of its mammalian host. This fungus exists as a commensal in most (healthy) individuals (Fig. 2), but when the delicate balance between the fungus and its host is disturbed, *Candida albicans* can cause 'superficial' infections of the mouth and vagina (thrush). Most women suffer at least one episode of vaginal thrush in their lifetimes, but these infections can become recurrent in some unfortunate individuals. Oral infections are common in new-born infants and in AIDS patients. In patients with a severely compromised immune system, *Candida albicans* can enter the bloodstream, become disseminated throughout the body and invade internal organs. Transplant patients on immunosuppressive drugs and cancer patients undergoing chemotherapy are most at risk. Many of these systemic *Candida albicans* infections are fatal. These fungal infections are becoming more prevalent worldwide because the size of the immunocompromised patient population is rising.

Virulence factors

Bacterial pathogens appear to rely upon a small number of key factors for their virulence. Purified cholera and tetanus toxins can themselves confer most of the effects of *Vibrio cholerae* and *Clostridium tetani*, respectively. Also, the inactivation of toxin genes can attenuate bacterial virulence. In contrast, knocking out gliotoxin production does not render *Aspergillus fumigatus* avirulent. Hence, fungal pathogens appear to display more complex virulence traits. Many factors appear to promote fungal virulence, and the expression of any single factor does not confer pathogenicity upon a benign fungus.

Several factors contribute to *Cryptococcus neoformans* virulence. A thick polysaccharide capsule protects this fungus from host immune defences (Fig. 3). The coat inhibits phagocytosis and modulates immune responses. Melanin production protects *Cryptococcus neoformans* from attack by reactive oxygen species, thereby reducing the potency of leukocyte killing. Virulence might also be promoted by the secretion of mannitol into the cerebral spinal fluid. Also, mating type is clearly linked to *Cryptococcus neoformans* virulence, because clinical isolates mostly have the MATa genotype. The explanation for this seems to be that mating and virulence factors are both regulated by the same signal transduction pathway.

Candida albicans also displays a battery of different virulence factors. This fungus expresses a large number of adhesins that help the fungus stick to host cells and gain a foothold in the early stages of infection. These adhesins include a family of agglutinin-like sequences (ALSs), an integrin-like protein and an Hwp1 protein that acts as a target for host transglutaminases that actually cross-link fungal cells to host cells. *Candida albicans* also secretes hydrolytic enzymes that presumably damage host tissue and possibly provide nutrients for the fungus and promote fungal invasion. Large gene families of secreted aspartyl proteinases (SAPs) and lipases (LIPs) are regulated differentially during disease progression in different host niches. This fungus has also learnt to adapt to the neutral pH of the bloodstream and more acidic pH of the vagina. *Candida albicans* virulence is attenuated if these pH responses are disrupted. Like *Cryptococcus neoformans*, *Candida albicans* exploits various strategies to evade host defences. For example, *Candida albicans* releases carbohydrates from its cell wall that modulate host immune responses, and it also undergoes rapid switching between different phenotypic forms. Virulence is affected if either of these events are blocked.

Cellular morphogenesis also plays an important role in fungal virulence. *Aspergillus fumigatus* is a filamentous mould, which generates infective spores. *Coccidioides immitis* also grows in a filamentous form in the environment, but it switches to a specialized growth form upon contact with the host. This fungus forms large spherules in the lung, each of which releases hundreds of endospores into the host. Similarly, the environmental and parasitic forms of *Histoplasma capsulatum*, *Coccidioides immitis* and *Paracoccidioides brasiliensis* grow with different morphologies. These fungi form mycelia in the environment, but grow in a yeast-like form inside their host. *Paracoccidioides brasiliensis* is particularly interesting, because the transition to the yeast form is inhibited by oestradiol. This probably explains why women are about 50 times less likely to suffer paracoccidioidomycosis than men.

Clearly, morphological transitions are important for the pathogenicity of these fungi. However, the situation is less straightforward in *Candida albicans*. This fungus exists in yeast-like, pseudohyphal and hyphal forms *in vivo*. It is often assumed that the hyphal growth form enhances tissue invasion, whereas the yeast form promotes dissemination of fungal cells in the bloodstream or between individuals. Although this assumption might prove to be correct, it remains to be confirmed experimentally. The problem is that yeast–hypha morphogenesis is intimately linked with the expression of other virulence factors, including

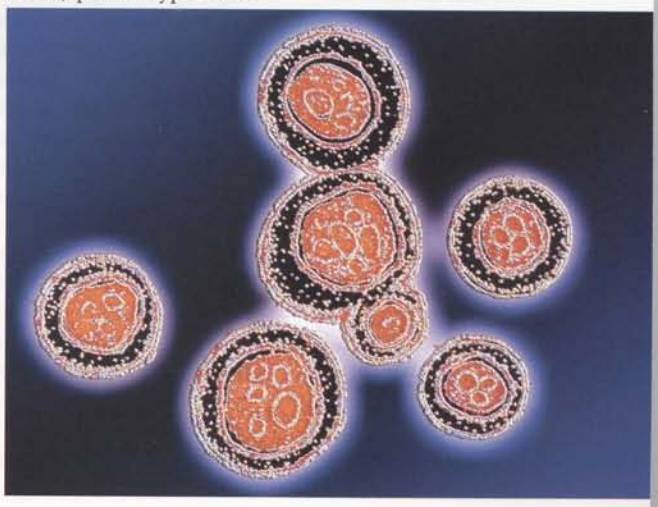


Table 1. Examples of common virulence strategies in fungal and bacterial pathogens

Virulence factors	Bacterial pathogens	Fungal pathogens
Toxins	Cholera, diphtheria, pertussis, tetanus, haemolysin	*Aspergillus fumigatus* gliotoxin, ribotoxins
Adhesion	Fimbrial adhesins of *Haemophilus, Helicobacter, Escherichia* species	*Candida* agglutinin-like sequences
	Afimbrial adhesins of *Bordetella, Salmonella, Staphylococcus* species	*Candida albicans* transglutaminase targets (Hwp1)
Invasion	*Mycoplasma, Yersinia, Salmonella, Shigella* species	*Histoplasma* invasion
		Candida albicans secreted aspartyl proteinases (SAPs) and lipases (LIPs)
		Morphogenesis in *Candida albicans, Paracoccidioides, Coccidioides, Histoplasma*
Evasion	Streptococcal, *Neisseria* capsules	Cryptococcal capsules
	Immunomodulation by *Mycoplasma, Escherichia* species	Immunomodulation by *Candida albicans*
	Pseudomonas, Streptococcus complement inactivation	*Candida albicans* phenotypic switching
	Salmonella, Neisseria antigenic variation	

Further reading

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Haynes, K. (2001). Virulence in *Candida* species. *Trends Microbiol* 9, 591–596.

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Van Burik, J.-A. H. & Magee, P.T. (2001). Aspects of fungal pathogenesis in humans. *Annu Rev Microbiol* 55, 743–772.

adhesins and proteases. These virulence factors must be dissected individually before we can assess their true contributions to the pathogenicity of *Candida albicans*. What is clear is that the pathogenicity of this fungus is complex: it is not dependent upon any single virulence trait.

Evolution of virulence

Bacterial pathogens produce adhesins and proteases as well as toxins. The genetic analysis of these traits has led to the major revelation that many are organized within 'pathogenicity islands'. These genes are located together in the bacterial chromosome, alongside genes encoding the specialized secretory apparatuses that target these virulence factors to the host. These pathogenicity islands may provide a means for the horizontal transfer of virulence genes amongst bacterial strains.

This is not the case in fungal pathogens. In general, fungal virulence genes are unlinked, and the regulatory mechanisms that control fungal pathogenicity must account for the distribution of virulence genes around the genome. There are some exceptions to this. For example, tandem copies of SAP and ALS genes exist in *Candida albicans*. Also, tandem copies of putative adhesin genes have arisen near the ends of *Candida glabrata* chromosomes. The location of some virulence genes close to telomeres might be no coincidence. Telomeric regions appear to evolve rapidly, allowing the rapid amplification (or loss) of niche-specific functions. These types of genetic event might have been particularly important in the evolution of fungal pathogens.

Invasion strategies

Routes of infection and sites of colonization vary for different microbial pathogens. Hence, there is enormous variety in the specific mechanisms by which microbes interact with their human host. However, despite the apparent complexity of fungal virulence attributes, many fungi and bacteria appear to adopt similar infection strategies (Table 1). Both fungal and bacterial pathogens must be capable of adhesion, invasion and colonization. They must both be able to grow well at 37 °C and they must evade the immunological defences of the host. However, the devil is in the detail.

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DNA damage responses: a combination of maintenance and fire-fighting

Fiona E. Benson & Antony M. Carr

The DNA in every living cell is constantly subjected to damaging events. Fiona Benson and Tony Carr describe how the integrity of genes is maintained.

All cells rely on DNA to transmit genetic information and it is vital to maintain the integrity of this information. This is underlined by the fact that in both prokaryotes and eukaryotes around 5% of the genes are devoted to encoding DNA repair and DNA damage response proteins.

DNA itself is fragile and undergoes a host of interactions with endogenous molecules in the cell. It has been estimated that every cell in our body suffers 10,000 DNA damaging events every day. Add to this the intrinsic infidelity of DNA replication and the exogenous damage induced by exposure to sunlight and other genotoxic treatments (smoking, X-rays, etc.) and it is clear that DNA damage responses are key to the survival of an unaltered genome. Preservation of a stable genome is critical; genome alterations have a fundamental role in initiation of cancer in higher eukaryotes.

The genome has often been likened to an encyclopaedia of technical information for building a complicated machine. The entries in the encyclopaedia are composed of just a four-letter base alphabet, comprising A for adenine, G for guanine, T for thymine and C for cytosine. It is the precise ordering of these four letters of the alphabet in each individual encyclopaedia entry, or gene, that provides the instructions for making the proteins that are the key cellular building blocks. In a simple eukaryote such as yeast there are approximately 12 million bases encoding 6000 genes. That's 6000 individual entries in a hypothetical encyclopaedia just to make a yeast!

In humans there are about 3000 million letters of DNA and about 30,000–40,000 genes. Now, if there are 10,000 spontaneous DNA damage events in each cell, then it's like somebody randomly erasing 10,000 letters in the encyclopaedia every day. Even though less than 2% of the human genome actually encodes proteins, a large number of these erasures will still affect an entry in our hypothetical encyclopaedia.

Fortunately, the double-stranded nature of DNA allows single base erasures to be fixed with high fidelity – information lost from one strand can be replaced by referring to the alphabet order on the other strand. Some forms of damage are more severe and delete letters opposite each other. This is a much more severe problem for a cell.

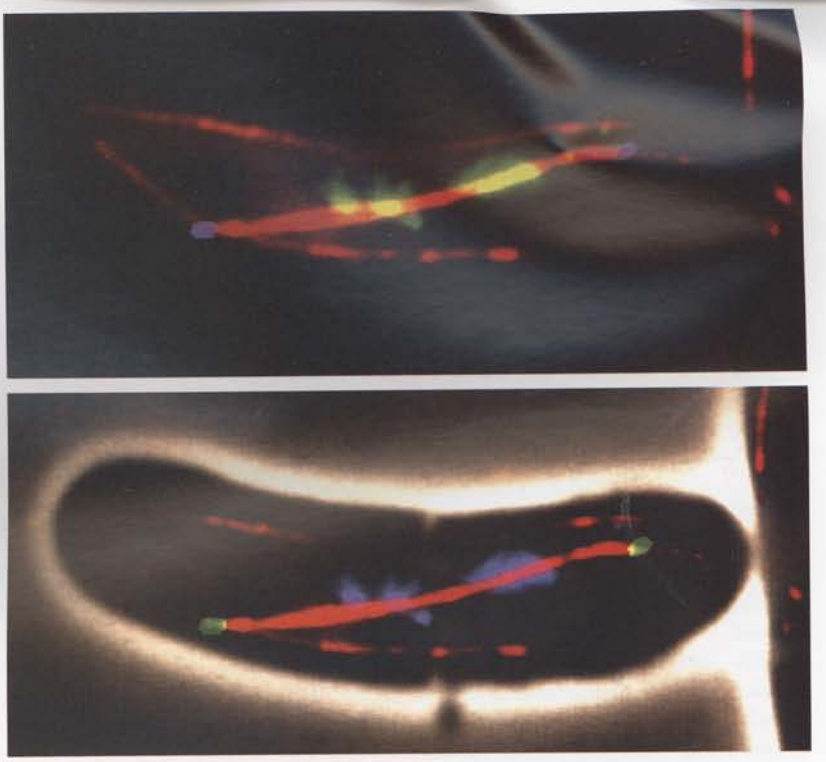
DNA repair pathways

How does a cell deal with all these problems? First, intrinsic damage to single letters is repaired by a variety of mechanisms designed to housekeep the encyclopaedia. These DNA repair pathways, which include base excision repair and mismatch repair, can essentially be thought of as maintenance workers which recognize inappropriate changes in the double-stranded DNA and put these right by copying from the undamaged strand. Probably these routine maintenance operations occur unseen, i.e. they are not monitored by the cell as a sign that something is wrong. However, induced DNA damage, such as distortions in the double helix which may result from exposure to the ultraviolet component of sunlight, or DNA strand breaks induced by ionizing radiation, require more complex repair pathways such as nucleotide excision repair (NER), homologous recombination repair (HR) and non-homologous end joining (NHEJ). These pathways can perhaps be considered as the emergency services, being recruited to sort out problems that hopefully do not occur too often and which, when they do occur, can have fatal consequences. Certainly it seems that these pathways are not silent, but are monitored in the cell by a series of mechanisms which are collectively called DNA-integrity checkpoints.

DNA-integrity checkpoint pathways

When the cell detects DNA damage or its repair (we still do not know precisely how this occurs), it responds in different ways, depending on the circumstances it finds itself in. For simple eukaryotes, such as yeast, every cell is going to reproduce, so the different responses are largely geared to keeping the encyclopaedia intact, thus ensuring that the blueprint remains unchanged. To do this it is necessary to arrest the cell cycle and co-ordinate DNA repair with whatever is on-going at the time. For example, if the cell is undergoing DNA replication, equivalent to making a copy of our entire hypothetical encyclopaedia, then the repair apparatus must interact with the replication apparatus and stop the latter temporarily, since copying damaged information is likely to exacerbate the problem. If however the DNA replication is complete, then it is important not to try and separate the replicated copies (i.e. undergo mitosis) until repair is complete. This is important for two reasons. First, if the DNA is physically broken (analagous to tearing a page out of our encyclopaedia) then pulling the two DNA molecules apart is going to result in the information (i.e. the page) being left behind. Second, if the DNA is broken, and still side by side with an intact copy, it is possible to use the information from the intact volume to effect repairs to the broken one. This process, homologous recombination, requires that the two identical volumes of the encyclopaedia are in close proximity until the repair is completed. Recent data suggests that co-ordination of homologous recombination is controlled by the checkpoint proteins.

In multicellular organisms, many cells are terminally differentiated and are not going to divide again. It is not clear exactly what the DNA damage responses are in such cells, since most work in laboratories is performed on dividing cultures. Clearly, stationary phase – or quiescent – cells can repair DNA damage and their



RIGHT:
A *Schizosaccharomyces pombe* checkpoint-defective cell following abortive mitosis. Top: DNA false-coloured in green, microtubules in red and spindle pole bodies in blue. Bottom: the same image superimposed onto an optical image of the cell (DNA blue, microtubules red, spindle poles green).
WITH THANKS TO IAIN HAGAN

checkpoint pathways still operate. Obviously, arresting the cell cycle is not an issue in a stationary-phase cell, and in this case checkpoint pathways seem to act mainly to induce other responses, for example, initiating transcription to ensure an adequate repair response and to make sure repair pathways are properly controlled. Another function of the checkpoint pathways is to help co-ordinate a cell suicide response, termed apoptosis. This response is thought to remove cells which have received particularly dangerous levels of DNA damage. It ensures that damage does not become fixed as a mutation, or permanently changes an encyclopaedia entry, which might result in a cell beginning to cycle again and potentially initiating tumour formation by inappropriate division.

In contrast to quiescent cells, stem cells are programmed to divide, primarily to give rise to differentiated cells of specific cell types, but also to self-renew, as part of the growth and maintenance of the whole organism. In these cells, it is particularly important to repair DNA damage and to monitor this so that the cell can respond appropriately. A dividing cell must be kept under strict control in a multicellular organism, since it is one step closer to forming a tumour than a quiescent cell simply by virtue of being programmed to divide. Perhaps unsurprisingly, stem cells appear to have a lower threshold of DNA damage for the cell suicide response than quiescent cells. The logic of this may be that, as dividing cells are more dangerous, it is better to sacrifice the individual cell when there is a chance of corrupting the blueprint, rather than potentially risking the integrity of the whole organism. The critical role of DNA repair and DNA damage response pathways is emphasized by the observation of the devastating consequences of inherited genetic defects in these pathways in diseases such as Xeroderma pigmentosum and Ataxia telangiectasia.

Similarities between prokaryotic and eukaryotic microbes

Prokaryotic organisms face a similar challenge to simple eukaryotes in the event of damage to their DNA. As each prokaryotic cell is destined to divide, the focus of the DNA repair and damage response is in protecting the integrity of the genome. Suicide is not an option! In bacteria DNA damage and repair are continually monitored and a primitive damage response, termed the SOS response, is activated to co-ordinate repair and cell division. Emergency repair pathways of nucleotide excision repair, homologous recombination and lesion bypass are induced as part of the SOS response, in parallel with temporary cessation of cell division. Once the DNA is repaired, the emergency repair systems are turned off and cell division is allowed to proceed. Remarkably, the mechanisms of DNA repair processes are essentially conserved from prokaryotes, through simple eukaryotes to complex multicellular organisms, such as man. In many cases, pivotal repair enzymes show a high level of conservation of sequence and structure from bacteria, through simple eukaryotes, such as yeast, to man. In view of the increased complexity of eukaryotic organisms it is perhaps not surprising, however, that the complexity of the enzymatic machinery that mediates repair is increased approximately 10-fold between bacteria and man.

From microbes to man

Study of prokaryotes has been important in elucidating repair pathways and providing a paradigm in the SOS response for study of eukaryotic DNA damage responses. However, studies of single-cell eukaryotes have proved to be of increased importance in delineating DNA repair and checkpoint responses of relevance to multicellular eukaryotes such as man. Clearly, such cells do not have a suicide response (it's better to try and divide, since there is nothing to lose). However, it is clear that the same fundamental eukaryotic surveillance pathways characterized in yeasts and other model eukaryotes report both to cell cycle regulators and the apoptosis system in multicellular systems.

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Going green: the evolution of photosynthetic eukaryotes

Saul Purton

The chloroplast is the site of photosynthesis in plant and algal cells. Saul Purton explains how this important organelle evolved from a photosynthetic bacterium.

Look around our macroscopic world and you see a rich diversity of photosynthetic eukaryotes. A fantastic range of plants covers our land and numerous different macroalgae (seaweeds) abound in our seas. Similarly, the microscopic world is filled with a wealth of exotic microalgae. However, all of these organisms share a common legacy – the chlorophyll-containing plastid (= chloroplast) that is the site of photosynthesis. This organelle has its ancestral origins as a free-living photosynthetic bacterium that became entrapped inside a primitive eukaryotic cell. The bacterium was retained rather than digested as food and a symbiosis was established in which the host cell provided a protected and nutrient-rich niche in return for the photosynthetic products generated by the bacterium. The story of how this bacterial endosymbiont evolved into a chloroplast and was then spread by subsequent symbiotic events to other eukaryotes is a fascinating and on-going one that involves the study of a wide range of microbial eukaryotes.

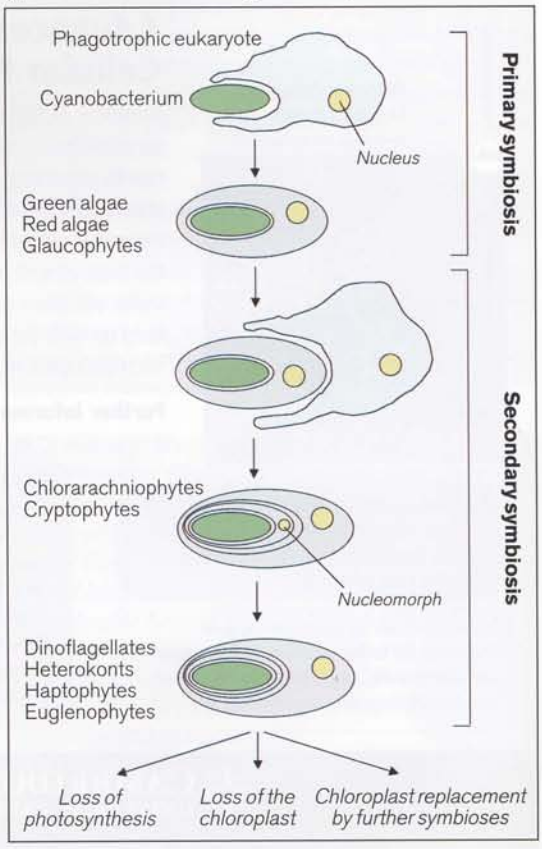
Coloured slaves

Early in the history of eukaryotic evolution a simple rule applied. Photosynthetic bacteria were the primary producers, utilizing the sun's energy to convert carbon dioxide to complex carbohydrates, and single-cell eukaryotes were the consumers, often acquiring their food by engulfing and digesting the bacteria or other eukaryotes. The cyanobacteria (also called blue-green algae) were particularly important producers since they carried out oxygenic photosynthesis in which the harvesting of light energy is coupled to the production of molecular oxygen from water. These early cyanobacteria probably contained several different light-absorbing pigments, including chlorophylls *a* and *b* and phycobilins, and could carry out photosynthesis using a wide range of light levels and wavelengths. Importantly, the cyanobacteria would still be able to photosynthesize even after being incarcerated within the colourless cell of a phagotrophic eukaryote. The normal fate of the captured bacterial cell would be death by digestion. However, for the eukaryote a continuous supply of fixed carbon and oxygen was perhaps an attractive alternative to a quick meal, and occasionally the death sentence would be commuted to life imprisonment. Under this arrangement, the bacterium would be allowed to grow and divide within its prison cell, and would therefore be retained and inherited by the eukaryote as it itself divided. Indeed, examples of such endosymbiotic associations are found amongst modern-day eukaryotes. For example, the cyanobacterium *Nostoc* survives inside the cells of the filamentous fungus *Geosiphon pyriforme*.

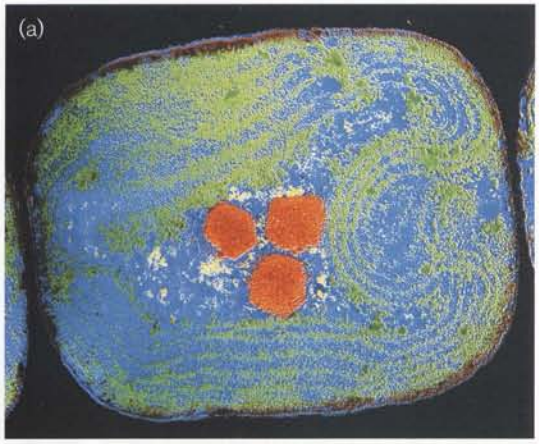
In one particular case, the interdependence between the master and his slave became closer and closer over evolutionary time. Ultimately, the once autonomous cyanobacterium became an integral and essential component of the eukaryotic cell – the chloroplast (see Figs 1 and 2). This first truly photosynthetic eukaryote is almost certainly the common ancestor of three major photosynthetic groups found today: the chlorophytes (green algae and all plants), the rhodophytes (red algae) and the glaucophytes. The divergent evolution of these three groups from the common ancestor has resulted in chloroplasts with different pigment composition and ultrastructure. The chlorophytes have lost the phycobilins, but retained chlorophyll *a* and *b*, whereas the red algae and glaucophytes have chlorophyll *a* only, together with phycobilins. Interestingly, the glaucophytes have also retained the cell wall of the bacterium and their chloroplasts are bounded by an inner membrane derived from the bacterial cell, a cell wall of peptidoglycans and an outer membrane derived from the food vacuole of the eukaryote. In the chlorophytes and rhodophytes, the cell wall has been lost and two membranes surround the chloroplast.

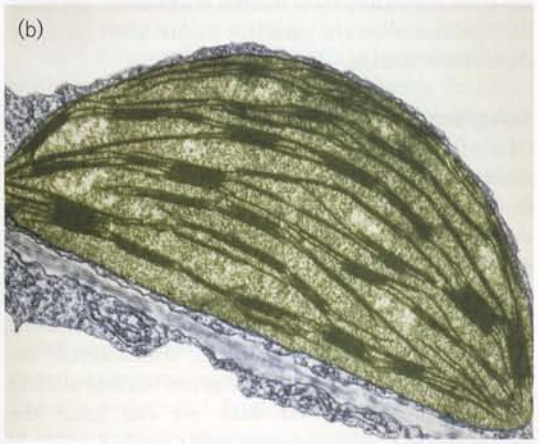
Centralization of power

Although the cyanobacterium escaped death by digestion, it was to pay a high price for its survival as a component of the eukaryotic cell. The several thousand genes the bacterium brought with it, and which allowed



RIGHT:
Fig. 1. The endosymbiotic origin of chloroplasts. Note that the chloroplasts of euglenophytes and dinoflagellates actually have three membranes rather than four. It is thought this reflects an alternative feeding mechanism in which the cell membrane of the prey alga is discarded.
COURTESY S.PURTON





LEFT:
Fig. 2. Transmission electron micrographs showing the similarity in ultrastructure between (a) a modern-day cyanobacterium (*Pseudanabaena*) and (b) the plant chloroplast (in this case in a tobacco leaf) that evolved from the cyanobacterial endosymbiont.
PHOTOS DR KARI LOUNATMAA (a) AND DR JEREMY BURGESS (b)/SCIENCE PHOTO LIBRARY

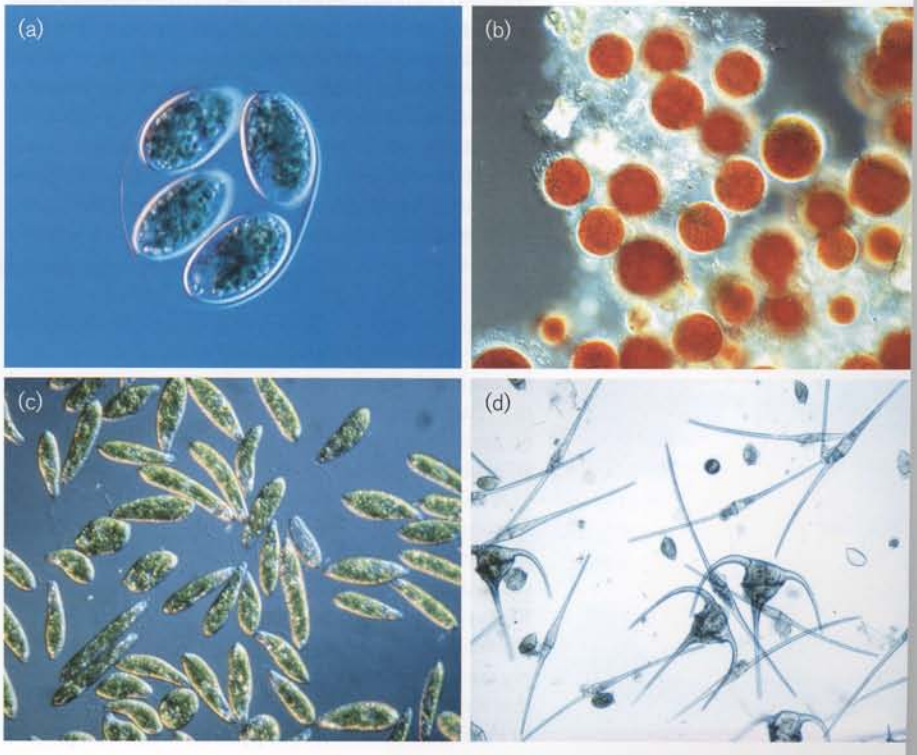
it to live an autonomous existence, were unceremoniously stripped from it leaving only a meagre genome of a few hundred genes. Genes no longer necessary for an intracellular existence (for example, those required for motility) were simply discarded. Others were eliminated by a process of gene substitution in which nuclear eukaryotic genes functionally replaced their bacterial counterparts. Finally, and perhaps most remarkably, there was a mass transfer of most of the remaining genes from the bacterial genome to the eukaryotic nucleus. The selective pressures that drove this gene exodus and the mechanism by which it occurred are poorly understood, but the implications for the evolving chloroplast were profound. First, it had lost control of its own destiny since it now possessed only a fraction of the genes needed for chloroplast biogenesis. The nucleus now controlled the growth and division of the organelle. Second, the expression of those genes that had remained in the chloroplast (mainly genes for components of the photosynthetic apparatus and the organelle's transcription/translation apparatus) needed to be tightly co-ordinated with the expression of the nuclear genes that encoded chloroplast components. The nucleus therefore developed elaborate control mechanisms in which nuclear-encoded factors were targeted into the chloroplast to regulate chloroplast gene expression. Finally, the photosynthetic eukaryote had to solve a major logistical problem. The products of the nuclear-encoded genes were now being synthesized outside the chloroplast in the cytosol, whereas previously they had been made inside the organelle. An early modification to the fledgling chloroplast was therefore the development of a protein import system able to recognize the necessary proteins and transport them across the two membranes.

From master to slave

The eukaryotic algae that evolved from the original endosymbiosis had an advantage over their non-photosynthetic kin. They didn't need to go hunting for food because they could synthesize it 'in house' from simple precursors using the power of photosynthesis. However, this meant that the algae also became targets for any hungry phagotrophic eukaryote. As with the cyanobacterial prey, the engulfed algal cells provided new opportunities for the establishment of symbioses, although in this case it was a eukaryote that was being enslaved within a eukaryote (a process termed secondary endosymbiosis; see Fig. 1). Once again, the endosymbiosis occasionally led to a permanent association between the two organisms and the evolution of the captured alga into a bona fide organelle. And once again the price for survival of the endosymbiont was high. Since the only important part of the alga was its chloroplast, other cellular components were rapidly discarded. Consequently, the algal cell was reduced to a chloroplast surrounded by additional membranes derived from the algal cell membrane and the vacuolar membrane of the phagotroph. Remarkably, the nuclear genes for the biogenesis of the chloroplast were once again moved en masse, this time from the algal nucleus to that of the new eukaryote host.

Various different algal groups appear to have evolved via this process and include the dinoflagellates, the euglenophytes, the heterokonts (which include the diatoms and the brown algae) and the haptophytes (see Fig. 3). The chloroplast of the euglenophytes evolved from a green alga, whereas the chloroplast of the other groups (with the exception of certain dinoflagellates – see below) is probably derived from a red alga. In all of

BELOW:
Fig. 3. Light micrographs of various microbial eukaryotes that possess chloroplasts. (a) A glaucophyte (*Glaucocystis*), (b) the red alga *Porphyridium*, (c) *Euglena*, a euglenoid alga that obtained its chloroplast from a green alga and (d) the dinoflagellate *Ceratium* that obtained its chloroplast from a red alga.
PHOTOS MICHAEL ABBEY (a), ASTRID & HANNS-FRIEDER MICHLER (b), ERIC GRAVE (c) AND LEPUS (d)/SCIENCE PHOTO LIBRARY



Further reading

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these groups, the old nucleus and all of the cytosolic components have been lost completely. However, in two other algal groups (the chlorarachniophytes and the cryptophytes) a vestigial nucleus called the nucleomorph remains in the intermembrane space, together with a genetic system that allows transcription and translation of the few hundred nucleomorph genes. Recent molecular analysis of the nucleomorph genome has revealed that it has undergone a remarkable process of compaction and miniaturization. The nucleomorph genes are crammed together on three tiny chromosomes, with non-coding DNA, such as introns and intergenic DNA, reduced to an absolute minimum. The formation of the nucleomorph genome in the chlorarachniophytes and cryptophytes represents an impressive case of convergent evolution since the two groups have clearly evolved from independent secondary endosymbiotic events. The chlorarachniophytes have green chloroplasts derived from a chlorophyte, whereas the cryptophytes obtained their chloroplast from a red alga. Thus chloroplast acquisition by secondary endosymbiosis appears to have occurred on at least six separate occasions, allowing the emergence of a wide variety of photosynthetic eukaryotes. However, it didn't stop there...

A change of colour

The dinoflagellates represent perhaps the most fascinating and complicated of all the algal groups. The majority of photosynthetic dinoflagellates probably obtained their chloroplast by secondary endosymbiosis of a red alga. These chloroplasts are distinctive in that they contain the xanthophyll pigment peridinin, which gives a golden coloration to the chloroplast. However, approximately half of all dinoflagellate species have no chloroplast at all and live life as phagotrophs. Others have green chloroplasts that appear to be of green algal descent, and others even have yellow-brown chloroplasts of haptophyte origin (a case of tertiary endosymbiosis!). Recent phylogenetic analysis suggests that all dinoflagellates have evolved from a common ancestor that had a peridinin-containing chloroplast. It would appear therefore that the chloroplast has been subsequently lost by some dinoflagellates that reverted to a phagotrophic existence. Others have discarded their original chloroplast in favour of a new one from green algae or haptophytes.

A further revelation has come from studies of the apicomplexan protists. These are obligate intracellular parasites and include the causative agents of malaria, toxoplasmosis and many other animal diseases. Remarkably, these organisms also seem to have a photosynthetic ancestry since they possess a non-pigmented plastid with its own tiny circular genome that is clearly a relic of a chloroplast genome, as described in Paul McKean's article on pp. 129–131. This plastid has attracted considerable interest as a possible target for therapeutics, since the parasites' animal hosts certainly do not have plastids.

A green ancestry for all?

One of the most contentious suggestions to have emerged recently is that the primary endosymbiotic event occurred much earlier in eukaryotic evolution than currently envisaged, and that many of today's eukaryotic microbes have evolved from this photosynthetic ancestor. Limited support for this has come from phylogenetic studies of various ciliates, oomycetes and amoeboflagellates, which reveal the presence of cyanobacterial-like genes in their nuclear genomes. Just how far back we can trace the photosynthetic ancestor must await further research, but it is clear that the chloroplast was a 'must have' accessory for many up-and-coming eukaryotes!

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New hope for the neglected diseases

Paul McKean

There is an urgent need to develop new drugs against protozoan parasites. Paul McKean explains how greater understanding of parasite biology and genome sequencing information may lead to a breakthrough.

As we enter the 21st century it is a sobering thought that many of the parasitic protozoan diseases that were thought to be under control, and indeed eradicated from some areas during the 1960s are again resurgent in many tropical countries. Diseases such as malaria, trypanosomiasis and leishmaniasis are once again exerting an enormous toll in terms of mortality and morbidity on the populations of developing countries (see Table 1).

Although there are reasons for this degenerating situation, including complex political and socio-economic factors (such as military conflicts, collapsing health programmes and population displacement) it is clear that the parasites themselves are also fighting back. There is widespread development of drug resistance in many parasitic protozoa, a worrying situation for diseases where the treatments are often unsatisfactory in the first place.

Although modern medicine has made enormous technological advances over the past 40 years, this has not been reflected in the field of tropical medicine. For instance, Melarsoprol, the most commonly used drug for the treatment of African trypanosomiasis or sleeping sickness, was introduced over 50 years ago. This arsenic derivative causes severe pain upon intravenous injection and actually kills up to 10% of patients due to severe side effects.

The neglected diseases

Although there is an urgent requirement for the development of new drugs against protozoan parasites, these organisms have been largely neglected by pharmaceutical companies in the developed world. At a recent meeting in New York organized by the French charity Médecins Sans Frontières (MSF) it was emphasized that whilst nearly 1,400 drugs have been introduced over the last 25 years, only 13 of these were for the treatment of tropical infectious diseases.

Clearly there is little financial incentive to develop drugs against diseases afflicting human populations in some of the world's poorest countries. However, the dearth of anti-parasite drugs is not just a financial issue. Our academic understanding of parasite biology has often not been at a level adequate for target identification.

New opportunities from the distinct biology of parasites

Despite this rather dismal picture of tropical disease and drug development there is now hope that progress in parasite molecular genetics, genome sequencing projects, as well as fundamental studies into the biology of parasites, will provide scope for new drug development.

Within the next 2–3 years, the genomes of four major protozoan pathogens (*Plasmodium falciparum*, *Leishmania major*, *Trypanosoma brucei* and *Trypanosoma cruzi*) will be completely sequenced. Careful interrogation of this wealth of information, allied to a greater understanding of parasite biology is creating exciting new opportunities for the development of novel chemotherapeutics. Nowhere is this approach better exemplified than by the recent advances in the identification of new targets for anti-malarial drug therapy, based in part on the realization that during its evolutionary history the malarial parasite *Plasmodium* 'ate a plant'.

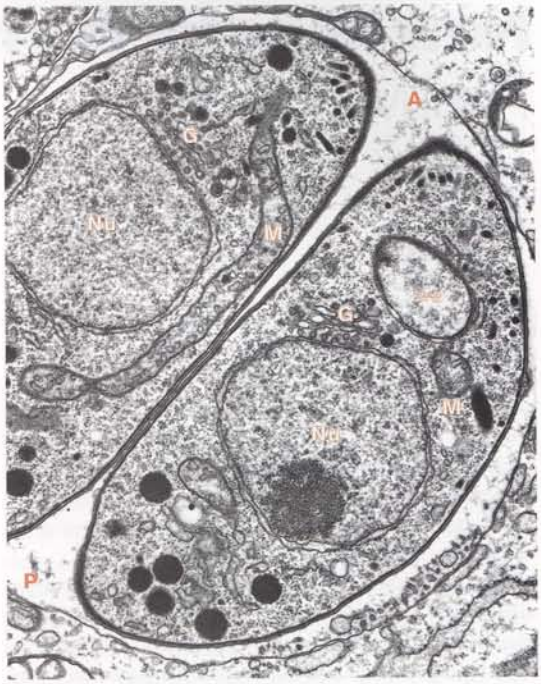
Plasmodium – a green parasite?

Plasmodium, along with all other parasites from the phylum *Apicomplexa*, contains three classes of DNA; a nuclear genome and two circular DNA elements of 6 and 35 kb in size. It was originally suggested that the 35 kb element could represent the mitochondrial genome of apicomplexan parasites. However, the subsequent identification of the 6 kb DNA element as the true mitochondrial genome presented

Table 1. Disease statistics associated with several important protozoan parasites

Disease	Parasite	Cases	At risk
Malaria	*Plasmodium falciparum* *Plasmodium vivax* *Plasmodium malariae* *Plasmodium ovale*	300–500 million	2,400 million
Leishmaniasis	*Leishmania major* *Leishmania donovani* *Leishmania mexicana* *Leishmania brasiliensis*	12 million	350 million
American trypanosomiasis Chagas disease	*Trypanosoma cruzi*	18 million	100 million
African trypanosomiasis Sleeping sickness	*Trypanosoma brucei gambiense* *Trypanosoma brucei rhodesiense*	300,000–500,000	60 million

Source: World Health Organization



RIGHT:
Fig. 1. Transmission electron micrograph of the apicomplexan parasite *Toxoplasma gondii*. The organellar structures containing the three genomes of this parasite; the nucleus (Nu), mitochondria (M) and apicoplast (**) are indicated. The golgi (G), and the anterior (A) and posterior (P) ends of the cells are also indicated.
PHOTO COURTESY PROFESSOR DAVID ROOS, DEPARTMENT OF BIOLOGY, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, USA

OPPOSITE PAGE:
Fig. 2. Schematic showing apicoplast metabolic pathways. Biosynthetic pathways within the apicoplast are dependent upon pyruvate. This is acquired through the import of sugars and/or phosphoenol pyruvate and the subsequent activity of the enzyme pyruvate kinase. Isoprenoids are synthesized via the DOXP-dependent pathway and are required for the isoprenylation of tRNAs and possibly other metabolic functions within the cell. Acetyl CoA is produced from pyruvate by the action of a pyruvate dehydrogenase complex and used to produce fatty acids via acetyl CoA carboxylase and a type II FAS complex. Although not discussed in the text it is also likely that the biosynthesis of haem is a metabolic function of the apicoplast.
DIAGRAM COURTESY P. MCKEAN (BASED ON A FIGURE BY PROFESSOR DAVID ROOS, DEPARTMENT OF BIOLOGY, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, USA)

a conundrum. Exactly where within the cell did this 35 kb DNA element reside and what possible function could it serve? Sequencing of the 35 kb DNA element clearly indicated that it resembled the plastid genome of non-photosynthetic algae. Research on a related apicomplexan parasite, *Toxoplasma gondii* (an important opportunistic pathogen in AIDS patients), localized the 35 kb DNA element to a small membrane-bound organelle adjacent to the apical end of the nucleus (Fig. 1). This structure, a relic chloroplast-like plastid termed the apicoplast, appears to have been acquired by an early progenitor of the apicomplexan phyla through a process of secondary endosymbiosis. It is proposed that a progenitor algal cell initially engulfed a cyanobacterial-like prokaryotic cell in a primary endosymbiotic event (see Saul Purton's article on pp. 126–128 for the development of chloroplasts in algae). The subsequent engulfment of this algal cell by the apicomplexan ancestor (secondary endosymbiosis) and the subsequent retention of the plastid gave rise to the apicoplast.

It is important to appreciate that the apicoplast (and indeed all plastids) retain a considerable degree of autonomy despite their intracellular existence within eukaryotic cells. This autonomy extends not only to retaining their own reduced genome, but also to the retention of transcription and translation systems that are fundamentally prokaryotic in nature.

Apicoplast genes and proteins

Sequencing of the plastid genome from *Plasmodium* and *Toxoplasma* revealed that many apicoplast genes were exclusively involved in gene expression, including large and small subunit rRNAs, 25 species of tRNA, subunits of eubacterial RNA polymerases and the translation elongation factor Tu. The presence of prokaryotic-like proteins explains the susceptibility of apicomplexan parasites to antibiotics that interfere with bacterial transcription and translation, such as rifampicin, erythromycin and doxycycline.

However many apicoplast-specific genes (probably more than 100) have also been transferred laterally to the nuclear genome of the apicomplexan cell. The targeting of nuclear-encoded proteins to the apicoplast presents a complex problem for cells as the apicoplast is surrounded by four membranes, reflecting the two endosymbiotic events leading to its formation. *Toxoplasma* has been instrumental in the elucidation of apicoplast-targeting sequences due to the exceptional ultrastructure of these cells. These studies demonstrate that nuclear-encoded apicoplast proteins encode an amino-terminal bipartite targeting signal. This consists of a typical amino-terminal secretory signal sequence immediately followed by a plastid-targeting domain. These two domains together are sufficient to target proteins with great efficiency to the apicoplast. The bipartite apicoplast targeting signal is well conserved phylogenetically, enabling nuclear-encoded apicoplast proteins to be identified from the *P. falciparum* genome sequencing project solely on the basis of primary sequence information (see below).

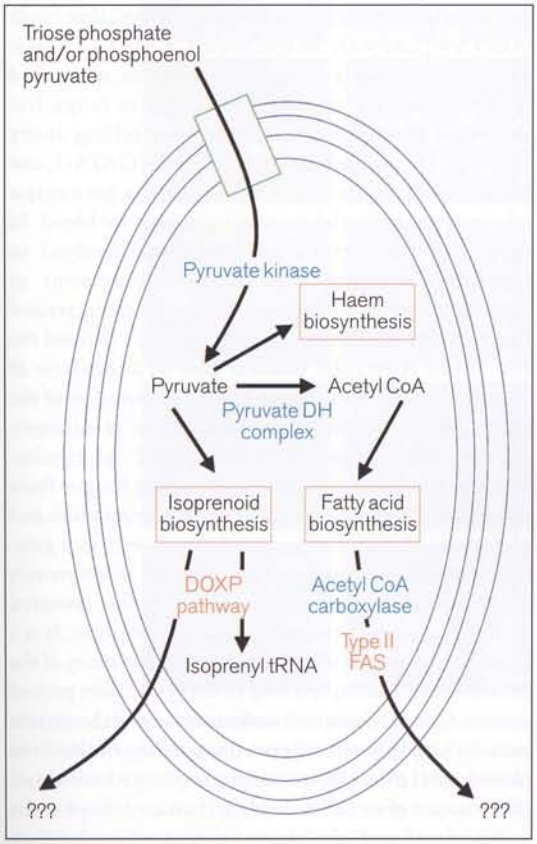
The apicoplast – the enemy within!

Whilst the unusual evolutionary history and cell biology of the apicoplast is clearly a fascinating area of academic research, the functional relevance of the apicoplast was initially obscure. However, the fact that apicomplexan cells had retained this organelle over millions of years of evolution strongly argued that it may have a vital cellular role. The precise nature of this is at last beginning to be unravelled, partly as a result of information derived from genome sequencing projects. Significantly, apicoplast metabolic pathways are more characteristic of bacteria and plants than animal cells. Obviously the cyanobacterial origin of the apicoplast now takes on added importance, as pathways fundamentally different from mammalian cells provide excellent targets for the design of new parasiticidal drugs.

Apicoplast metabolic pathways – the Achilles heel of apicomplexan parasites?

Isoprenoid biosynthesis. Isoprenoids represent a remarkably diverse group of essential lipids that include cholesterol and the respiratory chain electron carrier, coenzyme Q (ubiquinone). Isoprenoid synthesis depends upon the production of a critical subunit, isopentyl diphosphate (See Fig. 2). Synthesis of isopentyl diphosphate can proceed via two distinct routes, the melavonate-dependent pathway and the melavonate-independent pathway.

In mammals and fungi, isopentyl diphosphate is synthesized by the melavonate pathway, whereas in eubacteria, plants and algae this critical subunit is synthesized by the melavonate-independent or 1-deoxy-D-xylulose 5-phosphate (DOXP) pathway. Significantly, inhibitors of the melavonate pathway are ineffective as antimalarials, indicating that this pathway is absent in *Plasmodium*. However, two key enzymes in the



DOXP pathway have been identified in the *Plasmodium* genome; DOXP synthase and DOXP reducto-isomerase. The apicoplast localization of these two enzymes was strongly indicated by the presence of the bipartite apicoplast targeting sequence at the amino terminus.

Although the exact role of isoprenoid biosynthesis is still under investigation (as it is likely that *Plasmodium* salvages cholesterol from the host cell), this pathway is unquestionably important to *Plasmodium*. For instance, mice infected with the rodent malarial parasite *Plasmodium vinckei* can be completely cured of their infection by the administration of the antibacterial drug fosidomycin (an inhibitor of DOXP reducto-isomerase.

Fatty acid synthesis. The synthesis of fatty acids, which are important for cell growth, differentiation and general cellular homeostasis, represents one of the most critical biochemical pathways within cells. Fatty acids are synthesized *de novo* by most organisms, with two distinct types of fatty acid synthase (FAS) being described to date. Type I FAS is typically found in the cytosol of most eukaryotic cells, including man. Although the type II FAS pathway is widespread in bacteria, in eukaryotic cells it is almost exclusively limited to those organisms containing plastids. It is not surprising therefore that the type II FAS pathway has recently been identified in *Plasmodium*.

Crucially the two FAS pathways differ in susceptibility to inhibition by the drug triclosan (a broad-spectrum antibiotic); the type I FAS pathway is refractory, but the type II FAS pathway is inhibited. Administration of triclosan to malaria-infected mice results in the complete clearance of malarial parasites with no adverse effect on the mammalian host.

One of the major attractions of the apicoplast as a drug target is its prokaryotic character. This is not solely because apicoplast biochemistry is fundamentally different from that of the mammalian host, but also because considerable investment in antibacterial drug development now provides a pre-existing source of inhibitors that may be effective as anti-malarial drugs.

Unfortunately, trypanosomes and *Leishmania* do not harbour an apicoplast-like organelle to target for chemotherapy. However, with these pathogens too there is renewed optimism that the wealth of information from genome sequencing projects, allied to greater understanding of parasite biology will lead to better target identification and ultimately to the development of new and desperately needed drugs.

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Further reading

Website of *Médecins Sans Frontières*, the independent humanitarian medical charity: **http://www.msf.org/**

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What's for dinner, what shall I choose?

Mark X. Caddick

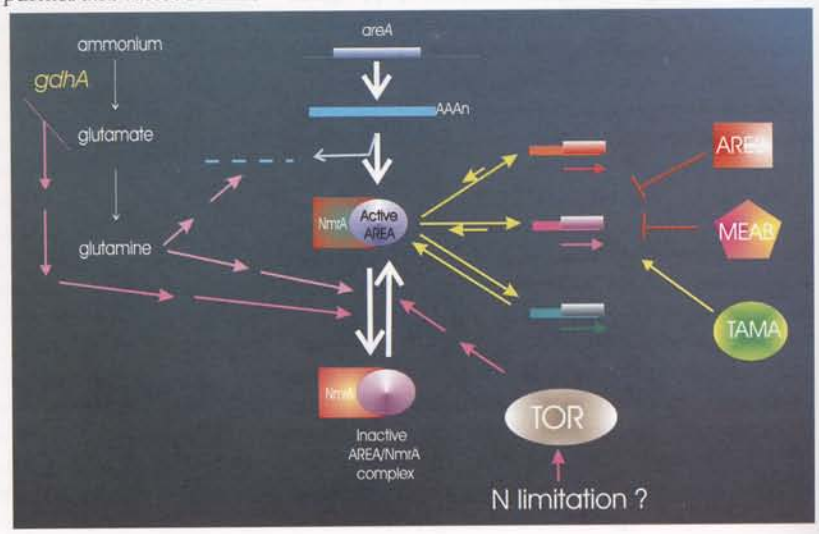
Fungi can metabolize a wide range of compounds, but when a variety is available a sophisticated control system determines the order in which they will be used.

As an undergraduate once observed, '*Escherichia coli doesn't have a very well developed nervous system*' and the same goes for fungi and most other micro-organisms. However, they are very accomplished at observing their environment and making appropriate decisions; an ability which puts many a human to shame. We often find it difficult to know what to eat, and a long menu can cause agonizing difficulties. I have a sister who takes at least 10 minutes to come up with an answer if you ask her what she would like to drink. This contrasts with the average fungal mould that shows a surprising ability to both consume what seems unpalatable and to do so in an impressively orderly fashion. At the beginning of the 1960s the French scientists François Jacob and Jacques Monod described such a decision-making mechanism in bacteria. '*I'll eat up my glucose before tucking into the lactose*' is the lesson that every self-respecting bacterium and undergraduate has learnt. Their classic work gave us the *lac* operon, which illustrated how gene expression can be switched on and off through the interaction of regulatory proteins (transcription factors) with a region of DNA (the promoter) just in front of the DNA that encodes a protein (the structural gene). Soon afterwards came descriptions of similar regulatory systems in fungi and other eukaryotes.

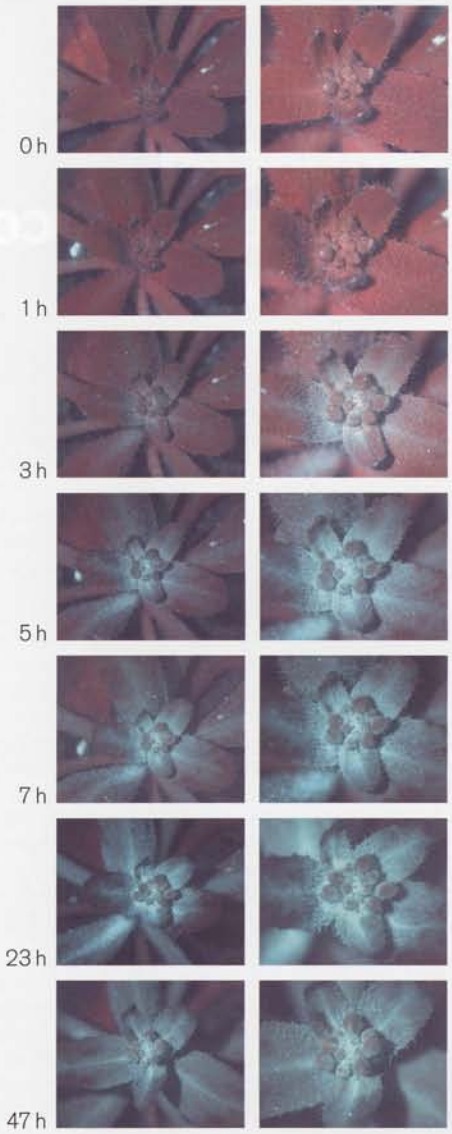
Among the best-characterized systems are those regulating nitrogen and carbon metabolism. Fungi are the champions among scavengers and the key to this is their metabolic versatility that in turn requires sophisticated control. In the mid-1960s the first observations were made of what is now called nitrogen metabolite, or ammonium, repression. This determines that if a good nitrogen source, such as ammonium or glutamine, is present then it will be utilized preferentially. Consequently, the genes and enzymes required for the metabolism of less favoured compounds such as nitrate, acetamide, purines and various amino acids are all turned off. This regulation has considerable subtlety; it is not just a simple on/off switch. The order of genes being turned on as the nitrogen is steadily depleted seems to be defined. Within this hierarchy some genes are only expressed under nitrogen-starved conditions and others are only repressed if high levels of ammonium or glutamine are present.

So how is this achieved? In most fungi it involves a transcription factor, bearing a four-cysteine zinc finger structure, that binds to DNA regions with the core sequence -GATA-. This is a member of a family of regulatory proteins, now called GATA factors, which are not restricted to fungi, but are found throughout eukaryotes controlling many activities. One of the best-characterized is GATA-1, one of the six vertebrate GATA factors, and it has a major role in controlling globin gene expression for blood. In fungi there are several GATA factors involved in regulating processes from sexual development to circadian rhythm. The first of these to be characterized was *areA*. Seminal work published in 1973 defined the role of this *Aspergillus nidulans* gene as a regulator of gene expression. It is required for the expression of the many genes involved in the utilization of nitrogen sources other than ammonium and glutamine. Mutations inactivating *areA* prevent the fungus from using most nitrogen sources other than ammonium and glutamine. A series of papers defined *areA* as a gene that encoded a protein which acts directly on promoters of the structural genes needed for using less favoured nitrogen sources to regulate their transcription. It is a tribute to the power of genetic analysis that many of the detailed conclusions relating to this gene have proved correct. Our fundamental understanding of the system remains largely unaltered even though the gene has been cloned, well over 100 mutations sequenced within it, the structure of its DNA-binding domain defined at the atomic level and the characteristics of its binding abilities analysed.

The *areA* gene produces a protein (AreA) whose activity is itself defined by several signalling mechanisms that report which nitrogen sources are out there. Among these is a protein, NmrA, which in the presence of high levels of intracellular glutamine represses AreA activity. This repression involves interactions with both the C terminus of the protein and its DNA-binding domain. A second mechanism modulates the amount



RIGHT:
Nitrogen regulation in *Aspergillus nidulans*.
COURTESY M. CADDICK



LEFT:
An induction time-course of GFP expression in *Arabidopsis thaliana*. Two 4-week-old soil-grown *alcR alcA::GFP* plants were monitored by fluorescence microscopy over a 47 hour period after induction by root drenching with 1 % ethanol.
COURTESY J. DOONAN

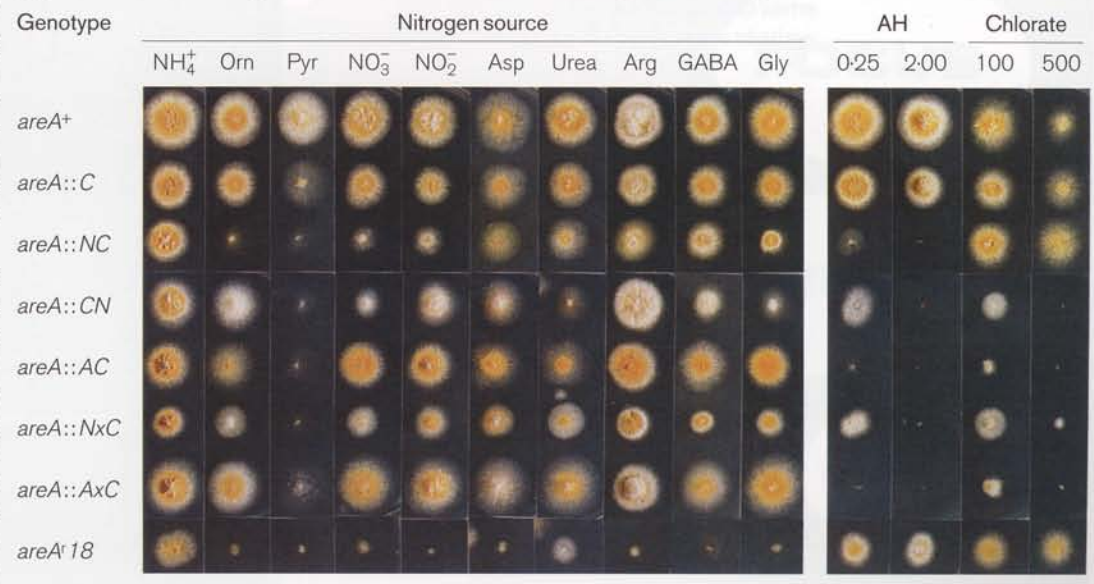
BELOW:
Aspergillus nidulans growth tests. A wealth of data can be obtained from simple plate tests. In this example a range of different strains are being tested for their ability to utilize different nitrogen sources as well as their resistance to toxic analogues. Abbreviations: Orn, ornithine; Pyr, 2-pyrrolidone; Asp, asparagine; Arg, arginine; GABA, γ-amino-n-butyrate; Gly, glycine; AH, DL-β-aspartyl-hydroxamate.
REPRODUCED WITH PERMISSION FROM CADDICK ET AL. (1997), GENES AND FUNCTION 1, 37–49 (© PORTLAND PRESS LTD, BLACKWELL SCIENCE LTD, THE GENETICAL SOCIETY AND THE PHYSIOLOGICAL SOCIETY)

of active AreA protein in the cell by altering the stability of the RNA message directing its synthesis such that it degrades rapidly if glutamine is present. These and other signalling mechanisms are actively monitoring the nitrogen levels within the cell and combine to define the level of active AreA. When it is active, AreA moves to the nucleus where it can bind to promoters and facilitate gene expression. The affinity of AreA for promoters defines a hierarchy of gene expression. Critically, the promoters of the genes it regulates have differing affinities for AreA, so when there are low levels of AreA within the nucleus only genes with high affinity will be activated, while in severe nitrogen shortages AreA levels increase and most of the genes within its regulatory domain can be switched on. Consequently, the genes that can utilize the preferred nitrogen sources are turned on first.

As with much of science there are always more questions than answers. For example, we now know that multiple signalling systems are involved, but we don't know most of their components or how they perceive nitrogen. We know AreA binds to DNA sequences with the GATA motif, but so do at least five other proteins, so how is functional fidelity retained? Perhaps most importantly we don't know all the activities that are regulated by AreA. AreA regulates nitrogen metabolism in *A. nidulans*, but this system appears to have additional roles in other fungi, such as regulating genes involved in pathogenicity, toxin production and antibiotic synthesis. The AreA regulatory system is not the whole story for nitrogen metabolism, either. In some single-celled yeasts, for example, nitrogen limitation leads to a morphological switch, so that the cells change shape to something much more like conventional fungal hyphae. This is very important in pathogenicity, particularly in animal pathogens such as *Candida albicans*. Shape-changing is triggered by various signals, but its regulation does not apparently involve *areA* homologues. When it comes down to it, nitrogen is not merely a nutrient, but is also an environmental marker that affects the fundamental biology of an organism.

In addition to global regulatory systems like *areA*, most metabolic pathways have a second level of regulation, asking whether a specific substrate is available. It is a bit like seeing what is in the fridge, and then deciding what you prefer. Many genes regulated by nitrogen metabolite repression require this second signal, so that only the presence of the specific substrate in addition to the absence of a better nitrogen source lead to their expression. Carbon metabolism also has a similar hierarchy of regulatory devices. In fungi, proteins from the zinc binuclear cluster family of DNA-binding proteins often do this job, regulating transcription of genes required to deal with a specific carbon source.

A good example is the *A. nidulans* transcription factor AlcR that is responsible for regulating alcohol metabolism. It interacts with the promoters of genes,



like *alcA*, needed to deal with ethanol, switching them on when alcohol is around. We have used AlcR to make a switch for genes in plants that is completely under the control of researchers. This works because the gene transcription machinery is conserved among eukaryotes, so that this regulatory protein functions in plants as well as fungi. Conventional genetic engineering techniques let us arrange for continuous production of AlcR within plants such as *Arabidopsis thaliana*. Then, provided a gene had an AlcR-regulated promoter, it would be expressed whenever alcohol was present. Of course, plants do not usually have this sort of promoter, which is precisely the reason for devising this switch. So, all you have to do is change the promoter of gene you are interested in, through some more genetic engineering, and then you can switch it on by watering with ethanol. The fact that the system can be transferred directly from fungi to plants suggests that AlcR detects the chemical signal directly, and there is no genetic evidence to suggest otherwise. The net result is that we now have an effective plant gene switch that allows transient expression of genes in a very well controlled manner – just water your plants with alcohol!

So in fungi we have regulatory systems that operate very much like animal and plant systems, providing fantastic model systems for experimentation. The biology they regulate is also important, whether you are interested in avoiding toxins, producing antibiotics or not getting a fungal disease. And finally we can put the expression systems into other organisms, whether we want to change the way they grow or, more often, simply try to understand how they work.

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Proposed UK Life Sciences Federation

Following the working dinner in November 2001, at which 16 of the largest UK life science learned societies were represented, a working party has been set up to consider the next steps in the formation of the proposed Life Sciences Federation (LSF). The working party – renamed as the Interim Executive Committee (IEC) – is chaired by Sir John Arbuthnott and has as its members Professor Colin Blakemore, Professor Neil Gow, Sir David Hopwood, Dr Nancy Lane, Dr Helen Ougham, Professor Nancy Rothwell, Sir David Smith and Professor John Whittaker, with Dr Brian Jamieson as secretary. Although the list contains several presidents or chairs of learned societies (including SGM) and other bodies, such as the Institute of Biology (IOB) and UK Life Sciences Committee (UKLSC), members are appointed as individuals, to cover a wide range of disciplines within the biosciences, rather than as representatives of particular constituencies or societies. Other members will be added as appropriate and advice taken from the professional staff of societies.

The IEC's first meeting included a wide-ranging discussion of possible activities for the LSF, operational structures, governance and sources of finance. Inevitably, there were different opinions about how much the LSF should try to do. It was agreed that the Federation should concentrate initially on public affairs and communications, dealing with generic issues affecting the biosciences. The next step will be to ask learned societies whether they are prepared to provide financial support, probably in the form of a capitation fee of £1 per member. This could be by transfer of support currently paid by societies to bodies such as the IOB and UKLSC. If sufficient support is forthcoming, the LSF could appoint a part-time director and arrange a temporary office in central London. It is envisaged that the director's first task will be to establish links with member societies so that their expertise can be the basis for the activities of the Federation.

One of the first public presentations of progress on formation of the LSF was given by Dr Nancy Lane, President of the IOB, at the IOB Affiliated Societies Forum on 11 June. There was an extended discussion by the many societies represented. A major difficulty is the future role of the IOB itself: many of the things that the LSF is intending to do are presently covered by IOB. The feeling was that the UK does not need two 'voices of biology'. It was recognized that the IOB is rather light on the more molecular end of the biosciences, and the fact that it is not a particularly wealthy organization limits the scope of its activities.

SGM Council's policy towards the Federation remains supportive, insofar as it shows potential to develop as a strong and respected voice on generic issues in the biosciences, but to retain full control of the Society's finances and core activities in microbiology, including meetings, publications, member services, education and public awareness. The IEC is scheduled to meet twice more in 2002: their proposals will doubtless be considered with great interest by the learned society community.

● ***Ron Fraser, Executive Secretary***

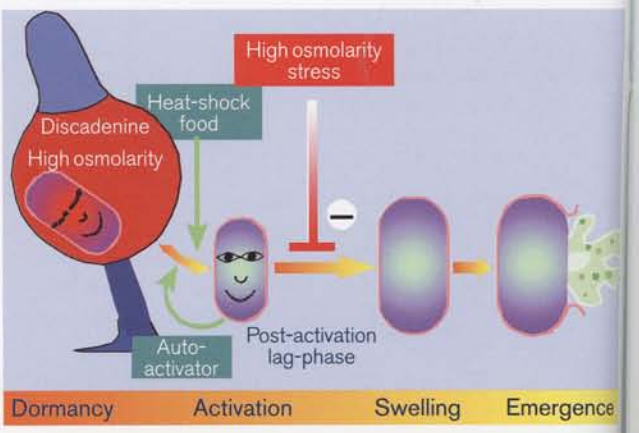
Survival by cAMP in social amoebae: an intersection between eukaryote and prokaryote signalling systems

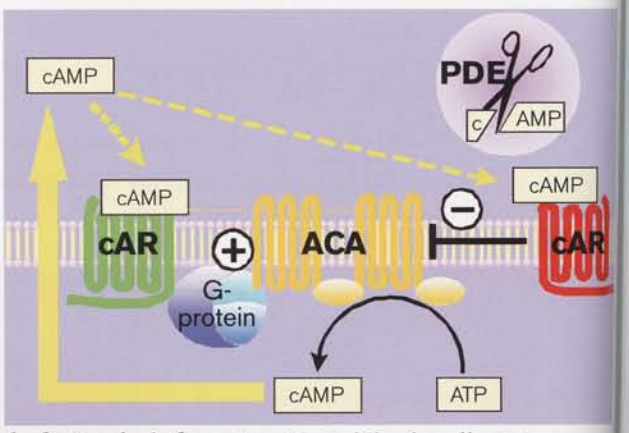
Pauline Schaap

Dictyostelium has a fascinating strategy for disseminating its spores to ensure survival. Pauline Schaap describes the sophisticated system of cell communication that enables this to happen.

Sporulation is a common strategy for most prokaryotic and eukaryotic microbes to survive food shortage and other environmental challenges. This essential response ensures the long-term survival of microbes in a quiescent state until conditions that are suitable for growth resume. Typically, sporulation involves the active elimination of water from the cell, cessation of metabolism and finally encapsulation in a protective cell wall. The process is remarkably effective as shown by the recent discovery and subsequent germination of spores that had been preserved in amber for millions of years.

Most spores do not need to wait millions of years for their environments to improve, and growth resumes predictably in a short amount of time. Some other microbes, rather than passively waiting around, tip the scales in their favour by placing their spores in locations that will allow their transport to better pastures. One of the most elaborate and magnificent examples of this latter strategy is seen in the social amoeba, *Dictyostelium discoideum*. These single-celled soil inhabitants first get together when food runs out. Up to 100,000 independent cells then collaborate to build a fruiting body that keeps the spores aloft and facilitates their dispersal by insects and other soil creatures. A sophisticated system for cell–cell communication has evolved to co-ordinate the functions, such as metabolism, movement and differentiation, that allow fruiting body formation to occur. cAMP, a well known mediator of hormone action in vertebrate cells, plays a crucial role at almost every stage of the sporulation process.





BELOW:
Fig. 1. The *Dictyostelium* life cycle.

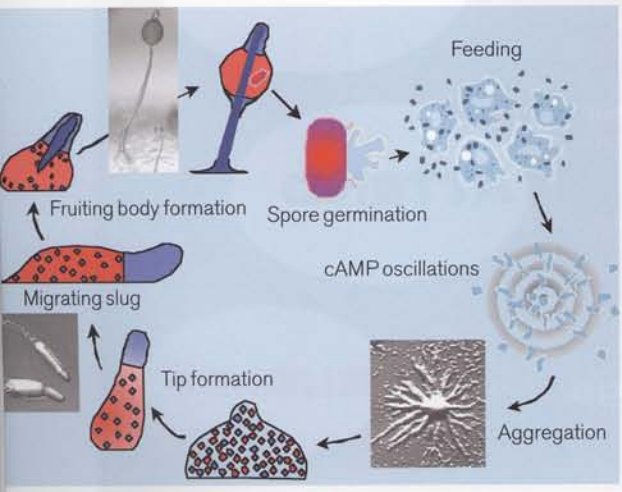
TOP RIGHT:
Fig. 2. Regulation of spore germination.

BOTTOM RIGHT:
Fig. 3. Adenylyl cyclase A is regulated by positive and negative feedback loops.

DIAGRAMS COURTESY P. SCHAAP

Extracellular cAMP

In the first stage, the starving amoebae use cAMP as a chemoattractant. Some cells start to secrete a pulse of cAMP every 6 minutes. The cAMP pulse induces surrounding cells to move towards the source of the signal and to secrete a cAMP pulse themselves. As a result, waves of cAMP propagate through the field of starving cells, which move collectively towards each other to form a multicellular aggregate (Fig. 1).



The aggregate then undergoes intriguing shape changes. A small extrusion, the tip, appears, which extends into a finger-shaped structure, the slug. The slug topples over and migrates towards the light until it reaches a location that is suitable for fruiting body formation. Meanwhile, the cells start to differentiate. About 75 % of the cells express genes that will ultimately cause them to transform into spores fated to survive. The remaining 25 % express genes that will cause their transformation into the stalk cells that are doomed to die. At first the two cell types are intermixed, but when slugs start to form, they sort out. The prestalk cells (blue in Fig. 1) move forwards to the front of the slug, while the prespore cells (red) remain at the back.

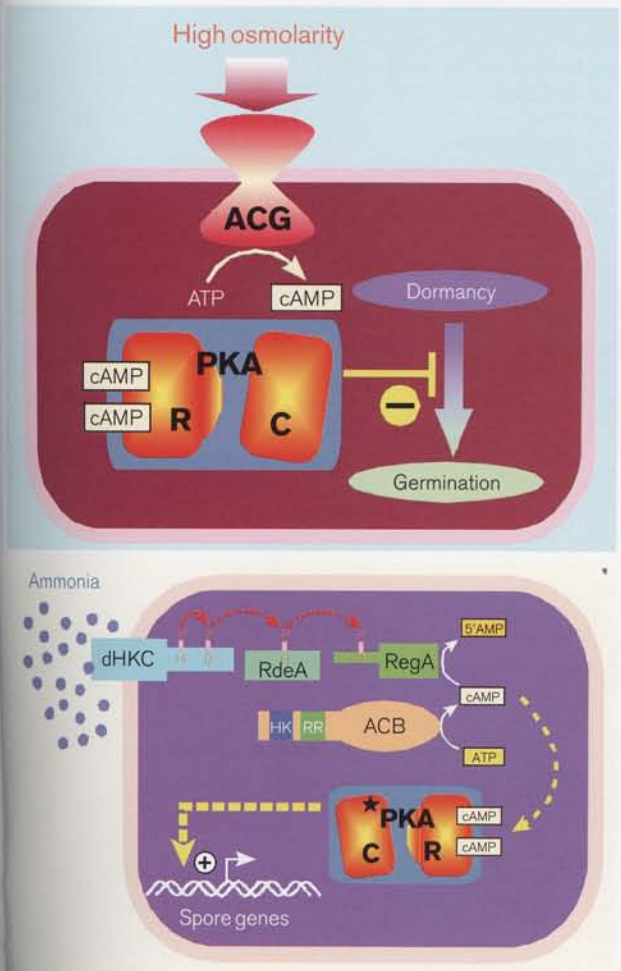
During fruiting body formation, the prestalk cells at the front synthesize a central cellulose tube and then move into it. While doing so they differentiate into stalk cells. This is quite a dramatic process; the cells swell by taking up water and deposit a shared layer of cellulose fibres that allows them to assemble into a rigid stalk. The prespore cells move up the stalk. They mature into spores by losing water and by constructing a thick wall from prepackaged spore coat materials.

The cell movements that allow slugs and fruiting bodies to form are controlled by the tip cells. They continue to secrete cAMP pulses, which travel through the slug in waves and cause cells to move towards the tip. The cAMP waves also cause the prestalk and prespore cells to sort, because the prespore cells gradually lose chemotactic responsiveness to cAMP and are left behind to occupy the rear of the slug.

Extracellular cAMP has a second important function: it induces the differentiation of the prespore cells. The prespore cells in turn secrete a small lipophilic factor, DIF, that induces the differentiation of the stalk cells.

Intracellular cAMP

Social amoebae are the only known organisms that use cAMP as an extracellular signal. Most prokaryotes and eukaryotes use cAMP as an intracellular messenger for a wide variety of physical and chemical external stimuli. In prokaryotes cAMP is usually detected by transcription factors, such as the catabolite repressor protein. In eukaryotes the most common target is the cAMP-dependent protein kinase (PKA). In *Dictyostelium*, intracellular cAMP acting on PKA induces the maturation of spore cells. Intracellular cAMP also regulates the very first step in the life cycle, the germination of the spores. Germination is a critical step in the life of any organism with a dormant phase, such as a cyst, spore or seed, because it must only occur under conditions that allow proliferation. Several constraints regulate spore germination in *Dictyostelium* (Fig. 2). In the fruiting body, spores are kept dormant by the presence of a plant cytokine type molecule, discadenine, and by high osmolarity, which is also a common inhibitor of the germination of plant seeds and fungal spores. Young spores require a stimulus such as food to germinate. Old spores secrete an autoactivator of germination and germinate in the absence of any stimuli. After being activated for germination, spores enter a lag phase before swelling and emergence are initiated. During the lag phase, spores sense whether the environment is suitable for germination, and if not, they return to dormancy. High osmolarity is also a constraint factor that induces return to dormancy and it does so by increasing intracellular cAMP.



TOP LEFT:
Fig. 4. Adenylyl cyclase G is an osmosensor that controls spore germination.

BOTTOM LEFT:
Fig. 5. RegA and ACB control the maturation of spores.

DIAGRAMS COURTESY P. SCHAAP

Adenylyl cyclases

Dictyostelium cells express three adenylyl cyclases that synthesize cAMP from ATP. Adenylyl cyclase A (ACA) is regulated by a positive and negative feedback loop to produce the cAMP pulses that control cell movement. This works as follows: starving cells secrete a small amount of cAMP, which acts on surface cAMP receptors (cARs) to stimulate ACA activity and initiate a cAMP pulse (Fig. 3). With a small delay, extracellular cAMP also triggers an inhibitory pathway that blocks further activation of ACA. An extracellular phosphodiesterase then degrades cAMP. cAMP receptors are now freed from cAMP and the cells become resensitized to respond to cAMP once more.

Adenylyl cyclase A (ACA) is homologous to the vertebrate adenylyl cyclases. These enzymes harbour two sets of six transmembrane domains interspersed with two catalytic domains. They are regulated by serpentine receptors that are coupled to heterotrimeric G-proteins. In vertebrates the β-adrenergic receptor, coupled to the G-protein Gs is the archetypal example of a signalling pathway that via activation of an adenylyl cyclase and PKA leads to glucose production. Glucose is required for the so-called fight or flight response that is triggered by an increase in blood adrenalin levels. In *Dictyostelium*, the serpentine cAMP receptors activate the G-protein (Fig. 3).

Adenylyl cyclase B (ACB) produces the intracellular cAMP for spore maturation. The ACB gene is homologous to that of adenylyl cyclases in cyanobacteria. In addition to the cyclase catalytic domain, it harbours a response regulator and a histidine kinase domain. These are very common components of the phosphorelay signal transduction systems in prokaryotes. The significance of these regions for regulation of ACB enzyme activity is not yet clear.

Adenylyl cyclase G (ACG) controls spore germination (Fig. 4). It is structurally homologous to adenylyl cyclases in *Trypanosoma* parasites with a single catalytic domain and a single transmembrane domain. ACG is strongly stimulated by high osmolarity. It produces

cAMP which activates PKA. PKA in turn blocks the transition from dormancy to germination.

Phosphodiesterases

The phosphodiesterases (PDEs) that degrade cAMP are of crucial importance for every step in the life cycle. PDE is an extracellular enzyme that degrades cAMP between pulses. This is necessary to generate steep gradients of the chemoattractant and to resensitize the cells for the next cAMP pulse.

RegA is an intracellular cAMP phosphodiesterase; its vertebrate-like phosphodiesterase domain is activated by its prokaryote-like response regulator domain. RegA acts antagonistically with ACB to control the process of spore maturation (Fig. 5). In migrating slugs, spore maturation is inhibited by ammonia which is produced in large amounts as an end product of protein degradation. Ammonia is detected by the histidine kinase dHKC. dHKC initiates a chain of events in which phosphate is first carried over to an intermediate, RdeA, and subsequently to the response regulator of RegA. RegA is then activated to degrade cAMP, which is continuously being produced by ACB.

When the spores are carried aloft during fruiting body formation, ammonia will be removed by diffusion into the atmosphere. dHKC, and therefore RegA, become inactive. At this point cAMP can accumulate and activate PKA. PKA triggers the expression of spore genes and mature spores are formed shortly afterwards.

In essence the function of cAMP during *Dictyostelium* development is to bring starving cells to the spore stage and to maintain dormancy until conditions improve. Signalling strategies from both the prokaryote and eukaryote kingdoms have been united to perform this unique feat of self-organization.

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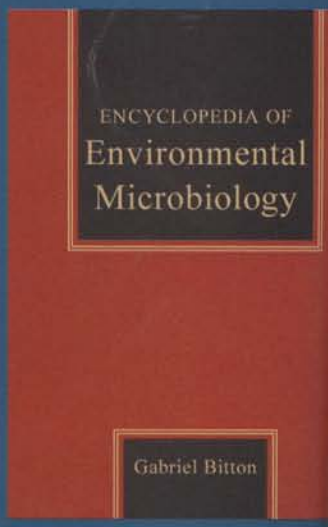
Book Review

Encyclopedia of Environmental Microbiology

Editor-in-Chief	Gabriel Bitton
Published by	John Wiley & Sons Ltd (2002)
Initial offer price	£1,330.00/ 2,111.80
Normal price	£1,480.00



This is the first attempt to publish an encyclopaedia, which exclusively deals with environmental microbiology. The Senior Editor, Professor Gabriel Bitton, has assembled an impressive editorial board, who are well respected in their fields of microbiology and include Robert Burlage, Douglas Capone, Charles Gerba, Mark Le Chevalier, Kate Scow and David White.

This six-volume set, with over 3,500 pages, contains 320 contributions from more than 420 scientists in 25 countries. As you would expect, the material in the volumes is presented alphabetically, with good use of cross-referencing of subject matter. At the front of each volume, the subject content is indexed and, in the final volume, there is a comprehensive index for the entire encyclopaedia. The information has been divided into 14 areas, which the editorial board considers to be the key areas on environmental microbiology: groundwater, freshwater, marine and estuarine waters, biofilms, soils, environmental biotechnology, air, wastewater, drinking water, pathogens, parasites and viruses, biodegradation, extreme environments and methodologies. Professor Bitton sees these volumes as a quick reference guide for environmental microbiologists at all levels, from undergraduate students to academics and other professionals working in this vast field.

The information is presented as small, peer-reviewed chapters, which are well structured. The authors make good use of sub-headings within each chapter, making it easier to isolate specific information. Furthermore, the chapters are well supported by the inclusion of figures and tables to augment the information contained within. Each chapter is well referenced, acting as a secondary source of information with which to delve further into the subject of interest.

My only criticisms of the encyclopedia are (i) a little difficulty in finding specific information; however, cataloguing and indexing are clearly difficult things to achieve for such a publication. (ii) The cost of the encyclopaedia is a significant constraint, precluding purchase by most interested parties. However, I think that for most academic libraries, this is a must for their reference sections. Perhaps something that the author and the publishers should consider is a CD-ROM version, containing a good search engine, which would be a useful asset to this extensive publication, allowing a lowering of the cost price, thereby providing greater accessibility to end-users as well as increased user-friendliness.

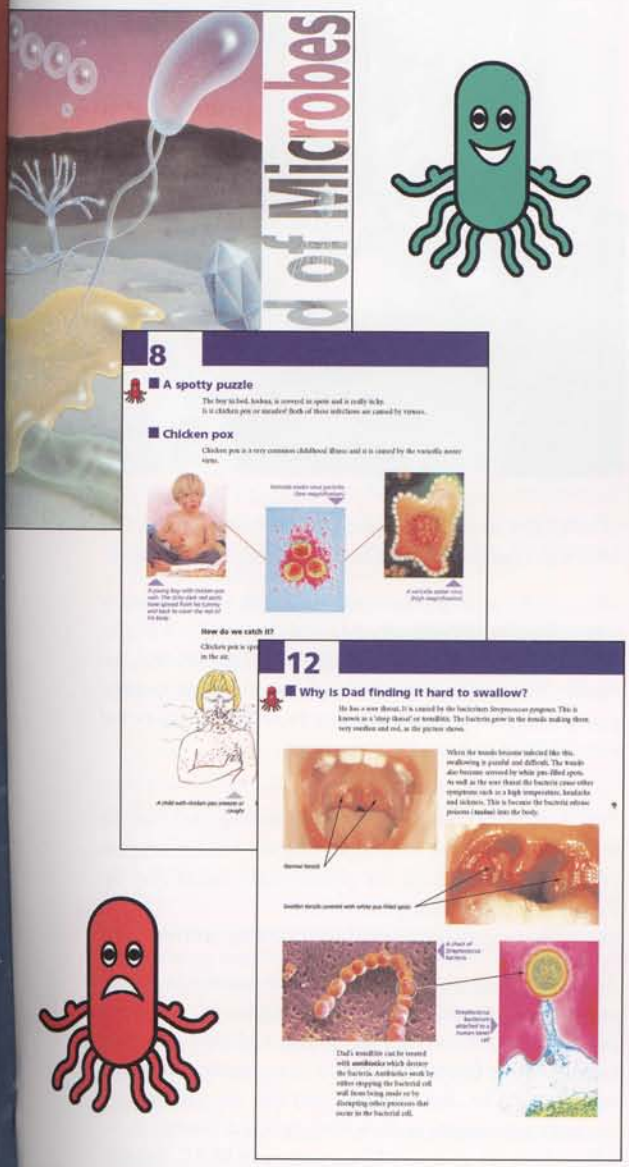
To summarize, this is a significant contribution to the environmental microbiological literature, which is well constructed and extremely useful to all interested in the subject area.

■ ***Kirk Semple, University of Lancaster***

SGM primary school competition: microbes – friend or foe?

SGM '*World of Microbes*' pack

Copies of the pack are available from the SGM Education Office, price £15 inc. p& p. Email **education@sgm.ac.uk** for further information.



The competition was organized to mark the launch of the SGM pack for primary schools, *The World of Microbes*. It is a requirement for all pupils at Key Stage 2 to study micro-organisms under the section 'Living things in their environment' as laid down in the National Curriculum for science SC25f. They have to be taught that micro-organisms are living organisms that are often too small to be seen, and that they may be beneficial or harmful. 'Unit 6B Micro-organisms' from the primary science schemes of work puts together a suggested format to show how SC25f may be addressed. *The World of Microbes* has been written for years 5/6 and supports the delivery of this unit. The children were invited to produce an attractive A3-sized poster which showed the harmful and beneficial roles that microbes play in our lives, suitable for display in the school library.

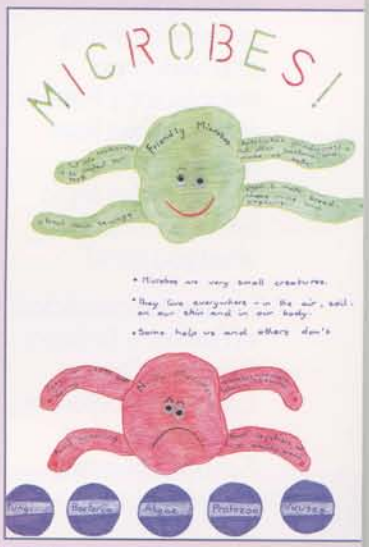
Over 400 entries were received from schools located across the whole UK, including Northern Ireland. Judging, carried out by a panel of microbiology education experts guided by Dariel Burdass, SGM Education Projects Administrator, was extremely difficult. Adjudication took account of originality, scientific content and accuracy, presentation and the effectiveness of the poster as a means of communicating with the peer group. Considering that many primary school teachers have no scientific training and microbiology is quite a specialist discipline which labours under the considerable disadvantage that the subject to be taught is invisible, the standard of entries was remarkably high.

The poster competition provided the teachers with an excellent assessment opportunity. The judges were particularly pleased to see that some pupils did not just focus on the role of micro-organisms in food production and disease. The more successful entries covered the important role that microbes play in decay, both beneficial, e.g. composting, and harmful, e.g. food spoilage, as well as the role of micro-organisms in the production of medicine.

The first prize of £150 for the school was won by **Lauren Meader**, aged 8, of the Abbey School, Reading. Her class will also have an outing to a local science centre. The second prize of £75 went to **Tristan Goodfellow**, aged 9, of Dulwich College Prep School and the third prize was won by **Chloe Varon**, aged 10 of St Paul's Junior School, Kingston upon Thames. Each winning pupil received a book token. Several other entries were highly commended or commended and received special certificates.

Every school entering the competition received a *World of Microbes* pack and each pupil was sent a certificate of entry.

BELOW:
Winning entries in the SGM primary school competition. Top: 1st prize, Lauren Meader. Middle: 2nd prize, Tristan Goodfellow. Bottom: 3rd prize, Chloe Varon. See text for full details.



Equal opportunities in microbiology research careers?

Liz Sockett

SGM Education Officer Liz Sockett explores some current equal opportunity issues which affect everyone training and working in microbiology. Further contributions from readers on any aspect of this topic are welcome. Tell us what you think!

Liz may be contacted at Genetics Division, School of Clinical Laboratory Sciences, Queen's Medical School, University of Nottingham, Nottingham NG7 2UH, UK (Tel. 0115 919 4496; email liz.sockett@nottingham.ac.uk).

At the Warwick SGM Meeting in April the External Relations Staff and Education Group put together a very successful careers evening for postdocs and graduate students. At the reception after the event I asked for comments from attendees as to what other careers information they would like. I was quickly surrounded by a group who requested more information on how women can build successful research careers and whether family considerations cause problems. I promised I'd publicize supportive schemes that are available. In addition, I want to take the opportunity here to flag up two other equal opportunities issues: encouraging more people from diverse ethnic groups to take up research careers and the impact that the recent extension to the Disability Discrimination Act will have on people with disabilities entering university, studying for first and higher degrees in microbiology and going on to research careers. I do not write as a professional in equal opportunities, but as a committed enthusiast for equality of opportunity for all, and as a female microbiology academic being a member of a minority group myself.

All microbiologists enjoy finding out about the massive diversity in the microbial world and we celebrate in our publications bugs with amazing and different capabilities. While it is true that the average undergraduate microbiology class in the UK will contain about 50:50 women to men, members of minority groups are underrepresented (compared to numbers in the whole population). At present it is also very rare to have a student with a physical disability in a microbiology degree class. Moving up through PhD to postdoc and academic posts in microbiology and other biosciences, the trend is towards a higher and higher percentage of white males in senior research posts. Now I have absolutely nothing against white males, being happily married to one myself, but recent equal opportunities policies aim to ensure that all members of society are encouraged and have access to career opportunities in all walks of life, including microbiology.

Schemes to help women scientists in research careers (and for men raising families/caring for relatives)

Although in 1998 50% of undergraduates were female, but only 9% were professors, things are changing and there are now schemes and policies that help younger women combine a career and have a family. Some of these are listed here and I hope that the information will be of use in career planning. The message I'm trying to give is that things are improving for the better and new schemes and opportunities are continually being developed. Eventually these will filter down to change the ethos of the workplace, including the way that maternity leave and career breaks are viewed. If you're a woman microbiology student or postdoc, get online and get informed.

PHOT

Your own university or institute should be a first port of call, they should have an equal opportunities policy which you can usually find on the 'Personnel' web pages.

The UK Athena project aims for '*the advancement of women in science engineering and technology (SET) in Higher Education*'. Its website, http://www.athena.ic.ac.uk/, has details of its mentoring schemes for women postdocs and young academics, discussion groups and conferences and a useful links page to other resources.

The Royal Society Dorothy Hodgkin Postdoctoral Fellowships (10 per year, 4 years funding each) are for research in natural sciences, offering the kind of support and flexibility which are particularly beneficial for female scientists (also open to men).
http://www.royalsoc.ac.uk/funding/fello_dhf.htm

The Daphne Jackson Trust, whose mission is '*returning engineers and scientists to work after career breaks*', also offers postdoctoral fellowships for women and men who have taken a career break of at least 3 years to care for family members. The fellowships include an element of retraining to update skills where required. Several of the fellowships are sponsored by agencies (BBSRC, NERC, Leverhulme Trust, etc.) that typically fund microbiology research as part of their contributions to female-friendly policies.
http://www.sst.ph.ic.ac.uk/trust/index.html

EMBO (European Molecular Biology Organization) has recently published a position paper on working together to achieve equal representation of men and women in the life sciences; see http://www.embo.org/projects/women/women_position_paper.pdf. They

PHOTO SGM

also have a range of research fellowships with flexible policies and career restarts after family breaks.
http://www.embo.org/projects/women/index.html

The Institute of Biology has a 'Women in Biology Working Group' (WIBWG) and has also just appointed its first female president, Dr Nancy Lane, an active promoter of women in science. The WIBWG is trying to promote activities that support women scientists in the UK and can be contacted at ruth.tittensor@faenol.freeserve.co.uk

● Changes to the Disability Discrimination Act to encourage students with disabilities into higher education

From September 2002 the 1995 Act incorporates the 'Special Educational Needs and Disability Act'. This will make it unlawful for higher education institutions to treat students and applicants for degree courses less favourably than someone else for a reason related to their disability without justification. This change will encourage more students with disabilities into higher education and puts the onus on institutions to make reasonable adjustments to their teaching methods to ensure that such applicants or students are not placed at a substantial disadvantage in comparison to someone who is not disabled.

In the microbiology arena this can mean adaptation of practical classes for students with visual or physical disabilities and in lectures the provision of information in new media, including tapes, discs or large print. HE institutions have Student Support Offices which facilitate compliance, but the onus is on every staff member to get informed and to conform. This is especially important given that the Act applies to people just enquiring about admission to a degree course as well as those studying on it. Lack of suitable adapted facilities to admit a student will no longer be a valid reason to deny them access to a course.

Speaking personally, having worked with a range of A-level biology students with visual impairments, I think we tend to greatly underestimate their practical abilities and a well planned lab bench can allow even students with no sight to do basic microbiology safely. See SchoolZone (p. 147) for details of a recent school visit to my lab to do some cloning. Working in a genetics department as I do, it is only logical that students with inherited conditions may be interested in studying for a degree here. Students with disabilities represent a substantial, virtually untapped pool of high quality intellects that can populate and enrich our classes and tutorials with their valuable insights given a small amount of adjustment by the receiving institution. We will be lucky to have them.

The Special Educational Needs and Disability Act can be found on the following website, but check your own institution's web pages for a digest of what it means to you.
http://www.parliament.the-stationery-office.co.uk/pa/ld200001/ldbills/018/01018–e.htm#

Skill: The National Bureau for Students with Disabilities has advice for academics on its site.
www.skill.org.uk

TechDis, an affiliated organization to LTSN, provides resources and advice on technologies and methods that make teaching accessible to students with disabilities.
http://techdis.ac.uk/

The National Disability Team work on behalf of HEFCE to enhance disability provision.
http://www.natdisteam.ac.uk/

● *Dr Liz Sockett, SGM Education Officer.*

Encouraging students from diverse ethnic backgrounds to become the microbiology researchers of tomorrow

- Are you considering a career in academia and don't know which way to turn?
- Do you consider yourself to be a member of an under-represented minority group?

The Annual Biomedical Research Conference for 'Minority' Students (USA) may be of use.

Sponsored by our American sister society, ASM, this conference aims to provide specific guidance and encouragement for students from 'under-represented minorities' to enter research careers. Attendees, who are final year undergraduates, or MSc or PhD students have to present and get feedback on posters on their project. They also attend seminars on professional development, transferable skills, current research opportunities and get extensive mentoring and advice from academics and researchers from minority groups who have made it to the top. One of the reasons for the initiative is to change the currently low numbers of people from minority groups in positions of leadership in universities. Details of the conference are at **www.abrcms.org**

SGM would like to evaluate the usefulness of this approach and so is willing to sponsor the attendance at the conference of two UK students from appropriate ethnic backgrounds in return for a report. The report will describe the benefits gained from attending and suggest which parts might be adapted for use in the UK. If you are interested in applying for one of these places and are considering a research career, please send a letter saying why you would like to attend, your CV and details of two referees (tutors, project supervisors, etc.) to Dr Liz Sockett at the address in the margin on p. 140. Please reply **on or before 13 September 2002**.

Other useful links

- African Caribbean Network for Science & Technology
  Tel. 0161 273 8808; email lizrasekola@hotmail.com
- Commission for Racial Equality
  http://www.cre.gov.uk/
- Ishango Science Clubs to encourage school children in science
  http://www.ishangohouse.com/Ishango%20Science%20Clubs.htm

SocietyNews

May Council Meeting

Nobel Prize Reception

● Council is joining with four other learned societies, The Biochemical Society, The Genetics Society, British Society for Cell Biology and British Society for Developmental Biology to host a reception in honour of **Sir Paul Nurse** and **Dr Tim Hunt**, winners with Leland Hartwell of the 2001 Nobel Prize in Physiology or Medicine at the Houses of Parliament on 8 October.

Areas of responsibility for Elected Council Members

As part of its strategy for improving the communication channels for ordinary members to Council, the first pairs of elected members accepted their new remits. **Professors Hilary Lappin-Scott** and **Dave Kelly** will have oversight of matters relating to postgraduate members and **Dr Pauline Handley** and **Professor Colin Howard** will concern themselves with industrial liaison. They are hoping to develop their ideas over the summer and would welcome input from members.

Delegates to the IUMS General Assembly, Paris 2002

Council confirmed the nominations of **Professors Sir David Hopwood** and **Alan Vivian**, and **Dr Liz Sockett** as its delegates to the IUMS General Assembly in Paris in July. They will take part in the election procedures for the appointment of new officers.

Proposed Life Sciences Federation

Council has reaffirmed its position on the Federation, namely that it would co-operate in generic activities in biological sciences, but would retain its rights in all matters relating to microbiology (see p. 134 for further details).

JMM on-line at HighWire

Council was pleased to hear that agreement has been reached for the *Journal of Medical Microbiology* to go on-line at HighWire, hopefully in August.

● *Alan Vivian, General Secretary*

Annual General Meeting 2002

The AGM of the Society will be held on **Tuesday 17 September** at the Society meeting at Loughborough University. Agenda papers, including reports from Officers and Group Conveners, the accounts of the Society for 2001 and a special resolution to amend Article 25 of the Articles of Association, are in the separate Annual Report booklet distributed to all members with this issue of *Microbiology Today*.

Address Book 2002

Members still just have time to notify the Membership Office at Marlborough House of any changes to their address, telephone/fax numbers or email details for inclusion in the new edition of the Society's Address Book, to be published later this year. Please send them immediately to members@sgm.ac.uk

Staff News

Welcome to **Dr Lucia Primavesi**, new Staff Editor on the JGV team. Lucia gained her qualifications at the universities of Durham, West of England and finally Leeds where she studied for a PhD. This was followed by a postdoc at Edinburgh University. Her researches have focused on the molecular biology of plant gene expression.

And farewell to **Dr Tracey Duncombe** who is relinquishing her post as Public Affairs Administrator to become Press Officer at the Institute for Animal Health. We wish her every success in this role.

Grants

International Research Fellowships

Recent recipients of awards are:

Dr Pablo Zunino, Instituto de Investigaciones Biologicas Clemente, Uruguay – up to £5,400 to study generation and characterization of *P. mirabilis* isogenic fimbrial mutants and sequencing of the UCA fimbrial operon

Dr Lioubov Vinogradova, All-Russia Research Institute for Fertilization, Moscow, Russia – up to £5,700 to study the phylogeny and nitrogen-fixing ability of a phenotypically identified *Agrobacterium radiobacter* (strain 204)

Dr Keith Firman, University of Portsmouth – up to £1,820 to study localization of the type IC restriction-modification enzyme *Eco*R1241 in liposomes

Dr Ahmad Rasheed, Mangalore University, India – up to £6,000 to study microbial profiles and toxin production in Indian monsooned malabar – speciality coffee

Dr Evdokia Pentcheva, University of East Anglia – up to £5,350 to study changes in the protein expression patterns after infection of various cell types with *Chlamydia* strains

Dr Natalia Kalinina, Moscow State University, Russia – up to £6,137 to study biomolecular interactions between virus-coded proteins and host proteins by surface plasmon resonance

Dr Oleg Reva, National Academy of Sciences of Ukraine – up to £6,500 to study the functional analysis of *Bacillus* genes that establish and sustain mutualistic interactions with plants and provide biocontrol activity

Dr Robert Reed, University of Northumbria at Newcastle – up to £1,900 to study the effects of sunlight on the pathogenicity of *Vibrio harveyi*

This 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 and all supplementary documentation must be submitted to the SGM Grants Office for consideration. The closing date for the remaining round of applications in 2002 is **30 November**.

International Development Fund

Members are reminded that funding is again available for competition this year. The purpose of the Fund is to assist microbiologists in developing countries and Eastern Europe. Members may apply for funding to run training courses in developing countries appropriate to the needs of those countries, or for any other small project to assist in technology transfer from Western Europe. The closing date for applications is **25 October 2002**.

Retired Member Conference Grants

Retired members are reminded that they may now apply for a grant to attend one SGM conference each year. The award covers en-suite accommodation and the Society dinner, up to a maximum of £250. Applications for grants to attend the SGM meeting at Loughborough are now invited.

Undergraduate Prizes

Higher education institutions are invited to nominate for an SGM Prize the undergraduate student who performs best in microbiology in their penultimate BSc year. Each student is awarded £50, a certificate and a free year's undergraduate membership. The prizes are intended to encourage excellence in the study of microbiology by undergraduates and to promote scholarship in, and awareness of, microbiology in universities. Nomination forms were sent out to departments in May, but further copies may be downloaded from the SGM website. The closing date for the receipt of applications by the Grants Office is **31 August 2002**.

Seminar Speakers Fund

The Fund aims 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. Written submissions should be sent to the Grants Office for consideration.

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. The closing date for applications to the Grants Office is **4 October 2002**.

Education Development Fund/ PUS Awards

Grants are available to members for projects intended to lead to an improvement in the teaching of any aspect of microbiology relevant to education in the UK. This might include the development of teaching materials (e.g. videos, slides, posters, CAL packages) or novel practical exercises. Funding is also available for small projects to promote the public understanding of microbiology, such as workshops, talks, demonstrations, leaflets, activities at science festivals. Applications will be considered on a first come, first served basis during the calendar year 2002.

Technician Meetings Taster Grants

Eligible microbiology technicians in universities, hospitals, research institutes, etc., may sample an SGM meeting with expenses of up to £200 being met by the Society. Full details were published on p. 83 of the May 2002 issue of *Microbiology Today*. Applications must be received by the Grants Office on the appropriate form before the meeting. If you wish to attend the Loughborough meeting, apply now.

Vacation Studentships

These 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 a laboratory-based science. Support is provided at the rate of £150 per week for a maximum period of 8 weeks. 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.

This year 54 applications were received (one more than in 2001) and studentships were offered to 41 applicants. A list of awardees is available from the SGM Grants Office.

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

The full rules of all Society grant schemes are available on the SGM website at **www.sgm.ac.uk** Please consult these before applying for an award. You can download the application forms for schemes where these are required. Click on the 'Grants & Funding' button for details.

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

Peter Wildy Prize 2002

John Grainger

Lecture title: *Heeding the unseen: a necessary life skill*

After studying bacteriology at the University of Birmingham, John moved to Reading for his PhD and was appointed to a lectureship there, eventually becoming Head of the Department of Microbiology. Involvement with schools began innocently enough in 1964 by providing courses on practical microbiology for teachers. He joined the SGM Teaching Group Committee in 1973 and became its representative on the Microbiology in Schools Advisory Committee. In 1984, the Society encouraged this work by funding a project at Reading to which Dr Paul Wymer was appointed. This then enabled John and Paul to secure DTI funding to found the National Centre for Biotechnology Education in 1985. Subsequent international developments included the European Initiative for Biotechnology Education in 1991 of which John is a founder member. Although retired from the university and as Director of NCBE, his work for schools continues, principally through SGM and as Chairman of MISAC.

Kathleen Barton-Wright Lecture

Al Brown

Lecture title: *Dissection of virulence attributes in the pathogen, Candida albicans – a Gordian knot*

A profile of Al Brown was published in the November 2001 issue of *Microbiology Today* (p. 195).

Meetings

Meetings on the web

Up-to-date information on future Society meetings is available on the website: **www.sgm.ac.uk**

On-line booking

On-line booking forms are now available on the SGM website.

Meetings organization

The SGM meetings programmes are organized by the committees of the special interest groups, co-ordinated by the Scientific Meetings Officer, Professor Howard Jenkinson. Suggestions for topics for future symposia are always welcome. See p. 162 for contact details of Group Conveners.

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

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 emailed to the Events Administrator, Mrs Josiane Dunn, at SGM HQ. 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.

Regional Meetings

Proposals are welcome for one-day regional meetings. These will usually be for postgraduates and first postdocs, with a keynote speaker and offered papers or workshop sessions. The objective is to provide a useful forum, particularly for younger microbiologists, outside SGM Ordinary Meetings. Funding is available to hold up to two of these regional meetings each year. Please submit proposals to the Scientific Meetings Officer, Howard Jenkinson.

Promega Prize

Are you

- a member of the SGM?
- a postgraduate or first postdoc in your first two years?
- 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.

Future Meetings

AUTUMN 2002 – 151st Ordinary Meeting

University of Loughborough 16–20 September 2002

● Main Symposium *Staphylococcus*

16–17 September
Organizers: S. Foster, C. Gemmell, D. Hodgson, H. Jenkinson & S. Patrick

● 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.

● Change of dates

Please note that the dates have changed from those previously advertised for the following symposia:

● Bacterial interactions with extracellular matrix components

Cells & Cell Surfaces Group

NOW 18 September
Organizers: Rod McNab (rmcnab@eastman.ucl.ac.uk) & Anthony Smith (prsaws@bath.ac.uk)

● Extremophiles and astrobiology – at the limits of life

Environmental Microbiology Group

NOW 19–20 September
Organizers: the late David Wynn-Williams & Andrew Ball (andrew@essex.ac.uk)

● Launch of new Eukaryotic Microbiology Group

19–20 September 2002

Top international speakers will participate in the first symposium of the new Group covering *The cytoskeleton as an integrator of cell function*. There will be a drinks reception amongst the posters on the evening of Thursday 19 September. See enclosed programme.

Organizer: Clive Price (c.price1@lancaster.ac.uk)

● Promega Prize Final

17 September

Promega sponsors this competition to encourage excellence in scientific communication by young scientists. Group Committees have now judged recent oral or poster presentations by members who are postgrads or first postdocs. The finalists from each Group or Branch go forward to compete for Promega Prizes at a special session of short oral presentations on their research. There are two prizes of £200 to be won and in 2003 the winners will go on to compete for the title of *Young Life Scientist of the Year* against finalists from other learned societies. The contestants are:

● Stefanie GEHRIG (Dept of Plant Sciences, University of Oxford) *Localization of the protein cluster producing an acetylated cellulose polymer in the plant-colonizing bacterium Pseudomonas fluorescens*

● David TURNER (Division of Microbiology and Infectious Diseases, University Hospital, Nottingham) *AspA, a novel, conserved, immunogenic and surface-exposed meningococcal autotransporter protein*

● Michelle BARR (School of Animal and Microbial Sciences, University of Reading) *Environmentally induced genes of rhizobia*

● Olivia CHAMPION (Dept of Infectious & Tropical Diseases, London School of Hygiene & Tropical Medicine) *Construction of a gene-specific composite Campylobacter jejuni DNA microarray*

● Douglas WEST (Centre for Veterinary Science, University of Cambridge) *Characterization of a ΔhasA allelic replacement mutant of Streptococcus equi subsp. equi*

● Natalie SIMPSON (Dept of Biochemistry, University of Cambridge) *Regulation of carbapenem production in Erwinia sp.*

● Andrew MACDONALD (School of Biochemistry and Molecular Biology, University of Leeds) *Functional consequences of interactions between HCV NS5A protein and Src family kinases*

● David L. WOODHALL (Dept of Medicine, University of Cambridge) *The human cytomegalovirus 72 kDa major immediate early protein interacts physically and functionally with a constituent of ND10 bodies, hDaxx*

● Social Events

Monday 16 September
Welcome Reception

Tuesday 17 September
Society Dinner

Wednesday 18 September
Pub Quiz – entrance fee for charity – prizes for the winning team!!

Thursday 19 September
Evening reception to mark the launch of the Eukaryotic Microbiology Group.

● Microscene Noticeboard

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

SPRING 2003 – 152nd Ordinary Meeting

University of Edinburgh
7–11 April 2003

● Main Symposium Microbial subversion of host cells

Organized by H.F. Jenkinson, D.G.E. Smith, C.D. O'Connor & A.R.M. Coates

7 April

M.J. HUMPHRIES (Manchester) *Current perspectives of the integrin field and their relationship to cellular microbiology*

G. FRANKEL (Imperial College London) *Pair protein interactions and structural analysis of enteropathogenic E. coli virulence determinants*

R. ISBERG (Boston, USA) *Setting up a nest and maintaining it: intracellular replication of Legionella pneumophila*

P. COSSART (Paris, France) *Entry of Listeria monocytogenes into mammalian cells: from cell biology to physiopathology*

G.L. SMITH (Imperial College London) *Vaccinia virus egress using the cytoskeleton*

E. GALYOV (Compton) *Induction of proinflammatory signals by Salmonella*

L. O'NEILL (Trinity College Dublin) *A52R and A46R from vaccinia virus as antagonists of Toll-like receptor signal transduction*

B. KENNY (Bristol) *Co-ordinate subversion of host cellular processes by enteropathogenic E. coli (EPEC)*

8 April

R. COMPANS (Atlanta, USA) *Regulation of viral glycoprotein traffic and virus-induced membrane fusion*

C.R. ROY (Yale, USA) *ARF-dependent transport of Legionella pneumophila to the endoplasmic reticulum*

J. PIETERS (Basel, Switzerland) *Molecular mechanisms involved in phagocytosis: lessons from the intracellular pathogen Mycobacterium spp.*

R.S. STEPHENS (Berkeley, USA) *Chlamydia-directed modulation of eukaryotic host cell functions*

C. MONTECUCCO (Padova, Italy) *Cellular and inflammatory activities of virulence factors of H. pylori*

P. SANSONETTI (Paris, France) *The proinflammatory response (Shigella)*

B. ROIZMAN (Chicago, USA) *Herpes simplex virus and apoptosis*

A. ZYCHLINSKY (Berlin, Germany) *Toll-like receptor-toxin interactions in Shigella*

● Other symposia and workshops

● Type IV secretion systems
Cells & Cell Surfaces Group
Organizer: I. Henderson

● Bacteraemia
Clinical Microbiology Group
Organizer: C. Gemmell

● Water- and environment-related infections
Clinical Microbiology/ Clinical Virology/ Food & Beverages Groups
Contact: T. Humphrey

● The management of outbreaks
Clinical Virology Group
Organizers: S. Cameron & P. Molyneaux

● Successfully surviving your PhD
Education Group
Organizer: J. Verran

● Biological control agents
Environmental Microbiology/ Systematics & Evolution Groups
Organizers: F. de Leij & G. Saddler

● Food fermentation biology
Fermentation & Bioprocessing/ Food & Beverages Groups with Scottish Microbiological Society
Organizers: J. Rattray, M. Collins & G. Hobbs

● Endothelial cell–pathogen interactions
Microbial Infection Group
Organizers: P. Langford & P. Oyston

● Molecular aspects of anaerobes
Physiology, Biochemistry & Molecular Genetics Group with Society for Anaerobe Microbiology
Organizer: N. Minton

● Vaccines (Symposium 1)
Virus Group
Organizer: M. Skinner

● Viruses and cancer (Symposium 2)
Virus Group
Organizer: K. Leppard

● Workshops
Virus Group

Oncogenic viruses
Pathogenesis
Gene expression
Virus vectors
Virus entry, morphogenesis and exit
Nucleic acid replication

● Offered papers and posters

These are welcome for all Group sessions. Please submit titles and abstracts to the SGM Events Administrator by the deadline of **6 December 2002**.

See notice on p. 144 for general conditions for submitting posters.

AUTUMN 2003 – 153rd Ordinary Meeting

UMIST, Manchester
8–12 September 2003

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

Other symposia include: Microbial sensing and signalling/ Analysis of biological data/ Molecular biology: detection and monitoring in the environment/ Post-genomics applied to processes: advances in eukaryotic microbiology/Production of DNA and protein/Genome-based detection/Gene expression *in vivo*/DNA 1952–2003: from structure to function

Irish Branch

Sensing and signalling in microbial populations

Dublin City University
5–6 September 2002
Organizer: Michael O'Connell (michael.oconnell@dcu.ie)

Microbial diseases and the immuno-compromised patient

Maynooth
Spring 2003

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

Other events

● Regional Bioinformatics Workshops 2002

The Society is sponsoring regional Bioinformatics Workshops throughout the UK in 2002. The workshops aim to give microbiologists who have a working knowledge of computational sequence analysis a firm grounding in the use of the latest genome analysis software (Artemis and ACT) developed at the Wellcome Trust Sanger Institute Pathogen Sequencing Unit. Artemis is a powerful annotation tool and DNA viewer that allows the user to analyse sequence data generated in-house as well as being able to upload and re-analyse data taken from EMBL or Genbank. ACT allows direct, and interactive, comparisons of multiple genomes/sequences. For more information about these analysis tools see **http://www.sanger.ac.uk/Software/Artemis/** or **http://www.sanger.ac.uk/Software/ACT/**

Each full-day course, managed by Dr Nick Thomson and colleagues from The Wellcome Trust Sanger Institute, will consist of several short talks dealing with current issues in genomics and demonstrating the utility of Artemis and ACT. However, the emphasis of the day will be for attendees to gain hands-on experience of using these packages with expert guidance and help.

One-day workshops will be held at: **University of Bristol** (Friday 30 August); **University of Liverpool** (Friday 13 September); **Hinxton Hall, Cambridge** (Thursday 7 and Friday 15 November). SGM members wishing to attend one of these workshops should complete the application form on the SGM website. A fee of £20 per registrant will be charged to cover administration, lunch and refreshments. The completed form, together with a cheque for £20 payable to the 'Society for General Microbiology', should be returned to the SGM meetings office. Early registration is advised to avoid disappointment.

Going Public

BUGs – bad, ugly and good

During National Science Week (8–15 March 2002) the School of Applied Sciences at Huddersfield University organized a one-day workshop entitled *BUGs – Bad Ugly & Good*; the theme for the day was based on food microbiology. The day involved pupils completing a circuit of 1 hour sessions on 'Bad bugs', 'Ugly bugs' and 'Good bugs', which included both laboratory and computer-based activities. 'Bad bugs' focused on food poisoning microbes. The 'Ugly bug' section concentrated on food spoilage microbes, whilst the 'Good bug' section examined the use of microbes in food production. We hosted 45 pupils from five schools in the local area; Salendine Nook, Sowerby Bridge, Ralph Thoresby, Rastrick High and Royds Hall.

Prior to the sessions all 'potential microbiologists' were introduced to the significance of microbes in each theme. This was followed by the all important safety talk on good practice in the laboratory. Pupils were then split into small groups before starting the circuit. Postgraduate demonstrators were assigned to specific sections and were available to help and answer any questions. Specially designed badges were handed out to the pupils to denote which themed section to start the circuit with. Some, however, with 'Ugly bug' badges seemed to think this a reflection of their looks! Several teachers were seen to have wry smiles on their faces during the distribution of good, ugly and bad badges!

The success of the day can be attributed to enthusiastic staff (thanks to all post-graduates and technicians who helped), and the wide variety of tasks involved in each themed section. For example, the 'Bad bug' section began with a computer-based learning programme on the use of a microscope before proceeding to examine prepared slides of food poisoning bacteria. Our forward thinking Learning Technology Adviser, Steven Bentley, had also prepared an IT exercise involving poor hygiene practice in food preparation. Variety was also a feature of the 'Ugly bug' section which encompassed such diverse activities as Gram staining, standard plate counts and the resazurin dye reduction test. Perhaps the most informative section, however, involved the 'Good bug' exercises. Pupils were very surprised to learn of the role of microbes in food and beverage production through an exercise that required the identification of microbes used in the making of a hearty three-course meal. Hands on experience of the role of 'Good bugs' was provided in the form of a fermented food lunch, served up in fast food style in Huddersfield University's normally tranquil Queensgate Restaurant.

The day ended with an inter-school quiz covering aspects of the day, with the winning team being awarded Huddersfield University calculators. All schools, however, received a prize: a beautifully illustrated and laminated set of 'Microbes & Food' posters provided by the SGM. Pupil evaluation questionnaires of the day were generally very positive and this indicates that SGM money was well spent for the second year in succession. A final big thank you to the SGM and Huddersfield University staff (too many to mention individually) in making this another successful, and hopefully inspiring, day.

● ***Dr Joy Perkins, Senior Lecturer in Microbiology, Department of Chemical & Biological Sciences, Huddersfield University, Huddersfield, HD1 3DH, UK. email j.perkins@hud.ac.uk***

LEFT:
Students anxious to gain hands-on experience.

TOP CENTRE:
No colony left uncounted!

ABOVE:
Looking for inspiration or a food poisoning bug!

PHOTOS J. PERKINS

Public Understanding of Science Grants

Are you planning any projects to promote the public understanding of microbiology?

SGM can help. Grants of up to £1,000 are on offer to fund your proposed activity. Applications are considered on a first come, first served basis. The funding year runs from June to May.

For an application form and details of the rules see the SGM website **www.sgm.ac.uk**

SchoolZone

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

Website:
www.microbiology online.org.uk

Enquiries:
education@sgm.ac.uk

Over to you...

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

What do you call 10^9 bacteria? A gigabug!

Visit by RNIB New College sixth formers to the Institute of Genetics at Nottingham University

Three A-level Biology students from the Royal National Institute for the Blind New College, Worcester, and their teacher Mr Norman Brown visited Dr Liz Sockett's lab for a day to experience at first hand some practical genetic engineering techniques, including PCR amplification, plasmid-based cloning and bacterial transformation that are part of the AS/A2 Biology specifications.

The three students were Emily, who is interested in physiotherapy or a Biology degree after her A-levels, and has partial sight and no colour vision, John, who has some sight in one eye, and Sarah, who has no sight at all and who reads Braille, unlike the other two who use large print.

During the visit the students met Helen Nankervis, who is currently designing SGM practicals for use in schools, and Karen and Matt, who are both researchers with Liz. Together we explained PCR and DNA sequencing and revised what the students knew about bacterial transformation, plasmids and reporter genes. We let them investigate lab equipment like PCR machines and micropipettes, then got them to set up a PCR amplification for a specific gene and to transform competent *E. coli* with a recombinant plasmid, and to make and pour selective ampicillin/X-Gal/IPTG LB plates to screen their transformants. We were quickly impressed by their knowledge, manual dexterity and enthusiasm. Even Sarah was fully able to pipette microlitre volumes in and out of Eppendorf tubes and to pour and inoculate her plates after a single run-though demonstration. Indeed, when we counted the transformants and sent the results to the school, her transformation efficiency was the best!

While we waited for our transformants to be ready we gave the students a tour of our lab, including our bacterial tracker which tests the motility of bacteria from videos of them swimming. The large video-screen images of the bacteria were visible to John and Emily after a few minutes acclimatizing to the lighting of the room. For Sarah we traced, with cardboard cut-outs, the journey of a single cell across the screen to give an idea of the speed. We also had an animated discussion about science and careers over lunch and later we visited the DNA sequencing service where Ingrid explained her role and opened up a sequencer for the students to investigate.

During the day we recorded what was being said on a small dictaphone and Sarah took the tapes home with her. As she said later, '*the descriptions on the tape are really good for revision, especially the details of how each of the individual protocols are carried out.* The students and the researchers really enjoyed the interaction. The students commented that '*doing the actual practical work makes it much easier to understand and the visit let us piece together all the different parts of the cloning process into the sequence that we are taught at school.*

From the lab side we did give up a day of the Easter vacation when we'd normally be doing research, but we gained a massive amount from the infectious enthusiasm of our visitors and were humbled by their intellects and manual skills. By the end of the day each of us could imagine how with only limited adaptations, we could work as undergraduate project students or even research colleagues. All that was needed was a well set out lab bench and a clear set of instructions. This is definitely a good thing to report as the new Special Needs and Disabilities Education Act starts to widen participation in higher education to more folk with physical impairments (see my article on p. 140).

From the school side it was a success too. Mr Brown, their teacher, emailed us the next day. '*What a brilliant day we had on Friday. The students asked questions almost all the way home! Please thank everybody for all the time and effort that they put in, it was much appreciated.*' Subsequently, we sent them their data so they could calculate their transformation efficiencies (scanning photos of the colonies on Petri plates on to tactile paper at our Student Support office for Sarah). Since then we've had emails from Mr Brown still reporting on their enthusiasm for molecular microbiology (and the odd 'gigabug' joke as above!)

We wish them well with their Biology exams and their future careers.

● ***Dr Liz Sockett is SGM Education Officer. She is based in the Genetics Division, School of Clinical and Laboratory Sciences, Queen's Medical School, University of Nottingham, Nottingham NG7 2UH, UK. Tel. 01159 194496; Fax 01159 709906 email Liz.Sockett@nottingham.ac.uk***

TOP RIGHT:
Sarah, who is blind, investigates a PCR machine before helping to set up an amplification.

RIGHT:
Sixth former John, who is partially sighted, gets used to small-scale pipetting watched by classmate Emily.

PHOTOS LIZ SOCKETT

Gradline

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

Soapbox!

Whether you're an undergrad or a postgrad, the SGM wants to hear from you. Anything goes as long as it's relevant to microbiology. Win £25 for the best letter published. Send your contributions to **soapbox@sgm.ac.uk**

SGM reserves the right to edit letters prior to publication.

A job in... Medical editing

Gradline Editor Tracey Duncombe talks to Emma Sheppard about her work as a medical editor and her aspirations of becoming a science journalist.

Profile

Name Emma Sheppard

Age 22

Present Occupation
Medical Editor, Science Press Ltd, London

Previous Employment
Editorial Assistant, Science Press Ltd

Education
BSc Microbiology and Virology, University of Warwick

Q *What does editing involve?*

'As a Medical Editor at Science Press I am involved in almost every stage of the publishing process. We publish books aimed at GPs to inform them of the latest drugs on the market. Our clients are the pharmaceutical companies who manufacture the drugs.

It's a varied job, which involves taking a book from the manuscript stage through to the final printed version. Some days I edit the text (for sense as well as content) and other days I edit on-screen, proofread or check advances from the printers. I've been trained how to edit properly according to our house style, using the special symbols editors use to denote what should happen to the text. Once I've edited a manuscript I then have to make changes to the Word document and mark the text and figures to be typeset. This is when the text is laid out on pages as it would appear in the final copy. After checking once more for errors the book then goes to the client. Sometimes they may query parts of the text and I have to liaise with the author to ensure that the final book satisfies the author, the client and Science Press, which can take some time! Once we get permission to go ahead the files are sent to the printer. My final task is to check the printer proofs to ensure that the colour is correct and the files have not corrupted.

It is very rewarding when I receive the book advances as the whole process takes many months from receipt of the manuscript to publication. As well as working on my own projects I proofread other people's work, including Spanish and Portuguese texts, which is very interesting as I speak neither language.

I've been very lucky in having such a good first job. It has provided me with a firm grounding in the basics of publishing and I've learnt many new skills that will help me to develop my career.'

Q *Where do you see your career developing?*

'My dream job has always been to write for *New Scientist* or a similar publication. I emailed *New Scientist* about getting work experience and ended up shadowing an Opinion Editor for the day. I learnt many useful techniques, including the standard notation used by sub-editors and how to edit a piece of work to fit a page, skills that I now use daily. I was shown the integrated nature of journalism and the links between each department, which are needed to produce the perfect publication. He convinced me that publishing was a good way to get into writing.'

Q *Do you think you've got what it takes?*

'I hope so. While I was at university I tried to get lots of relevant experience to set me above other candidates. In my first year I joined my student newspaper, the *Warwick Boar*, and wrote weekly for the News section. I enjoyed writing in this style as it was informative, like scientific writing, and it was fun to interview people and create a slant on each story. I entered the *Daily Telegraph Young Science Writer of the Year Awards 2000* and was very surprised to reach the finals with a piece on the role of *Campylobacter* in food poisoning.

I have been interested in writing scientific material since doing my A-levels and was very pleased to discover that a Science Communication course was one of the available modules in my degree. The course comprised a series of workshop sessions run by an ex-*New Scientist* journalist. Our group carried out role-plays of interviews and came up with ideas for museum exhibits and National Science Week. It all culminated in the production of a small portfolio of work that demonstrated how I could communicate science in different ways. The coursework varied from interviewing a member of staff about research and writing an article on it to planning a radio show and designing a leaflet to inform the general public about stem cell research. I put a lot of hard work into my portfolio as I was determined to do well. I was over the moon when I got the result. I got a first class mark. It was confirmation that I was actually good at doing something I enjoyed so much.

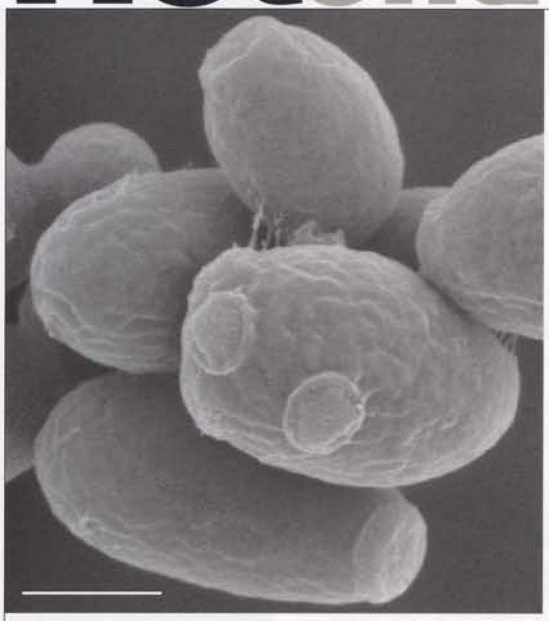
To get a job in the media you must have a lot of experience and useful contacts. I decided to make the most of my university holidays by getting some relevant experience. As well as shadowing someone at *New Scientist*, I arranged to shadow an Anglia TV news presenter to see what television work was like. After standing outside a courthouse for most of the day without getting an interview I decided that perhaps television was not the career for me! I instead chose to follow a career in print and I'm now trying hard to expand my portfolio and get more work published.'

Q *Where do you go from here?*

'I'm trying to create more opportunities for myself by approaching different companies for freelance work. I have recently passed a test for a website that produces health news so hopefully I'll be carrying out work for them in the near future. I'm also writing a chapter in a biology textbook, which I'm looking forward to seeing published. Maybe my next job will have more of a writing role, but I'm pretty happy with what I've achieved so far.'

Hot off the Press

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



TOP:
Scanning electron micrograph of a small cluster of cells of *Candida davenportii*. Bar, 1 μm.
COURTESY MARK KIRKLAND AND MALCOLM STRATFORD, UNILEVER R&D COLWORTH

Wanted – dead or alive!

Microbiologists would like to know how to tell when bacteria are really dead, and when they are alive but unwilling to grow. Obviously, if the microbes have just been cooked in an autoclave, they are not shamming death, but many situations are less clear-cut. Researchers can often see bacteria on grains of soil, or samples of animal tissues, but cannot grow the same ones on culture media. In a similar way, tools from molecular biology have revealed the existence of vast hordes of microbes in every possible environment, few of which will grow in the laboratory.

Apart from philosophical interest, there are very practical reasons for wanting to understand what is happening in these situations. If apparently viable but 'non-culturable' pathogenic bacteria can ever be induced to grow again, they could be medically important, rather than a scientific oddity. Tuberculosis is one of the diseases where there is an argument about whether, and how, bacterial cells can persist in the body for years before becoming active and causing disease.

Researchers at the Bakh Institute of Biochemistry in Moscow and the University of Wales, Aberystwyth, have been collaborating for several years to study 'non-culturable' bacteria. They have studied both an avirulent strain of *Mycobacterium tuberculosis*, the bacterium that causes TB, and its non-pathogenic relative *Rhodococcus rhodochrous*. They have discovered that several days after *R. rhodochrous* has used up all the food in the growth medium, there is a discrepancy of up to 10,000-fold between the number of bacteria that are visible and the number that can be induced to grow by changing the growth medium. However, adding a small amount of liquid from growing cultures decreased these differences. The reason turns out to be minute amounts of a small protein called Rpf, released by the growing bacteria. The same sort of phenomenon happened with *M. tuberculosis*, where even 5 months after the cells had apparently ceased growth, adding Rpf, or liquid from a growing culture, triggered their revival. If *M. tuberculosis* cells can really enter a state of deep dormancy, this may explain why TB can suddenly re-appear years after the infection was ostensibly cured. Finding ways to block this resuscitation may eventually offer new treatments for this disease.

Shleeva, M.O., Bagramyan, K., Telkov, M.V., Mukamolova, G.V., Young, M., Kell, D.B. & Kaprelyants, A.S. (2002). Formation and resuscitation of 'non-culturable' cells of *Rhodococcus rhodochrous* and *Mycobacterium tuberculosis* in prolonged stationary phase. *Microbiology* **148**, 1581–1591.

Spoiling the picnic

Soft drinks are a hostile environment for most microbes because they are so acid. However, a select few are able to live in this acidic, sugary environment, and their growth spoils the flavour and appearance of the drink. Researchers at Unilever R&D, working with colleagues at the National Collection of Yeast Cultures, have just added *Candida davenportii* to this exclusive band, named after the late Professor Bob Davenport, whose work with spoilage yeasts in soft drinks is legendary. The trail started with a common wasp lying dead next to a few drops of syrup from the sampling tap of an external sugar syrup tank at a European soft drinks factory. Although the yeast isolated from the wasp looked perfectly ordinary, biochemical and DNA tests showed that it was sufficiently different from the other 800 known types of yeast to be a new species.

Its most notable characteristic was that it was more resistant to acetic acid than almost all other spoilage yeasts and could grow even at pH 1·4. Another interesting feature was that *C. davenportii* and other closely related yeasts are associated with bees and wasps. Most of them have been isolated from these insects and may be carried by them to infect, and so spoil, sugary foods. So not only is there a hazard from being stung by wasps at a picnic, but they may be carrying yeasts that could spoil the soft drinks.

Stratford, M., Bond, C.J., James, S.A., Roberts, I.N. & Steels, H. (2002). *Candida davenportii* sp. nov., a potential soft-drinks spoilage yeast isolated from a wasp. *Int J Syst Evol Microbiol* **52**, 1369–1375.

A tasty bit of hot property

There is a big market for monosodium glutamate, the ubiquitous taste enhancer listed as MSG in many prepared and oriental foods. Worldwide production exceeded 1 million tonnes in 1996. Much of it comes from bacteria of the genus *Corynebacterium* that secrete large amounts of glutamic acid as they grow in vast industrial fermenters. One problem is that the growing bugs generate so much heat that they die unless complicated cooling systems keep the temperature down.

One solution would be to use bacteria that enjoy higher temperatures. Japanese researchers from Ajinomoto, the world's largest producer of MSG, and from the University of Technology, Toyohashi, have now discovered a new species with exactly this characteristic. In trials, *Corynebacterium efficiens* pumped out over 1·0 g glutamic acid l^{-1} while growing vigorously at 45 °C. The bacteria were originally isolated from soil and an onion bulb, and described in a Japanese patent application. They could now be a piece of hot intellectual property.

Fudou, R., Jojoba, Y., Seta, A., Yamada, K., Kimura, I., Nakamatsu, T., Hiraishi, A. & Yamanaka, S. (2002). *Corynebacterium efficiens* sp. nov., a glutamic-acid-producing species from soil and vegetables. *Int J Syst Evol Microbiol* **52**, 1127–1131.

RIGHT:
Symptoms of Japanese hydrangea phyllody phytoplasma (*Phytoplasma japonicum*) infection on a Japanese hortensia plant (*Hydrangea macrophylla* f. *macrophylla*). A diseased flower, showing typical phyllody symptoms (development of the floral parts into leafy structures) is shown (bottom) below a normal flower (top). Diseased plants also show virescence (the development of green flowers and loss of normal flower colour), proliferation of auxiliary shoots, resulting in a witches' broom appearance, necrosis in the phloem, dieback of branches and eventual decline.
PHOTO COURTESY DR SHIGETOU NAMBA

OPPOSITE PAGE:
A reminder of the FMD crisis in the UK in the summer of 2001.
PHOTO IAN ATHERTON

DNA recombination and diversity in phytoplasmas

Phytoplasmas are very small, wall-less bacteria that live exclusively within the phloem of plants. They have among the smallest numbers of genes of any living organisms, being able to rely on their unwitting hosts for many materials. The main reason for being interested in phytoplasmas is that their parasitic lifestyle causes disease. To date, over 600 diseases in at least 300 plant species have been ascribed to phytoplasmas, but because they cannot easily be separated from their hosts they are very difficult to study. The only way to maintain a phytoplasma for research is in infected plants in a greenhouse. Since the phytoplasma is transmitted in the saliva of sap-sucking insects, the plants have to be within insect-proof containment, and a suitable insect has to be available to propagate the phytoplasma to new plants.

Researchers at the University of Tokyo have been studying the phytoplasma responsible for onion yellows disease (OY-W). This produces a wide variety of symptoms in its plant host, including excessive greening of the flowers, and flowers with leaf-like petals and sepals, yellowing of the leaves, stunting, and excessive proliferation of shoots. They maintained the phytoplasma on garland chrysanthemums and used a leafhopper to transmit it from plant to plant. At one point a variant of the phytoplasma (OY-M) arose that produced much milder symptoms than the original strain. The researchers immediately wondered what change had occurred in the OY-M line.

They knew that the genes for pathogenicity in bacteria are frequently not carried on their chromosome, but instead on small extra pieces of DNA, called plasmids. They had already discovered two classes of plasmids within OY-W, the smaller of which was missing from OY-M. The Japanese group have now reported their most recent findings in *Microbiology*, which give further insight into the evolution of these two phytoplasma lines. They have found a third class, present in both OY-W and OY-M, which looks as if it has arisen by recombination of the two other classes and has lost some of its virulence along the way.

Although this is a first for phytoplasmas, recombination between plasmids is a well-known feature in bacteria that plays a major evolutionary role by creating genetic diversity and provides the potential for rapid adaptation to new environmental conditions. Since phytoplasmas are so dependent on their hosts, any mechanism for increasing their biological diversity could be of great significance for their pathogenicity.

Nishigawa, H., Oshima, K., Kakizawa, S., Jung, H.-y., Kuboyama, T., Miyata, S.-i., Ugaki, M. & Namba, S. (2002). Evidence of intermolecular recombination between extrachromosomal DNAs in phytoplasma: a trigger for the biological diversity of phytoplasma? *Microbiology* **148**, 1389–1396.

FMD revisited 1 – pinpointing the genes responsible for infectiousness and virulence

The outbreak of foot-and-mouth disease (FMD) in the UK in 2001 did not end without a massive effort, involving restrictions on farming and access to the countryside for months, as well as the slaughter of millions of animals. The progress of an outbreak of FMD in Greece in 1994 was very different. Although it started with a lot of illness in sheep flocks, the number of cases declined sharply after a month and the disease finally appeared to die out of its own accord. This sort of behaviour has been recorded before in outbreaks among small flocks. If it really occurs, it could shed some light on exactly why FMD is so virulent.

Researchers at the Institute for Animal Health at Pirbright, UK, collaborating with the Centre for Tropical Veterinary Medicine at the University of Edinburgh, in the UK, set up an experiment to see whether the Greek strain of FMDV really did become less infectious as it spread. They infected one small group of sheep with the virus and then let them meet with other sheep, in an arrangement designed to mimic the spread of disease between flocks in real life. The amount of virus in the blood of infected animals usually correlates well with the infectiousness of that animal, and it turned out to be lower in sheep that were infected later on.

If an infectious agent is to maintain itself through an unbroken chain of infections, it must maintain the level of infectiousness of each newly infected individual, or it will inevitably die out. In this experiment, the peak amount of virus in new infections decreased by about 50 % over only 3 weeks, suggesting that this strain really could not maintain its transmission, which agreed with the records of its behaviour in Greece in 1994. How long it would really take to disappear in real life would depend on a host of factors, but the researchers now want to find out how this strain differs from others, to pinpoint the genes that control its infectiousness and virulence.

Hughes, G.J., Mioulet, V., Haydon, R.T., Kitching, R.P., Donaldson, A.I. & Woolhouse, M.E.J. (2002). Serial passage of foot-and-mouth disease virus in sheep reveals declining levels of viraemia over time. *J Gen Virol* **83**, 1907–1914.

Capsules and carriers – the puzzle of meningitis pathogenicity

Bacterial meningitis is caused by *Neisseria meningitidis* which can be detected in the nose and throat of many normal, healthy people. The proportion of such carriers varies considerably, but can be over 40%. However, only *N. meningitidis*, and one other member of its genus, are capable of causing disease. Researchers would like to know why some people very occasionally become seriously ill, while most live all their lives with *N. meningitidis* as a harmless inhabitant.

One of the distinguishing features of the bacterium is its thick coat of complex lipids and polysaccharides, called a capsule. This can protect it from the immune system during an infection, and may have the more biologically important role of preventing the bacterial cells from becoming dried up in the air so that they can spread from person to person in coughs and sneezes. The detailed structure of the capsule lets researchers assign each strain to one of 13 groups. Virtually all infections come from only five of these groups, although even then most people carrying these strains do not fall ill. Nevertheless, researchers are convinced that understanding more about the capsule may help them understand why a few strains are pathogenic while most are not.

Researchers led by Ulrich Vogel at the University of Würzburg in Germany, collaborating with Martin Maiden from the University of Oxford in the UK, recently tested 8,000 healthy schoolchildren and young adults from Bavaria for *N. meningitidis*. Just over 10% carried the bacterium, and 16% of these strains lacked several of the genes that are required to synthesize a capsule. Synthesizing the capsule is quite complicated. The bacteria have to build a series of special lipids and sugars, transport them onto the surface of the cell and then join them together. A large number of genes control this biosynthesis.

When the researchers examined exactly why these bacteria no longer made capsules, they discovered that the acapsulate strains fell into at least four distinct groups. Genes for the synthesis, lipid modification and transport of the capsular polysaccharide had been replaced by a short length of DNA that did not encode anything. The researchers obviously wondered where this had come from. They were not entirely surprised when they worked out that it originated in the species *Neisseria lactamica* and had been transferred to *N. meningitidis* on several different occasions. The species of *Neisseria* are well known to be genetically diverse, and to exchange genes among themselves, and with other species of bacteria.

Although the biological role of the meningococcal capsule is still unclear, the fact that it is absent from particular groups of the species suggests that these are less dependent on a capsule for protection during transmission than other groups. The reason for this still awaits discovery.

Claus, H., Maiden, M.C.J., Maag, R., Frosch, M. & Vogel, U. (2002). Many carried meningococci lack the genes required for capsule synthesis and transport. *Microbiology* **148**, 1813–1819.

FMD revisited 2 – limiting the spread

The recent UK FMD outbreak was a heart-rending example of how this highly contagious virus disease of livestock can result in personal despair for people dependent on agriculture and rural businesses, as well as the culling of millions of animals to control the infection. The highly contagious nature of FMD, and the drastic measures used to eradicate it, were shown on the television for months. Sheep played a major role in the spread of the disease because the clinical signs often are mild in sheep. This means that the virus can be transmitted from infected sheep to other animals through their breath or by contact before anyone realizes there is a disease problem.

Veterinary scientists at the Institute for Animal Health at Pirbright, UK, have now reported a study into how readily the virus can be spread among sheep, and also how much airborne virus sheep actually excrete as the disease progresses. The researchers kept 10 Dorset crossbred ewes in a biosecure building, and infected six of them with the strain of the virus that caused the UK epidemic. From then on, they examined the sheep for signs of disease every day, collected samples of blood, and took nasal and rectal swabs to test for the virus. They also collected samples of air from the room housing the sheep so they could measure whether there was virus in their breath.

FMDV multiplied rapidly in the sheep, and the infected sheep shed virus into their breath and surroundings only 24 hours after they were injected. The amount of virus in the air was enough to let a sheep breathe in an infectious dose in only 5 minutes, and the other four sheep rapidly became infected. These initially showed very little sign of illness but excreted airborne virus maximally within 48 hours. By the sixth day, all the sheep were obviously ill, but by that time, although the researchers could detect virus in the swabs, there was none in the breath of the sheep. Antibodies to FMDV in their blood indicated that the immune systems of the sheep were getting the infection under control by this time. This matched with the decreasing amounts of live virus within the blood samples or swabs. One month after the start of the experiment, the researchers could still detect very low levels of virus in throat samples from half of the sheep, indicating that they were now virus carriers.

The reason that the sheep became infected so quickly was probably the large amount of the virus they were exposed to. In real life, the disease would be transmitted less quickly if the sheep were scattered across fields or hillsides, but could travel swiftly if they were brought together for any reason, such as shearing. The fact that sheep are most infectious before there are any obvious signs of illness is very important for working out strategies to contain FMD. The researchers hope to use the detailed results from this experiment to develop improved computer models for predicting the spread of the disease, as well as recommending practical steps to limit its spread.

Alexandersen, S., Zhang, Z., Reid, S.M., Hutchings, G.H. & Donaldson, A.I. (2002). Quantities of infectious virus and viral RNA recovered from sheep and cattle experimentally infected with foot-and-mouth disease virus O UK 2001. *J Gen Virol* **83**, 1915–1923.

International Development Fund report

SGM helps microbiologists in developing countries and Eastern Europe through this fund, usually by supporting training courses and other small technology transfer projects. The closing date for the current round of applications to the fund is **25 October 2002** (see p. 142 for details).

Improving water quality in China

■ Gwyn Jones

This was my fifth visit to China, specifically to Hebei Province which surrounds Beijing, and where I had been involved in advisory work in the past. The province has a population of about 55 million and the industrial city of Shijiazhuang accounts for about 3 million people. Past visits have been under the auspices of the British Executive Service Overseas (BESO) or by special invitation of the Chinese Academy of Sciences. BESO is a registered charity that collaborates with countries in Africa, South America and Asia that require specialist advice, usually from retired experts. I have, at times, thought of this process as VSO for the wrinklies but, in so doing, I am sure that I am doing a great disservice to my fellow volunteers. Whilst past visits provided the opportunity to advise on environmental problems on a day-by-day basis, there was little chance to examine a single problem in depth.

The bulk of the expertise in this arid zone is in agriculture and horticulture, and the organization with which I had established the most productive contact was the Institute of Agricultural Modernization. More recently, the Institute has been charged with solving water quality problems in the region, specifically the eutrophication of the massive Dalangdian Reservoir and the gross faecal pollution of the City River. The earlier visits had shown that the transition from soil to freshwater microbiology was going to be a major step, with little understanding of how lakes, reservoirs and rivers function, particularly in relation to the scale of microbially mediated redox reactions.

I was, therefore, delighted to hear that my application to the SGM International Development Fund had been accepted. Even more so, that Janet Hurst and her colleagues provided me (at extremely short notice) with educational materials, including excellent posters and copies of *Microbiology Today*. In addition, I took out several textbooks, and the grant covered about £1000 worth of membrane filtration equipment. John Walker on the China desk of BESO was delighted to be a co-sponsor and covered my UK travel costs as well as using the organization's excellent contacts to obtain a visa at short notice and provide insurance and diplomatic cover.

So, I was well equipped and on my way. I was introduced to the students (the class size ranged from 40 to 100 depending on daily commitments) by the Principal of the University, and then left to get on with it. The first barrier to be broken down was one of formality. There was a great tendency to try to write down every word I spoke and on no account was I to be interrupted. This clearly was not going to work, as I wanted interaction with the students and I wanted them to think about what I said and to question me as soon as they did not understand anything. We managed to overcome this on the first day when I wrote on the board that my name was 'Gwyn' and they should stop me at any time to ask questions. Luckily, the age range of the students was from 21 to 40 and some of the older and more confident ones took the lead. I also emphasized that the whole course content was in the text books that I had taken out with me, so there was no need to take notes. They could, of course contact me by email to ask questions, and I am happy to report that several have done so since my return.

Having broken down the barriers of formal teaching, things went very well. It was not long before a student said '*You don't have to speak so slowly – we do understand you*'. This, I suppose, was a throwback to my teaching experiences in Argentina when I was told that everyone was '*fluid*' in English – and they weren't! By the second day the students were quite happy to stop me if I had used a term that they did not understand. Once written on the board, they tapped it into their hand-held translation devices and, after a brief stoppage, this resulted in a class gasp of '*Ahh – that's what he's on about*'. Thereafter, this worked quite well and I felt that we had established some rapport.

The course started with the basics of freshwater physics and chemistry and then developed into how microbes mediate the reactions, particularly under conditions of stratification. Clearly, the processes of anaerobic respiration and the scale on which they occur represented totally new information. We then progressed to sources of pollution that, in this part of the world, is largely faecal, with industrial overtones in the form of heavy metals. I decided to concentrate on the former, as there was not enough time to deal with metal toxicity. My equipment included some samplers for counting coliform bacteria. Each student was given one and asked to dip it in a water body of his or her (the majority of students were female) choice, not

forgetting to test the tap water in the building. Bear in mind that, even in the best hotels in Beijing, the tap water is not fit for human consumption. You either drink bottled water or boiled water that is provided in your room or on any train journey that you make. If you have any sense, you purchase some of the excellent Chinese green teas to add to the boiled water and this makes a refreshing drink. The only other options are Western beverages such as Coke and Seven Up.

Although the University did not have appropriate incubation facilities, prolonged incubation at a lower temperature provided results adequate enough to convince the students of the shortfall in water quality. We then examined what constituted a significant difference in the results. Although well versed in computer-based statistical packages the students were unaware of the limitations imposed when small samples are taken and subjected to statistics based on the normal distribution curve. We examined the use of non-parametric statistics and how such tests may prove more powerful in detecting significant differences when small numbers of samples are taken. Luckily, the results of algal counts on the membrane filters (almost always a Poisson distribution) proved the point nicely.

I had planned to end each day with a case study. I had assumed that the students would be fairly tired after 5 hours of solid teaching in a foreign language, so this was a good opportunity to get over the message that microbiology combined with active management can result in improvement of the environment. The examples that really seemed to catch their imagination were phosphorus stripping to reduce cyanobacterial blooms, the use of *Bacillus thuringiensis* to control insect pests such as the Blandford Fly and the use of anaerobic bacteria to generate base in waters subject to acid pollution.

I mentioned above that I thought that the students might find the course a little tiring. I had not allowed for the excellent Chinese hospitality during the week. Each lunch break we went to a nearby restaurant and consumed far more than my usual 'soup and a roll'. Whilst this was delightful, if only for the opportunity to talk informally to the students (different groups were invited each day), we were all fairly soporific at the end of such large meals. The University, however, was well prepared for such an eventuality, and I was provided with a bedroom for an hour before the afternoon lectures began. I have to admit that, on the first day, I slept very well. Thereafter, it was a good opportunity to sharpen up the afternoon's lectures.

At the end of the course I gave a signed certificate to each student who had completed the course.

These bore the name of the SGM to emphasize the contact and were much appreciated by all.

We were also able to visit Dalangdian reservoir and use it as a case study closer to home. This water body is large (17 km^2) and is filled by canalized water from the Yellow River (85 × 10^6 m^3 volume) over an astonishingly short 3 weeks in winter. For those of you who know the Lake District, that is greater than the total volume of Haweswater, our largest reservoir. Thereafter, water is drawn down to a depth of one metre and, as summer progresses, blooms of the cyanobacterium *Microcystis aeruginosa* develop, rendering the water unusable for anything but irrigation. The students quickly registered that a slower filling regime combined with treatment (possibly by phytoremediation) was required. However, events have overtaken any possible remedial measures, as plans are well underway to transfer water from the Yangtze River to the Yellow River and to treble the size of the reservoir. I am currently involved in discussions, following the publication of a joint paper with a graduate student, on the possibility of introducing the water into a wetland before it enters the enlarged reservoir. This would provide the opportunity for plant/microbe interactions in a reed bed system to strip much of the excessive load of phosphorus. Hopefully, some of the future students will be able to study this process.

I hope that the course demonstrated that microbes can be used effectively to improve water quality. The response from the students was more than encouraging, so I am very grateful to the SGM for the opportunity to take this message to China.

■ ***Professor J. Gwynfryn Jones was formerly Director of the Institute of Freshwater Ecology and the Freshwater Biological Association, Windermere. He may be contacted at The Orchard, Oldfield Road, Windermere LA23 2BY, UK. email gwynfryn@btinternet.com***

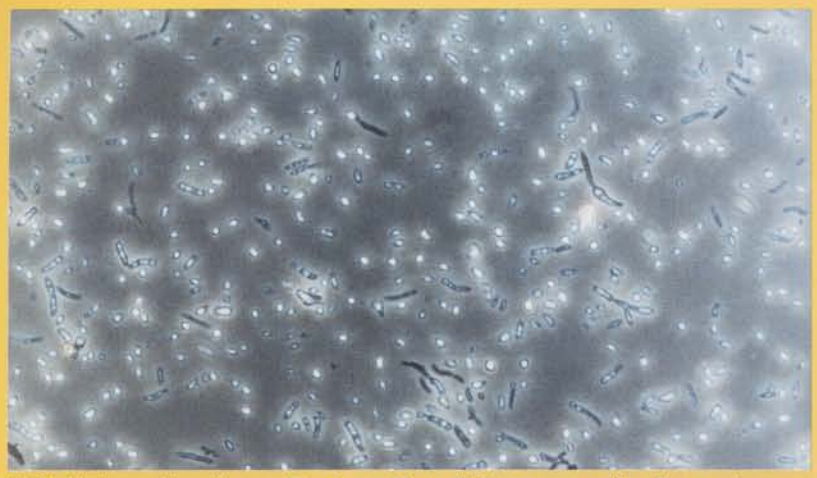
ABOVE:
Professor Jones with two students outside the University.

TOP LEFT:
The course is announced.

BOTTOM LEFT:
Sampling the massive Dalangdian Reservoir.

PHOTOS J.G. JONES

International Research Fellowship report



SGM International Research Fellowships enable scientists to travel to or from the UK and Ireland to carry out a defined piece of research in any field of microbiology. Visits may last up to 3 months. The final closing date this year is **30 November 2002**. See SGM website for full details and an application form.

RIGHT:
A premature neonate in the intensive care unit. Note the large number of tubes and attachments.
PHOTO A. LECK

ABOVE:
The yeast *Candida parapsilosis*. The cells are characteristically elongated.
PHOTO RICHARD BARTON

Typing *Candida parapsilosis* strains from neonates

■ Roma Batra

Being an enterprising mycologist, my joy knew no bounds when I was given an opportunity by the SGM to work at a world famous mycology centre – the Mycology Reference Centre at the University of Leeds. I arrived at Manchester Airport on 30 April 2001, full of enthusiasm to undertake the research project. Then I boarded a train to Leeds. I was very much impressed by the beautiful countryside, as it was my first visit to the UK.

On arriving, I was given a warm welcome by Dr Richard Barton. He introduced me to other lab personnel who were equally warm and friendly. Therefore, working in the mycology research laboratory was a pleasure.

The objective of my study was to do molecular typing on *Candida parapsilosis* isolates from a neonatal intensive care unit. Greater numbers of low-birth-weight infants now survive in neonatal intensive care units (NICU) because of the introduction of new medical therapies. Unfortunately, the survival of these infants has been associated with an increase in the incidence of disseminated candidal infections. One of the reasons is that cellular immunity, which plays an important role in protection against fungal infections, is almost negligible in neonates. Also, these infants are subjected to broad-spectrum antibiotics and prolonged hospitalization, using adhesive tape to fix venous catheters, endotracheal tubes and monitoring electrodes that strip the skin on removal, thereby increasing vulnerability to fungal infections.

Candida infections commonly seen in neonates are usually superficial lesions of the mouth (thrush) and rashes of the perianal and groin regions. Sometimes, deep-seated infections may also be present. *Candida albicans* is the most frequently isolated species, but the proportion of non-*albicans* species has increased recently. *C. parapsilosis* is isolated particularly in the case of neonates. In fact, it represents the second most prevalent *Candida* species causing bloodstream infections. A large number of *C. parapsilosis* strains which required typing were isolated from the NICU patients at Leeds.

The epidemiology of nosocomial *C. parapsilosis* infection is complex and poorly defined and may involve colonized patients and hospital personnel. It has a unique ability to adhere to plastic biomedical devices and survives on environmental surfaces. Restriction fragment length polymorphism (RFLP) analysis with and without probes, randomly amplified DNA (RAPD) analysis, pulsed field gel electrophoresis (PFGE) and other PCR-based methods are used to investigate outbreaks of candidiasis. These methods are primarily used to identify individual strains and to detect possible cross-infection. One of the most versatile is southern-blot hybridization with species-specific complex DNA probes which has been reported to be particularly effective with *C. albicans*. Therefore, it was decided to

use this method to type *C. parapsilosis* strains to determine if there was any horizontal transmission of infection and also to determine if there was any specific strain that predominated in the colonized neonates. A new probe, Cp3-13, was used which is very efficient as it has a high level of discrimination and reproducibility and the results can be subjected to computer analysis. My aim was to type as many isolates as possible in the limited period of 3 months and that proved to be quite challenging.

Molecular typing revealed possible nosocomial transmission. The results suggest exogenous acquisition of *C. parapsilosis*. The mechanism of transmission may have been by indirect contact via the hands of hospital personnel or from the hospital environment. Also strains from multiple sites within the same individual were different. The data still has to be subjected to computer analysis.

I enjoyed my stay in Leeds immensely as the research work was very enjoyable and challenging. I am grateful to Professor E.G.V. Evans, Dr Richard Barton and Dr A. Chakrabarti who made it possible for me to come from India and carry out this research. I am indebted to the SGM (International Research Fellowship) for their generous financial support.

■ ***Dr Roma Batra is Senior Scientist at Mediprobe Laboratories, Unit A1,501 Alliance Avenue, Toronto, Ontario, Canada M6N 2J1***

Book Review

Encyclopedia of Life Sciences
(20 volumes)

Managing Editor
D. Atkins
Project Manager
M. Calais
Published by
Nature Publishing (2001)
North America
US$4,200
(ISBN: 1-56159-274-9)
UK & ROW
£2,595
(ISBN: 0-333-726219)

Online subscription
Academic subscription for 1–3 users (annual).
A signed licence agreement must be completed.
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(ISBN: 1-56159-238-2)
UK & ROW
£1,000
(ISBN: 0-333-947886)

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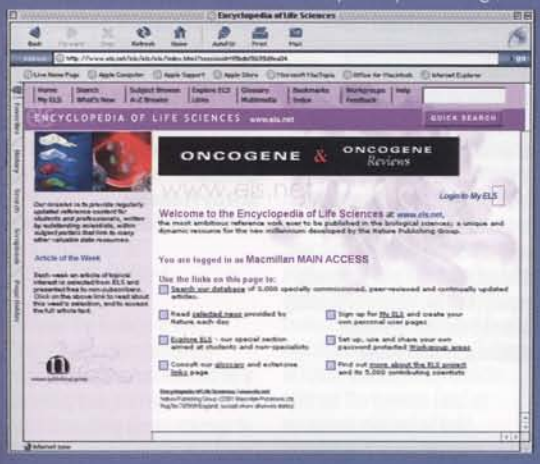
from US$4,860
UK & ROW
from £3,100
(ISBN: 0-333-7947894)

Recent advances in computer technology and the expansion of the Internet have revolutionized the communication of scientific information. The *Encyclopedia of Life Sciences* (ELS) is part of this revolution. It comprises a print set of 20 volumes and a web product that allows for online searching, browsing, cross-reference linking and much more. Within the ELS database, the articles, indices, appendices, glossaries and illustrations are superbly networked and a few additional mouse clicks take you to the Internet with its assortment of powerful search and retrieval systems (e.g. *Entrez*). The ELS site also provides its readers with specific links including, for example, sophisticated interactive tutorials on protein structure and function and access to the *Nature Science Update* pages. The bound volumes of ELS are elegant and a pleasure to handle, but what makes ELS an educational resource par excellence is the electronic version. This is how most undergraduates and postgraduates access information and ELS makes optimal use of the technology. I sincerely hope that the Nature Publishing Group can sustain their promise to revise, update and expand the ELS website (www.els.com). It would be a great pity, indeed, if it grew old.

The subject matter of ELS is biology and the coverage is awesome. There are over 3,000 articles ranging from *Acantharia* (marine protozoa) to *Zygomycota* (a group of saprotrophic fungi). And in between, there's not much missing. Biochemistry, clinical medicine, developmental biology, ecology, evolution, functional and comparative vertebrate morphology, genetics and molecular cell biology, immunology, microbiology and virology, neuroscience, plant science, structural biology, science and society: it's all there and it's all-encompassing. At the same time, however, attention to detail has not been sacrificed. The articles are organized into three levels, introductory, secondary and special, and are written by acknowledged experts in a style that is both authoritative and accessible. By and large, the scientific accuracy is remarkable and the ELS text alone will suffice for most undergraduate and postgraduate students. In particular, the illustrations are excellent and they are sure to appear regularly in essays and course work. For the scientist and researcher, the ELS database will be a starting point for access to the primary literature and a portal to information on the Internet. For the teacher, ELS is a unique resource for the construction and preparation of lectures and slide presentations (the 'permission to reproduce' request form is provided online).



How about the microbiology content? Free text searches for the words bacteriology, virology, mycology, protozoology and phycology produced 157, >200, 40, 36 and 30 article hits, respectively. A closer examination of the articles on 'virology' (my own particular interest) reveals that almost every topic that should be included in a 3-year undergraduate course is covered in depth. I think you could hardly ask for more from a single information source. My colleagues in immunology, cancer biology and genetics were just as impressed and I can only conclude that the *Encyclopedia of Life Sciences* is a justified title for this comprehensive reference work.

So, would you buy it? Probably not, as it would set you back almost £2,600 for the print edition and £1,000 per year for an annual online subscription. But should you encourage the library to enter into negotiations for a multi-user online subscription? Most certainly yes. If nothing else, your students will be everlastingly grateful.

■ ***Professor Stuart Siddell, Editor-in-Chief, JGV***

Reviews

If you would like your name to be added to our database of book reviewers, please complete the book reviewer interests form now available on the SGM website.

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

Compendium of Potato Diseases, Second Edition

Edited by W.R. Stevenson, R. Loria, G.D. Franc & D.P. Weingartner
Published by APS Press (2001)
US$49.00, pp. 144
ISBN: 0-89054-275-9

To those with an interest in potatoes or plant pathology, this book is invaluable and, thankfully, competitively priced. It is a substantial update on the first edition and includes comprehensive information on diseases and disorders worldwide. The expanded use of colour photographs is helpful, as is the language and structure, which ensure wide accessibility. Diseases of microbial origin are well covered and up-to-date, but brief. This is not a book of methods or recipes, more an overall picture or an easy entry into new areas. I was particularly struck by a detail in the introduction concerning the denunciation of potato consumption from some Scottish pulpits soon after its introduction. From this rocky beginning, potatoes have gone on to become Scotland's fourth most important crop. It would be interesting to reflect on how the current debate on GM crops is viewed in the future or whether they will have similar impact or acceptance.

■ ***Gerry Saddler***
Scottish Agricultural Science Agency, Edinburgh

Fungi in Bioremediation. British Mycological Society Symposium Series, Vol. 23

Edited by G.M. Gadd
Published by Cambridge University Press (2001)
£80.00/US$120.00, pp. 481
ISBN: 0-521-78119-1

This 23rd volume in a well-respected series of symposia provides an overview of the current status of fungi in environmental bioremediation and highlights the potential for further exploitation of this very versatile group of organisms. Through its 17 chapters, 29 internationally renowned authors discuss the physiology and chemistry of a variety of organic and inorganic pollutant transformations. Not surprisingly several authors include discussion of the ligninolytic properties of the wood-degrading white-rot fungi, exemplified by *Phanerochaete chrysosporium*, providing varying amounts of detail on the specific enzymes involved. This has inevitably resulted in the duplication of information across some chapters. However, other fungi are by no means neglected, with three chapters devoted to the fungal treatment of metal-containing waste materials and the last two chapters focussing on the potential of mycorrhizal fungi in soil remediation. Recommended to anyone (not just mycologists) with an interest in the expanding field of environmental biotechnology.

■ ***Vicki Tariq***
The Queen's University Belfast

Biological Systems Under Extreme Conditions: Structure and Function. Biological and Medical Physics Series

Edited by Y. Taniguchi, H.E. Stanley & H. Ludwig
Published by Springer-Verlag (2002)
69.95/sFr116.00/£49.00/US$74.95, pp. 282
ISBN: 3-540-65992-7

I found this a most interesting and informative volume. It encompasses the physics of water at low temperature, the behaviour of proteins under extreme pressure as studied by NMR and FTIR spectroscopy and X-ray scattering, melting temperature determination and stopped-flow enzyme kinetics. The effects of pressure on haemoprotein intramolecular electron transport, on the dynamics of cell structure, and on the survival of micro-organisms are elaborated. Deep sea adaptations in marine micro-organisms are summarized and the possibility that deep sea hydrothermal vents may have been suitable sites for the origin of life discussed. Most of the contributors are not microbiologists but physical scientists. As a consequence we learn more about problems than about solutions. If we wish to find out more about organisms of the abyssal depths, the high stratosphere, or perhaps the outer reaches of the Universe, we cannot know too much chemistry or physics. Not an easy read, but highly recommended.

■ ***David Lloyd***
Cardiff University

The Changing Face of HIV and AIDS. British Medical Bulletin, Vol. 58

Edited by R.A. Weiss, M.W. Adler & S.L. Rowland-Jones
Published by Oxford University Press (2001)
£40.00, pp. 223
ISBN: 0-19-922486-2

This collection of 12 excellent essays reflects contemporary study and understanding of the virus and disease of AIDS. Each review is concise and informative, and the book as a whole is highly recommended. Almost all aspects of the subject are covered from the evolution of the virus and its interaction with the host cell to the global economics and epidemiology of AIDS. The pathogenesis, prevention, intervention and management of AIDS are all discussed. Indeed, the diversity of the topics that are addressed mirrors the myriad problems and concerns that arise from a virus that devastates the immune system; that is spread sexually and through blood contact; that mutates extremely rapidly; that has disproportionately affected the less developed nations and their poorer inhabitants; for which prophylatic drugs are expensive to take and to monitor, and which may be poorly tolerated; and for which there is no vaccine.

■ ***Jon Clewley***
Central Public Health Laboratory, Colindale

Bacterial Adhesion to Host Tissues: Mechanisms and Consequences. Advances in Molecular and Cellular Microbiology, Vol. 1

Edited by M. Wilson
Published by Cambridge University Press (2002)
£60.00/US$90.00, pp. 328
ISBN: 0-521-80107-9

About 20 years ago, there was a spate of books and symposia on bacterial adhesion and identification of specific bacterial adhesins and the host macromolecular receptors to which they bound. Since then, things have moved on with an increasing appreciation of the considerable range and diversity of adhesins produced even by a single bacterial species, and of the multifarious physiological and genetic means of their regulation. Of even greater significance is the realization that we are not just talking about binding, but about interaction so that the responses triggered in the host cell by binding of bacteria (and vice versa) are of central importance in pathogenic processes. This book is a collection of 13 independent reviews, each of a standard roughly of what might appear in *Microbiology* or *Molecular Microbiology*. It is thus a compact source of information on the current state of the art in a selection of bacterial–host systems.

■ ***Roy Russell***
University of Newcastle

Immunology of Infectious Diseases

Edited by S.H.E. Kaufmann, A. Sher & R. Ahmed
Published by American Society for Microbiology (2001)
US$115.95, pp. 520
ISBN: 1-55581-214-7

There are a large number of immunology text books available, most of which devote only one chapter to the control of infectious diseases, the reason why the immune system evolved in the first place, while the remainder of the book discusses various malfunctions or unfortunate manifestations of the system, such as autoimmunity and allergy. This multi-author book attempts to expand upon those single chapters and to fill the gap between immunology and infectious disease text books which concentrate on the pathogen or the disease caused. The book succeeds in this aim, and should be a valuable resource for academics and graduate students working in this area, and for undergraduates in immunology. It is, however, probably a little too specialized for medical students or undergraduates in microbiology, as a certain level of understanding of immunology would be required to make use of this volume.

■ ***Andy Heath***
University of Sheffield

The Mycota. A Comprehensive Treatise on Fungi as Experimental Systems for Basic and Applied Research. Vol. VIII: Biology of the Fungal Cell

Edited by K. Esser
Volume Editors: R.J. Howard & N.A.R. Gow
Published by Springer-Verlag (2001)
DM318.86/sFr274.99/£110.00/ US$159.00, pp. 307
ISBN: 3-540-60186-4

To cover the biology of the fungal cell comprehensively within a single volume would be a daunting task, and in fairness to the Editors they do not attempt to do this. Rather their aim has been to provide a selection of topics they regard as '*at the forefront of fungal cell biology*'. The volume is divided (unnecessarily) into two parts. The first covers growth (hyphal, yeast and colony), morphogenesis (in *Candida albicans*) and pathogenicity (of plant pathogens), while the second, entitled '*Structural Continuum*', provides an overview of hydrophobins, various cellular components (including the cell wall, microtubules and vacuole systems), and fungal genomics. Individual chapters are supported by extensive and up-to-date bibliographies. The volume is well illustrated and certainly realizes the primary aim of '*The Mycota*', namely to highlight developments in both basic and applied research into fungal systems. Recommended for purchase by institutional libraries, but rather pricey for most individuals.

■ ***Vicki Tariq***
The Queen's University of Belfast

The Mycota. A Comprehensive Treatise on Fungi as Experimental Systems for Basic and Applied Research. Vol. X: Industrial Applications

Edited by K. Esser & J.W. Bennett
Volume Editor: H. D. Osiewacz
Published by Springer-Verlag (2002)
DM425.86/sFr367.01/£147.00/ US$199.00, pp. 414
ISBN: 3-540-41583-1

The latest volume in this series provides an overview of both traditional and novel industrial applications of fungi, from their role in the production of bread, cheese, fermented foods, beer and wines, to their potential in bioremediation. The former topics are covered in the first three chapters, which include summary flow diagrams that teachers and students alike will find useful. Ten of the remaining 18 chapters review the wide diversity of fungal metabolites and enzymes. Editors of future volumes may wish to address the overuse (and on occasions misuse) of bold typescript in some chapters, e.g. Chapter 4, which proved mildly irritating. Researchers may be disappointed that some bibliographies do not contain a higher proportion of references to post-1995 literature.
A pity this text is so expensive, since it represents a useful source of information for undergraduates as well as their teachers and researchers. Recommended for purchase by academic libraries.

■ ***Vicki Tariq***
The Queen's University of Belfast

Algal Adaptation to Environmental Stresses. Physiological, Biochemical and Molecular Mechanisms

Edited by L.C. Rai & J.P. Gaur
Published by Springer-Verlag (2001)
DM383.06/sFr329.56/£132.00/ US$194.00, pp. 421
ISBN: 3-540-41938-1

This is an interesting book that suffers from an effort to generalize physiological responses over a set of organisms (the algae) that are not phylogenetically related (paraphyletic). Some chapters deal with this problem by restricting the range of the review, while others sail blithely on regardless. The topic of stress covers both the concept of organisms growing outside their normal comfort zone as well as how the group(s) generally deal with environmental extremes, particularly nutrient deprivation. Here, however, a focus on the photosynthetic property that makes them algae does not always lead to a clear picture. We now realize that an awful lot of the micro-algae are, in fact, mixtrophic to some degree: dealing with nutrient depletion from a strictly botanical perspective is not always appropriate. Don't get me wrong; the authors have provided an extremely stimulating set of reviews and I am pleased to have this book on my shelf.

■ ***Dave Roberts***
The Natural History Museum, London

Secret Agents: The Menace of Emerging Infections

By M. Drexler
Published by Joseph Henry Press/ National Academy Press (2002)
£17.95, pp. 316
ISBN: 0-309-07638-2

Several recent books have dealt with emerging infections and future microbiological threats. For the lay reader or student, *Secret Agents* is one of the best. There is also something to learn for the professional microbiologist, though not too much. Madeline Drexler writes a good story line which is scientifically accurate with a minimum of technical jargon. Moreover, she is bang up-to-date with a chapter on the issues since last September and the anthrax scare that followed. Yet she observes, '*The most ceaselessly creative bioterrorist is still Mother Nature. Her microbial operatives are all around us, ready to pounce when conditions are right. From airborne anthrax to West Nile virus, from the deadly organisms hiding in our food to the next, inevitable 'flu pandemic, we're up against a perpetual war with germs*'.

■ ***Robin A. Weiss, UCL***

Manual of Commercial Methods in Clinical Microbiology

Edited by A.L. Truant
Published by American Society for Microbiology (2002)
US$115.95, pp. 502
ISBN: 1-55581-189-2

The Editor's stated aim was to provide an overview of commercially available manual and automated test systems available for use in clinical microbiology laboratories. Despite the enormity of the task, this book by and large achieves its objective. Two particular strengths are the judicious use of well laid-out and informative tables, and the inclusion of a large number of photographs which greatly aid understanding of equipment or tests that the reader may not be familiar with. One drawback for the non-American reader, however, is the bias towards systems used in American laboratories, which is particularly marked in the discussion of laboratory information systems, although it is less so in other subject areas covered. Although laboratory technology continues to advance, this book should prove valuable for comparing the merits of newer systems with those currently available. This book should interest all those involved in the practice of clinical microbiology.

■ ***Alan Johnson***
Central Public Health Laboratory, Colindale

An Illustrated Guide to the Protozoa, Second Edition. Organisms Traditionally Referred to as Protozoa, or Newly Discovered Groups

Edited by J.J. Lee, G.F. Leedale & P. Bradbury
Published by Society of Protozoologists (2000)
US$135.00, pp. 1,432
ISBN: 1-891276-22-0

This long-awaited book is enormously disappointing. The publishers started taking people's money in 1995; the title page gives the publication date as 2000, but it has only just appeared (February 2002). The most recent reference I could find was 1998. This is an hugely exciting time to be involved in protistan systematics, with new ideas appearing so frequently, but consequently the useful life of such texts is around 5 years. This one has been so long in production that most of that lifetime has gone. Final submission dates for the chapters would have been a useful guide for readers. The book has grown to two volumes, largely because the layout is in large type, and it looks amateurish. Editorial production standards are disappointing. If you are in the field, you need to have access to it, but it could and should have been so much better.

■ ***Dave Roberts***
The Natural History Museum, London

DNA Microarrays: Gene Expression Applications. Principles and Practice

Edited by B.R. Jordan
Published by Springer-Verlag (2001)
42.95/sFr81.32/£31.50/ US$49.00, pp. 140
ISBN: 3-540-41508-4

The authors have provided a current practical guide and review of gene expression analysis using DNA microarrays. The various approaches to DNA microarraying are described in different chapters, including glass slide DNA microarrays, oligonucleotide chips and nylon membranes. The examples and protocols are mostly based on work with eukaryotic organisms but many procedures are generally applicable to research in this field. There is a very useful chapter on DNA microarray data analysis and a wealth of references to helpful Internet sites and published literature throughout the book. Individual organizations as well as individuals are likely to find this book a useful resource for setting up and working with DNA microarrays in the laboratory. The book is up-to-date with developments in this field and describes future trends. However, this technology is developing at a fast rate and it is possible that some of the approaches described in the book may be superseded in the near future.

■ ***Jerry Wells***
University of East Anglia and Institute of Food Research, Norwich

Viral Co-infections in HIV: Impact and Management. State of the Art Series

Edited by J. Lalezari & G. Moyle
Published by ReMEDICA Publishing (2001)
£20.00, pp. 144
ISBN: 1-901346-40-4

Co-infections with viruses and other micro-organisms are a crucial feature in HIV infection: indeed, many of these secondary infections define the clinical syndrome of AIDS. This volume concentrates on viral co- or superinfections of HIV-infected patients, mainly due to human cytomegalovirus, hepatitis viruses A–C, human herpesvirus type 8, Epstein–Barr virus, and human polyomaviruses. Whilst HIV infection can substantially accelerate the natural course of infection with the other viruses, the introduction of highly active antiretroviral therapy has reduced viral opportunistic infections. The individual chapters concentrate on some of the natural history and epidemiology of the co-infecting viruses, but mainly on clinical presentation, diagnosis, prognosis, management and antiviral treatment. Resistance to antiviral drugs and their side effects are reviewed. References are up-to-date to approximately 2000. The research progress in this area is fast as, for instance, the data on co-infection with HIV and GB virus C [*N Engl J Med* (2001) 345, 707, 715, 761] testify. The chapters are written by teams of clinicians and scientists. In my opinion, the book will benefit mainly busy clinicians of all specialties as HIV infection has now established a firm place in the differential diagnosis of disease in practically all areas of medicine.

■ ***Ulrich Desselberger***
Addenbrooke's Hospital, Cambridge

The Life of a Virus: Tobacco Mosaic Virus as an Experimental Model, 1930–1965

By A.N.H. Creager
Published by University of Chicago Press (2002)
H/B US$75.00/£47.50; P/B US$27.50/£16.00, pp. 352
ISBN: H/B 0-226-12025-2; P/B 0-226-12026-0

When the 'centenary' of tobacco mosaic virus (TMV) was celebrated in 1998, attention was drawn to the many scientific advances in which it has been involved. This book attempts to describe how TMV came to hold such a prominent position as a model system. An obvious criticism is that the book is US-centred, perhaps betraying the author's original intention to write a history of Wendell Stanley and the Virus Laboratory at Berkeley. The work of Bawden and Pirie and of the Tübingen group is described largely in terms of its interaction with events in Stanley's group, but much other work done outside the US gets short shrift. Nevertheless, it is fascinating to read about the circumstances that propelled research in particular directions at different times, and I recommend this book to anyone who is interested in why science proceeds in the way it does.

■ ***David Robinson***
Scottish Crop Research Institute, Dundee

The Nidoviruses (Coronaviruses and Arteriviruses)

Edited by E. Lavi, S.R. Weiss & S.T. Hingley
Published by Kluwer Academic (2001)
US$145.00/£101.50/ 166.75, pp. 742
ISBN: 0-306-46634-1

The virus families *Coronaviridae* and *Arteriviridae* have recently been brought together in the order *Nidovirales*. This book describes the *Proceedings of the 8th International Symposium on Nidoviruses* held in Pennsylvania in May 2000. These viruses have comparatively very large genomes of single-stranded RNA of positive polarity (13–32 kb), and thus handling of these genomes, as well as dissection of their functions, is not a trivial exercise. The highlight of this meeting was the presentation of success in obtaining infectious cDNA clones of several *Nidovirales* by research groups in Germany, Spain and the United States. This achievement will greatly improve further study of this exciting group of viruses that have various pathological presentations (infections and disease of the gastrointestinal and respiratory tracts, of the CNS, vasculitis, etc). The book is a treasure for details on various replication functions as well as virus–cell interactions, pathogenesis and vaccine development. The quality of the presentations is excellent. This book should be studied by every 'RNA virologist', but the intricate replication strategies and other features of these viruses are of general interest to all virologists. Although the price of the book is relatively steep, it is worth the expense and is highly recommended.

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Protocols in Lichenology. Culturing, Biochemistry, Ecophysiology and Use in Biomonitoring

Edited by I. Kranner, R.P. Beckett & A.K. Varma
Published by Springer-Verlag (2002)
DM213.89/sFr184.04/£74.00/ US$109.00, pp. 580
ISBN: 3-540-41139-9

This is a welcome addition to the series because lichenological methods are seldom documented in texts on mycology, phycology or plant science. Methods described are wide-ranging, most are lab procedures, but some are field-based or more applicable to the herbarium. Instructions are more explicit than is usually permissible in a research paper, and include useful tips, warnings of potential pitfalls, and sections on troubleshooting. As the Editors point out, the manual is not exhaustive; for example, it is published almost simultaneously with another dedicated to methods in lichen biomonitoring, a topic restricted to three chapters here. Nonetheless, this pleasingly produced volume is a creditable starting point. It is essential buying for lichenologists and deserves a place in institutional libraries where it might tempt mycologists and phycologists to extend comparative studies to include lichenized species, and where students will find it useful for project work.

■ ***Peter Crittenden***
University of Nottingham

Principles and Practice of Clinical Parasitology

Edited by S.H. Gillespie & R.D. Pearson
Published by John Wiley & Sons Ltd (2001)
£175.00, pp. 670
ISBN: 0-471-97729-2

This impressive volume draws on the expertise of 44 specialist authors, to give a comprehensive overview of parasitology. The book begins with a historical account, fascinating in its description of parasitology's 'golden age', between about 1850 and 1930. The subsequent epidemiology chapter emphasizes how failure to understand this discipline can lead to counter-productive control measures, and also explains the value of new technologies such as satellite imaging and computer mapping. The remainder of the book consists of thorough and thoughtful disease-specific reviews, beginning (naturally) with malaria. Many chapters include discussions of the emerging role of new molecular diagnostic and typing techniques. I would like to see future editions include more thematic chapters, such as parasites in immuno-deficiency, or chemotherapeutic agents. Nonetheless, this is an excellent book, suitable for every microbiology/infectious disease department, and for individuals with a particular interest in this intriguing specialty.

■ ***Aodhán Breathnach***
St George's Hospital, London

AIDS in the Modern World

By I.E. Alcamo
Published by Blackwell Publishing (2001)
£18.95, pp. 90
ISBN: 0-632-04474-8

This book states its aims to 'present principles of the AIDS epidemic in a format that is easy to understand and comfortable to read'. It uses simplistic format, with each chapter introduced by a 'Review and Preview' section

(aka a summary), key sentences in blue ink and three questions presented at the end to focus the reader on key learning points. While the layout may meet the objectives of the author, the content is confusing – is this a text book or not? Basic virology and immunology is described which the lay reader (stated target audience) will find hard to assimilate and relate to the HIV scientific information presented. Current issues in HIV are not well covered, rather the history of the epidemic. The lay person with an interest could access a similar standard of HIV/AIDS knowledge from reading newspaper reviews.

■ ***Sheila M. Burns***
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Viruses & Human Disease

By J.H. Strauss & E.G. Strauss
Published by Academic Press (2002)
£32.95, pp. 383
ISBN: 0-12-673050-4

This book is one of the best general virology texts I have seen. The detailed and yet very user-friendly style, taken together with its reasonable price means that it will very likely become a popular student text. Having said that, the book will also be very useful to more experienced researchers wanting a concise summary of a field of virology outside their own. The book describes viruses of bacteria, plants and animals but focuses on those causing diseases in humans, pathogenic mechanisms and the use of viruses in attempts to treat disease. The numerous tables and figures are very clear with extensive use of colour. This book is designed to be an overview of virology, however, extra references to more specific and detailed articles at the end of each chapter would be helpful. Despite this, I cannot recommend this text more highly.

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

Enzymes in the Environment. Activity, Ecology, and Applications

Edited by R.G. Burns & R.P. Dick
Published by Marcel Dekker Inc (2002)
US$195.00, pp. 614
ISBN: 0-8247-0614-5

This topic is certainly ripe for the comprehensive treatment delivered here, as there has been little since *Soil Enzymes* (Academic Press, 1978). *Enzymes in the Environment* goes much further in its 21 chapters from contributors who attended the conference of the same name in Spain in 1999. It is, however, not merely a 'proceedings', but is much more authoritative and ordered. The book sets off with three long chapters covering enzymes in soil, lakes and the sea – heavily referenced and detailed. Chapters of varying length follow, dealing with more specific topics (rhizosphere, biofilms and mycorrhiza, for example) and applied aspects (bioremediation, biosensors, biocontrol). The final chapter takes us back to the fundamentals of enzymes in soil to finish off this large book in good style. The Editors and contributors have stuck to the task well and there is no doubt that this is a reference text for libraries everywhere and, in that context, good value for money.

■ ***Alan McCarthy***
University of Liverpool

Bacterial Pathogenesis: A Molecular Approach, Second Edition

By A.A. Salyers & D.D. Whitt
Published by American Society for Microbiology (2001)
US$56.95, pp. 560
ISBN: 1-55581-171-X

The first edition of bacterial pathogenesis proved to be an extremely popular textbook with its clear explanations, excellent diagrams and summaries. This second edition has been extensively re-written in many areas and updated to take account of the revolution in our understanding of bacterial pathogens brought about by genome sequencing and genomics. Each chapter on individual pathogens now contains a short biography of the organism at the beginning and a useful summary outline of the information in the chapter at the end, so students will really find this book invaluable to augment lecture notes and to revise from. One of the best features of this book is undoubtedly the extremely readable text which has been written in a very personal and communicative style which maintains the interest of the reader. The numerous figures are also excellent and many have been retained from the first edition. In summary this is a fantastic textbook which will be useful for undergraduates and postgraduates alike.

■ ***Dave Kelly***
University of Sheffield

Principles of Gene Manipulation, Sixth Edition

By S.B. Primrose, R.M. Twyman & R.W. Old
Published by Blackwell Science (2001)
£27.50, pp. 390
ISBN: 0-632-05954-0

Even though a new edition has long been overdue, the current popularity of this book is proof for enduring success among its audience. The authors are to be congratulated for their courageous effort to bring the new edition up-to-date in an area that is a technological hallmark of the 21st century. The book has been revised throughout covering modern cloning vehicles and technologies, for a wide range of organisms. It now includes an expanded chapter on some important applications of gene technologies. It is well structured and easy to navigate. The starting level is still well suited to advanced undergraduates, but it quickly leads to specialized sophisticated technologies and applications. Some of the material will be a challenge to beginners. Overall, the scientific content of this book is seriously impressive, its coverage comprehensive and it will undoubtedly become an important resource to students, course organizers and young scientists.

■ ***Irina R. Tsaneva***
University College London

Nitrification and Denitrification in the Activated Sludge Process. Wastewater Microbiology Series

By M.H. Gerardi
Published by John Wiley & Sons Ltd (2002)
£37.50, pp. 193
ISBN: 0-471-06508-0

Mike Gerardi's synthesis of the field is commendable with a very accessible, if brief, overview of the topic and then a detailed examination of the processes from a theoretical, operational and troubleshooting perspective that will be of benefit to students and practitioners alike. While the inclusion of the Gram stain procedure as an appendix does not really add to the context, the consistent lack of SI units in the calculations for plant loading parameters is the only significant short-coming in an otherwise well written and presented text.

Donald Reid
Water Services Unit, Scottish Executive, Edinburgh

Fermentation and Food Safety

By M.R. Adams & M.J.R. Nout
Published by Aspen Publishers (Kluwer Academic) (2001)
156.50/US$138.00/£95.50, pp. 300
ISBN: 0-8342-1843-7

'Wholefood' enthusiasts often assume that 'natural' fermented foods are intrinsically safe. This is a dangerous myth, but existing texts on food fermentations do little to correct it. I therefore welcome this authoritative text edited by two experts with an impressive panel of authors from industry, academia and the WHO. I would have valued a contribution from a developing country, where traditional village fermentations can present problems. However, many contributors draw on their direct experience of these problems. Both the risks and benefits of fermentation are fairly represented in the book, although I was surprised to find nothing specific on possible contributions of fermentation to the welfare of weaning infants and lactating mothers. Chapters on worms, etc., and endogenous chemical hazards are very welcome. The clear presentation, useful tables and diagrams and striking illustrations of parasite life cycles will make this book an asset to most food-related courses but its price will limit its sales to LDCs.

■ ***Brian J.B. Wood***
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Microbiology Video Library CD

By A. J. Cann
Published by Department of Microbiology and Immunology, University of Leicester (2002)
US$75.00
To order, see http://www-micro.msb.le.ac.uk/video/cd.html

The CD contains basic comprehensive microbiology information on over 300 topics. Included in the CD price is a site licence for a LAN or Intranet. On the positive side this is the first UK example of a general CD microbiology teaching aid. Particularly impressive are the wide variety of easily downloaded high quality images and short QuickTime movies. These may be particularly useful for staff to use in PowerPoint lectures and for student presentations. However, the purchaser must be aware that the 'so-called' online resources are nothing more than online marketing for book purchases. Add to this the rather amateur packaging and unattractive homepage, there is certainly room for improvement; an accompanying booklet for example is a must. These criticisms aside, this CD provides a useful source of information for both staff and students who might otherwise have to rely on the questionable quality of much Internet-based information.

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Comment

Confusion over bovine tuberculosis in badgers, cattle and humans?

TB was virtually eradicated from cattle in the UK by the 1970s, apart from small areas in SW England. Transmission from badgers was blamed for these and a controversial government-funded culling trial began. The BSE crisis of the late 80s and early 90s led to cutbacks in proven measures of controlling bovine TB and the recent foot-and-mouth outbreak led to the suspension of testing. TB in cattle is now rising and spreading rapidly. Are badgers really to blame?

Progress in politics and science often happens by serendipity and an unexpected effect of the 2001 foot-and-mouth epidemic will be on bovine TB. The routine testing of cattle and the badger culling trial were both suspended for over 10 months, so cattle TB will be much worse, the badger trial has been compromised and the risks to public health will have increased. Before considering these issues, it is important to understand that the justification for the controversial badger culling part of the cattle TB eradication programme depends on four main claims which have become 'accepted wisdom':

1. the SW England cattle TB problem is due to its higher population of badgers than in the rest of the UK;
2. badgers cause 80–90 % of TB outbreaks in cattle herds;
3. TB is transmitted from badgers to cattle, not vice versa;
4. badger culls 'work' in reducing cattle TB outbreaks.

In fact none of these claims stands up to scrutiny. Much of the confusion over TB has arisen because veterinary students no longer have a solid training in disease pathogenesis and the classic studies by Francis in the 1940s and 1950s have been largely overlooked.

Cattle TB is a slow but progressive bronchopneumonia which has two pivotal implications:

1. An 'undisclosed reservoir'. The long incubation and progression from microscopic or non-visible lesions (NVL) to tubercle lesions visible (VL) at abattoir inspection may take a year or so. Hence, early 'latent carriers' may be NVL, non-reactors to the skin test and not very infectious. This explains why annual testing is the gold standard worldwide: it removes TB cases before they can pass on the disease within the herd or to other herds if stock is sold. Repeat testing may be needed to weed out latent carriers as they come on stream. Switching to longer herd test intervals of 2–4 years may simply allow TB to build up within herds, and carriers to be exported before TB is diagnosed and movement restrictions imposed.
2. Transmission. Francis drew a clear distinction between primary and secondary lesion complexes. Cattle TB may be transmitted almost entirely by the respiratory route with lesions in the pulmonary lymph nodes appearing before those in the lung tissues which they drain. As these lesions grow, bacilli shed into the blood may set up secondary lesions in other lymph nodes and sites, including liver, kidneys, brain or bone. Since early on in TB the lesions are usually confined to the thorax, indicating transmission by inhalation, it is hard to see how badgers could pass TB to cattle.

   Transmission via ingestion is revealed by lesions in lymph nodes of the head and neck or around the gut. But the infective dose needs to be up to a million times greater than by inhalation. Cattle thus may be at little risk even from pasture highly contaminated with cattle faeces. Unfortunately, many studies of both cattle and badger TB lesions present uncritical accounts of the wide range of sites, but fail to distinguish the primary sites which indicate route of infection, and secondary spread. The pivotal misunderstanding about badger TB is that it '*is 80 % via the respiratory route*', whereas it often starts in the submandibulars and is clearly of dietary origin, e.g. when the animals are worming under infected cow pats. Transmission from cattle to badger is far more likely than vice versa.

Returning to claims for badger 'guilt', the protocol for attribution of the source of TB in herd breakdowns leads in practice to looking at other cattle or badgers, since other domestic stock, wildlife or human sources are rare. However breakdowns are often of untraceable origin, e.g. 69 % in Cornwall (1972–8), 76 % in 1993 in the non-SW and, even with a fully computerized cattle database, 32 % in Ulster. Blaming badgers for most breakdowns hence overlooks the 'undisclosed' cattle reservoir and that the badgers found with TB have merely caught it from cattle.

Likewise, badger culling since 1975 has failed to prevent the current cattle TB crisis, with spread from the SW to Midlands areas which had been TB-free for 40 years.

The cases of badger culls 'working' often cited overlook the simultaneous removal of the 'undisclosed' cattle reservoir. For example at Steeple Leaze, Dorset, where there were up to five cattle TB tests a year in 1973–5, 244 reactors were removed from the cluster of farms, a third being VL, so curing the chronic problem with just one reactor found in 1976–7. Culling badgers subsequently was irrelevant.

Cattle TB crisis

A century of experience of cattle TB schemes worldwide suggests that success depends on annual testing of ALL cattle, and since the test is only 80 % accurate, a movement ban from TB areas is the only guaranteed way of preventing spread to TB-free areas. Britain had a textbook scheme with the whole country under attestation by 1960, and a low point by 1979 of only 89 herds infected and 600 cases. Working from

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

LEFT:
A storm brewing over farmland in Cornwall, in the far south west of the UK.
PHOTO IAN ATHERTON

north to south had reduced TB to a few high density cattle 'hotspots' in the SW. Depopulating these would probably have eradicated TB but the Ministry of Agriculture, Fisheries and Food (MAFF) was overstretched at the height of the BSE crisis in 1992–3, so longer TB test intervals were introduced with fewer cattle tested, and there were massive stock movements. SW herds with TB nearly doubled from 121 to 232 and there were new outbreaks on Exmoor and in Worcestershire. By 1999, over 50 % of new breakdowns were in areas TB-free for 10 years, including Avon, Cornwall, Devon and even in 'frontier' counties such as Derbyshire, Shropshire and Staffordshire. Statistics for infected badgers show that these were unlikely to be the cause. For example, TB was detected in only 11 out of 1,204 badgers tested in Somerset between 1972 and 1993.

With the 10 month suspension of TB testing due to foot-and-mouth, reactors in herds are into double figures; restocking has already let TB into Cumbria and Scotland. It wouldn't be surprising if TB has not doubled again from the 1,031 herds and 9,000 cases of 2000, and with almost no movement restrictions TB will spread far and wide and blight the cattle industry for the next decade.

Risk to human health

Mandatory milk pasteurization is normal in cattle TB schemes, as in Scotland and Ireland. England and Wales still have some 400 'greentop' milk producers, and attempts to ban raw milk have been thwarted politically. With TB so widespread there is increased risk, particularly to farmers consuming the home product. Transmission of TB from meat seems less of a risk.

Badger cull trial compromised?

The validity of the Krebs/Bourne trial was open to doubt from the outset. It is well behind schedule, farmer co-operation is only 50 % in West Cornwall and animal rights groups interference with traps has compromised the results as in Sussex in 1986. But more critically, some 135 herds have been lost in trial areas and unrestricted movement of some 700,000 replacement cattle untested for TB must invalidate the data. Badger culling should have ended years ago for four reasons.

(a) It is based on flawed science, as already discussed. Much of the rationale comes from MAFF's high density badger study in Woodchester. These data have been used to make computer models in which TB is supposedly endemic and self-sustaining and lacks outside inputs from cattle or other sources. These models aim at a prevalence of TB of 11–22 % in badgers, overlooking the real levels which are often substantially higher. Therefore, whilst TB was confined to a few social groups of badgers for years, the cattle TB outbreaks in the 1980s and 90s meant that the disease spilt over to new badger clans. Badger TB peaks after cattle.

(b) It is uneconomic. An earlier model suggested culls did not work and that the 1975–6 drop in cattle TB was due to bans of Irish imports. In 1975–83 badger culls cost £9·7m for alleged preventative benefits of £1·9m, a net loss of £7·8m. All of the methods suggested for badger control (cull, fertility control or vaccination) are labour intensive and too costly. Removing each badger with TB in the Bourne trial has cost £35,000 against an average farmer income of only £8,200 per annum. And so apart from the

(c) ethical doubts over culling a legally protected species,

(d) as McInerney says, '*in the last analysis the problem of badgers and bovine tuberculosis is fundamentally a political one*'.

The unforeseen impact of foot-and-mouth may finally demonstrate conclusively that cattle are the problem, and badgers merely innocent bystanders, thus clarifying decades of confusion.

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Diary

august 02

54TH HARDEN CONFERENCE: ENZYMOLOGY: EMERGING TRENDS AND FUTURE PROSPECTS

St Martin's College, Ambleside
20–24 August 2002

CONTACT: The Meetings Office, Biochemical Society, 59 Portland Place, London W1B 1QW (Tel. 020 7580 3481; Fax 020 7637 7626; email meetings@biochemistry.org)

BIOFILMS IN INDUSTRY, MEDICINE AND ENVIRONMENTAL BIOTECHNOLOGY: THE SCIENCE

Galway, Ireland
24–29 August 2002

CONTACT: Dr Therese Mahony (email therese.mahony@nuigalway.ie; www.nuigalway.ie/microbiology/mel800/bio-imeb.html

55TH HARDEN CONFERENCE: DYNAMICS OF MEMBRANE TRAFFIC

St Martin's College, Ambleside
25–30 August 2002

CONTACT: The Meetings Office, Biochemical Society (see above)

ESBES-4 LIFE: SCIENCE AND TECHNOLOGY. 4TH EUROPEAN SYMPOSIUM ON BIOCHEMICAL ENGINEERING SCIENCE

Delft, The Netherlands
28–31 August 2002

CONTACT: email esbes-4@tnw.tudelft.nl; www.esbes4.tnw.tudelft.nl

aug–sept 02

CELLULAR AND MOLECULAR BASIS OF REGENERATION. EUROCONFERENCE ON THE STEM CELLS INVOLVED IN TISSUE REPAIR AND REGENERATION PROCESSES

Castelvecchio Pascoli, Italy
31 August–5 September 2002

CONTACT: Dr J. Hendekovic, European Science Foundation, EURESCO Unit, 1 quai Lezay-Marnésia, 67080 Strasbourg Cedex, France (Tel. +33 388 7671 35; Fax +33 388 36 69 87; email euresco@esf.org; www.esf.org/euresco/02/lc02177)

september 02

CURRENT FRONTIERS IN PARASITIC PROTOZOA. BRITISH SECTION OF THE SOCIETY OF PROTOZOOLOGY (BSSP)

Linnean Society, London
2 September 2002

CONTACT: Harriet Jones (harriet.jones@uea.ac.uk) or the BSSP website (www.bssp.org)

PROTEIN TECHNIQUES. A TWO-DAY LABORATORY COURSE

University of Hertfordshire Hatfield, 2–3 September 2002

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://herts.ac.uk/natsci/STC)

NUCLEIC ACID TECHNIQUES. A THREE-DAY LABORATORY COURSE

University of Hertfordshire, Hatfield
4–6 or 11–13 September 2002

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://herts.ac.uk/natsci/STC)

EIGHTH EUROPEAN WORKSHOP ON VIRUS EVOLUTION AND MOLECULAR EPIDEMIOLOGY

Leuven, Belgium
4–11 September 2002

CONTACT: Prof. Anne-Mieke Vandamme, AIDS Research Unit, Rega Institute & University Hospitals, Minderbroedersstraat 10, B-3000 Leuven, Belgium (email annemie.vandamme@uz.kuleuven.ac.be; www.kuleuven.ac.be/aidslab/veme.htm)

DANGEROUS PATHOGENS 2002

Center Parcs, Longleat
9–11 September 2002

CONTACT: Sonya Rowe, Chemical and Biological Sciences, Room A201, Building 7, Dstl Porton Down, Salisbury SP4 0JQ (Fax 01980 614307; email scrowe@dstl.gov.uk)

10TH BIENNIAL AND CENTENARY CONFERENCE OF THE CHALLENGER SOCIETY FOR MARINE SCIENCE

Plymouth, Devon
9–13 September 2002

CONTACT: email challenger@mail.pml.ac.uk; www.challenger2002.org.uk

UNDERSTANDING THE USE OF MASS SPECTROMETRY IN PROTEOMICS. A ONE-DAY LECTURE COURSE

University of Hertfordshire, Hatfield, 18 September 2002

CONTACT: Prof. John Walker (see above)

VIROLOGY FOR THE NON-VIROLOGIST

Harrington Hall, London
19 September 2002

CONTACT: Management Forum Ltd, 48 Woodbridge Road, Guildford GU1 4RJ (Tel. 01483 570099; Fax 01483 536424; email info@management-forum.co.uk; www.management-forum.co.uk)

THE IMMUNOLOGY OF VACCINES AND VACCINE DEVELOPMENT

Harrington Hall, London
25 & 26 September 2002

CONTACT: Management Forum (see above)

BIOTECHNOLOGY FOR THE NON-BIOTECHNOLOGIST

The Rembrandt Hotel, London
26–27 September 2002

CONTACT: Management Forum (see above)

october 02

CHINA HI-TECH FAIR/BIOTECH 2002

Shenzhen, PR China
12–17 October 2002

CONTACT: Brenda Yau, Coastal International Exhibition Co. Ltd, Room 3808, China Resources Building, 26 Harbour Road, Wanchai, Hong Kong (Tel. +852 2827 6766; Fax +852 2827 6870; email general@coastal.com.hk)

january 03

'LAB ON A CHIP' - DIAGNOSIS AND ONSITE TESTING, WINTER MEETING OF THE SOCIETY FOR APPLIED MICROBIOLOGY

Holiday Inn, Birmingham
8–9 January 2003

CONTACT: Dr. John Coote (email j.coote@bio.gla.ac.uk)

may 03

ACHEMA 2003: 27TH INTERNATIONAL EXHIBITION-CONGRESS ON CHEMICAL ENGINEERING, ENVIRONMENTAL PROTECTION AND BIOTECHNOLOGY

Frankfurt am Main, Germany
19–24 May 2003

CONTACT: DECHEMA eV, PO Box 150104, D-60061 Frankfurt am Main, Germany (Tel. +49 69 7564 0; Fax +49 69 7564 201; email achema@dechema.de; www.achema.de)

june 03

5TH INTERNATIONAL SYMPOSIUM ON *E. COLI*-VTEC 2003

Edinburgh
8–11 June 2003

CONTACT: Mia Walker, In Conference Ltd, 10b Broughton Street Lane, Edinburgh EH1 3LY (Tel. 0131 556 9245; Fax 0131 556 9638; email mia@in-conference.org.uk; www.vtec2003.com)

july 03

22ND ANNUAL SCIENTIFIC MEETING OF THE AMERICAN SOCIETY FOR VIROLOGY

Davis, California
12–16 July 2003

CONTACT: Sidney E. Grossberg, Secretary-Treasurer, American Society for Virology, Department of Microbiology and Molecular Genetics, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226-0509, USA (Tel. +414 456 8104; Fax +414 456 6566; email segrossb@mcw.edu; www.mcw.edu/asv)

december 03

13TH INTERNATIONAL SYMPOSIUM ON THE BIOLOGY OF THE ACTINOMYCETES

Melbourne, Australia
1–5 December 2003

CONTACT: Dr I. Kurtboke, University of the Sunshine Coast, Faculty of Science, Maroochydore DC, Queensland 4558, Australia (Tel. +61 (07) 5430 2819; Fax +61 (07) 5430 2881; email ikurtbok@usc.edu.au)