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Microbial evolution in action

Adaptation of bacterial populations

RNA virus evolution

Evolution of antifungal resistance in *Candida*

Fast-track bacterial evolution to combat pollution

Serial endosymbiotic theory

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Above: An artist's impression of the primeval Earth. *David A. Hardy / Science Photo Library*

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Microbiologists confront evolution in action on a daily basis in their work. In this issue we consider various aspects of microbial evolution.

Richard Lenski, who has conducted a long-term experiment with populations of *E. coli*, gives an overview of the theme on p. 158, while Paul Rainey asks 'are the bacteria that you started your experiment with the same at the end?' His cautionary tale (pp. 160–162) about the adaptation of pseudomonads to their environment, should make everyone think.

Viruses also evolve at a frightening speed. Peter Simmonds describes on pp. 163–165) how the adaptation of RNA viruses to new environments, selection pressures and hosts can make drug treatment of diseases such as HIV very difficult indeed.

Fungi are different from bacteria in that they have no plasmids or other natural mechanism for transferring genetic material between strains. This makes the evolution of antifungal resistance much slower in opportunistic pathogens such as *Candida*, as Frank Odds explains on pp. 166–167.

Peter Williams informs us on pp. 168–170 that the role of plasmids in expediting bacterial evolution can, however, be beneficial, allowing the microbes to degrade previously unknown compounds such as synthetic dyes, thus helping to clean up pollution.

Finally Lynn Margulis gives her perspective of major evolutionary transitions in the history of life on pp. 172–174.

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

Articles

Regular Features

Other Items

Microbial evolution in action

Richard E. Lenski

In his introduction to this issue on microbial evolution, Richard Lenski describes his own research into *E. coli* populations and puts the other articles into context.

Most of us first encountered evolution as children, when we saw the fossil remains of dinosaurs and other extinct organisms in museums. As biologists, we also see the grand sweep of evolution recorded in the genomes of living organisms and, as microbiologists, we see on-going evolution in the emergence of microbes resistant to antimicrobial agents. Until recently, few viewed evolution as an experimental science. This is now changing as microbes are increasingly used in designed experiments to test various hypotheses about evolutionary dynamics, patterns and mechanisms.

For decades, some microbes served as model organisms in genetics and molecular biology. The same advantages – ease of culture, rapid generations and large populations – that served those fields also make micro-organisms ideally suited to experimental evolution. The advances in those fields, from technical approaches to whole-genome sequences, provide a powerful toolkit and a wealth of knowledge for analysing and interpreting results of evolution experiments with microbes. Many evolutionary questions are being addressed: the dynamics of adaptation by natural selection, the genetic changes underpinning that adaptation, tradeoffs between different aspects of performance, the specificity of adaptation with respect to environmental variables, the causes and consequences of hypermutability, the effects of population size, the maintenance of genetic diversity, conflict and cooperation in social interactions, effects of sexual versus asexual reproduction and co-evolution of hosts and parasites.

Evolution experiments with microbes are often quite simple, at least in concept. Populations start from an ancestral strain and are propagated in defined environments for many generations. The ancestor is frozen away, as are samples taken from the evolving populations at various generations. Later, ancestral and derived types can be revived and compared to determine what phenotypic changes occurred and to identify the genetic bases of those changes. One can even perform competitions between the ancestral and descendant types to measure the net change in Darwinian fitness that occurred during an experiment. (In human terms, it is as though we could bring back fossil hominids – not just their bones or bits of DNA, but the living beings – and challenge them to some competition – say, football or chess – to test whether and how much we have improved on our distant ancestors.) A genetic marker is often introduced to distinguish more readily the ancestral and evolved competitors. It is important to realize that the relative fitness of any two types depends on the environment, so the finding that a population has become more fit than its ancestor under one set of conditions does not imply that it would be more fit elsewhere.

BELOW:
Fig. 1. Twelve *E. coli* populations, evolving in and adapting to identical environments, provide a test of the repeatability of evolutionary dynamics and outcomes.
COURTESY R.E. LENSKI

Some years ago, I began a long-term experiment in which 12 populations of *Escherichia coli* began from the same ancestral strain and have evolved in identical, defined environments for more than 20,000 bacterial generations (see Fig. 1). My two main objectives were to examine the reproducibility of evolution and to explore the coupling between phenotypic and genomic changes. In short, all the populations have become much more fit in the glucose-limited environment in which they evolved; at the end of 20,000 generations they grow about 75 % faster than the ancestor when they compete head-to-head for glucose. There is much work still to be done on the genetic front, but one exciting result has been that global gene-expression profiles show strikingly similar evolution across replicate populations, yet sometimes these parallel changes involved mutations in different genes. I have reviewed our findings elsewhere.

In this issue, Paul Rainey reviews his experiments showing the rapid diversification of *Pseudomonas fluorescens* from a single genotype into several lineages adapted to different ecological niches that stably coexist even within a simple microcosm. He concludes that all microbiologists should realize that any experiment involving bacterial growth opens the door to evolutionary change. Of course, bacteria are not the only microbes that evolve: Peter Simmonds describes the tremendous speed with which viruses, especially RNA viruses, can evolve and adapt to different host environments. Frank Odds examines the troubling problem of antimicrobial resistance in *Candida*, an opportunistic fungal pathogen. We can take some comfort from evidence that fungal mutants suffer a physiological cost of evolved resistance, which reduces their fitness in the absence of antifungal compounds and thereby slows their spread.

Peter Williams describes rapid plasmid-mediated evolution of bacteria, which allows cells to degrade synthetic compounds that were never encountered in their prior evolutionary history. This article reminds us that many bacteria are friends, not foes, and evolution may sometimes work to our advantage in helping solve environmental problems. Finally, Lynn Margulis describes major evolutionary transitions in the history of life that emerged from endosymbiotic associations between micro-organisms. Remarkably, many of the hypothesized intermediate stages in these relationships can still be found among living microbes and subjected to investigation. Her perspective reminds those of us fascinated by studying evolution in action that our experiments are a mere drop in the deep ocean of evolutionary time.

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Further reading

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Bacterial populations adapt – genetically, by natural selection – even in the lab!

Paul Rainey

Microbes are constantly adapting to their environment. In this thought-provoking article Paul Rainey describes the results of his studies on cultures of *Pseudomonas fluorescens* which confound many preconceptions commonly held by microbiologists.

Evolution by natural selection is an inevitable and inescapable feature of life. Organisms multiply, vary and have heredity; as a consequence, populations of organisms evolve. In this regard we can be certain that the bacterial culture retrieved from the incubator this morning will be different from the population used to found the flask 16 hours and 10 generations ago.

Despite the fact that microbiologists confront the stuff of evolution on a daily basis, our understanding of this process is at best fuzzy and at worst just plain wrong! Unfortunately there is nothing new here and the situation is unlikely to improve without a rethink of the way undergraduate microbiologists are trained. In the 1940s Salvador Luria damned bacteriology as 'the last stronghold of Lamarckism'; a similar sentiment followed publication of John Cairns' paper in *Nature* in 1988, and of course vestiges of the 'directed mutation' debate rumble on. But this is just the tip of the iceberg: it is interesting to note that the motivation for Luria & Delbrück's fluctuation test published in 1943 stemmed less from a wish to test the randomness of mutation and more from a desire to show that bacteria are organisms that have a genetic makeup and are subject to the forces of Darwinian evolution.

A peculiar perspective on evolution

Ironically, the perception of evolution as peculiar or irrelevant to our immediate dealings with microbes stems largely from advances in bacterial physiology and genetics. Studies over the last 50 years have shown that bacteria have a remarkable capacity to respond to environmental change. Ask a microbiologist how such a response is wrought and almost certainly the answer will involve a description of phenotypic acclimation – the process by which an individual organism alters some aspect of its behaviour, morphology or metabolism in response to an environmental cue. Reference will be made to regulatory systems, signal transduction and ensuing effects on gene expression. So comprehensive and far-reaching is the capacity for phenotypic acclimation that the notion that bacteria respond to environmental challenge by any other means is rarely considered. With all that genetic circuitry (the argument goes) there can be few phenotypes worth expressing that are not genetically 'programmed'. The end point of such thinking is the notion that bacteria are equipped to deal with every conceivable environmental challenge – that every phenotype, from the complex structures of biofilms, through virulence, is regulated by a genetic programme under the control of 'global regulators'.

It is important to recognize that phenotypic acclimation is just one way that a population responds to environmental challenge. Equally significant (and equally common) is genetic adaptation – a process whereby the genetic composition of a population changes as a result of natural selection. The large population sizes and rapid generation times of many microbes means that genetic adaptation is a particularly potent force for change.

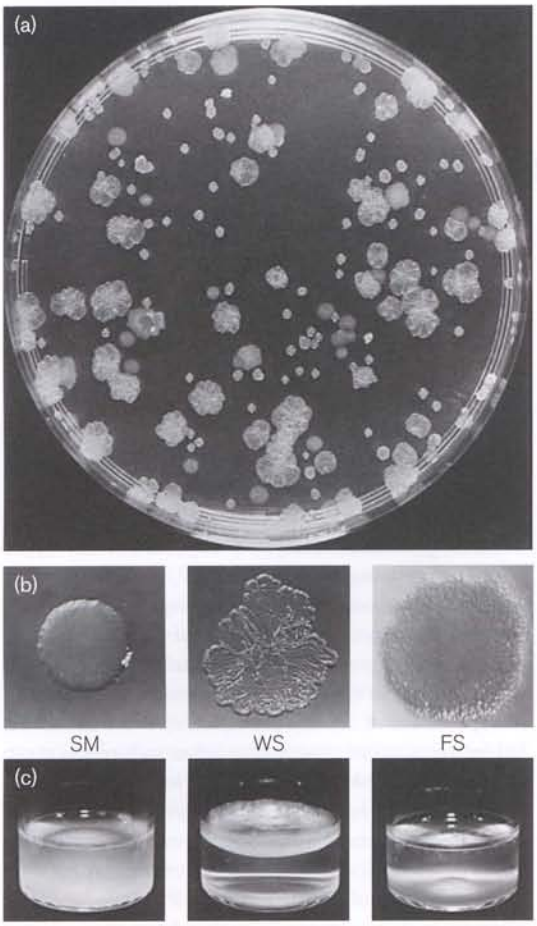
Studies with microbes reveal the workings of evolution

Over the last three decades there has been increasing interest, particularly from evolutionary biologists, in using microbial populations to test predictions made by, and transpiring from, Darwinian Theory. Arising from these studies have been some of the clearest examples of genetic adaptation by natural selection. Richard Lenski and colleagues, for example, having propagated replicate populations of *Escherichia coli* for many generations in a simple defined laboratory medium, have been able to show emphatically that natural selection can lead to adaptation. The simple proof came from experiments in which the ancestral genotype was put in direct competition with derived (evolved) genotypes. In every instance derived genotypes out-competed the ancestral genotype and the magnitude of the difference increased with the number of generations of selection: adaptation (which manifests as an increased competitiveness in the struggle to leave offspring) is caused by natural selection – just as Darwin predicted! Recent studies have identified many of the causal mutations and thus begun to provide the basis for mechanistic insight into evolutionary change.

Our own work has used experimental populations of *Pseudomonas fluorescens*; the motivation being to understand the evolutionary causes of ecological diversity. To this end we allowed replicate populations to evolve in two environments (microcosms) that differed in the degree of spatial structure. A spatially homogeneous environment was obtained by incubating microcosms in an orbital shaker, whereas a spatially heterogeneous environment was obtained by incubating microcosms without shaking. After 5 days, populations propagated in the heterogeneous environment had diversified (see Fig. 1), whereas populations propagated in the homogeneous environment remained uniform. Interestingly, the dynamics of diversification (in the spatially structured microcosms) are highly repeatable with similar patterns of diversity arising each time the experiment is repeated – an outcome to note in light of following comment.

The response of bacteria to environmental challenge

These experiments have allowed testing of long-standing ideas surrounding the role of ecological opportunity and competition in diversification. However, they also have relevance for how we think more generally about the response of bacteria to their environment. In our experiments the only difference between the two treatments was the degree of spatial structure afforded to the growing populations, and yet the response of populations in each treatment was quite different.



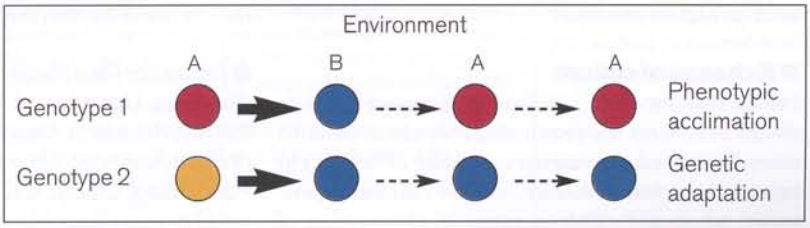
LEFT:
Fig. 1. Phenotypic diversity and niche specificity among *P. fluorescens* SBW25 colonies propagated in a spatially heterogeneous environment. Microcosms were incubated without shaking to produce a spatially heterogeneous environment. (a) After 7 days, populations show substantial phenotypic diversity which is seen after plating. (b) Most phenotypic variants can be assigned to one of three principle morph classes: smooth (SM), wrinkly spreader (WS) and fuzzy spreader (FS), although there is substantial variation within a class and additional minor types. (c) Evolved morphs showed marked niche preferences.
REPRODUCED FROM P.B. RAINEY & M. TRAVISANO (1998) *NATURE* **394**, 69–72.

A model is needed to account for the different outcomes and to aid subsequent experimentation; indeed, two models can be invoked: one involving phenotypic acclimation, the other genetic adaptation. The phenotypic acclimation model requires, within each cell, a genetically determined pathway comprised of a sensor, that in this case recognizes 'spatial structure' (or some component thereof), and a means of transducing this information to affect the expression of genes controlling a diverse array of colony morphologies. Such a system, were it to exist, would be reflective of a long evolutionary history in which repeated exposure of ancestral types to spatially structured versus unstructured environments has led to the evolution of a genetic network that produces an optimal response depending upon a specific environmental cue. The genetic adaptation model requires that spontaneous mutation can produce one or more beneficial variants that increase in frequency through natural selection. In the absence of a molecular understanding how can the most appropriate model be identified? A simple scheme is outlined in Fig. 2 which involves comparison of the phenotype of ancestral and derived populations in the ancestral environment.

Turning attention back to the *Pseudomonas* populations: when cells that experienced the spatially heterogeneous environment were plated alongside cells of the 'ancestral' genotype (that had not experienced this environment) obvious phenotypic differences in colony morphologies were observed. All colonies from the ancestral genotype were of the normal smooth type, whereas colonies from the cells that experienced the spatially heterogeneous environment expressed a range of different phenotypes (see Fig. 1). When the cells that experienced the spatially homogeneous environment were compared with the ancestral genotype no differences in colony morphology were observed; however, a comparison of the competitive fitness of the two populations revealed the derived population to be more fit. In both cases genetic adaptation by natural selection is implicated.

To some, an outright rejection of phenotypic acclimation might seem uncalled for, but without tortuous modification, this model stumbles from the outset. Even in the absence of a direct comparison between ancestral and derived populations the phenotypic acclimation model cannot easily explain the diverse array of colonies shown in Fig. 1. A model invoking phenotypic acclimation requires that all cells in the same environment behave in the same way – at least on average. Examination of the agar plate reveals a diverse array of colonies and yet all the cells growing on the plate experience more-or-less the same environmental conditions. Now, it is true that both populations experienced different environmental challenges during the time that they were propagated in microcosms, but the likelihood that these past differences could continue to manifest some 15 or so generations after removal from the microcosm is unlikely. Nevertheless, by propagating different colony types in different environments for a few generations and then transferring these back to the original medium we could see whether the phenotypes bred true – indeed they did. Thus the phenotypes are heritable and therefore highly likely to be genetically determined: the phenotypic acclimation model collapses.

One further experiment is required to examine an apparent discrepancy between a central expectation of the genetic adaptation model and our observations. I mentioned that the patterns of diversity arising in spatially structured microcosms were similar across replicate microcosms – the same types emerging at the same time and reaching similar population sizes. This deterministic outcome appears to be inconsistent with the randomness of mutation, but it need not be. Imagine that one in every 5×10^7 cells is a niche specialist mutant; a microcosm that harbours $\sim5\times10^{10}$ cells (as ours do) will harbour many niche specialist mutants. Provided these types are favoured by natural selection (which they are), then the dynamics of diversification will be reproducible. Of course it follows that if reproducibility is a consequence of large population size and strong selection, then reproducibility ought to disappear once the population size is reduced. Indeed, reproducibility is lost once the population size falls below $\sim1\times10^7$.



BELOW:
Fig. 2. Distinguishing phenotypic acclimation from genetic adaptation. Two different ancestral genotypes (1 & 2) are grown in environment A and their phenotype recorded: one red; the other yellow. Both genotypes are exposed to environment B and their phenotype in this new environment recorded: in both cases it is blue. To determine whether the cause of the phenotype change is phenotypic acclimation or genetic adaptation, both genotypes are transferred back to 'ancestral' environment A and their phenotypes scored, however, before scoring, each genotype is passed again through A. The phenotype of each genotype is now compared with the phenotype of the ancestral genotype (also in environment A). The phenotype of genotype 1 is identical (red) after experiencing environment B and therefore the blue phenotype expressed in environment B is likely to be a result of phenotypic acclimation. This is not true of genotype 2: although it expressed the blue phenotype in environment B, it no longer expresses the yellow phenotype when returned to the ancestral environment A – not even after two passages. As such it is likely to be genetically distinct from the ancestral genotype, indicating genetic adaptation.
COURTESY P. RAINEY

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Acknowledgements

I thank Tim Cooper for discussion and comment.

The power of natural selection

Over the years we have progressed with genetic dissection of the diverse morphs. The evidence (which ranges from estimates of mutation rate, to identification of many causal mutations) points to diversification being wrought by genetic adaptation: natural selection acting on spontaneous mutation. Upon entering a novel environment replete with ecological opportunity, the ancestral genotype experiences strong diversifying selection (which is not experienced in the spatially unstructured environments). Selection favours particular mutants because of the fitness benefits they engender. Competition among competing beneficial mutations – particularly for oxygen – fuels the diversification process.

When I first began to study the strange world of bottle-bred *Pseudomonas* I was spurred on by a suspicion that diversification was likely to be controlled by some complex stress-inducible mutagenesis system, and was reflective of an adaptive 'life history strategy': after all, the complexity shown in Fig. 1, the speed with which niche specialist types arise, the degree of fit between organism and environment and so forth, could not possibly be determined by chance alone. But it is. And therein resides an extraordinary revelation of the power of natural selection.

Are we missing something?

A fortuitous feature of our *Pseudomonas* populations is the correspondence between niche specialist genotype and colony morphology on agar plates. This means that it has been possible to look at the dynamics of genetic diversification simply by scoring the frequencies of colony variants. Put another way, it has been impossible to ignore evolution. Had evolutionary diversification not manifested in a visible way, we would have overlooked the phenomenon. This leads us to wonder whether evolution in bacterial populations is overlooked, moreover, whether it being overlooked is problematic.

With certainty, evolution occurs, is overlooked, ignored, or incorrectly interpreted. Depending on the particular questions asked, this may or may not matter. The way forward is first to recognize that no environment is benign. For a freshly isolated bacterium entering the laboratory environment selection for mutants that grow more rapidly *in vitro* will be intense. Moreover, initial fitness improvements are likely to involve loss of traits not required *in vitro*, the problem here is that many of these traits may be relevant to the life of the bacterium in its natural environment!

A change of culture

I think that one of the most useful things we could do would be to alter the terminology we use to describe everyday laboratory practices. Instead of 'overnight culture', 'enrichment culture', or 'flow chamber experiment' we should think in terms of the number of generations and the intensity of selection. The moment we recognize that an overnight culture is really a '12-generation selection experiment', or enrichment culture a '1000-generation selection experiment for types capable of growing on compound X', the effects of that selection regime ought to come into question. In many circumstances there may be little that can be done other than to recognize the fact that evolution occurs and to account for its effects in experimental design and interpretation of results. However, in some situations failure to recognize genetic adaptation and its effects can be seriously problematic, resulting in the formulation of implausible hypotheses, the design and execution of meaningless mutant hunts and incorrect conclusions about the ecological significance of genes and regulatory networks – even of the organism itself. While no area of microbiology is immune from this difficulty, one area that seems to be at risk of being misled (if it hasn't already succumbed) is that concerned with 'biofilms'. Studies in this area rely heavily on experiments performed in flow chambers – environments that impose intense selection for surface-colonizing mutants: a cell that doesn't stick is washed from the chamber and is effectively dead. Moreover, flow chamber experiments are typically run over the course of days, thus providing ample opportunity for natural selection to operate. At the very least flow chamber experiments should include a control in which the derived population (the population taken from the flow chamber at the end of the experiment) is competed directly with the ancestral population (the population used to found the original flow chamber). I suspect that in most instances evidence that the flow chamber population has adapted genetically by natural selection to the flow chamber will be overwhelming.

Two processes are relevant to how we think about the response of bacterial populations to environmental change: phenotypic acclimation and genetic adaptation by natural selection (in fact the two processes are not mutually exclusive). For reasons that are complex and worthy of further exploration in their own right, microbiologists have tended to overlook or misinterpret genetic adaptation by natural selection, assuming that phenotypic acclimation is sufficient to account for the majority of responses to environmental challenge. This oversight has serious implications for how we think about and study microbes: for the kinds of models we develop to inform and instruct our investigations, for the way we think about evolution in bacteria and for our understanding of the function of bacteria in natural environments.

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RNA viruses – evolution in action

Peter Simmonds

'Survival of the fittest', Darwin, elephants lumbering across the arid African plain, selfish genes, Neanderthals, introns, junk DNA, the mathematical horrors of population and quantitative genetics, neutral theory, creationism, the geological record, Dolly the sheep. This jumble of thoughts often springs to mind when the word 'evolution' is mentioned. They contrast the basic simplicity of the principle of inherited variation with the peculiar and often unfathomable complexity in which it is expressed, and reveal its fundamental importance not only in biology, but also for our world view and philosophy. Even to biologists, the coldness and cruelty of biological determinism and ruthless, meaningless extinctions often remain unreconciled with frequent anthropomorphic interpretations of their own work. To others, the theory of evolution is additionally difficult to comprehend and win universal acceptance because it operates so slowly and imponderably on the most important objects of study, ourselves and the primates from whom we descend.

With RNA viruses, however, we have the opportunity to observe evolution in action, and empirically test those principles of mutation, inheritance and fitness selection on which Darwin's theory depends. Three attributes make RNA viruses particularly suitable objects of study.

- First, they replicate extremely rapidly, with generation times of as little as 30 minutes in the case of bacteriophages.
- Second, their extremely error-prone replication provides a rich source of mutations on which selection acts.
- Third, they can achieve huge population sizes (up to 10^{12} replicating virions in the body of an HIV or HCV-infected individual), leading to intense fitness selection far beyond that found in the evolution of larger organisms such as mammals.

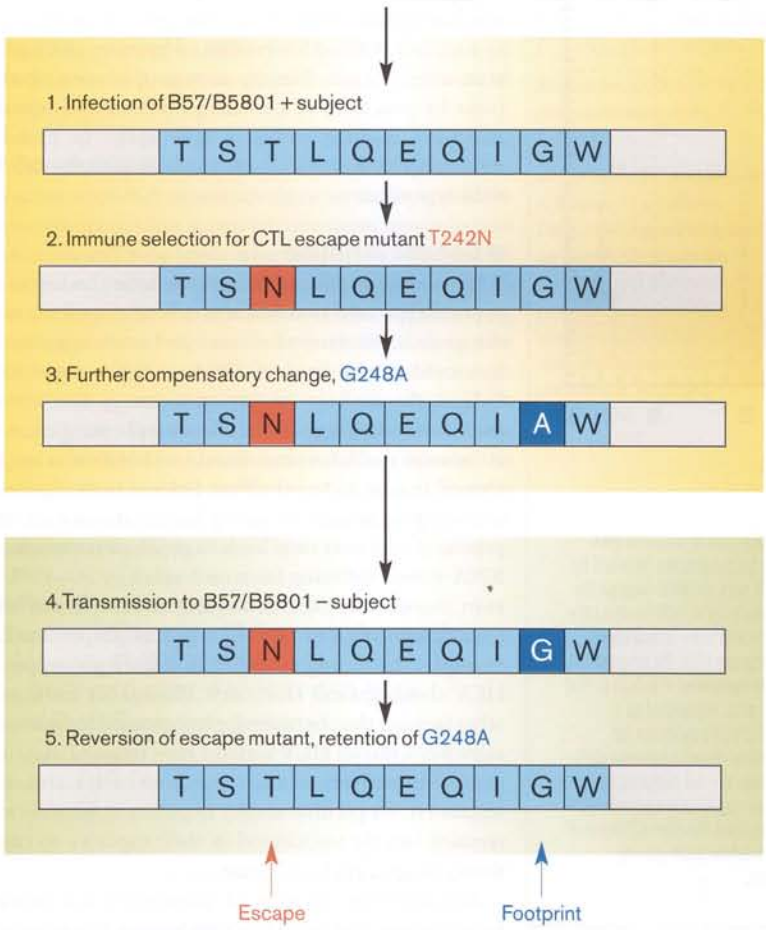

Fig. 1. Virus sequence changes and the immune system
Immune-mediated selection for an amino acid change in one of the anchor residues in a major class I epitope occurs reproducibly and rapidly each time an individual with a B57 or B5801 HLA type becomes infected. The T→N change at position 242 in the $p24^{gag}$ gene is associated with a subsequent further change in the epitope, G→A at 248, and at other sites in the p24 gene to help recover virus fitness. Further transmission of the mutated virus to non-B57 or B5801 individuals is associated with rapid reversion to the wild-type amino acid residue at position 242, indicating that its previous immune escape strategy was associated with substantial fitness cost to the virus. The retention of the compensatory alanine mutation in these further transmission cases, and its frequent presence in the published database of HIV sequences is a kind of evolutionary 'footprint' or relic of the selection process and provides an example of how much of the observed virus diversity may be shaped by past selection processes.
MODIFIED FROM LESLIE *ET AL.* (2004); SEE FURTHER READING

Natural selection

In both natural history and *in vitro* studies, there are several dramatic examples of 'positive' or 'Darwinian' selection, in which selection for, and inheritance of, phenotypic changes in mutant virus leads to complete population replacements over short observation periods. For example, each time an HIV-infected individual is treated with the antiviral agent AZT, a clinically resistant population of HIV rapidly emerges bearing the same 2–4 amino acid changes in the part of the reverse

RNA viruses are characterized by a remarkable capacity to adapt to new environments, new selection pressures and new hosts when opportunity arises. Peter Simmonds describes the evolutionary activities of these amazing life-forms.

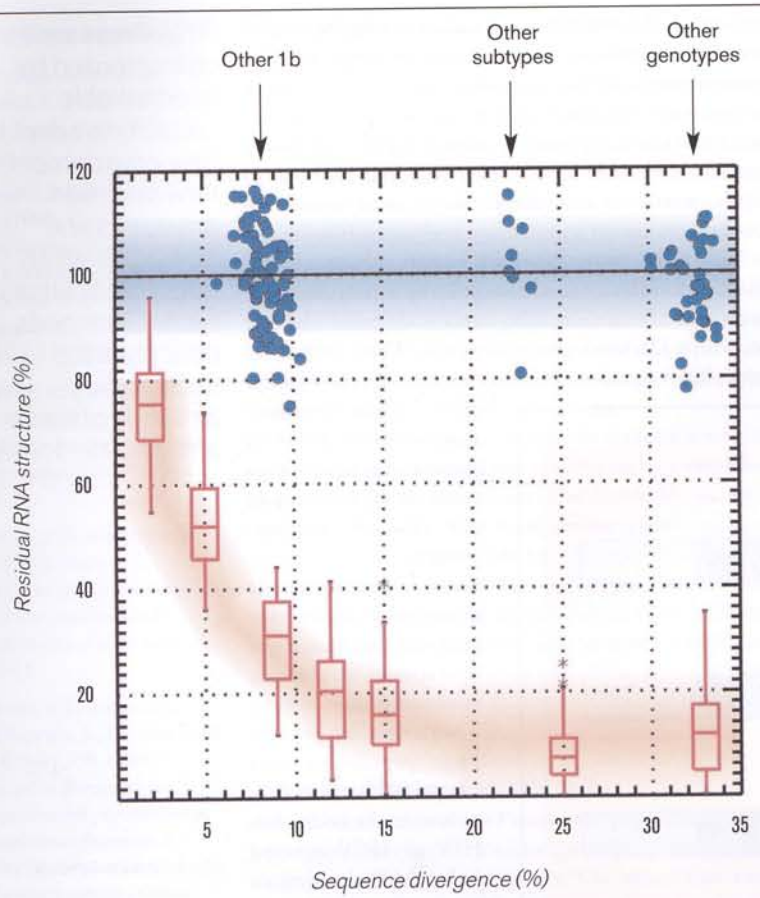

Fig. 2. Virus evolution and RNA structure
RNA folding requirements constraints. The failure of simulated 'neutral' sequence drift to preserve RNA secondary structure when introduced into the HCV genome indicates the powerful constraints imposed by RNA-folding requirements. To demonstrate this, a genotype 1b sequence of HCV was mutated through the introduction of nucleotide substitutions that reproduced naturally occurring variability in HCV (such as the transition/transversion ratio, synonymous to non-synonymous substitution ratio and base composition observed in native sequences). HCV variants were created from 2 to 35 % divergence from the original sequence (*x* axis). The formation of RNA structure in the mutant sequences was compared in extent to that of the native sequence using a thermodynamic prediction algorithm (MFOLD; *y* axis; expressed as a percentage). Mutants differing by as little as 2 % in sequence from the original showed evidence for disruption and loss of RNA structure formation (red symbols), while those with introduced sequence drift of greater than 10 % produced mutants that were totally unstructured. In contrast, the full range of naturally occurring variants of HCV, differing by up to 33 % from the 1b sequence (blue symbols), showed complete conservation of RNA structure. The inevitable conclusion from this comparison is that the diversification of HCV operates under very specific constraints, and the evident requirement for internal base-pairing conserved in native sequences must constrain even its very short-term evolution.
FIGURE MODIFIED FROM SIMMONDS *ET AL.* (2004); SEE FURTHER READING

transcriptase enzyme that determines substrate recognition. Similarly, many virus infections show evidence for positive selection in response to activity of the immune system. Over the course of an epidemic, the external haemagglutinin of influenza A shows dramatically accelerated evolution, keeping it ahead of the neutralizing antibody response mounted by the host. Primary infection with HIV is associated with a burst of rapid sequence change that eliminates specific MHC class I recognition motifs in several virally encoded proteins, therefore preventing destruction of the infected cell by cytotoxic T cells. It has recently been shown that immune-mediated changes in the *gag* gene in individuals with HLA types B58 and B5801 revert back to wild type on further transmission to individuals with different HLA types, indicating the fitness compromise that this form of evasion may have to incur (see Fig. 1).

Reversion on a larger scale was observed in a classic series of experiments in the 1980s and 1990s, where populations of the bacteriophage MS2 were shown to be able to repair sections of their genome that had been artificially mutated or even deleted. For example, removal of 19 bases from an intercistronic region that regulates translation of the coat protein of MS2 led to a >1 billion-fold fitness drop. However, the highly attenuated viruses blindly rebuilt the missing sections by processes of random mutation and mutant selection, leading within a few weeks to pseudo-revertant viruses with fitness levels close to that of the wild-type virus.

Genetic variation

Surprisingly, sequence changes occurring in response to phenotypic selection makes very little contribution to the genetic diversity of viruses and other organisms, measured at the level of DNA or RNA sequences. Indeed, the majority of sequence change that occurs over time has no significant effect on phenotype (i.e. it is 'neutral') and becomes fixed in the population by chance. In what seems a baffling contrast to the dramatic phenotypic changes made by single mutations, the process of drift over time leads to genotypes or species of RNA viruses differing from each other by 30–40 % or even more in nucleotide sequences, each remaining remarkably similar in their biological properties. For example, the coding sequence in the six genotypes of HCV shows greater than 30 % divergence from each other (greater than between typical genes of humans and ostriches!), but all HCV variants have retained identical genome organizations and replication cycles, and each retains HCV's peculiar ability to persist in humans and remains largely unchanged in their capacity to cause slowly progressive liver disease.

Although the fixation of phenotypically neutral substitutions that takes place on sequence drift should occur at a constant rate over time, it is nevertheless difficult to date times of divergence of different virus variants, genotypes or species. From the epidemiological distribution of different genotypes of GB virus-C (GBV-C), a non-pathogenic flavivirus cousin of HCV, it appears that its current sequence diversity (11–13 %) arose extremely slowly, potentially as long as the 150,000 year period during which anatomically modern human population groups re-populated the world from Africa.

RNA structure

In the case of GBV-C, HCV and other persistent RNA viruses, we have recently found that their sequence drift is limited by a lack of truly 'neutral' sites. The nucleotide sequences of their genomes are organized to form evolutionarily conserved, extensive RNA secondary structures, termed genome-scale organized RNA structures (GORS), which may in some way modulate the activity of host-cell defences that recognize double-stranded RNA. GORS is destroyed by even minimal nucleotide changes that would typically be regarded as 'neutral', such as those at third codon positions that do not alter the encoded protein sequence (Fig. 2). GORS may therefore place some viruses in an evolutionary 'straightjacket' in which only a minority of changes that retain base pairing are tolerated. Such RNA viruses are clearly not the progressively evolving and ephemeral entities of popular imagination.

Conclusions

In summary, RNA viruses are characterized by a remarkable capacity to adapt to new environments, new selection pressures and new hosts when opportunity arises. In established virus–host interactions, however, RNA viruses may show extreme conservatism, representing closely optimized replication, transmission dynamics and frequent persistence in the extraordinarily tough environments created by sophisticated animal and plant host defences. The tempo and mode of these contrasting aspects of RNA virus evolution fully embody the principles expounded in the *Origin of Species*; Darwin would have been delighted by this new branch of evolutionary biology.

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Micro Shorts

Lister Institute Research Prizes

The first winners of these prestigious prizes have been announced. **Dr Oliver Billker** (Imperial College London), **Dr Nia Bryant** (Glasgow University) and **Dr Paul Lehner** (Addenbrooke's Hospital, Cambridge) have each won £150,000 to spend as they wish on their research over the next 3 years. This is a new source of funding for young clinical and non-clinical biological researchers. Applicants must have at least 3 but less than 10 years of postdoctoral experience. Their work must address the Institute's charitable aim of enhancing understanding in biological and biomedical sciences relevant to preventative medicine. The Prizes are awarded based on both the past achievements of applicants and the scientific quality and potential implications of their proposed research. The money can be spent on any aspect of research other than personal salaries. Applications for the 2005 round of awards are invited. See **www.lister-institute.org.uk** for details.

Foresight into Infectious Diseases

A new UK Foresight project sponsored by Defra aims to produce a challenging and long-term vision for the detection and identification of infectious diseases in plants, animals and humans. The vision will take account of: the evolving risk of diseases; changing user requirements for detection and identification; and cutting edge science. The project aims to inform policy at national and international level. Experts or stakeholders are invited to register their interest in the project via the web at **www.foresight.gov.uk**

Scientific Instruments

The Scientific Instrument Society aims to provide a forum for those who have developed a fascination for the history and development of scientific and technical instruments, the varied forms which they take and the role which they have played in the development of science and technology. SIS organizes meetings and study tours and publishes a regular Bulletin. For further information email **patrickmill@btopenworld.com**

The evolution of antifungal resistance in *Candida* species

Frank Odds

The problems of antifungal resistance are different from those of antibacterial resistance. Frank Odds describes aspects of the evolution of resistance to antifungals by *Candida albicans*, a major opportunistic pathogen.

Resistance to antimicrobial agents is big news. MRSA (methicillin-resistant *Staphylococcus aureus*) has become a topic for discussion by politicians, and many recent articles have appeared on the threats posed to public health by the increased prevalence of 'superbugs' resistant to most known antibiotics. By contrast, with the vociferous pressures for new drugs and better hospital hygiene to combat the 'nightmare epidemic' of bacteria resistant to antimicrobial agents, discussion of antifungal resistance has been relatively sober. The agents used to treat fungal infections work differently from antibacterial agents and belong to different chemical classes. The problems of antifungal resistance are different in many ways from those of antibacterial resistance. This article focuses on the polymorphic yeast *Candida albicans*, which is the major opportunist fungal pathogen causing potentially fatal disease in immunosuppressed human hosts, and aspects of the evolution of resistance to antifungals in a eukaryote bounded by a rigid cell wall.

Clinical importance and mechanisms of antifungal resistance

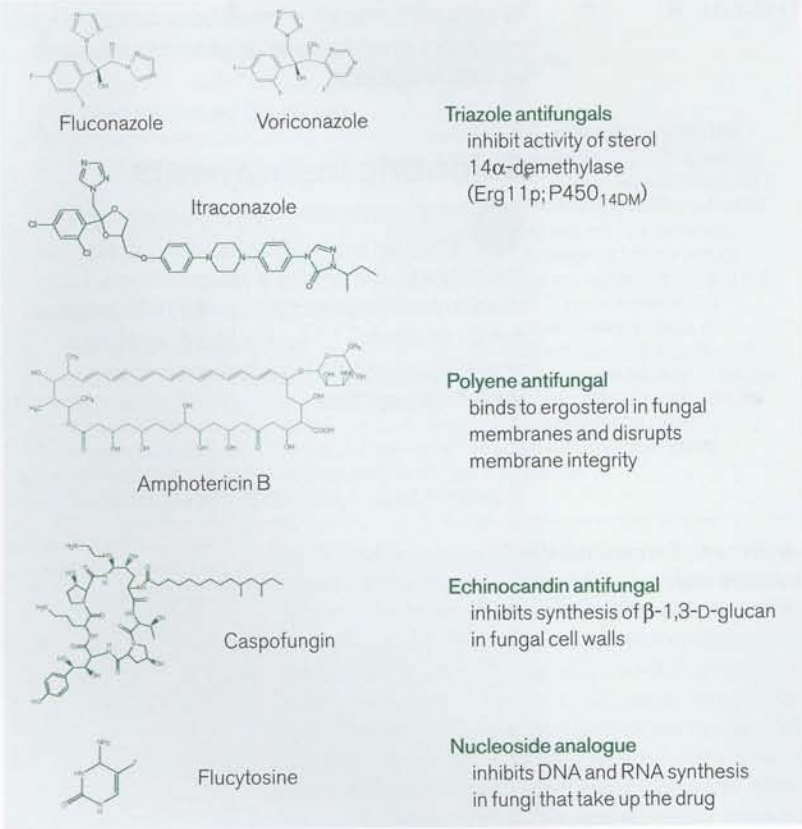
Fungi differ from bacteria in one very important respect: they have, so far as we know, no plasmids or other natural mechanism capable of transferring genetic material between strains. This means that a strain of *C. albicans* that has become resistant to an antifungal agent cannot pass on the gene(s) encoding the resistant phenotype to other strains. The potential for rapid emergence of resistance that has been seen with many types of bacteria is therefore much smaller in *C. albicans*. We have already seen how antifungal resistance emerges in clinical practice. Before effective therapy to combat AIDS was available, around 20 % of patients infected with HIV who were repeatedly treated with the agent fluconazole for *Candida* infections of their mouths ended up with infecting strains that were many-fold less susceptible to fluconazole than the strains that caused the first bouts of infection. Yet it was rare to find any replacement of an individual's infecting strain with another that clearly differed in molecular typing tests: resistance almost always emerged by a process of 'micro-evolution' within each patient's own isolate responding locally to the selective pressure of fluconazole exposure.

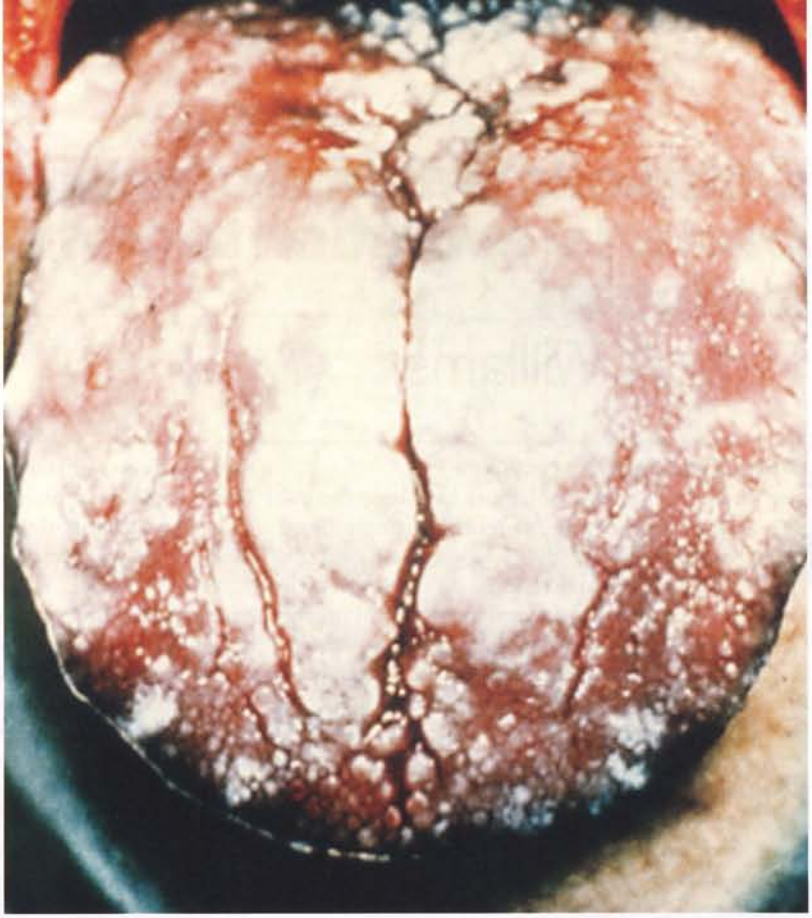
In the best known example of this process, a set of 17 consecutive oral isolates of *C. albicans* was obtained over a 2-year period from one patient as his CD4+ cell count deteriorated. The fluconazole susceptibility of each new isolate was as low as, or lower than its predecessor. Yet the isolates were indistinguishable by a variety of DNA typing tests. The mechanisms of resistance expressed in each of the isolates were determined. In isolate number 3, the gene *MDR1*, a fluconazole efflux pump, was over-expressed. In isolate number 13, mutations were detected in the gene *ERG11*, which encodes the enzyme that is the target for fluconazole; the mutation was found in both alleles of the gene (*C. albicans* is diploid). Moreover, the mutated *ERG11* was also over-expressed. Isolates numbers 16 and 17 added over-expression of another gene encoding an efflux pump, *CDR1*, to the other mechanisms of resistance. So these last isolates had evolved to express at least four different mechanisms of fluconazole resistance in each cell. However, there is no evidence that these multiple-resistant strains were transferred to other AIDS patients. Of course, patient to patient transfer of resistant strains can occur, but this means of spread is far less efficient than would be the case if the fungi could transfer DNA from strain to strain.

Loss of fitness as a penalty for antifungal resistance

Evolution to an antifungal resistant genotype is not a cost-free experience for the fungus. Fitness, typically defined as reproductive output over a specific time interval, may be reduced in a strain that has evolved to antifungal resistance as compared with its susceptible predecessor. Trade-offs of fitness in exchange for acquisition of survival-enhancing characters in a specific environment form an inevitable part of evolutionary processes. With *C. albicans*, Dr James Anderson and his colleagues in Canada have experimentally investigated the evolution of fitness and susceptibility in initially

BELOW:
Fig. 1. Antifungal agents in clinical use for serious infections and their mechanisms of action.
COURTESY F. ODDS





LEFT:
Fig. 2. Oral *Candida* infection in an AIDS patient, breeding ground for antifungal resistance.
COURTESY F. ODDS

clonal populations of a fluconazole-sensitive isolate that was sequentially subcultured in a medium with and without additions of fluconazole. They found that fluconazole exposure led to different levels of resistance development in different subpopulations, that resistant populations initially paid a penalty in fitness for the mutation to resistance, but that fitness returned to normal with further exposure to the fluconazole-containing environment. Microarray experiments with the sensitive and resistant strains showed that expression of no fewer than 301 genes altered significantly as the populations adapted to fluconazole resistance! The expression changes could be assigned to three fairly general patterns, which were associated with different stages of resistance development.

Are there over-arching mechanisms determining antifungal resistance?

Although *C. albicans* has a diploid genome, recent research has shown that the fungus contains genes homologous to the mating-type genes of *Saccharomyces cerevisiae*, and several groups of investigators have now succeeded in inducing isolates that are homozygous *a* or α type at the mating-type-like (MTL) locus to undergo a mating process, though not yet with the completion of meiosis. Intriguingly, clinical isolates of *C. albicans* that are fluconazole-resistant are far more likely than others to be homozygous at the MTL. Recent data from my own lab show that MTL homozygosity is also significantly associated with *C. albicans* resistance to flucytosine, an antifungal with a totally different mode of action from fluconazole (Fig. 1). As DNA-level strain typing methods for *C. albicans* have progressed, ever more reliable population structure analyses of the species show that the majority of isolates of the yeast can be assigned to one of four major, closely related clades. Dr David Soll and his group in Iowa have shown that almost all isolates of *C. albicans* expressing resistance to flucytosine belong to a single clade. Moreover, all flucytosine-resistant isolates from that clade owe their resistance to a single point mutation in a target gene. Perhaps resistance mechanisms to other agents will ultimately prove to be restricted to particular clades.

Antifungal resistance: more questions than answers?

Studies of the evolution of antifungal resistance in *C. albicans* have reached a particularly exciting point. We know that mutation to one or more triazole resistance mechanisms occurs readily in response to fluconazole exposure, and that the changes involved can require collateral alterations in levels of expression in as much as 5 % of the *C. albicans* genome. We know that fluconazole- and flucytosine-resistant isolates are significantly more often (though not always!) homozygous at the MTL locus, suggesting that mutation to resistance is possibly linked to recombination events involving a mating process. And we know that a common mechanism of mutation to flucytosine resistance pertains to isolates in one of the four major clades of the global *C. albicans* population. What we do not know is how these processes are triggered and regulated; why strains need to mutate to constitutively over-express efflux pumps (why don't they just over-express when the drug is present and turn down the gene expression when it is not?); why just one clade of related strains should have a near monopoly on mutation to flucytosine resistance?

Research on *C. albicans* has been well supported and has itself evolved rapidly over the past 20 years. We may soon have answers to some of the intriguing questions posed by the evolution of antifungal resistance in *Candida* species; meanwhile we can take comfort in recent surveillance data which show unequivocally that antifungal resistance among clinical isolates of *Candida* species is growing slowly, if at all. We appear to have time to understand the mechanisms well before any clinical resistance problem arises.

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Catabolic plasmids: fast-track bacterial evolution to combat pollution

Peter A. Williams

Bacteria can evolve incredibly fast to degrade new synthetic compounds such as dyes or solvents. Peter Williams explains the role of catabolic plasmids in this process.

Microbes as waste recyclers

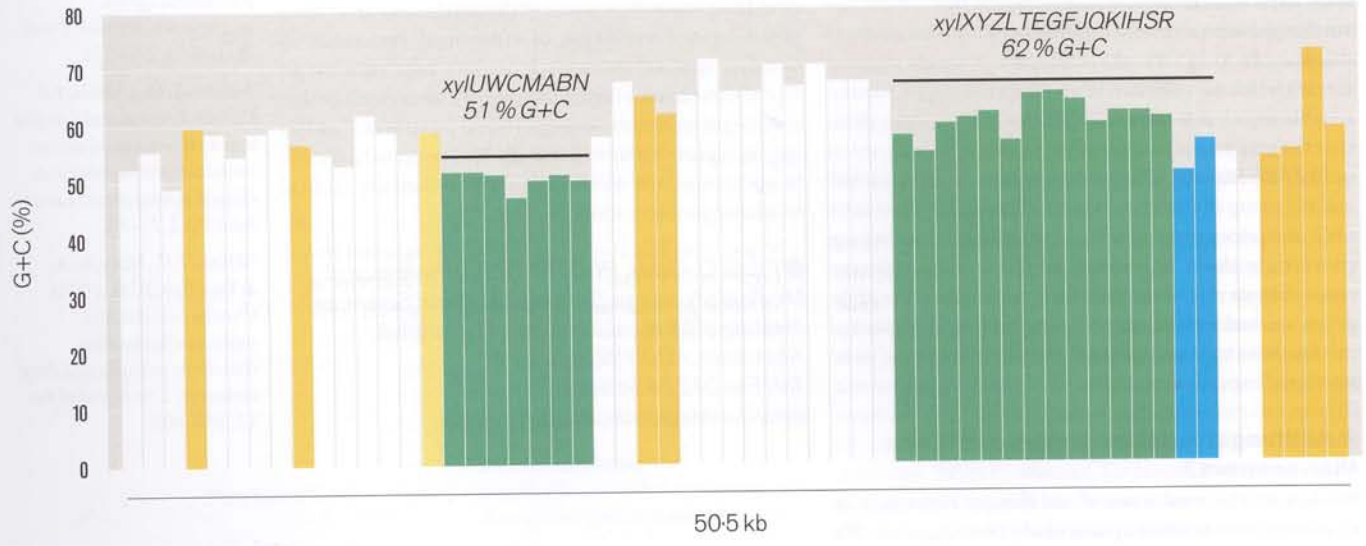
For several billion years microbes have been the unsurpassed recyclers of waste materials. Their combined ability to consume natural waste products as their 'foodstuffs' (growth substrates) and thereby recycle them has been a critical factor upon which all life has depended. During their long evolutionary history bacteria have evolved novel and often exotic catabolic pathways for this purpose, very few of which have been passed on to their eukaryotic descendants.

Since the development of organic chemistry in the 19th century, hundreds of thousands of novel compounds previously unknown to biology (xenobiotics) have been synthesized. Many have found such uses as agrochemicals, fuels, dyes, drugs, plasticizers, explosives or solvents and have been synthesized on industrial scales. Their deliberate or inadvertent release into the environment has presented microbes with entirely new potential growth substrates. Many of these compounds are toxic to higher organisms, and their removal from the environment relies on the almost limitless capacity for biodegradation of the microbial population. Microbes have risen to the challenge and, within decades, have fast-tracked evolution to arrive at solutions for degrading most (but not all) of the introduced xenobiotics. The mechanism for this rapid evolution is the same as that which has caused the rise of antibiotic-resistant bacteria in hospitals, namely the ability of DNA to move between both replicons and individual bacteria via plasmids and transposable elements.

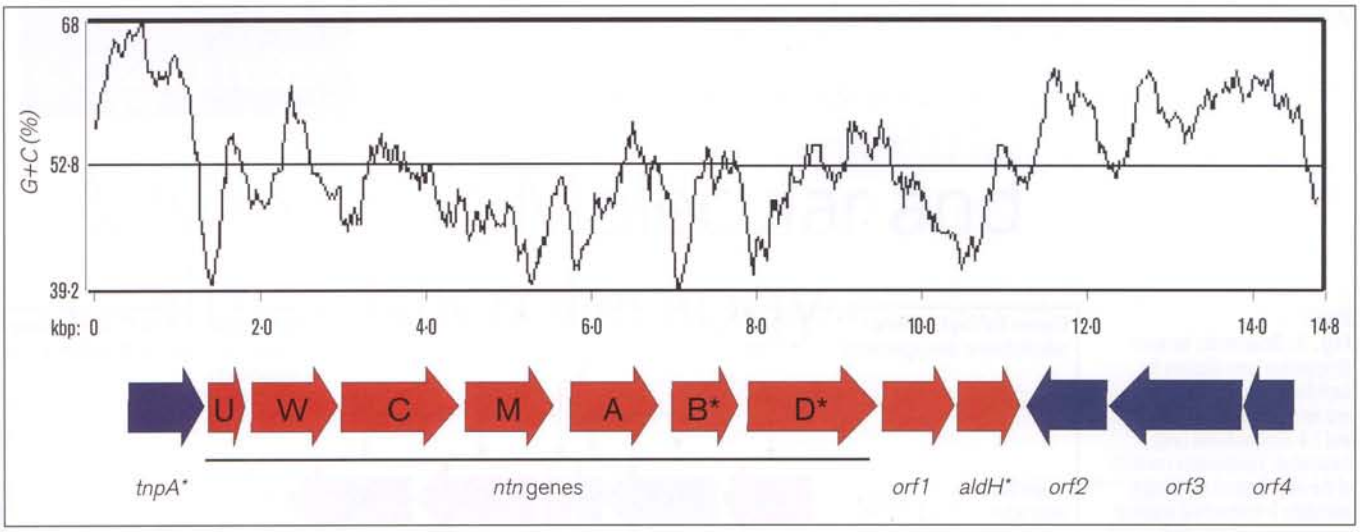
Catabolic plasmids

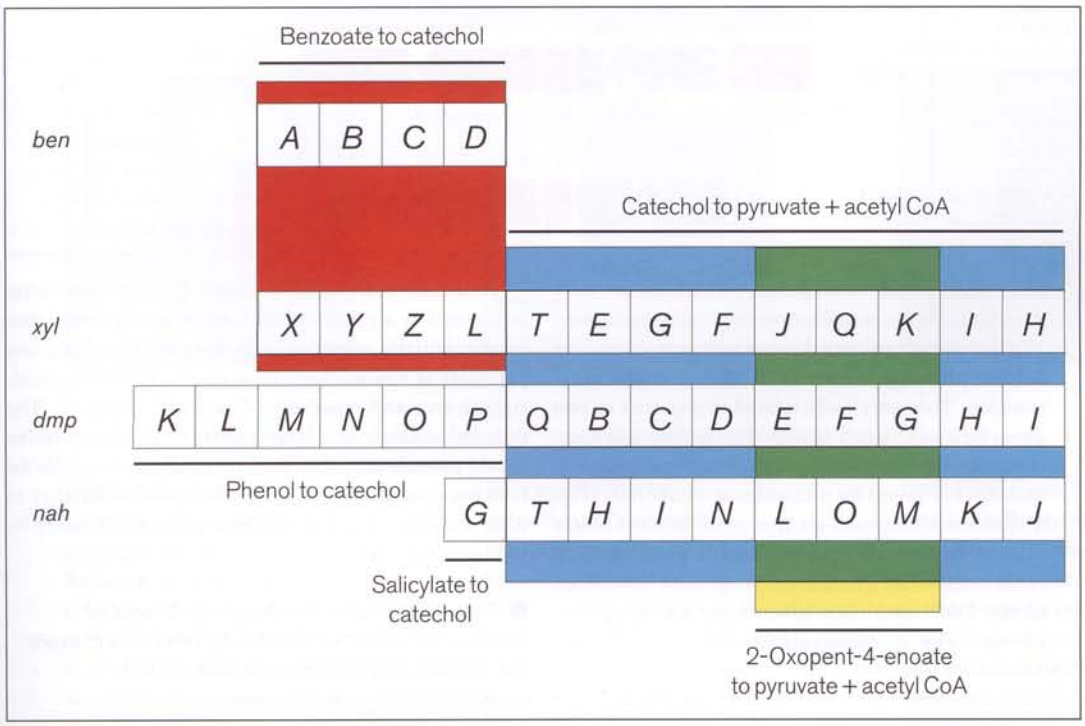
The first reports of catabolic pathways encoded by plasmids were made in the early 1970s. These were for catabolism of camphor, octane, naphthalene, salicylate (a metabolite of naphthalene) and toluene and were all found in strains of the Gram-negative genus *Pseudomonas*. None of these particular substrates are truly xenobiotic, being found naturally in plants or in oil, and the plasmids therefore probably do not represent the result of recent evolution. However, it was not long before a plasmid determining the catabolism of a true xenobiotic, the herbicide 2,4-dichlorophenoxyacetic acid (2,4-D), was reported in a *Ralstonia* strain. Subsequently, catabolic plasmids in many different genera have been reported and almost all determine the utilization of substrates which *Escherichia coli* microbiologists would regard as 'exotic' and many of which are true xenobiotics: there are very few examples of plasmid-encoded catabolism of more 'conventional' substrates such as sugars, amino acids or other common biological molecules, for which a chromosomal location appears the norm. By contrast, for some 'exotic' substrates, such as toluene and naphthalene, many different and diverse plasmids have been described and a plasmid location of the genes appears to be the norm. This suggests an evolutionary segregation of catabolic genes into two groups: (a) 'housekeeping' catabolic genes, chromosomally located and essential to the cell for regular use; and (b) 'peripheral' catabolic genes, required on a less frequent basis and which are plasmid-encoded.

The size and diversity of the saprophytic microbial population and its combined ability to degrade essentially all natural products, means there is a huge pool of catabolic genes. The freedom of these genes to move between hosts on plasmids and thereby become exposed to rearrangements by means of genetic recombination can lead to plasticity in the organization of these genes. Add to this the fact that many catabolic enzymes have a broad substrate specificity, then DNA rearrangements giving rise to new combinations in new genetic contexts can result in novel catabolic phenotypes



BELOW:
Fig. 1. Diagrammatic representation of region of TOL plasmid pWW0 carrying the two *xyl* catabolic operons (green). This shows the difference in G+C content of the two operons and also the high concentration of transposition-related genes in the vicinity (yellow). Each gene is represented by a bar of constant width, not related to its size.
COURTESY P.A. WILLIAMS





ABOVE:
Fig. 2. Structure of 4-nitrotoluene (*ntn*) genes. The genes are of low G+C content (red), but embedded within a sequence with higher G+C content (blue) more typical of the host *Pseudomonas*. Also adjacent to the ntn operon is a functionless pseudogene for a transposase (*tnpA**) frequently found in the vicinity of such catabolic gene clusters. An asterisk signifies a pseudogene no longer specifying an active protein.
COURTESY P.A. WILLIAMS

LEFT:
Fig. 3. Modular structure for catabolic genes. The *xyl*, *dmp* and *nah* genes are found on plasmids and code for xylene, phenol and naphthalene respectively. The early genes for each operon are unique to each, but the nine genes for further metabolism of the common substrate catechol (in blue) are all homologous and in the same gene order. The *xyl* genes converting benzoate to catechol (red) are found in the chromosomal *ben* genes of *Pseudomonas* strains converting benzoate to catechol in a different pathway. A subgroup of three genes (yellow) found within the catechol 'module' (blue) is also found as a cluster within genes converting biphenyl. Genes are not drawn to scale.
COURTESY P.A. WILLIAMS

resulting simply from 'repackaging' of genes already in existence.

Molecular archaeology of catabolic genes

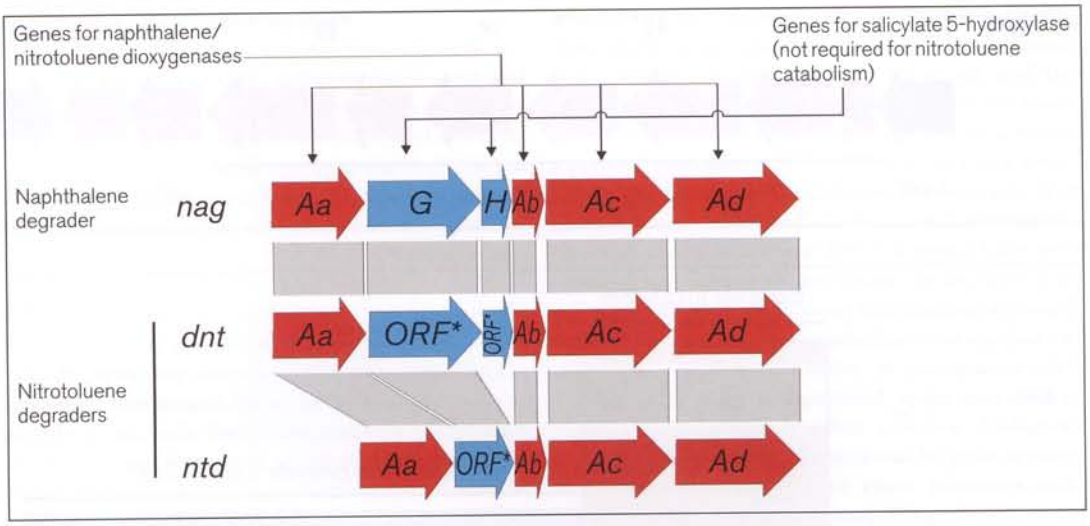
Strong evidence for a gene transfer/recombination scenario for the evolution of new catabolic traits comes indirectly from molecular archaeology – the analysis of sequence data both from the limited number of complete plasmid sequences available and from large chunks of catabolic genes sequenced (which may or may not be plasmid-encoded):

(a) Transposition-related genes are found at a high frequency in very close proximity to catabolic sequences (see Fig. 1): this is true even for gene clusters which have not been definitely shown to be on plasmids. The TOL (toluene/xylene) plasmid pWW0 carries 12 transposase-like genes, some of them still active, and the present structure of the plasmid appears to have occurred by a series of sequential recombination/transposition events.

(b) There are often significant and abrupt differences in base composition between catabolic genes and the surrounding DNA or between different segments of the catabolic genes (Figs 1, 2). These discontinuities indicate they have come together from different origins.

(c) Some of the plasmid-encoded catabolic operons appear to have been constructed from modules: subsections of them turn up in operons for other pathways with the relevant genes sharing the same gene order and high homologies (Fig. 3).

(d) As in real archaeological remains, non-functional remnants of a previously functional catabolic sequence are occasionally found. This indicates that a region of DNA has been removed *en bloc* and relocated in a new position (and probably in a new host strain). Within the new genetic context and in combination with adjacent genes, its gene(s) are able to confer a novel phenotype, but the relocation event may have fortuitously carried with it genes which are no longer required in the new location. For example, in a number of strains degrading mono- and dinitrotoluene, synthetic precursors of the explosive TNT (2,4,6-trinitrotoluene), the initial enzymic step is by a



RIGHT:
Fig. 4. Relationship between dioxygenase gene clusters for naphthalene (*nag*) catabolism and for 2-nitrotoluene (*ntd*) and 2,4-dinitrotoluene (*dnt*) catabolism. Functionless residues of the *nagGH* genes encoding a salicylate 5-hydroxylase required for catabolism of naphthalene, but not nitrotoluenes, are found in the *dnt* and *ntd* cluster, showing their evolution from a *nag*-like ancestor. COURTESY P.A. WILLIAMS

multicomponent dioxygenase which must have originated from a naphthalene degradative pathway. Within the nitrotoluene dioxygenase gene cluster one or two pseudogenes are intercalated in the same position. They are clearly related in sequence to two genes for a salicylate 5-hydroxylase present and functional in the corresponding naphthalene pathway, but no longer required for nitrotoluene catabolism (Fig. 4). Since nitrotoluenes are true xenobiotics of recent origin, the presence of the redundant pseudogene(s) must result from a recent rearrangement/relocation of the DNA and may, given time and selection, ultimately be completely eliminated.

At a time when whole bacterial genomes are being sequenced at a phenomenal rate, it seems ironic that relatively little attention is being paid to sequencing plasmids of environmental, as distinct from medical, significance and especially of catabolic plasmids. The detailed analysis of a large number of such replicons would provide arguably the best evidence available for how bacteria can evolve with extraordinary rapidity to cope with the complex challenges thrown at them by industrial society.

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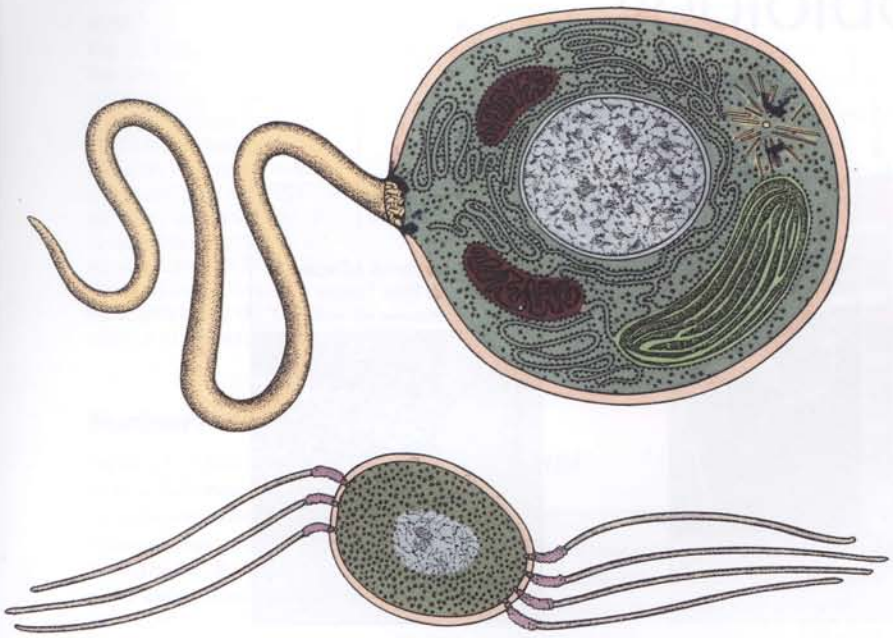
Serial endosymbiotic theory (SET) and composite individuality

Transition from bacterial to eukaryotic genomes

Lynn Margulis



Distinguished evolution expert and writer Lynn Margulis discusses the serial endosymbiotic theory of the transition from bacteria to eukaryotes.

ABOVE:
Fig. 1. Comparison of the two types of cells. *Top*: eukaryote cell with membrane-bounded nucleus that contains chromatin, undulipodium, centriole-kinetosomes, mitochondria, plastid, large ribosomes and intracellular motility. *Bottom*: prokaryote cell with rotary motor flagella, nucleoid, small ribosomes and peptidoglycan cell walls.
DRAWINGS BY CHRISTIE LYONS

OPPOSITE PAGE, TOP:
Fig. 2. A walled oxygenic photosynthetic cell (top) compared with an intracellular organelle from a chlorophyte (green) alga (bottom). Both contain chlorophylls *a* and *b* in a ratio of 1:3.
SEE MARGULIS (1993), PP. 116 & 337

The living world's highest taxa: bacteria and eukarya

The Russian–American *Drosophila* geneticist Theodosius Dobzhansky wrote that '*nothing in biology makes sense except in the light of evolution*'. I paraphrase him by suggesting that today nothing in molecular biology makes sense except in the light of the evolutionary history of organisms in specific paleoenvironments. As Darwin noted, our classification systems should become genealogies. If our taxa classify, identify and name life accurately, our grouping will reflect evolution; this is possible because strong inferences concerning the past are embodied in the living. The contribution to evolution of microbiology (*sensu lato*, the study of both bacteria and their protist descendants) has only recently begun to be appreciated. The cells of microbes are the units of life, hence the recognition of their importance in their own evolution and evolution of larger life forms is bound to increase.

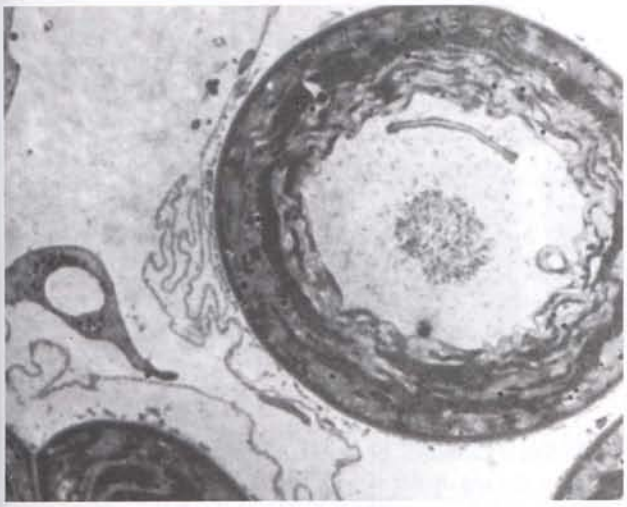
The living world unambiguously is divided into two definitive never-overlapping categories: prokaryotes and eukaryotes (Fig. 1). In spite of the immensely useful 'three-domain' 16S rRNA classification scheme proposed by Carl Woese, only two fundamentally different kinds of life exist on Earth. No evidence from either the fossil record or the living world can be mustered for any 'progenote' or other deviation from the prokaryote–eukaryote rule. This prokaryote–eukaryote divide (=Prokarya–Eukarya) remains the largest discontinuity in the living world. First recognized by Edouard Chatton and first analysed by the Delft School of Microbiology (e.g. A.J. Kluyver, Cornelius van Niel and Roger Stanier) the list of differences between Archaebacteria, Eubacteria and Eukarya unequivocally shows that the two prokaryote groups are far more closely related to each other than each of them is to any eukaryote. The cell, whether bacterial [where its genome is chromonemal (see below) and unbounded by membrane] or mitotic (nucleated, where a lipoprotein membrane bounds the proteinaceous chromosome) is the unit of all life.

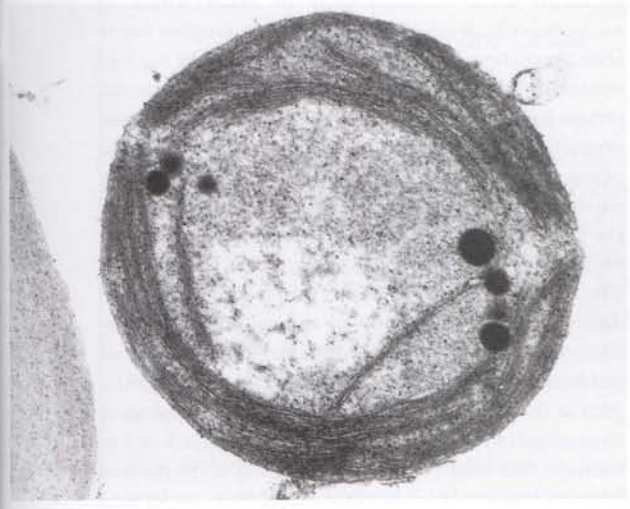
No system of matter and energy flow less complex than a cell is alive. The presence of the nucleus is the only feature that uniquely defines the eukaryotes and distinguishes them from bacteria. The origin of the bacterial cell is the origin of life itself, whereas Serial Endosymbiotic Theory (SET) describes the subsequent origin of the nucleated cell by symbiogenesis.

To proceed we need to explain how the ecological concept of 'symbiosis' differs from the evolutionary term 'symbiogenesis'. Symbiosis refers to the living together of organisms of different species. Endosymbiosis, a topological condition, is a kind of symbiosis where one partner lives inside of another. Symbioses usually, if not always, have environmentally contingent outcomes. Symbiosis, not an evolutionary process *per se*, refers to physiological, temporal or topological associations with environmentally determined fates. Symbiogenesis, however, implies the appearance of new tissues, new organs, physiologies or other new features that result from protracted symbiotic association. Two great classes of eukaryotic cell organelles, plastids and mitochondria, evolved symbiogenetically. Oxygen-respiring, heterotrophic α-proteobacteria were probably phagocytosed by anaerobic motile protists (like today's mastigamoebae). Genetic and metabolic redundancies were selected against as once free-living eubacteria evolved into the organelles we recognize as mitochondria. The descendants of this merger include most heterotrophic protists such as most amoebae, cryptomonads, chilomonads and chytrids,

Definition of *chromonemal*

The term chromosome does not apply to bacteria, even though it is often used. Chromosomes (*chromo*-coloured, *soma*-body) are the staining bodies, approximately 40% DNA by weight and 60% histone protein, that are segregated by the mitotic apparatus to the opposite ends of nucleated cells. The unit fibre is 100 Å diameter in chromosomes. Nothing resembling chromosomal mitosis has ever been found in any prokaryote, although it was claimed to be present in cyanobacteria. The much smaller unit fibre of bacteria, about 25 Å and nearly entirely composed of DNA does not take up Fuelgen and other cytological stains; it is properly referred to as 'chromoneme' and is the typical organization of nearly all bacterial nucleoids. The nucleoid refers to the electron microscopical appearance of the chromonemal DNA organization, if visible, in prokaryotic cells.





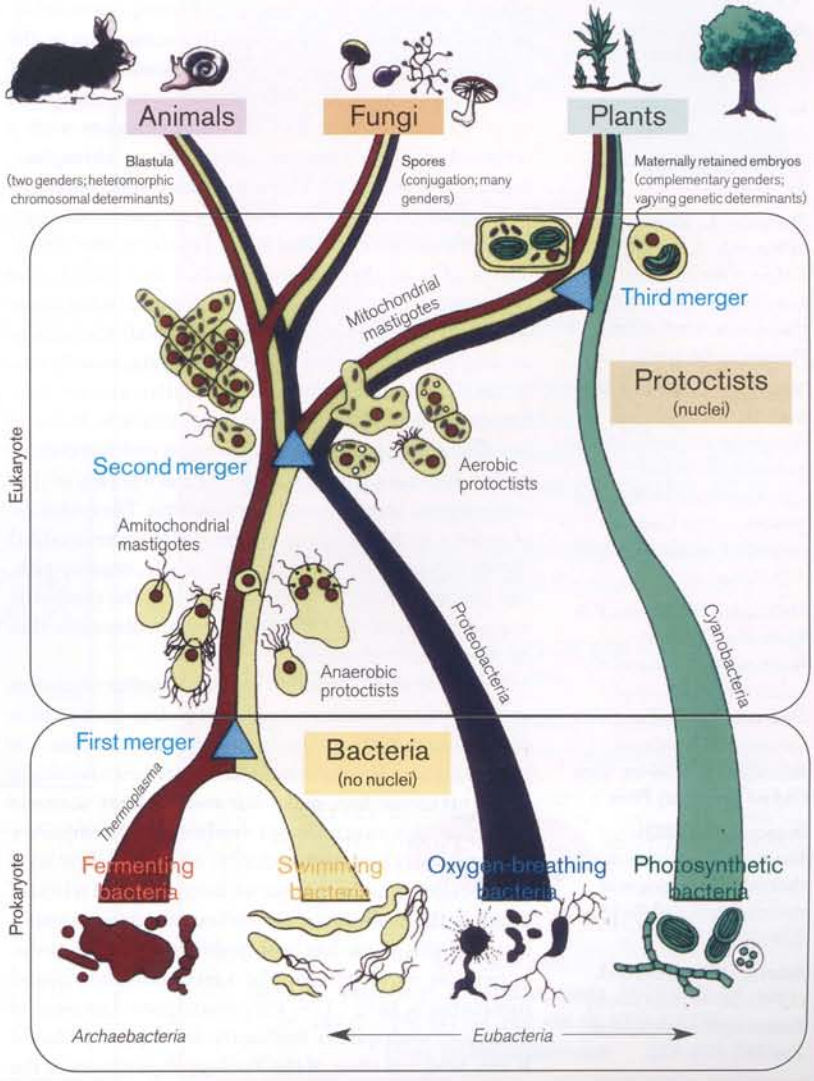
oomycotes (like *Phytopthora infestans*, the potato blight organism). No doubt some motile protists ingested, but failed to digest, food – cyanobacterial cells – that eventually became symbionts. The retention of undigested cyanobacteria in well-lit waters led to permanent unions in which, once again, natural selection favoured the reduction of genetic and metabolic redundancy. In this way algae, eukaryotic organisms that bear photosynthetic organelles in their cytoplasm, evolved and some became, eventually, the ancestors to the land plants. The Apicomplexa (a phylum which *Plasmodium*, the genus to which the malarial parasite is assigned) apparently evolved from one lineage of such algae. The members of this phylum, including *Toxoplasma* have retained a residuum plastid with its DNA, but they are no longer capable of photosynthesis. The principle of 'use it or lose it' can be invoked. Natural selection does not plan ahead; the unused plastids that began as cyanobacteria were severely reduced as they evolved. The striking resemblance of some free-living bacteria (such as cyanobacteria) to certain intracellular organelles (such as green algal chloroplasts) bolsters the concept that certain bacteria have been trapped inside other cells for millennia (Fig. 2).

With respect to the acquisition of mitochondria from free-living α-proteobacteria and that of plastids from free-living cyanobacteria, no one any longer doubts that the oxygen respiratory and photosynthesizing organelles evolved by symbiogenesis (Fig. 3).

Modern symbioses, both intra- and extracellular, that can be subjected to experimental analysis are of extraordinary importance for understanding evolution. How cells merge and how redundancy is reduced is especially relevant to the appearance of the first eukaryotes (which, by definition, were the first protists). Ironically, although most disease conditions are variations on the general theme of cyclical symbioses, few protistologists and microbiologists are familiar with the insightful, burgeoning literature that analyses these nearly ubiquitous associations.

No 'missing link' exists in our hypothetical evolutionary scenario on the origin of the complex individuality of Eukarya; every hypothetical event can be observed in extant microbes. This is why we have been able to make the 17 minute video entitled *Eukaryosis* (see www.sciencewriters.org). The study of genomics and proteomics will confirm or falsify this historical reconstruction that was made primarily based on observations of live organisms. Organismic biology coupled with direct knowledge of the fossil record are indispensable to evolutionary reconstruction. The techniques of molecular biology and sequence analysis by themselves are inadequate to the creation of testable evolutionary hypotheses.

BELOW:
Fig. 3. The minimal four prokaryotes of the plant cell. Swimming eubacteria (1) merged with sulfidogenic archaebacteria (2) and formed archaeprotists (amitochondriate mastigotes). O_2-respiring eubacteria (3) in the second merger produced ancestors to eukaryotic heterotrophs. Some acquired cyanobacteria (4) as undigested food and became algae with the third merger. All eukaryotes evolved from symbiotic mergers, whereas prokaryotes did not. Past (at bottom) to present (at top) is represented by the Archean Eon dominated by prokaryotes, the Proterozoic Eon of protoctists and the upper level Phanerozoic Eon, marked by the abundance of plants, animals and fungi.
DRAWING BY KATHY DELISLE



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Complex individuality and the evolution of the tethered nucleus

How did the distinctive nucleus evolve? What was the first eukaryote? In the past decade, since the publication of the second edition of my book *Symbiosis in Cell Evolution*, with close colleagues (Drs Michael Dolan and Dennis Searcy) we have further developed the SET. New sets of data from three sources have permitted us to make good progress toward understanding the crucial step of the origin of the nucleus. We reconstruct the transition from the earliest prokaryotic (bacterial level of organization) during the Archean Eon (3500–2500 million years ago) to the complex individuality of the first eukaryotes. The Proterozoic Eon (2500–541 million years ago) was the backdrop for the appearance of cells at the protist level of organization. All eukaryotes, in the SET, are products of symbiogenesis whereas no prokaryote cell evolved by merger of whole-cell predecessors.

Sulfur syntrophy, we hypothesize, united thermoplasmic archaebacteria (such as *Thermoplasma acidophilum*) with motile *Spirochaeta*-like eubacteria in the evolution of the karyomastigont organellar system of swimming protists. The first eukaryotes were composed of at least two integrated bacterial genomes with a tethered nucleus (nuclear connector or rhizoplast, kinetosome-axoneme). This organellar system called the 'karyomastigont' has been known to protozoologists since it was first described by C. Janicki in the 1930s. Think of it as the nucleus attached by fibres to the kinetosome-centrioles of the undulipodia: what those who know nothing about bacteria would call 'the nucleus attached to basal bodies and their flagella, usually two or four'. We interpret this organellar system [the karyomastigont of the so-called flagellates (which should be called mastigotes), zoospores of water molds and slime molds, many motile algal cells, etc.] as a legacy of that first genomic integration of these bacteria. The evolution of mitosis with its histone-coated, nucleosome-studded chromatin occurred under anoxic, acidic, organic-rich, and probably muddy conditions prior to the symbiotic acquisition of oxygen-respiring α-proteobacteria that became the mitochondria.

New biochemical data on the role of sulfur oxidation and reduction in nucleated cells and on free-living sulfur consortia, as well as geological information on the prevailing conditions of aquatic environments during the Proterozoic Eon make our evolutionary scenario plausible. We continue our studies of contemporary archaeprotists (amitochondriate, often multinucleate single-celled organisms) that we interpret to be relicts of stages in the evolution of the earliest motile eukaryotes. Much of this work has been published or is in press. It permits us to present the karyomastigont model summarized here. The karyomastigont concept of mastigont multiplicity brilliantly developed by Harold Kirby, who was chair of the Zoology department of the University of California, Berkeley, when he died in 1952, refers to the organellar system known to be present, although often inconspicuous in many kinds of nucleated cells. By definition, the karyomastigont has at least these three components: the nucleus, the nuclear connector and the kinetosome/centriole-axonemes. (In certain protists other components of the karyomastigont organellar system are routinely present, such as axostyles, peltas and Golgi apparatus, the latter known as the parabasal body.) We argue that the earliest nucleus was in the form of the minimal karyomastigont and that this organellar system was a response to selection pressure. The nucleus with the combined genomes of at least two different prokaryotes evolved to assure genetic continuity of the now integrated archae- and eubacterial symbionts. The nucleus itself began in the karyomastigont as the integrated symbionts, in an act homologous to conjugation between very different bacteria, fused to form the first eukaryote. The untethering of the nucleus in many lineages led to the free nuclei. Free nuclei seen today in animals, plants and fungi we interpret as the derived state. Tethered nuclei evolved simultaneously with the first protist. No missing links need to be hypothesized. Certain amitochondriate eukaryotes always were confined to anoxic environments and never had mitochondria. The nucleus, in this scenario preceded both the mitochondria and the plastids. Indeed, in the bowels of xylophagous insects (wood-ingesting roaches and termites) and in anoxic muds all 'intermediate stages' that we envision as steps in the origin of nucleated cells are still found today.

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New Council Officers

With effect from 7 September 2004, **Dr Ulrich Desselberger** commences his 5-year term as General Secretary, **Professor Hilary M. Lappin-Scott** commences her 4-year term as Scientific Meetings Officer and **Professor George P.C. Salmond** his 5-year term as International Secretary. Biographies of new Officers appear below.

Ulrich Desselberger

After studying Medicine in Germany and France, Ulrich initially worked as a histopathologist in Berlin (1967–68) and then specialized in medical microbiology (virology), gaining the 'Habilitation' at Hannover Medical School in 1976. After postgraduate work at Mount Sinai School of Medicine, New York (1977–79), he became a Senior Lecturer at the Institute of Virology, Glasgow (1980–87), Director of the Regional Virus Laboratory, Birmingham (1988–91), and Consultant Virologist at the Clinical Microbiology and Public Health Laboratory, Addenbrooke's Hospital, Cambridge (1991–2002). His main interests are the molecular biology and epidemiology of RNA viruses and clinical virology. Since 2002 he has also worked as a Visiting Research Fellow at the Unité de Virologie Moléculaire et Structurale, CNRS, Gif-sur-Yvette, France.

Ulrich is not a complete stranger to the SGM: he was an Editor of JGV (1989–95), on the Editorial Board of *Microbiology Today* (1999–2001) and an elected Member of Council (1998–2001). He is very much looking forward to his new activities at SGM.

Hilary Lappin-Scott

Hilary graduated in Environmental Sciences and did her PhD in environmental microbiology at the University of Warwick. Her first postdoctoral position was at the Institute for Biotechnological Studies, London, but a chance meeting with Bill Costerton led to an invitation to do postdoctoral research into biofilms at Calgary University, Alberta. She returned to England to work at the University of Exeter where she has greatly increased the range of microbiological research.

Hilary's existing research interests include biodegradation, bioremediation and biofilms. She has strong links with research sponsors in industry, was heavily involved in the development of the new Peninsular Medical School and has senior responsibilities for this and the new University of Exeter in Cornwall.

Hilary is a Fellow of the American Academy of Microbiology, Vice President of the International Society for Microbial Ecology and is Chair Elect of Q Division (Environmental Microbiology) of the American Society for Microbiology.

George Salmond

George studied microbiology at Strathclyde University and took a PhD on phages at Warwick University followed by postdoctoral studies on *E. coli* cell division in Edinburgh. He lectured in the Universities of Kent and Warwick, in the latter as Professor until 1996. He also worked at Celgene Corporation, New Jersey, and in the CNRS labs in Marseille. In 1996 he was appointed to the Chair of Molecular Microbiology in the Biochemistry Department in Cambridge University. His broad research interests have included development and exploitation of genetic tools (particularly using phages) in diverse bacteria to study cell division, protein secretion systems, molecular phytopathogenesis, methanotrophy, quorum sensing, and regulation and biosynthesis of antibiotics.

He served previously on the CCS and the PBMG Group committees, and was also an Elected Member of the SGM Council. He is currently the Convener of the PBMG committee. His other community roles have included serving on several BBSRC research funding committees, and membership of the Governing Councils of the John Innes Centre and the Scottish Crop Research Institute.

News of members

The Society notes with regret the death of **Professor S. T. Williams** (member since 1963).

Staff news

Welcome to new Staff Editor **Julia Trusler**, who joined us in June. Julia gained her first degree at the University of Cambridge before starting her career in publishing with BioMed Central. Staff Editor **Tobias Allinson** left SGM in September and we wish him well in his new job as a medical writer in London.

Technician membership

This new category of membership is open to microbiologists employed as technicians, research assistants (not registered for a PhD) and biomedical scientists in universities, research institutions, hospitals and commercial organizations. Their salary must be no higher than £21,500 (gross or euro equivalent) and they must be resident in the UK or Republic of Ireland.

For only £20 a year Technician Members will enjoy:

- Attendance at SGM meetings free or at reduced registration fees
- The opportunity to apply for a grant to attend one SGM meeting a year
- Scientific sessions approved for CPD by the IBMS
- Special workshops and events
- Networking with other microbiologists
- *Microbiology Today*
- Discounted prices on SGM publications

Please publicize this new scheme to your staff. Attractive promotional material is available and application forms can be downloaded from the web or obtained from the Membership Office (members@sgm.ac.uk)

Jobs on the web

- Do you have a post to fill?
- Are you seeking a job or a PhD studentship?

SGM can help!

Microbiology job vacancies, studentships and postdocs are now advertised on the SGM website. This service is currently free for SGM members. See the SGM *Jobs Page* to browse the latest vacancies or find out how to advertise a post. Follow the links from the Noticeboard page: **www.sgm.ac.uk/noticeboard.cfm**

For further information contact Faye Jones (f.jones@sgm.ac.uk).

New Elected Members of Council

Professor Iain Hagan

University of Manchester

Iain works at the Paterson Institute for Cancer Research in Manchester. His main field of interest is the cell cycle. He uses fission yeast as a model system in which to address the following specific interests: the formation and function of the mitotic spindle; the structure and function of the spindle pole body; the regulation of commitment to mitosis; the regulation of exit from mitosis; and the role of the cytoskeleton in the maintenance of spatial organization.

Iain was a member of the Cells & Cell Surfaces Group Committee (1994–1997), during which time he organized a symposium on *Nucleus and nucleoid* at City University. He was also a co-organizer of the main symposium at Southampton in 1997: *Checkpoints and non-linear dependency relationships.*

Professor Bertus Rima

Queen's University of Belfast

Bert was appointed Professor of Molecular Biology at the Queen's University, Belfast, in 1993. His main research interest is to apply molecular

biological and genetic techniques to virology and infectious diseases in general. He has an interest in human viruses (mumps and measles) as well as animal viruses such as rinderpest, canine distemper and seal and dolphin viruses of the same group. His work now centres primarily on how viruses are attenuated for vaccines and what barriers exist that prevent human viruses from infecting animals and vice versa. He served as Editor of JGV from 1998 to 2003.

He is Deputy Director of the Centre for Cancer Research and Cell Biology at Queen's University and a member of the Veterinary Products Committee of the Veterinary Medicines Directorate.

Professor Katherine Smart

Oxford Brookes University

Katherine completed a BSc in Biological Sciences at Nottingham in 1987 and was awarded the Rainbow Research PhD Scholarship to investigate yeast cell adhesion at Bass Brewers, Burton-on-Trent. She then moved to Cambridge to take up an appointment as a Postdoctoral Research Fellow in the Department of Plant Sciences where she worked on bioactive surfaces, biofouling and the contamination of non-alcoholic beverages. In 1992, Katherine became a Lecturer and then 1 year later Senior Lecturer in Microbiology and Fermentation at Oxford Brookes University. In 1999 she was awarded the Institute and Guild of Brewing Cambridge Prize for her contribution to brewing science and in 2000 was appointed the Scottish Courage Reader in Brewing Science. In 2001 she was awarded a Royal Society Industrial Fellowship and some 2 years later an Enterprise Fellowship for her contribution to applied research. In the last 2 years she has received several awards, including the Save British Science Award and a NESTA crucible award. In September 2004 Katherine Smart was appointed to a personal chair at Oxford Brookes University.

Katherine is a member of several societies and has served on society committees and journal editorial boards. Until July of this year she was Chairman of the Institute and Guild of Brewing International Section and the American Society of Brewing Chemists International Director. She has served on the Fermentation and Bioprocessing and Cells and Cell Surfaces Groups of the SGM.

Industrial Member Forum report

SGM members from a range of companies met on 30 June with Council Members Jeff Cole, Pauline Handley and SGM External Relations Office staff to discuss issues arising from the industrial member survey carried out in 2002. Following presentations on the Society and the reasons for holding the meeting, delegates were divided into two discussion groups. Ideas were then fed back to the whole group and a consensus reached. It soon became clear that although many industrial members work for companies focusing on fermentation, a significant number of other interests is represented by this group. This leads to widely differing needs; activities that would suit one sector could be entirely irrelevant to another group.

Topics under discussion included organization and marketing of scientific meetings, the appointment of an Industrial Liaison Officer to Council and recruitment of graduate and postgraduate microbiologists. A number of action points were proposed including:

- Interest Groups should co-opt an extra committee member from industry. This will provide an opportunity to give input to session content. The term of office should be no longer than 2 years (to allow for the short time scale and the rapidly shifting focus of these individuals' work).
- Identify topics for workshops by surveying delegates at the next SGM meeting and/or requesting suggestions via an online form.
- Develop ways to promote networking between industrial and academic members.

At the SGM Council meeting on 6 July 2004, Pauline Handley presented a report of the Industrial Member Forum that stimulated much discussion. There was support for the suggestion to co-opt industrial members on to Group committees. This will require an amendment to the byelaws of the SGM Memorandum of Articles and Association that will be ratified at the Council meeting in November 2004. Jeff Cole and Pauline Handley were asked to develop a job description for the new post of Industrial Liaison Officer.

A second meeting of the Industrial Member Forum will take place at 1730, Monday 4 April 2005 at Heriot-Watt University (room to be confirmed). The Scientific Meetings Officer and Group Conveners will also be invited.

If you would like a full copy of the Industrial Member Forum report or if you would like to attend its next meeting at Heriot-Watt, please contact Jane Westwell in the External Relations Office (j.westwell@sgm.ac.uk).

Details of all grant schemes are available on the SGM website at **www.sgm.ac.uk**. Please consult these before making an application. You can download the application forms for schemes where these are required.

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].

Grants

IUMS Congresses San Francisco, 23–28 July 2005

SGM Travel Grants

Grants to provide a contribution towards registration fees, accommodation and travel to the congresses are available to eligible members of the Society. Full details of the rules and an application form are on the website. The fund is aimed, in the first instance, at SGM members who are ineligible for a Royal Society grant (see below), such as postgraduate student members and research assistants. The closing date for applications is **18 February 2005**.

Royal Society Conference Grants

www.royalsoc.ac.uk
email conferencegrants@royalsoc.ac.uk

Eligible SGM members should apply to the Royal Society in the first instance. Applicants must be of at least PhD status and normally resident in the UK. Civil servants, employees of research councils, government-funded bodies and commercial concerns are NOT eligible for these awards. Ordinary Members applying to the SGM will have to provide evidence that their application to the Royal Society has been unsuccessful.

ASM/SGM Joint Meeting Vancouver, 13–16 July 2005

Prokaryotic Development

Travel Grants

Grants of up to £500 to provide a contribution towards registration fees, accommodation and travel to the meeting are available for eligible SGM members. The full rules and an application form are posted on the SGM website. Postgraduate students may also apply for an ASM student bursary, provided they are presenting work and their abstract has been accepted (see www.asm.org). This will not affect any award that they may receive from the SGM. The SGM fund is capped and applications will be dealt with on a first come, first served basis. The closing date for applications is **25 March 2005**.

Undergraduate Microbiology Prizes

The scheme to encourage excellence in the study of microbiology by undergraduate students continues to be well received in universities in the UK and Republic of Ireland. Institutions offering an appropriate microbiology course were invited to nominate a student for an SGM prize, based on good performance in microbiology in the penultimate year of study for a BSc. The department was able to choose the type of assessed work for which the prize was awarded. Of the 64 departments circulated, 49 made nominations. Each prizewinner receives a certificate, a cheque for £100 and a year's free Undergraduate Membership of the Society. Undergraduate Microbiology Prizes are awarded annually and the invitations for nominations in 2005 will be announced next May.

President's Fund

New rules for research visits

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

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

Larger awards are available for short research visits.

1 & 2 Smaller Awards

Maximum grants are:

- £125 for attendance at meetings/courses in the country of residence
- £200 for travel to another European country
- £300 for travel outside Europe
- £300 for attendance at a UK GRADschool

Applicants may apply for one GRADschool grant and one travel grant during the period of their studentship or first postdoctoral position. They may also apply for a research visit grant.

3 Larger Awards – Research Visit

The rules of this part of the scheme have been amended. Funding will be capped and awards will be made by competition. Starting in 2005 there will be TWO closing dates each year for the receipt of applications, which will be considered by a small award panel.

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

All applicants must be resident and registered for a higher degree, or in a first postdoctoral position, in a country in the European Union. Only one application may be made for a research visit grant during the term of a studentship or fellowship.

Postgraduate Conference Grants

Postgraduate Student Members of SGM currently resident and registered for a higher degree in the UK or another European Union country are eligible for a grant to cover the costs of accommodation and travel in attending ONE of the following Society meetings in 2005: Heriot-Watt University, April; Keele University, September; or any other SGM Group or Branch meeting. Application forms giving full details of the scheme were sent to all Student Members in the EU with their subscription invoices. A form can also be downloaded from the SGM website.

Public Understanding of Science Awards

Are you planning any projects to promote the public understanding of microbiology? Have you got a National Science Week event in mind? SGM can help. Grants of up to £1,000 are available to fund appropriate activities. Applications are considered on a first come, first served basis throughout the calendar year.

Vacation Studentships 2005

The Society offers a limited number of awards to enable undergraduates to work on microbiological research projects during the summer vacation. The purpose of the awards is to provide undergraduates with experience of research and to encourage them to consider a career in scientific research. The studentships provide support at a rate of £160 per week for a period of up to 8 weeks. An additional sum of up to £400 for specific research costs may also awarded. Applications on behalf of named students are now invited from SGM members in higher education institutions and research institutes.

The closing date for applications is **25 February 2005**.

Seminar Speakers Fund 2004/2005

The purpose of the Seminar Speakers Fund is to promote talks on microbiological topics in departmental seminar programmes. Applications are invited from Higher Education Institutions where microbiology is taught for grants of up to £200 towards the travel, and if necessary, accommodation, expenses of an invited speaker. See website for full rules. Applications will be dealt with on a first come, first served basis during the academic year, which is defined as running from September 2004 to June 2005. Written submissions should be sent to the Grants Office at SGM Headquarters.

Back issues of SGM journals required

At its meeting in July, SGM Council approved funding for the project to put older back issues of the Society's journals online at HighWire. The objective is eventually to go back to volume 1, issue 1 in each case.

Digitization of the back content will involve de-spining paper issues and scanning the separated pages, using a specialist contractor. De-spining means that the process is essentially destructive, so we cannot use the bound archive/reference copies we have at Marlborough House.

Since February, we have been trying to assemble complete back runs of older issues of each journal, up to the year when we can take spare copies from our back-sales stocks. Thanks to the help and generosity of three SGM members, we now have a complete back run of *Journal of General Virology*, and we have plugged large gaps for *Microbiology / Journal of General Microbiology*. We are still looking for the following:

- *Journal of General Microbiology*
  Volumes **1** (1947)–**29** (1962)
- *Journal of Medical Microbiology*
  Volumes **1** (1952)–**46** (1997)
- *International Journal of Systematic and Evolutionary Microbiology*
  Volumes **1** (1951)–**30** (1980) and volume **31** issue 2

  (remember that *International Journal of Systematic and Evolutionary Microbiology* was *International Bulletin of Biological Nomenclature and Taxonomy* from 1951 to 1965, then *International Journal of Systematic Bacteriology* from 1966 to 1999.)

If you or your institution's library have any of these issues and would be willing to donate them, please contact Ron Fraser at SGM (r.fraser@sgm.ac.uk; Tel. 0118 988 1812). Please don't send anything without checking first: we don't want more than we need! SGM will of course pay for packaging and shipping costs.

● *Ron Fraser, Executive Secretary*

BugView

David Leader of Glasgow University, in association with colleague Tim Mitchell, has written BugView, software for visualizing and comparing genomes. It can be also be used to view individual genomes. BugView is a standalone application and is available free for non-commercial work. It was written for comparative studies of bacterial genomes, but handles eukaryotic genomes equally well. Version 1.3 was released in July 2004.

For further information contact David on d.leader@bio.gla.ac.uk or see the dedicated webpages at www.gla.ac.uk/~dpl1n/BugView

SGM membership subscriptions 2005

The following rates were agreed at the AGM of the Society on 7 September 2004.

Membership category	Annual subscription		Additional subscriptions for publications (print only)							
			Microbiology		*JGV*		*IJSEM*		*JMM*	
	£	US$	£	US$	£	US$	£	US$	£	US$
Ordinary	47	82	90	162	90	162	90	162	48	84
Postgraduate Student	20	35	40	75	40	75	90	162	48	84
Retired	20	35	40	75	40	75	90	162	48	84
Technician	20	NA	40	75	40	75	90	162	48	84
Undergraduate	10	NA	NA	NA	NA	NA	NA	NA	NA	NA
School	10	NA	NA	NA	NA	NA	NA	NA	NA	NA
Corporate *Tier 1*	350	NA	NA	NA	NA	NA	NA	NA	NA	NA
Corporate *Tier 2*	500	NA	NA	NA	NA	NA	NA	NA	NA	NA

For airmail despatch of *Microbiology Today*, add £15/US$25 to subscription

Members are reminded that their 2005 subscriptions are due for payment by **1 December 2004**.

As in previous years, no journal or meetings information will be despatched to members who are in arrears, and there will be no guarantee of provision of back numbers of journals for members who pay their subscription late.

Payment by direct debit or continuous credit card

Subscription notices were despatched recently to all members paying by direct debit or by continuous credit card arrangement. To continue your present status and journal requirements, no further action is necessary. However, if you pay by continuous credit card, you should check that the card number and expiry date on the subscription notice are correct. To change your membership status or journal requirements for 2005 or your credit card details, you should have amended your subscription notice and returned it to the membership office by **12 November 2004**. However, if you have missed this deadline, your amended notice will be accepted if it is submitted immediately.

Payment against invoice

Invoices were despatched recently to all members who pay by this method. If you did not receive one, please inform the Membership Office.

Subscriptions waived for unemployed members

As in previous years, subscriptions may be waived at the discretion of the Society for unemployed members under the age of 35 who are resident in the UK. If you are eligible and wish to benefit in this way in 2005 you should send a signed statement that you are currently unemployed to the Membership Office before **30 November 2004**. (Please note that no increase in journal requirements will be permitted.)

Income tax relief on membership subscriptions

Members who are liable for UK income tax are reminded that their annual subscriptions to the Society have been approved by the Inland Revenue as qualifying for income tax relief. Any member who would like further information or has difficulty in obtaining this relief should contact the Executive Secretary.

Meetings

Meetings on the web

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

Meetings organization

The SGM meetings programmes are organized by the committees of the special interest groups, co-ordinated by the Scientific Meetings Officer, **Professor Hilary Lappin-Scott**. Suggestions for topics for future symposia are always welcome. See p. 202 for contact details of Group Conveners.

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

Offered papers and posters

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

Offered posters

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

Abstracts

Titles and abstracts for all presentations are required in a standard format and should be submitted through the SGM website. Deadlines for submissions are published in *Microbiology Today* and on the web. For further information contact the Events Administrator.

Abstracts Book

155th Meeting, Trinity College Dublin

The full text of the abstracts book is now available as a PDF file on the SGM website.

Future Meetings

SPRING 2005 – 156th Meeting

Heriot-Watt University, 4–7 April 2005

● Plenary: Molecular pathogenesis of virus infections

Organizers: P.E. Digard, H.F. Jenkinson, A.A. Nash & R.E. Randall

● Speakers

J.L. WHITTON (Scripps Research Institute, USA) *Adaptive immune response*

G. SCREATON (John Radcliffe Hospital) *Immune responses to Dengue virus*

S. BORROW (Jenner Institute for Vaccine Research) *Immune response to HIV*

J.K. FAZAKERLEY (Edinburgh) *Persistent RNA virus infections*

S. NICHOL (CDCP, USA) *Exotic virus pathogenesis*

S. SIDDELL (Bristol) *Coronaviruses and SARS*

J. MANSON (IAH, Edinburgh) *Transmissible spongiform encephalopathies*

R. WEBSTER (St Jude Children's Research Hospital, USA) *Influenza virus pathogenesis*

R. ANDINO (California, USA) *Antiviral potential of RNA silencing*

R.L. HENDRICKS (University of Pittsburgh, USA) *Herpes simplex virus*

S.M. LEMON (Texas, USA) *Molecular pathogenesis of HCV*

S. HERRINGTON (St Andrews) *Papillomaviruses & human neoplasma*

O. HALLER (Freiburg, Germany) *Intracellular antiviral defence mechanisms*

A. ALCAMI (Autonoma, Madrid, Spain) *Poxvirus immune evasion*

L.K. DIXON (IAH Pirbright) *African swine fever*

J.P. STEWART (Liverpool) *Molecular pathogenesis of gammaherpesviruses*

● Other symposia and workshops

● Special Symposium: Emerging diseases of wildlife and farmed animals

7 April – Organizers: G.C. Schild & C.R. Howard

● Molecular typing and epidemiology

Clinical Microbiology/ Systematics & Evolution Groups

4 April – Organizers: S.C. Clarke, N.A. Logan & G.S. Saddler

● Antibiotic resistance

Clinical Microbiology Group/ BSAC

5 April – Organizers: P. Hawkey & M.B. Avison

● Emerging infections: dangers to human and animal health

Clinical Virology Group

6 April – Organizers: D. Paton & P. Simmonds

● Virology: is it practical?

Education & Training Group

7 April – Organizers: R.J. Cooper & B.A.B. Martin

● Microbe–pollutant interactions: ecology, function and applications

Environmental Microbiology Group

6 April – Organizers: G.I. Paton & K.T. Semple

● Evolving bacteria and emerging food-borne disease

Food & Beverages Group

6–7 April – Organizers: M. Peck & B.M. Lund

● Alternative models of infection

Microbial Infection Group

5 April – Organizer: J.N. Fletcher

A leaflet about the meeting is enclosed with this issue. An A3 poster is also available from the Events Administrator if you would like to help publicize the meeting.

● Bacteriophage evolution, ecology and applications

Physiology, Biochemistry & Molecular Genetics/ Cells & Cell Surfaces/ Education & Training/ Microbial Infection Groups

4–5 April – Organizers: M.C.M. Smith & G.P.C. Salmond

● Virus cell tropism and host range

Virus Group

7 April – Organizers: L.K. Dixon & R.E. Randall

● Virus Group Workshops

6 April

RNA viruses – Organizers: P.E. Digard & J. McLauchlan

DNA viruses – Organizer: D.J. Blackbourn

Virus pathogenesis – Organizer: A.A. Nash

Virus, immunity and vaccines – Organizer: N.M. Almond

Plant viruses – Organizer: J. Carr

Prions – Organizer: N. Mabbott

Email addresses of all organizers are available on the SGM website.

● Special events

Monday 4 April – Welcome Reception: Get to know your fellow delegates over a glass of wine on the first evening of the conference.

Tuesday 5 April – Society Dinner and ceilidh: A four course meal with inclusive wine and pre-dinner drink will take place on campus, followed by an ever-popular ceilidh where you can practise your skills at traditional Scottish dancing.

Wednesday 6 April – Retro Disco: Dance the night away to those familiar tunes from yesteryear. There will be a cash bar until late.

Wednesday 6 April (postgraduate student members only) – 'Surviving Your PhD' – An interactive session in the early evening with experts on vivas, writing and managing your supervisor, will be followed by drinks and a buffet reception. The event will end before the disco starts!

● The venue

This spring we are returning to Heriot-Watt University, an attractive, self-contained campus on the outskirts of the historic City of Edinburgh. A packed programme of symposia and workshops has been planned, with some social events to enjoy in the evenings.

● Accommodation

A new policy at Heriot-Watt means that only en-suite rooms will be available for delegates. These are excellent value at only £30 per night for bed and breakfast, but fewer rooms will be on offer than in previous years. If you wish to stay on campus, particularly on the Tuesday and Wednesday nights, book early to avoid disappointment. Bookings will be accepted on a strict first come, first served basis. Once the rooms have all been allocated, delegates will be responsible for obtaining their own accommodation in the city's numerous guesthouses and hotels. Please note that little is available close to the university.

● Registration fees

£30 per day will be payable by SGM members for this meeting. Non-member registration fees are £85 per day. Fees include refreshments, lunch, the abstracts book, all conference literature, the welcome reception, ceilidh and disco. Student Members, Retired Members, Technician Members and Honorary Members are exempt from registration fees.

● Postgraduate conference grants

These will be available, subject to the usual conditions. As lunch is included in the complimentary registration fee for Postgraduate Student Members, subsistence allowances will no longer be available. For full details, a form and allowances for travel see **www.sgm.ac.uk/grants/pg.cfm**

● Registration

Register for the meeting through the SGM website. You can either register online (www.sgm.ac.uk/regforms/156/regform.cfm) or download a PDF of the booking form and fax or post it to the Meetings Office with your payment (**www.sgm.ac.uk/meetings/mtgpages/HWregform.pdf**)

We are no longer printing registration forms. Anyone who experiences problems with registering through the website should contact the Meetings Office (Tel. 0118 988 1805; email **meetings@sgm.ac.uk**)

Deadline for early registration: **Friday, 4 March 2005**. Thereafter a late booking charge will be incurred.

AUTUMN 2005 – 157th Meeting

University of Keele, 12–15 September 2005

● Plenary: Micro-organisms and earth systems – advances in geomicrobiology

Deadline for receipt of abstracts for offered papers and posters: **13 May 2005**.

Irish Branch

Environmental genomics

University College Cork, 28–29 April 2005

Organizer: J.R. Marchesi

Rapid molecular diagnostics in medical microbiology

University of Ulster, Coleraine September 2005

Organizer: C.J. Lowery

Mechanisms of microbial adherence and invasion

Trinity College Dublin April 2006

Organizer: S.G. Smith

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

Other Events

● American Society for Microbiology/ Society for General Microbiology Joint Meeting

Prokaryotic Development

13–16 July 2005; Vancouver, Canada

The meeting aims to provide a forum for the exchange of current information on topics related to prokaryotic development. This includes both the well studied model developmental systems of *Bacillus*, *Caulobacter*, *Myxococcus*, *Streptomyces* and *Anabaena*, and opportunities for new emerging systems. Session themes include:

- Cell cycle
- Morphogenesis
- Differentiation
- Cell division
- Cell–cell signalling
- Multicellularity
- Symbiosis

Organizers Jeff Errington (Oxford) & Heidi Kaplan (Texas)

SGM members will be able to register at ASM member rates. Postgraduate Student Members will be able to apply for ASM student bursaries. There will also be a separate SGM travel grant scheme – see p. 179 for details.

For programme and registration information, see the ASM website: **www.asm.org**

● IUMS Congresses

23–28 July 2005; San Francisco, USA

See advertisement on p. 203 for details. Information about the SGM grant scheme is on p. 179.

● Norwegian Microbiology Societies/ Society for General Microbiology Joint Meeting

27–30 September 2005; Bergen, Norway

Themes include:

- New and re-emerging infectious diseases
- Antimicrobial and antiviral resistance
- Marine microbiology and fish vaccinology
- Microbiology education

For further information, see the SGM website: **www.sgm.ac.uk**

Gradline

Gradline aims to inform and entertain SGM members in the early stages of their career in microbiology. Contributions from undergraduate and postgraduate students or postdocs are always welcome. If you have any news or stories, or would like to see any topics featured, contact Jane Westwell (j.westwell@sgm.ac.uk).

A job in...
A research institute

Profile

Name Tracy Palmer

Age 37

Present Occupation
MRC Senior Non-Clinical Research Fellow, John Innes Centre (2004–2009)

Previous Employment
1996–2004 *Royal Society University Research Fellow, John Innes Centre*
1992–1996 *Postdoctoral researcher, then Fellow, Dept of Biochemistry, University of Dundee*

Education
PhD Biochemistry, University of Birmingham, 1992
BSc Biochemistry, University of Birmingham, 1988

Q *What attracted you to microbiology research?*
I studied biochemistry at university, but I found myself particularly enjoying the lectures on bacterial physiology, photosynthesis and gene regulation. When it came to choosing a PhD I followed up this interest by working with photosynthetic bacteria, and I've worked with microbes ever since.

Q *How did you find the transition from postdoc to research group leader?*
Very difficult and quite traumatic! Nothing prepares you for the absolute responsibility of supervising PhD students and postdocs. During our training we acquire the ability to think scientifically, but we are not trained in people management skills and you just end up having to pick them up along the way!

Q *Can you describe a typical day?*
There isn't really a 'typical' day, although more often than not I manage to find at least a couple of hours to work at the bench. I have never given up benchwork, it's the thing I enjoy most about my job and one of the main reasons why I am a perpetual fellow! One of the great attractions of working in a research institute is the access to central facilities such as a media kitchen, which has saved me countless hours preparing LB and autoclaving tips! The rest of my time is taken up with grant and paper writing and reviewing, other bits and pieces of admin and the odd conference here and there.

Q *How do you fund your research?*
My research is funded by a combination of funding bodies – currently the BBSRC, MRC, Royal Society and European Union. In the past I have also enjoyed funding from the Leverhulme Trust and the Wellcome Trust. Local funding bodies, the John Innes Foundation and the University of East Anglia have been particularly helpful for funding for PhD projects.

Q *Is it possible to achieve a good work–life balance as a researcher?*
This is a difficult one. It's a job that constantly encroaches on your time in one form or another. From working late meeting grant deadlines, to inoculating overnights on a Sunday, to attending meetings, it's almost impossible to have what most people would consider a 'normal' home life. As a working mother I try to restrict my working hours between 9 am and 6 pm during the week, and be away as little as possible at weekends, but it feels like a constant battle!

Q *What is rewarding about your job?*
My job is rewarding in lots of ways. The prospect of making new scientific discoveries is still very exciting to me. It's great to see people in the lab enjoying their research, and very rewarding to have a hand in their career development. Getting papers published and grants funded is something we always celebrate in the lab, and it makes up for the disappointments. Finally the opportunity to travel to conferences, particularly in exotic places, is a definite perk of the job!

Q *How do you see your future?*
I'm very happy with my current job, and I see my long-term future as a project leader here at the John Innes Centre. Norwich is a fantastic place to do microbiological research. Apart from the John Innes Centre, there are microbiologists and bacterial biochemists at the University of East Anglia and at the Institute of Food Research, and, in future, medical microbiology particularly will be strengthened with the construction of the Biomedical Research Centre (BMRC) at UEA. Although I expect my administrative load to increase over the coming years, I will be very disappointed if I have to hang up my Gilsons for good!

Q *What advice can you offer people planning a career in microbiology research?*
I can only really offer advice on a career in academic research, since this is the only experience I have. Choose PhD and postdoc positions carefully – publications are very important, so try and pick labs that have a good publishing record. Volunteer to supervise lab visitors – good experience for training students in future and it helps hone those all important people management skills! Finally, work on something that interests you – and be prepared to work long hours and weather quite a lot of disappointments along the way.

Further information

John Innes Centre – **www.jic.bbsrc.ac.uk**

The MRC offers grants, including Career Development Awards to postdoctoral non-clinical scientists with 2–7 years experience – **www.mrc.ac.uk/index/funding/funding-personal_awards.htm**

Postdoctoral researchers in biomedical sciences can apply for funding from the Wellcome Trust. Schemes include Advance Training Fellowships and Research Career Development Fellowships – **www.wellcome.ac.uk/funding/biomedicalscience/iid/**

The Royal Society schemes for postdoctoral researchers include Dorothy Hodgkin Fellowships, UK Relocation Fellowships and University Research Fellowships – **www.royalsoc.ac.uk/funding/**

The BBSRC offers David Phillips Fellowships to scientists who have demonstrated high potential during their research training and initial years of postdoctoral research – **www.bbsrc.ac.uk/funding/fellowships/Welcome.html**

Sense About Science
Voice of young science

17 September 2004

This event, organized by Sense About Science and held at the Science Media Centre in London, set out to identify the problems and challenges of representing science in the media and to encourage young scientists to speak about their research.

The first session, *Science and the media*, was a discussion on the changing image and role of science and scientists in the public domain, led by three scientists who have all had dealings with the media.

Trust was considered an important factor. Scientists have to trust that journalists will report their science correctly, while journalists have to trust that a scientist is giving them qualified results that the majority of the scientific community will agree with.

However, one panellist observed that an obvious problem is that 'bad news' or scare stories sell newspapers, whereas 'good news' or educational stories tend be boring in comparison.

Although all of the scientists could recount incidences of misquotes in articles or sensationalist headlines, they agreed that the majority of their science was correctly reported in all media forms and that it is important to communicate with the press.

The emphasis on speaking to the press was also backed by the panel of journalists who led the second session, *What journalists are looking for*, which considered how the media works and where things can go wrong.

The journalists present insisted that the press doesn't intentionally make mistakes with stories to sensationalize science or sell more newspapers. The media works on reputation and if they are known to deliberately sensationalize, people stop giving them good stories.

Advice on dealing with the press from a journalist's viewpoint was that it is always better to speak to the press than to decline. The urge to make news is just too strong and if scientists don't speak to the media and give them the correct facts, a story could run anyway without this input, or even with obviously incorrect 'facts' from an alternative or opposition viewpoint.

There are many ways in which scientists can help to keep articles accurate – including being clear, not using jargon, using analogies and being willing to give a bit on precision.

Taking a realistic approach to science reporting was an explanation of how scientific news is communicated, typical difficulties and areas of misunderstanding, as well as practical guidance on how to make your voice heard in debates about science. Fiona Fox from the Science Media Centre, a press office for all UK science, gave a great example of how one badly reported story could be carried through the media as far as Government without the actual facts behind it being checked.

Her advice was not to be complacent about the risks from the media and that preparation makes a huge difference – know what you want to say, as well as what you are not saying, think about any contentious questions that may arise and have answers ready. It was also considered very important to discuss any risks associated with your work – let's face it, life itself carries many risks. Other good tips included using press offices – most universities and institutes have them; using science reporters – because they specialize in science issues; and not being afraid of the broader debate – scientists do bring respect to debates.

There are many researchers and scientists who believe that younger colleagues should be taking over and speaking to the press, and the journalists attending the event were unanimous in their approval of young scientists putting themselves forward as experts.

■ ***Faye Jones, Public Affairs Administrator***

Young Microbiologist of the Year Competition

The Dublin meeting saw the finals of the SGM's science communication contest. Nine keen postgrads and postdocs, who had been selected as finalists by the Special Interest Groups and Irish Branch on the basis of their offered presentations (either oral or poster) at recent SGM meetings, gave 10 minute talks on their research. Five minutes was allowed for questions to each speaker. The standard was amazingly high and the judges, provided from the Group Committees and chaired by Jo Verran, Convener of the Education and Training Group, had a very difficult job. The winners were announced at the 'Irish Night' later that evening. The first prize of £500 went to **Nolwenn Jouvenet** (pictured above) of Institute of Animal Health, Pirbright, for her presentation *Transport of African Swine Fever virus from assembly site to the plasma membrane*. The second prize of £200 was won by **Gavin Byrne** (University College Dublin) and third prize of £100 went to **Sheila Ryan** (University College Cork). The other finalists received a cheque for £25 in recognition of their efforts and everyone will get free membership of the Society in 2005.

Further details of the competition and an entry form are available on the meetings page of the SGM website. Why not enter by submitting an offered poster or oral presentation for the spring meeting at Heriot-Watt next year? The closing date for abstracts is **3 December 2004**, so get cracking!

Biosciences Federation Careers Conferences 2004

- 6 November – King's College, London
- 20 November – Leeds
- 27 November – Glasgow

These all day conferences are for life science undergraduate (graduating in 2005 or 2006) and postgraduate students. Each conference includes a range of talks on career choices and further training, an exhibition and a CV clinic. Don't miss the chance to attend the nearest event to your institution – further information and a booking form are available on the web: **www.bsf.ac.uk/careers**

Organized by bioscience learned societies, including SGM.

GRADschool Grants

Up to £300 is available to support GRADschool attendance by postgraduate student members who are unable to obtain sponsorship from certain funding bodies (BBSRC, MRC, EPSRC or the Wellcome Trust). Grants will be available for courses in 2005. See **www.sgm.ac.uk/grants** for an application form.

Surviving Your PhD

Workshop, 6 April 2005

This evening workshop will take place at Heriot-Watt University and include interactive sessions on *Managing your supervisor, Getting through your viva* and *Thesis and report writing*. The event will be followed by a buffet and drinks reception.

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 teaching resources and discounted fees on SGM training courses and workshops. Application forms are available at **www.sgm.ac.uk**

Enquiries: education@sgm.ac.uk

Education website: www.microbiologyonline.org.uk

Teaching evolution

'Microbiology Today' Editor Gavin Thomas describes some of the available resources to support the teaching of evolution.

Unfortunately, evolution is a relatively small part of the curriculum and post-16 specifications in the UK, but there are increasing numbers of high-quality resources available on the internet to support this fundamental area of biology. Type evolution into Google and you get over 18 million hits! Where to start and where is the reliable information for teachers and students?

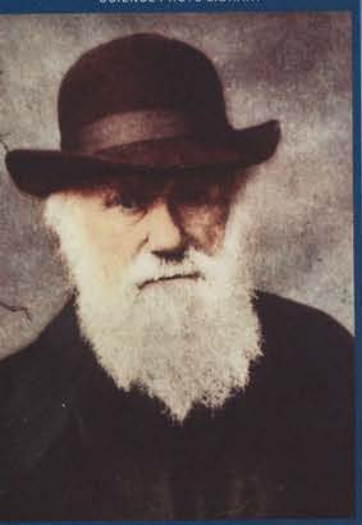
Web resources for teaching evolution

By far the best site is *The Evolution Project* run by the USA Public Broadcasting Service (PBS), which accompanies a TV series they produced in 2001 and covers many aspects of evolutionary theory. The site contains many excellent resources, including multimedia learning aids in the 'Teachers and Students' section. The material has been produced for US schools and is of professional quality.

The high quality of this site reflects the mobilization of the scientific community into actively supporting evolutionary teaching in the face of rising Creationist teaching in many states in the US. As a more direct response to this development, another US group called the National Centre for Science Education has a site with many well written and useful articles about teaching evolution, the arguments used by scientific creationists and the best ways to counter them. The group also contributes to another good site run at the University of California. This may become an issue in the UK as some schools have opened in the North East of England which teach creationism.

UK efforts are sadly not so good. The BBC has a simple site with a few features that could be useful in the classroom, but most of the material is fragments from various television programmes and it does not provide particularly useful teaching aids. However, the section on 'Darwin – the man and his legacy' has some good essays from expert writers. After the PBS site, the lack of multimedia is striking, the only content being short video clips in the 'Natural Selections' section.

BELOW:
Coloured portrait of Charles Darwin (1809–1882). English naturalist and author of the *Origin of Species*, photographed in 1874.
SCIENCE PHOTO LIBRARY



Evolution of antibiotic resistance in bacteria

A classic example of evolution related to microbiology is the emergence of bacteria that are resistant to antibiotics. There are two mechanisms by which a population of bacteria can become resistant. The first is that one of these bacteria has, by chance, picked up a mutation in its DNA that then confers resistance to the antibiotic, for example by altering the site of action. As these microbes then grow and divide their offspring also have this mutation and these cells eventually take over the population. As the spread of the resistance phenotype is due to passing the mutation from generation to generation down the 'family tree' it is known as vertical transmission. This mechanism is how resistance to antifungals has developed in *Candida albicans* and is outlined in the article by Frank Odds in this issue. The second mechanism, that has lead to the evolution of pathogens like methicillin-resistant *Staphylococcus aureus* (MRSA), is what is known as 'horizontal gene transfer'. In this mechanism, bacteria pick up existing resistance genes from the environment, and not from their parents. This 'short cut' allows bacteria to become resistant rapidly to a number of antibiotics. The mechanisms by which these genes are spread are also important in evolution of other properties, and the article by Peter Williams describes how horizontal gene transfer is used to evolve new biochemical pathways that bacteria can use to degrade poisonous chemicals.

Accurate information for teaching this area is harder to come by on the web, but there is a good teacher study aid available from the Woodrow Wilson Foundation and some useful material in *MicrobeWorld*. Also, the PBS site contains an interesting expert panel discussion on how to reduce antibiotic resistance.

Popular science texts for students and teachers

The increasing popularity of general science writing has seen books about Darwin and his world stacking up on the shelves in increasing numbers. This is partly due to the huge amount of research into Darwinism in the last 20 years. This 'Darwin industry' is exemplified by the Darwin Correspondence Project, which aims to catalogue and publish every known letter written or received by Darwin! A site about the UK's most prominent evolutionist, Richard Dawkins, is to be recommended and although it hasn't been updated since 2001, it still contains many articles and essays. For an interesting and accessible introductory text to supplement teaching I would recommend Dawkins' book *River Out of Eden*.

Web resources

General sites

The Evolution Project – www.pbs.org/wgbh/evolution/

National Center for Science Education – www.natcenscied.org/

Understanding Evolution – evolution.berkeley.edu/

BBC Evolution site – www.bbc.co.uk/education/darwin/index.shtml

Evolution links – www.biozone.co.uk/biolinks/evolution.html

Evolution of antibiotic resistance in bacteria

Woodrow Wilson Foundation – www.woodrow.org/teachers/bi/2000/Antibiotic_Resistance/introduction.html

Microbeworld – www.microbeworld.org/htm/cissues/resist/resist_0.htm

The Evolving Enemy (PBS) site – www.pbs.org/wgbh/evolution/survival/enemy/index.html

Other links

Darwin Correspondence Project – www.lib.cam.ac.uk/Departments/Darwin/

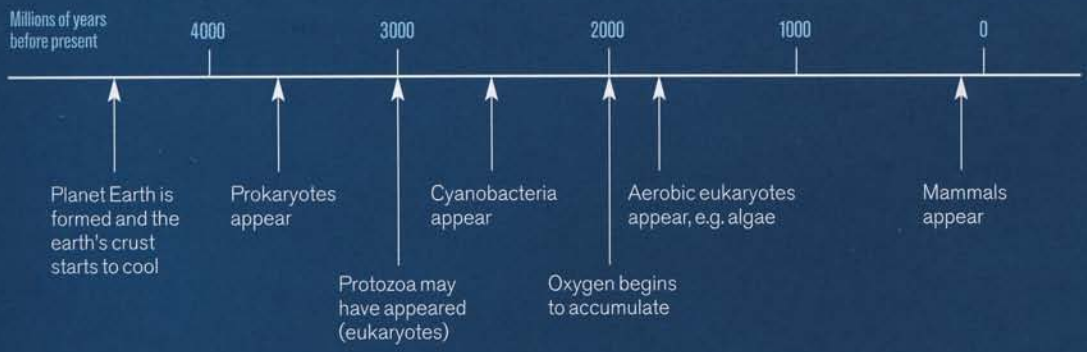
The World of Richard Dawkins – www.world-of-dawkins.com/index.shtml

Gavin Thomas is lecturer in the Department of Biology, University of York, PO Box 373, York YO10 5YW, UK (Tel. 01904 328678; email ght2@york.ac.uk)

The Evolution of Microbes

Dariel Burdass

Microbes have been around for at least 3,500 million years and were the only life forms on earth for most of that time. The rich diversity of the microbial world can be explained by the long period in which they have had to evolve compared with plants and animals.



As the earth cooled, liquid water formed and the first microbial life appeared. In the inhospitable conditions the colonizing organisms were prokaryotes. They were also anaerobes, as there was negligible oxygen present. The first microbes probably resembled the *Archaea* (extremophiles), as they were able to live in extreme environments such as the high temperature found on the cooling planet.

During this early period the ozone layer was not fully formed, leaving the earth's surface exposed to ultraviolet radiation. As a result, most microbes probably lived and developed below the surface of the land and sea where they were protected from the effects of the harmful rays. It is possible that a bacterium called *Deinococcus radiodurans* was able to survive on the earth's surface. *D. radiodurans*, which literally means 'a strange berry that withstands radiation', is a polyextremophile which can endure many extremes, including radiation. It is listed in the Guinness Book of Records as 'the world's toughest bacterium'. It can withstand doses of radiation 3,000 times greater than the amount fatal for humans, thanks to an efficient system for repairing its own DNA, often within hours. Scientists are hoping to use this microbe in bioremediation.

Cyanobacteria

Around 2,800 million years ago, cyanobacteria (formerly known as blue-green algae) probably appeared. This was an important development as these were the first organisms able to carry out aerobic photosynthesis, using light energy to produce glucose and oxygen from carbon dioxide and water. Prior to this only anaerobic photosynthesis was carried out by organisms similar to today's purple and green sulfur bacteria. It is likely that cyanobacteria were largely responsible for raising the level of oxygen in the earth's atmosphere from less than 1 % to the 21 % of the present day. With the presence of oxygen in the atmosphere came the formation of the ozone layer. This facilitated the evolution of new aerobic species of microbes, which began to colonize every ecological niche.

Different species of cyanobacteria formed complex microbial communities, often with bacteria and the other types of micro-organisms as they evolved, and these communities have left an extensive fossil record. They are found in rocks which are millions of years old. Their existence is also preserved in the complex structures they created, large dome-shaped mounds formed by the incorporation of mineral sediments into microbial mats, known as stromatolites. Cyanobacteria predominate in these microbial mats. Interestingly, there are still living stromatolites, such as those found on the coast in Western Australia. They are formed in two ways: one by trapping fine sediment with a sticky film of mucus secreted by the cells which are bound together by calcium carbonate precipitated from the water; the other by the cyanobacteria precipitating their own carbonate framework, with little integration of sediment. Some present-day stromatolites may well be 1,000 years old (see photograph above).

ABOVE:
Stromatolites exposed at low tide at Hamelin Pool, Shark Bay, 600 km north of Perth, Australia.
COURTESY K.J. MCNAMARA, WESTERN AUSTRALIAN MUSEUM

ABOVE LEFT:
An evolutionary time line.

Eukaryotes

It was originally thought that the first eukaryotes appeared 2,000 million years ago when the oxygen levels were high enough to support them. However, some modern protozoa can survive in conditions without oxygen, so it is possible that protozoa appeared earlier, around 3,000 million years ago.

Scientists believe that eukaryotic cells arose when free-living prokaryotes lived inside larger prokaryotes as endosymbionts. These symbionts eventually became integrated into their host cell forming a single unit. Analysis of rRNA gene sequences from mitochondria and chloroplasts shows that they are most closely related to the sequences of a purple bacterium (possibly an ancestor of three modern groups of purple non-sulfur bacteria, *Agrobacterium*, *Rhizobium* and *Rickettsia*), and a cyanobacterium respectively. It is believed that the nuclear envelope and endoplasmic reticulum probably evolved from internal folds of the plasma membrane of prokaryotic cells.

Fossil evidence from around 650 million years ago shows the existence of multicellular animals, including primitive arthropods. 400 million years ago primitive land plants developed along with fungi. Through their metabolic activities, the latter enabled plants to colonize nutrient-poor soils, leading to the symbiotic mycorrhizal associations that are found today between the roots of most plant species and fungi. Mammals and flowering plants are relative newcomers and only appeared around 100 million years ago.

Useful resources

McNamara, K.J. (1992). *Stromatolites*. Perth: Western Australian Museum. ISBN: 0 7309 5215 0.

http://helios.bto.ed.ac.uk/bto/microbes

http://science.nasa.gov/newhome/headlines/ast14dec99_1.htm

http://www.genomenewsnetwork.org/articles/07_02/deinococcus.shtml

Dariel Burdass, Education Projects Administrator

Post-16 Summer School

12–16 July 2004, Leeds University

SGM's second Summer School for post-16 biology teachers was held in the School of Biochemistry and Microbiology at the University of Leeds. The staff worked extremely hard to make us feel welcome and participated in the programme with enthusiasm. In particular we would like to acknowledge the role Dr David Adams played in making the event so successful by facilitating the arrangements, organizing speakers and providing practical workshops.

The programme was carefully planned to reflect the microbiology content of the current post-16 examining body specifications, including the new pilot specification from Salters/Nuffield. The microbiological issues studied throughout the week were then set in the context of real-life applications, making the content both relevant and stimulating There was a mixture of cutting edge talks by experts on topics such as tuberculosis, malaria, drug development, fungal protein and microbial immunology.

Afternoons were spent in the laboratory where the teachers carried out microbiology investigations. The new, state-of-the-art facilities were much appreciated. Biorad supplied the new ELISA Immuno Explorer Kit. This enabled teachers to use the same antibody-based test that is used in diagnostic laboratories to detect diseases such as HIV/AIDS and SARS, and to trace pathogenic agents in water, food or the air.

The teachers also attended a workshop on science communication with Dr Bernard Dixon, the well-known science writer, and were required to put their skills to the test in small teams by producing a scientific poster. *Microbiology Today* Editor Gavin Thomas came over from York to join the judging panel, which also included SGM Education Officer Sue Assinder.

On the last day, the delegates heard about the latest initiatives in biology education such as the new Salters/Nuffield Advanced Biology course, the Science Learning Centres and the DfES Standards Unit. The 'Ask the Doc!' session with MISAC chairman John Grainger masquerading as an agony aunt was particularly popular, enabling the teachers to resolve knotty problems they had encountered running practicals in school.

An enjoyable evening social events programme provided light relief after each day's intensive study, including an evening cruise down the River Ouse in York and a gala dinner at University House.

Feedback from the teachers was extremely positive. This comment typifies the responses the SGM has been receiving:

'*A most interesting, stimulating and valuable week of work and enjoyable socially of course!*

Dariel Burdass, Education Projects Administrator

ABOVE:
Teachers listening to a talk in the seminar room (top) and attending the gala dinner (bottom).

PHOTOS JANET HURST, SGM

FEMS at the Summer School

SGM was delighted to welcome a small delegation of representatives from FEMS societies to the Summer School. The purpose of the visit was twofold: (a) for them to observe our teacher training in action and talk to UK teachers; and (b) to hold a meeting to discuss ways of promoting microbiology in schools throughout Europe.

The working group was formed after the successful roundtable on microbiology education that I organized last year at the 1st FEMS Congress in Ljubljana. At this it became clear that our countries shared many difficulties, such as raising the public profile of our discipline, ensuring that biology teachers are properly trained in microbiology and getting school students interested in the subject so that they want to study it at university. Across Europe there appears to be a shortage of professional microbiologists.

FEMS is willing to support a modest initiative and the working party, after many deliberations, came up with a cost-effective proposal which would be relevant to all microbiology teaching in Europe. This was put to the FEMS Executive at their recent meeting and I am delighted to report that it was accepted. As a result, FEMS societies will be able to put forward microbiologists in universities and research institutes who have a proven interest in microbiology at school level to attend a two-day course in the UK hosted by the SGM. This will involve observing teachers at one of our *Basic Practical Microbiology* courses before participating in a 'trainer of trainers' session to learn how to run similar courses for local teachers from their home institution. SGM will provide a pack of course materials which can be translated as required. FEMS will sponsor the travel and accommodation of the participants. Further details will be available soon from FEMS. It is hoped to run the first session in summer 2005.

In the meantime, please contact me if you would like to know more about the initiative.

Janet Hurst, SGM External Relations Manager
email j.hurst@sgm.ac.uk

ABOVE:
The FEMS working party writing their report. *From left to right*: Janet Hurst (SGM), Johanna Sollid (Norway), Richard Braun (Switzerland), Gosse Schraa (The Netherlands), Ragnheidur Magnusdottir (Iceland) and Erika Toth (Hungary).

MISAC 2005 Schools Competition

Fungi in Your Shopping Basket

Sponsored by British Mycological Society

This year secondary school students are being asked to produce an eye-catching poster to inform the public of the importance of fungi in the foods, drinks and other goods they find in the shops. Entries will be judged in two age groups (Key Stage 3 and GCSE).

Cash prizes are up for grabs as follows

	School	Pupil
1st	£200	£30
2nd	£100	£20
3rd	£50	£10

In addition every school entering the competition receives a pack of microbiology teaching resources; each student submitting an entry of scientific merit is sent a certificate.

Entry forms can be downloaded from www.microbiologyonline.org.uk/misac. The closing date is **31 March 2005.**

MISAC wishes to express its sincere thanks to the British Mycological Society for sponsoring the 17th competition.

Schools Training Courses 2004/5

Basic Practical Microbiology

Thanks to the SGM members who are hosting courses this year. Venues and dates (where known) are as follows:

Sir John Deane's College, Cheshire	19 November 2004
Reading University	29 November 2004
University of Birmingham	15 December 2004
Isle of Man	February 2005 (tbc)

Microbes, Maths & ICT

Post-16 Microbial Investigations for Statistical Analysis

This new, advanced course will take place at the University of Reading on 24 November 2004.

Details of all courses, fees and booking forms are available at www.microbiologyonline.org.uk

ASE Annual Meeting

6–8 January 2005, Leeds University

SGM will be involved in a range of activities at the meeting. Apart from our usual stand in the exhibition (come and find us on C10, alongside MISAC), we are participating in *Biology in the Real World* – a day-long programme of talks on Friday 7 January organized by bioscience learned societies, research councils and charities under the NUCLEUS umbrella. There will be two parallel sessions on *Cure the World* and *Feed the World*. Professor Dick Killington is speaking in the SGM slot on *The reality of HIV*. We are also launching our Food Microbiology e-source on the School-science website and stand. Full details of the Annual Meeting programme are on the ASE website: **www.ase.org.uk**

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MISAC 2005 Schools Competition

MiSAC
MICROBIOLOGY IN SCHOOLS ADVISORY COMMITTEE

bms British Mycological Society promoting fungal science

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E-sy learning

Education & Training Group Symposium, Trinity College, Dublin, September 2004

Sue Assinder

Conversations about e-learning frequently get bogged down in jargon – VLEs, MLEs, online communities and reusable learning objects. For many of us, e-learning begins and ends with putting our lecture notes on the web (usually at the risk of then lecturing to an empty room). The aim of the Education & Training Group Symposium in Dublin was to demonstrate that there is much more to e-learning than simply supplying online resources to support conventional teaching. In the course of a fascinating afternoon, delegates discovered how e-learning is being imaginatively applied in a variety of learning contexts, ranging from web-based support of single modules through to fully online courses and global collaborative research projects.

Alan Cann, a previous winner of the SGM Peter Wildy Prize for Microbiology Education, began the session by demystifying some of the jargon, in particular the difference between a VLE (virtual learning environment) and an MLE (managed learning environment). A VLE, such as blackboard or Web-CT, provides an integrated system for managing online learning, including a delivery mechanism, student tracking and assessment plus access to discussion, support and resources, whilst an MLE additionally contains integrated links to other management information systems (e.g. student records, library, finance systems). From the student viewpoint, a key feature of a VLE is consistency of navigation, so that all modules have an identical interface. Alan stressed that using these tools requires institutional commitment, in particular training for lecturers who face the challenge of a diversity of students with a variety of learning styles, computer and communication skills.

Having laid the foundations, we went on to look at some examples. In the US, there has been an upsurge in online masters courses designed to meet the needs of school teachers for professional development. Spencer Benson described a Master in Life Sciences programme at the University of Maryland College Park, and Paul Kemp talked about the Masters of Education programme at Stony Brook University in New York. Although expensive to enrol on such courses (in the region of US$10k for the whole programme), the costs are to a large extent offset by the increase in salary that a teacher can expect upon graduation. Although the US leads the field in this area, the UK is catching up fast. Jonathan Ball described the development of an e-learning, postgraduate certificate in molecular biology at the University of Nottingham. A common problem with such developments is that lecturing staff are put off by the thought of having to master the technology. At Nottingham, the solution has been to construct the course using a database of 're-usable learning objects'. These are modular packages of teaching material that staff can enter through an easy interface, so that they can develop online resources without having to master the complexities of web authoring.

RIGHT:
Fig. 1. The virtual microscope website (www.wartburg.edu/biology/fluorescentmicro/index.htm).

A theme that came through many of these talks was the importance of actively engaging students in the learning process. A major advantage that VLEs offer compared to traditional teaching approaches is the opportunity for threaded online discussions. Many of the speakers felt these to be critical aspects of the teaching and learning process, and assigned a substantial proportion of the module assessment to the quality and frequency of the students' questions and answers. This was well illustrated by Sharon Zablotney's talk, in which she described the virtual tutorials that she runs with her class at the State University New York, Fredonia. This employs student-led discussions and team case studies, both of which require the student to become actively involved in material through a question and answer process. This 'virtual classroom' facilitates learning by removing barriers that might inhibit student participation in similar discussions in the traditional classroom.

Another area where online materials can be particularly useful is in a virtual laboratory environment. Online simulations and animations are helpful for topics where practical work is expensive or reliant on equipment that is not readily available. Roy Ventullo from Wartburg College, Iowa, demonstrated the virtual fluorescence microscope (Fig. 1), which allows students to learn the parts of the microscope and their function. By working through the interactive website prior to attending the lab session, students have the opportunity to acquire the necessary skills in an environment that is free of risk, either to themselves or to the precious equipment. The final talk of the afternoon from Kathy Takayama (University of New South Wales) put the virtual laboratory into a global context. 'Visualizing the Science of Genomics' (www.omnium.unsw.edu.au/courses/vsg_2003s1/base/index.php) was an international online project designed to enable students to experience the thrill of collaborative research, using 3-D modelling and genomic analysis to examine how

Microbiology in the Regions report

the HIV-1 virus mutates and the implications for vaccines. Students from 24 universities across 11 different countries worked in teams to develop their own research questions and appropriate methodology for investigation. The project resulted in the creation of a global online research community through multidisciplinary collaboration.

E-learning approaches do not necessarily save staff time. All of the speakers had invested much energy into developing their online resources and running them required substantial ongoing effort. Indeed, the salaries of staff teaching the Maryland course were supplemented to reflect the extra workload, a somewhat unfamiliar concept for UK academics! Nevertheless, it was clear that the speakers were witnessing tangible rewards in terms of student engagement, performance and enjoyment, and hopefully some of the audience were inspired to take their involvement in e-learning to the next level.

● *Sue Assinder, SGM Education Officer and Head, School of Biological Sciences, University of Wales, Bangor, Gwynedd, LL57 2UW*
Tel. 01248 382604; Fax 01248 370731
email s.assinder@bangor.ac.uk

2nd All-Wales Microbiology Meeting, Gregynog Hall, 15–17 March 2004

■ Gareth W. Griffith

With devolution in Wales has come the possibility of funding for research from the Assembly Government and also encouragement for collaboration between the constituent colleges of the University of Wales and other research institutions in Wales. Microbiologists from Aberystwyth and Cardiff have met annually at Gregynog Hall (www.wales.ac.uk/newpages/ external/e3650.asp), the university's residential centre near Newtown Powys since 1972. These meetings were originally instigated by Professors Gareth Morris from Aberystwyth and David Hughes from Cardiff, and many alumni of the two departments, including a number of eminent SGM members, will remember the 25th anniversary meeting in 1996.

In 2003 it was decided to broaden the scope of the meeting to include microbiologists from Bangor and Swansea in the first All-Wales Microbiology Meeting. This year's meeting was further expanded to include scientists from IGER and benefited greatly from a grant from the SGM/SfAM regional meeting fund. The grant covered the costs of guest speakers and also allowed us to focus the meeting on lectures given by younger microbiologists. The majority of the 27 presentations were given by postgraduates, with some talks from undergraduates and postdoctoral researchers (the full programme can be found at http://users.aber.ac.uk/gwg/gregynog/). All the talks were of a very high standard, but the £150 Microbiology Communication Prize for the best talk by a younger scientist was won by George Tordoff, Cardiff, on Interactions between collembola (springtails) and saprotrophic basidiomycete fungi, with Amy Bishop (Swansea), Prysor Williams (Bangor) and Kathryn Wakeman (IGER) as close runners-up.

As a mycologist I see it as my duty to constantly remind my colleagues that microbiology is more than just bacteria, so it was pleasing that there were several fungal presentations, including that of our guest speaker Dr Jonathan Leake from the University of Sheffield who enthralled the audience with a lecture entitled *Mycorrhizal mycelial networks – key pathways of nutrient and energy flow in ecosystems.* We were also fortunate to have a presentation by Dr Alan Thomas, newly appointed Director of the Wales Centre of Excellence for Waste Research, about future funding possibilities in this important area of applied microbiology.

The meeting included an 'ice-breaker' quiz hosted by Hywel Griffiths (Aberystwyth) – there seemed to be an inverse correlation between success in the quiz and academic seniority (even in the microbiology rounds!). There was also time to tour the magnificent grounds as part of a nature walk led by Al Venables (Cardiff) or to help 'aerate' one of the lawns in the traditional Gregynog football match.

I am grateful to all 50 delegates who attended the meeting for their support and hope to see them again next Spring (14–16 March 2005). I do have an extensive mailing list of microbiologists working in Wales, but if I failed to reach any SGM members who would like to know more about the forthcoming meeting, please email me on gwg@aber.ac.uk

■ ***Gareth W. Griffith, Institute of Biological Sciences, University of Wales Aberystwyth, Ceredigion SY23 3DD***

SGM/SfAM Joint Regional Meetings Grants aim to promote microbiology in the UK at a local level. Information on the scheme is available at **www.sgm.ac.uk/grants**

BELOW:
Gregynog Hall, Newtown Powys, Wales.
COURTESY G.W. GRIFFITH

International Development Fund report

SGM helps microbiologists in developing countries through this fund, usually by supporting training courses and other small technology transfer projects. See the website (**www.sgm.ac.uk**) for the rules. The annual closing date for applications is in October.

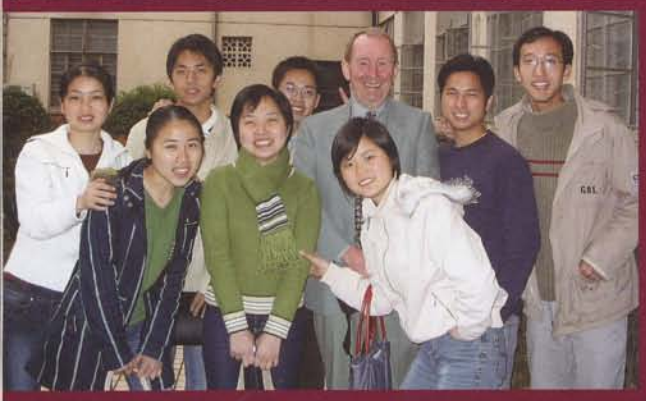
From rainstorm to sandstorm – environmental microbiology in China

Gwyn Jones

This was my seventh visit to China and the second under the sponsorship of the SGM. I had been in Fuzhou in October 2003, advising the Environmental Monitoring Station and the Environmental Research Station on water quality problems. During that visit, Yuping Su, Deputy Director of the Environmental Sciences Department of Fujian Normal University had attended several of my seminars, asked lots of questions and, at the end of my visit, asked if it was possible for me to teach a course on environmental microbiology. Thanks to the SGM's International Development Fund, I returned in March of this year to do just that.

Fujian Normal University was established 100 years ago and has 25,000 full-time undergraduates, 2,000 postgrads and 2,400 staff. The library holds over 3 million books and work on the university's two campuses now also encompasses distance- and life-long learning courses. My meeting with the Vice-President included a long discussion on the role of the Open University in the UK.

Teaching started at 8 a.m. and usually finished at 5.30 p.m. although, on several days, it continued into the evening at my hotel adjoining the campus. Luckily, the cost of meals there was such that I was able to invite postgrads to join me for discussions on individual research projects. These discussions are continuing by email. The average class size was around 35, comprising lecturers, graduates and undergraduates, increasing on occasions when students who just wanted to improve their English attended. Two 'large' lectures, to audiences of around 200 were also organized. During all these, the level of competence in English surprised me. Although Yi Xiaoe, who preferred to be known as 'Grace', acted as my translator, there were long periods when the Deputy Director stopped the translation and told students that they must now concentrate and work only in English. There were no signs of the hand-held translation machines experienced further north in China and the questioning was fast and furious. During one 'large' lecture I noticed that 'Grace' was visibly relieved to stop translating; it was only afterwards that I discovered that her microphone was giving her electric shocks!



RIGHT:
A banner at Fujian Normal University announcing the course.

BELOW (TOP)
Two of the Chinese students taking water samples with Gwyn.

BELOW (BOTTOM):
Gwyn surrounded by a group of students from the course.

COURTESY G. JONES

We covered subjects such as how to determine bacterial and algal populations and spent a great deal of time on microbially mediated geochemical activities and their use in environmental remediation. With my background, the bulk of the course related to water quality problems but, with the free flow of questions, this expanded to discussions on environmental engineering (What did I think of the Three Gorges Dam? Was it a good idea to transfer water from the Yangzi to the Yellow River?).

Practical classes included the use of dipsticks to test for coliforms and the use of membrane filters. Our sampling expeditions were a bit of an eye-opener, especially when I explained to the enthusiasts that they should not use their bare hands to dip bottles in largely untreated sewage effluent. When this warning came too late, they were surprised about my concern that they should wash thoroughly. On the plus side, the membrane filtration equipment that I had been able to take out was an endless source of interest, particularly when it was realized that a water sample could be filtered, the filter dried and cleared for microscopic examination – all in a matter of minutes – a rapid method of assessing water quality. It was during these practical sessions that several students came to me, quite unprompted, and asked me to thank the SGM for making the course possible.

Perhaps I should explain the title to this report. Before I left home I had emailed to ask about weather conditions and was relieved to hear that temperatures were 25 °C+. I was concerned about the weight of material I was carrying so was glad to take only light summer wear. By the time I arrived the temperature had dropped to 10 °C and the rain put the Lake District to shame. I was never gladder of my tiny umbrella and the duvet on my bed (the hotel air-conditioning only provided cooling – heating is not normally required!). On my return to Beijing the temperature was 25 °C and the capital was in the grips of a powerful sandstorm from Inner Mongolia. The local Foreign Expert Bureau had arranged for me to give a seminar on my final, stopover, day in the capital. I addressed the Beijing Hydraulic Research Institute and the Beijing Water Resources Board for 2 hours in the morning. After lunch we visited a number of 'problem' lakes. The fine sand and winds hardly made this a pleasant experience. My eyes and lungs have now recovered thanks to a couple of good walks in the Lake District.

It is difficult to convey the gratitude of staff and students at Fuzhou, but I can certainly add my own in thanking the SGM for a great teaching experience.

Professor J. Gwynfryn Jones, The Orchard, Oldfield Road, Windermere, LA23 2BY, UK. email gwynfryn@btinternet.com

International Research Fellowship report

A worm's eye view of immunity

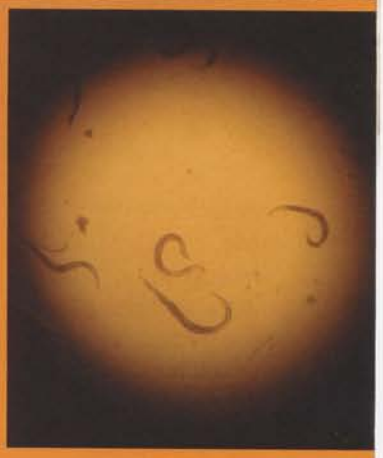
George Salmond

The SGM fellowship enabled me to visit Dr Jonathan Ewbank's lab in the CIML, Marseille, France, where the worm *Caenorhabditis elegans* is used as a model for the study of the innate immune system response to bacterial challenge. In particular, his group has investigated the various interactions between *C. elegans* and *Serratia marcescens*, the subject of my visit. My visit had two main purposes: (1) to pick up the *C. elegans* assay systems, and (2) to assist the Marseille group by extending development of genetic analysis of their chosen *Serratia* strain (Db11), the genome of which is currently being sequenced at the Wellcome Trust Sanger Institute.

As a novice, my starting point was getting to know the various stages of the worm developmental cycle, from textbook drawings and pictures to identifying the real beasts while gazing down the microscope. The controlled predictability of these various stages helps to give good control over the bacterial virulence assays. Susceptibility to the adverse effects of bacterial infection is developmental stage-dependent and so it is important to infect worms at the same stage.

It has to be said that *C. elegans* leads a pretty depressing life in the lab. I guess it has the self-indulgent fun of hermaphroditism, but crawling around on agar plates and eating bacteria all day as a prelude to self-fertilization, then laying eggs, is not the most exciting career choice. Part of the virulence assay involves getting the worms at developmental stage L4 to eat the tasty bacteria that will eventually kill them. (The fact that this choice of prokaryotic cuisine provides daily sustenance, but ultimately kills the worm, has ironic echoes with our current human obesity problems!) The worms burrow into thick patches of bacterial growth and start munching. Plates are incubated, allowing the worms to enjoy their gastronomic delights in a nice warm environment. By assessing the rate of worm killing (e.g. comparing a wild-type and a mutant strain for virulence), it is possible to determine the impact of a particular mutation in pathogenesis. This involves lots of staring down stereomicroscopes and hand-picking the worms one-by-one as they move on the agar – a bit tricky for the uninitiated – but it gets easier with practice. A more high tech approach to the selection of L4 worms is the use of the worm 'sorter' that can be used to enrich for pools of worms of similar sizes (and developmental stages).

In my group in Cambridge, Ian Foulds had isolated a series of new bacteriophages that infected strain Db11. In collaboration with Dr Elizabeth Pradel in Jonathan's group, I was able to test these phages for their ability to infect various mutants of Db11 affected in virulence in the worm assay. One of the Db11 mutants most heavily attenuated in virulence was defective in LPS production and it was also resistant to multiple phages, implying that LPS is their receptor. But other phages, some of which are possibly temperate, didn't use LPS for adsorption and these are now under investigation back in Cambridge. Elizabeth was also interested in extending the genetic tractability of the Db11 strain, but we found that the immediate progenitor (Db10) had several genetic advantages and so she made a gridded transposon insertion library of Db10 for use in subsequent virulence screens. We used some of Elizabeth's tagged mutants for transduction assays and generated preliminary evidence that one of the LPS-dependent phages was a generalized transducer. This phage might prove useful as a new tool for functional genomics of the Db11 strain, once the final genome sequence is available.



TOP:
The view from the lab window!

MIDDLE:
The worm sorter.

BOTTOM:
C. elegans infected with *Serratia*

COURTESY G. SALMOND

We also tested multiple strains and mutants of *Serratia* in the *C. elegans* assay and backed up anecdotal evidence that prodigiosin can be a virulence factor in this pathogen. Using mutants generated by Sarah Coulthurst in my group, our collaboration also uncovered evidence that the AI-2-based quorum sensing system can play a role in modulating virulence in some *Serratia* strains.

So what was the overall value of this International Fellowship? Well, I think it was very successful – for such a short visit. Under the expert tutelage of Leo Kurz, Elizabeth, Jonathan and others, I picked up the basic technology for worm growth and propagation and the pathogenesis assays. I was introduced to the value and uses of the worm sorter and the limitations of both the agar plate-based assay and issues of comparability with the liquid-based assay. I think I am now competent to import worm pathogenesis techniques into my own lab.

The Marseille group was very friendly and supportive, showing generous Provençal hospitality and an endless tolerance of my rather naive questions about *C. elegans*. The visit was mutually beneficial in that I learned a lot about worms and my hosts learned something about genetic tricks for the chosen strain(s). I made good contacts with experts in the area and this pump-priming interaction will be useful for future collaborations. I thank the SGM for the generous support and, not surprisingly, I am convinced that this was money well spent. The visit provided important technical education for me that should underpin future research applications.

Some of the collaborative work with the Marseille group is cited in a paper recently published in *Microbiology* [Coulthurst *et al.* (2004), 150, 1901–1910].

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Hot off the Press

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

ABOVE:
Bottles of essential oils with loose herbs, including cinnamon and bay leaves.
ERIKA CRADDOCK / SCIENCE PHOTO LIBRARY

Microbial 'aromatherapy'

Staphylococcus aureus is an important pathogen of humans, causing diseases such as toxic shock and scalded skin syndromes, as well as food poisoning. Proteins liberated from the bacterial cells cause many of the symptoms, and researchers are keen to devise new ways to prevent this happening. One exciting development is the realization that plant extracts, especially essential oils, can have effects on bacteria.

Researchers at the Department of Dietetics, Nutrition and Biological Sciences at Queen Margaret University College, Edinburgh, and the University of Edinburgh Medical School, have collaborated to investigate the effects of five plant essential oils on the production of key toxic proteins by *S. aureus*. They added bay, clove, cinnamon, thyme and nutmeg oil to growing bacterial cultures at low levels that did not inhibit bacterial growth, and then tested the amounts and activities of bacterial proteins present in the growth media. There was no change in the overall amount of protein, but some toxic effects were significantly reduced, with a simultaneous reduction in the relevant toxic protein. Bay, cinnamon and clove oils were particularly effective.

The researchers already knew that some antibiotics and plant extracts affect the production of bacterial toxins, but this is the first time that the effect of plant oils has been shown so clearly on *S. aureus* toxins. With increasing interest in new and natural food preservation methods, as well as a need for new therapies against antibiotic-resistant bacteria, these results add to the interest in plant essential oils for the food and pharmaceutical industries.

Smith-Palmer, A., Stewart, J. & Fyfe, L. (2004). Influence of subinhibitory concentrations of plant essential oils on the production of enterotoxins A and B and α-toxin by *Staphylococcus aureus*. *J Med Microbiol* **53**, 1023–1027.

Virus evolution in action

Viruses depend on animal, plant or bacterial cells for life. They take over cells and force them to make new copies of the viral particles. Of course, this is often lethal, so cells have a vested interest in spotting and eliminating viruses. The viruses respond with subtle changes to evade detection. Indeed, a mechanism to generate variation is built into the way in which some viruses replicate. Elizabeth Chare and Edward Holmes at the University of Oxford have been studying how these selection pressures work in viruses that require both plants and animals for replication, compared with ones that require plants alone.

The diseases caused in plants by viruses are responsible for billions of pounds of economic losses every year, wasting food and human effort. Very many are transmitted by insects that move from plant to plant, spreading the virus as they feed. Modern agricultural practices that grow a single crop over hundreds of acres positively encourage viral disease. Researchers know that the role of the insect is more than simply mechanical, because changes in the outer covering of some viruses can prevent transmission. Indeed, some viruses multiply within both the insect vector and plants. The question that the Oxford researchers asked was whether there was any difference in the way mutations accumulated in the genes of the two types of plant viruses, those that needed an insect vector and those that did not.

They selected 36 virus species and trawled international gene sequence databanks for records of the capsid protein (CP) gene, which encodes the protein that makes the outer coating of each species. They reasoned that as this was the viral surface exposed to the vectors and plant, it should be most affected by any selection pressures. In all, they found 1,001 CP gene sequences and used computer methods to organize and compare them. The comparisons were based on the fact that some changes in the genetic code of a gene do not affect its function, while others do. The researchers discovered that the vector-borne viruses were under significantly more selective constraints than the non-vector-borne viruses. It means that although many variations are created during the transmission of plant viruses, most of them are not well-suited to their hosts and are therefore removed from the population. Viruses that have to please the complex environment within both an insect and a plant are under even more severe constraints for what makes a viable virus particle. As well as its relevance to the study of evolution, increased understanding of the limits of viral variation could be of value in the practical world of devising treatments for viral diseases.

Chare, E.R. & Holmes, E.C. (2004). Selection pressures in the capsid genes of plant RNA viruses reflect mode of transmission. *J Gen Virol* **85**, 3149–3157.

Abnormal prions in a human cancer cell line

Prion diseases were a backwater of medical microbiology until Mad Cow Disease hit the UK in the late 1980s. Now, words like BSE and variant Creutzfeldt–Jacob Disease (vCJD) have entered everyday language. Despite researchers' continuing efforts, prion diseases are still difficult to diagnose and impossible to cure.

The prion protein that is a normal part of the surface of brain cells causes the disease, but only after, for an unknown reason, it has changed shape. The abnormal proteins clump together into insoluble aggregates that interfere with normal brain functions. Exposure to abnormal prions appears to be one way to trigger the shape change. However, if the conversion process was completely understood, it might be possible to devise treatments that halted or reversed it.

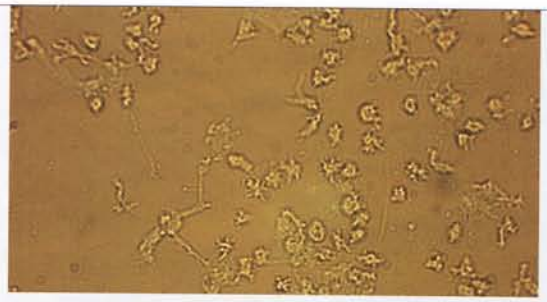
Researchers who want to study these changes in living cells have had to use cell cultures derived from mouse brains, because until recently there were no suitable human cell cultures. However, Yutaka Kikuchi and his colleagues at the National Institute of Health Sciences and Hiroshima University in Japan have discovered that a line of human cancer cells can develop abnormal prion proteins. The cell line, called T98G, was derived from a glioblastoma multiforma tumour in a 61-year-old man in the late 1970s and is used widely in scientific research. The Japanese researchers found that if the cells were left in culture for a very long time, there was an abnormal protein in the cell-surface membrane. Tests showed that some of its features were the same as those of the abnormal prion protein. There were a few differences, and the researchers are continuing to investigate this. Nevertheless, this discovery provides a new and valuable addition to the resources for studying prion disease, as well as a warning to other researchers using this cell line to take extra care.

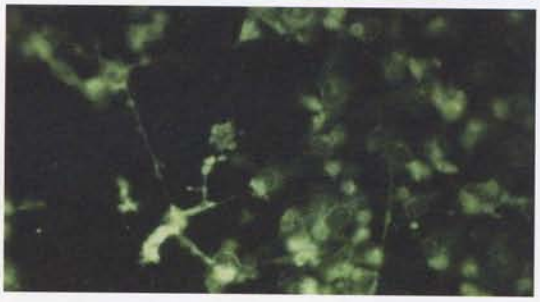
Kikuchi, Y., Kakeya, T., Sakai, A., Takatori, K., Nakamura, N., Matsuda, H., Yamazaki, T., Tanamoto, K.-i. & Sawada, J.-i. (2004). Propagation of a protease-resistant form of prion protein in long-term cultured human glioblastoma cell line T98G. *J Gen Virol* 85, 3449–3457.

Killer amoeba

Balamuthia encephalitis is an insidious disease with an incubation period from days to as long as 2 years. The amoeba *Balamuthia mandrillaris* causes a granulomatous amoebic encephalitis disease while growing within the brain. The symptoms include general malaise, headache, fever and neurological effects such as confusion, nausea and seizures. It was first identified as the cause of death of a pregnant mandrill baboon in the San Diego Zoo Wildlife Animal Park in 1990, but since then there have been over 100 human cases from around the world. The patients have ranged from babies to the elderly, and because the symptoms are so non-specific, it is usually diagnosed after death. The amoeba probably enters the human body through the air or wounds and then spreads to the brain via the blood.

The question of where the amoebae are found in the environment is not entirely clear. One major problem has been that, unlike many amoebae, *B. mandrillaris* appears to feed on other amoebae and grow very slowly. The standard methods used to isolate amoebae do not work. Researchers at the State of California's Viral and Rickettsial Disease Laboratory and Ohio State University in the USA have now carried out a comprehensive study of the growth requirements of the species. They worked out how to isolate the amoebae from soil, first growing them alongside bacteria and then transferring them to feed on animal cell cultures. This took several months and they also discovered that slightly raising the temperature killed other amoebal species, but not *B. mandrillaris*. The researchers managed to isolate and grow enough pure cultures of amoebae to check that characteristic stretches of DNA matched authentic *B. mandrillaris*.





Although the researchers obtained *B. mandrillaris* from only one of four soil samples, their work shows that it is a free-living member of the soil ecosystem. They are now in a good position to carry out a comprehensive survey of the distribution of this pathogenic amoeba in the environment.

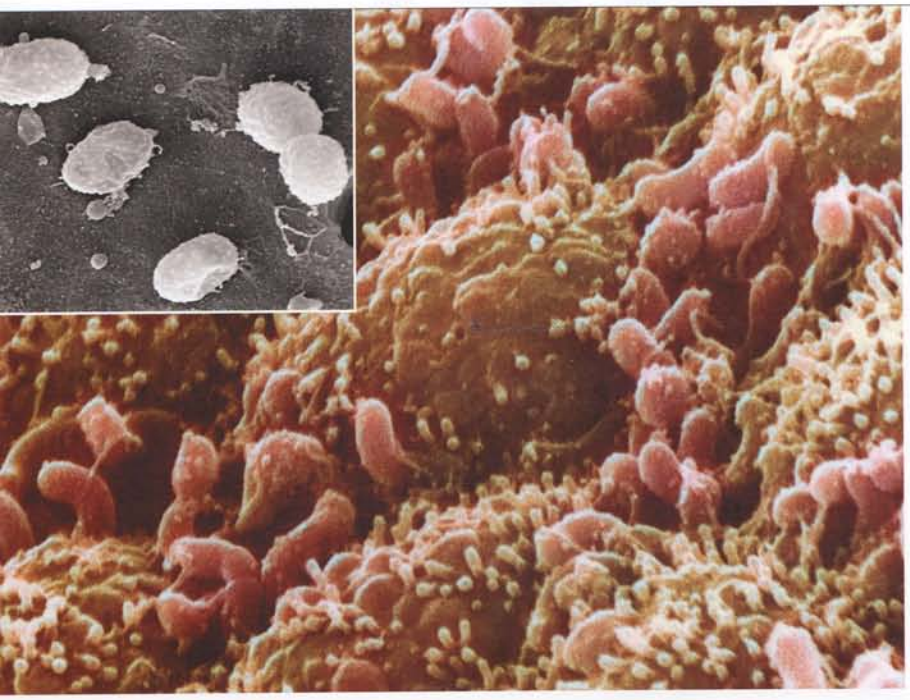
Another difficulty with *B. mandrillaris* is the difficulty of diagnosis and lack of treatments. One way to address this is to develop model systems to study how it affects brain cells and this is precisely what has been done in a collaboration between researchers at Birkbeck College of the University of London, the London School of Hygiene and Tropical Medicine and King's College Hospital in the UK. They have devised a system to isolate *B. mandrillaris* from brain and cerebrospinal fluid using human brain microvascular endothelial cells (HBMEC). The researchers successfully cultured amoebae from post-mortem samples taken from a previously healthy young man who became ill subsequent to suffering skin lesions which developed following a traffic accident in Bolivia. Although it took around a month and a half before the amoebae were numerous enough to be visible, the researchers went on to start investigating how the amoebae affected brain cells and to work towards more sensitive diagnostic methods.

The accumulating information about *B. mandrillaris* should lead to better information on its distribution and pathogenicity as well as improvements in diagnosis and treatment.

Dunnebacke, T.H., Schuster, F.L., Yagi, S. & Booton, G.C. (2004). *Balamuthia mandrillaris* from soil samples. *Microbiology* 150, 2837–2842.

Jayasekera, S., Sissons, J., Tucker, J., Rogers, C., Nolder, D., Warhurst, D., Aslam, S., White, J.M.L., Higgins, E.M. & Khan, N.A. (2004). Post-mortem culture of *Balamuthia mandrillaris* from the brain and cerebrospinal fluid of a case of granulomatous amoebic meningoencephalitis, using human brain microvascular endothelial cells. *J Med Microbiol* 53, 1007–1012.

ABOVE:
Balamuthia mandrillaris under light (top) and UV (bottom) microscopy. To obtain these images, HBMEC were grown on coverslips and then *B. mandrillaris* was added. The plates were incubated until the amoebae had consumed all the HBMEC.
COURTESY NAVEED AHMED KHAN, BIRKBECK COLLEGE UNIVERSITY OF LONDON



ABOVE:
Coloured scanning electron micrograph of intestinal bacteria on the surface of the duodenum.
BIOMEDICAL IMAGING UNIT, SOUTHAMPTON GENERAL HOSPITAL / SCIENCE PHOTO LIBRARY

INSET:
Scanning electron micrograph of *Akkermansia muciniphila* strain Muc^T.
M. DERRIEN *ET AL.*, WAGENINGEN, THE NETHERLANDS

A mucus-degrading bacterium found in the human gut

Many bacteria live within the human gastrointestinal tract. Researchers would like to know more about them because of their effects on human health. The diversity of bacterial DNA in faeces comes from bacteria that inhabit the gut and provides abundant evidence of species that have never been grown within the laboratory. These may be perfectly normal, harmless or even beneficial, but it is difficult to be certain without knowing more about each species. Obtaining living, growing cells is therefore important. Illnesses caused by digestive problems are sufficiently important within the European Union that the European Commission has financed a Euro2.2 million project to learn about bacteria within the gut and how they affect health.

This research has led to the discovery of a new species of bacteria that can degrade the mucus that lines the gut and the development of a technique to grow it in the laboratory. Mucus, a viscous gel made of polymers from proteins and sugars called mucins, protects the underlying human gut cells from physical and chemical damage as food passes along the digestive tract, and is a barrier to pathogenic micro-organisms. However, it is obviously also an ever-present source of food for bacteria, and removal of the mucin will expose the human cells to damage or pathogens. Indeed, the ability of some bacteria to degrade mucin is an important factor in their pathogenicity.

Researchers at Wageningen University in the Netherlands used a combination of old-fashioned microbiology and high-tech DNA analysis to grow a small oval-shaped bacterium from healthy human faeces. It was very abundant and fast-growing – provided that the growth medium contained mucin as the sole source of food and oxygen was completely absent. These unusual conditions explain why it has never been cultivated before. The researchers have named it *Akkermansia muciniphila*, to commemorate the microbial ecologist Antoon Akkermans and the bacterium's need for mucin. The question of its role in human health or disease remains to be discovered.

Derrien, M., Vaughan, E.E., Plugge, C.M. & De Vos, W.M. (2004). *Akkermansia muciniphila* gen. nov., sp. nov., a human intestinal mucin-degrading bacterium. *Int J Syst Evol Microbiol* 54, 1469–1476.

A key event in the colonization of *Bordetella*

Several members of the bacterial genus *Bordetella* cause disease. *B. pertussis* and *B. parapertussis* cause whooping cough in children and *B. pertussis* can give adults a chronic cough. Another species, *B. bronchiseptica*, infects many mammals, causing effects ranging from no symptoms to acute damage to the respiratory tract. It is the source of the infectious disease of dogs called kennel cough, which fortunately usually ends after a few weeks but can make the dog susceptible to further infections.

Medical scientists would like to understand better how the bacteria produce the disease symptoms, so that they can devise better treatments. The disease results from the interaction of the bacteria with several types of cell. They include the cells that cover the surface of the trachea with short hair-like structures, called cilia. These beat in synchrony to remove any dirt or mucus to produce a wave that propels everything up from the lungs to the larynx. Researchers already know that the bacteria stop the cilia moving, and also affect mucus production. Inflammation and visible damage to the tissues also occur. However, the relationship between these events is unclear. Studies with *Bordetella* using human volunteers are forbidden in the UK and researchers at the Centre for Veterinary Science of the University of Cambridge have used tiny pieces of the trachea from dogs to investigate the disease. They kept them on a jelly-like cell culture medium in a sterile atmosphere and saw that the cilia continued to beat in synchronized waves that cleared minute latex beads from the surface for over a day.

Although a few cells of *B. bronchiseptica* had no effect, when the researchers dropped larger numbers onto the tracheal surface, the cilia stopped moving within an hour, despite looking perfectly healthy. The stickiness of the bacteria was crucial, because when the researchers tried out bacteria that had lost the ability to stick to cell surfaces, the cilia continued to move. During the day, a sheet of mucus dotted with bacterial cells built up over the piece of trachea, although the amount of mucus was very variable. One explanation might be that the 5 mm^2 pieces of trachea had different numbers of goblet cells. These specialized cells synthesize mucus as condensed granules, which expand up to 600-fold once released.

The researchers now know that preventing clearance of debris from the trachea by the cilia is the first visible event in the disease. Once this defensive barrier is breached, the infection can escalate.

Anderton, T.L., Maskell, D.J. & Preston, A. (2004). Ciliostasis is a key early event during colonization of canine tracheal tissue by *Bordetella bronchiseptica*. *Microbiology* **150**, 2843–2855.

Cultivation-independent study of vaginal microbial communities

Like every accessible surface in the human body, the healthy vagina is colonized by micro-organisms that help keep undesirable organisms at bay. This provides some protection against yeast and urinary tract infections, sexually transmitted diseases, bacterial vaginosis and even HIV. Researchers are therefore keen to know all about the normal inhabitants and how they can be encouraged.

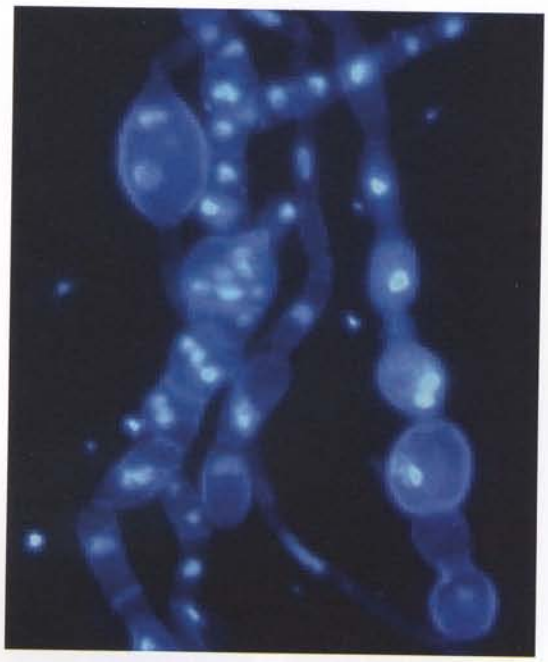
The first microbiological study of the vagina was by Albert Döderlein in 1892, and since then information has accumulated so that now the common wisdom is that lactobacilli dominate the normal vaginal microflora of post-pubertal women. These bacteria are supposed to keep out potential pathogens by secreting lactic acid and a range of antimicrobial substances. However, almost all studies have relied on identifying and counting the bacteria from vaginal samples that grow in laboratory media. Microbial ecologists know that this method gives a biased and incomplete impression of the identity and abundance of the microbes in many habitats. This is because it is impossible to provide the correct environment in the laboratory for all the billions of bacteria that make up microbial communities. Attention has therefore turned to culture-independent methods that rely on sequence analysis of bacterial genes for more accurate information. DNA extracted from the environment is analysed and the information obtained is used to identify the bacteria as well as to estimate the abundance of each species.

Researchers led by Larry Forney of the University of Idaho, in collaboration with Proctor and Gamble, have carried out the first in-depth cultivation-independent study of the vaginal microflora in five healthy adults. After sequencing over 1,200 pieces of DNA, the researchers had a good idea of the identity and proportion of bacterial species. One of the most interesting results was that the bacterial population in each woman's vagina was different. A *Lactobacillus* species certainly predominated in four of the women, although not always the same species. However, the vagina of the fifth woman contained hardly any lactobacilli. Instead, almost all the DNA came from the species *Atopobium vaginae*, which also produces lactic acid, but only grows in an oxygen-free environment. This species has only once before been recorded as present within a vagina. In addition, bacteria from the genera *Megasphaera*, *Leptotrichia*, *Gardnerella*, *Peptostreptococcus*, *Veillonella*, *Aerococcus* and some that did not match any previously known species were present in the women.

Special conditions are needed to grow several of these species in the lab, so it is not surprising if they have been under-reported in the past.

Although these results reinforce the view that the vaginal bacterial community is dominated by species that produce lactic acid, the bacteria need not be lactobacilli. Future studies will be needed to discover whether the bacterial populations of these five women are typical of the over 3 billion women in the world.

Zhou, X., Bent, S.J., Schneider, M.G., Davis, C.C., Islam, M.R. & Forney, L.J. (2004). Characterization of vaginal microbial communities in adult healthy women using cultivation-independent methods. *Microbiology* **150**, 2565–2573.



ABOVE:
Fluorescence microscopy (with DAPI and CWF staining) of a *Fusarium oxysporum* Δ*chsV* mutant lacking a class V chitin synthase.
COURTESY M. MARTÍN-UDÍROZ, M.P. MADRID & M.I.G. RONCERO, UNIVERSIDAD DE CÓRDOBA, SPAIN

Microbiology special issue

Fungal cell wall biogenesis: building a dynamic interface with the environment

Volume **150**, part 10
October 2004

The Fungal Cell Wall Biogenesis section of this special issue of *Microbiology* presents a collection of papers bringing together some of the latest research by leading international groups in this active and wide-ranging field. The collection was edited by César Nombela and Angel Durán, with help from Judith Berman, Dan Burke, Lorna Casselton, Jean-Paul Latgé, Maria Molina, Jesús Pla, Pedro Moradas-Ferreira, Dominique Sanglard, Han Wösten and Oded Yarden.

Copies of the issue can be ordered via the journal website: **http://mic.sgmjournals.org**

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A list of publishers' website addresses is given on p. 201.

Hepatitis B and D Protocols: Vol. 1: Detection, Genotypes, and Characterization. Methods in Molecular Medicine, Vol. 95

Hepatitis B and D Protocols: Vol. 2: Immunology, Model Systems, and Clinical Studies. Methods in Molecular Medicine, Vol. 96

Edited by R.K. Hamatake & J.Y.N. Lau
Published by Humana Press (2004)
Vol. 1: US$125.00, pp. 368
ISBN: 1-58829-105-7
Vol. 2: US$135.00, pp. 650
ISBN: 1-58829-108-1

Both volumes provide an excellent reference for background information and detailed experimental investigations for both Hepatitis B and Hepatitis D. A major attribute of the volumes is that as they cover a wide range of subjects, the reader has the opportunity to access information they would not normally encounter.
Each chapter opens with relevant details describing the principles of the protocols to be presented, which often include a very informative diagram relating to the technique. Additional information is presented within the experimental procedure to clarify the purpose of that specific manipulation within the overall investigation. Each protocol is very well presented and the reader is guided through the experimental procedures in a step-by-step manner, with troubleshooting and potential pitfalls clearly identified. All equipment and reagents required to perform the experiment are listed.
The *in vitro* and *in vivo* models may have a restricted appeal to clinical laboratories, but provide easy-to-follow procedures to investigate the immune response to infection and the development of antiviral agents for those laboratories involved with studying HBV and HDV pathogenesis. The chapters describing the molecular methods associated with viral detection, genotyping and resistance analysis of HBV and HDV and the impact on disease progression and treatment would be an extremely valuable reference for many clinical virology laboratories, in particular those with hepatitis reference laboratory commitments. As knowledge regarding the impact of HBV and HDV genotypes increases, the application of the molecular methods described will become more routine.
Volumes 1 and 2 are an excellent reference source and the methodologies described present the opportunity for both new and experienced researchers to study the molecular aspects of HBV and HDV infection.
■ ***Jeff Connell***
University College Dublin

Probiotics for Crohn's & Colitis

By P. Cartwright
Published by Prentice Publishing (2003) (www.prentice-publishing.co.uk)
£9.99/US$14.95/Euro14.95, pp. 128
ISBN: 0-9544438-0-2

Peter Cartwright has written an interesting and highly readable book on the use of probiotics and dietary manipulation as possible treatments for Crohn's disease and ulcerative colitis. Although it is difficult to accurately identify the target audience for this book, it would be of interest to junior scientists and medical students and also informed lay people. The information is presented in a way which makes it highly accessible and the book also contains a number of useful references to both scientific and non-scientific literature. Although the book is clearly written by someone who has a firm belief in the advantages of pre- and probiotics, it does present quite a balanced picture and provides useful information on the influences of diet and lactic acid bacteria on gut microflora, function and immune development. My only concern about the book is that it contains quite a few throwaway lines and bold statements which are sometimes not supported by references to peer-reviewed publication. For example, the book states '*the normal microflora has been shown, on balance, to be slightly more harmful than beneficial*'. There are many microbiologists and nutritionists who would challenge this statement.
■ ***Tom Humphrey***
University of Bristol

Laboratory Correlates of Immunity to Influenza – A Reassessment. Developments in Biologicals, Vol. 115

Volume Editors: F. Brown, L.R. Haaheim, J.M. Wood & G.C. Schild
Published by Karger (2004)
CHF160.00/Euro114.50/US$145.50, pp. 164
ISBN: 3-8055-7735-4

The gold standard for assessing the protective immune response to influenza vaccines, the haemagglutinin inhibition (HAI) test is showing its age, despite several face-lifts to format it for the high throughput age. Technical limitations aside, new generation mucosal targeted vaccines will potentially evoke site-specific immunity involving *sigA*. Consequently, the HAI test may no longer measure the appropriate parameter (serum IgG against HA). This book discusses where to go from here and spotlights the surprising extent of the gaps in our knowledge regarding immunity in the very young and old; cell-mediated immunity; the importance of other viral antigens; and the logistics of measuring and interpreting mucosal immune responses. Sufficient background information on host response correlates with immunity and test methodologies are provided for the uninitiated reader. Suitable easy reading for anyone looking for an overview of the influenza vaccine world.
■ ***Laurence S. Tiley***
University of Cambridge

Real-Time PCR: An Essential Guide

Edited by K. Edwards, J. Logan & N. Saunders
Published by Horizon Bioscience (2004)
US180.00/£90.00, pp. 346
ISBN: 0-9545232-7-X

This book is written by experts in the field and I recommend it as a standard text for real-time PCR users. Scientists of all levels will appreciate the clear writing style and presentation, whilst there is plenty of useful detail to interest those with more substantial expertise. There are numerous genuinely useful figures, tables and real life examples that complement the text. Critical aspects of the technique, such as chemistries, controls, cDNA preparation and assay validation are thoroughly covered, whilst chapters on real-time NASBA and ARMS PCR go beyond the standard assays that many labs run routinely. The concentration on general principles combined with examples of data from a variety of platforms means that unlike other books covering this fast moving field, it is likely to have a longer shelf life. This book represents excellent value for libraries and individuals or groups that already perform or are considering real-time PCR.
■ ***Chantelle Ward***
GlaxoSmithKline, Stevenage

A Clinician's Dictionary of Pathogenic Microorganisms

By J.H. Jorgensen & M.A. Pfaller
Published by American Society for Microbiology (2004)
US$29.95, pp. 282
ISBN: 1-55581-280-5

This compact, lab-coat pocket-sized volume is unlikely to be the sort of book a practising clinician would whip out on rounds to prompt a correct diagnosis. It is more likely to be useful to microbiology or medical undergraduates cramming for exams, and would be handy to researchers reading papers on

unfamiliar organisms or diseases. The book covers bacteria, fungi, parasites and viruses, although the virus section seemed a little thin. It is lightly referenced with suggested reading sections for bacteria and viruses. There is very little discussion of treatments in the short, but information-dense, definitions. However, I suppose this is not part of the book's remit as it is, after all, a dictionary and not an encyclopedia.
I believe it would be better to own this book individually than institutionally, as it may be the sort that you'd like to keep close at hand for occasional dipping.
■ ***Tobias Allinson***
SGM, Marlborough House

Emerging Infections 6

Edited by W.M. Scheld, B.E. Murray & J.M. Hughes
Published by American Society for Microbiology (2004)
US$84.95, pp. 228
ISBN: 1-55581-242-2

This is an impressive, modest-sized book comprising an eclectic mix of chapters on emerging viruses, bacteria, fungi and parasites. There is a recurring gripe over the use of the term 'emerging' by books and journals, but congratulations to this one where the balance of emergent infections is very good. I note the absence of hardly any 2003 references and this probably explains why, somewhat surprisingly, SARS has not been included as a subject. The chapters are largely excellent accounts of their topics by well-placed authors. I particularly enjoyed the two chapters dealing with clostridial infections in intravenous drug users – truly 'emerging' infections – and also the account of yellow fever vaccine-associated disease. The book is, I suspect, destined for the library shelf and will be used particularly by those who need to be updated on a wide variety of infectious threats to public health.
■ ***Mark Wilcox***
Leeds General Infirmary

North American Parasitic Zoonoses. World Class Parasites: Volume 6

Edited by D.J. Richardson & P.J. Krause
Published by Kluwer Academic (2003)
Euro165.00/US$182.00/£114.00, pp. 224
ISBN: 1-4020-7212-0

American Trypanosomiasis. World Class Parasites: Volume 7

Edited by K.M. Tyler & M.A. Miles
Published by Kluwer Academic (2003)
Euro112.00/US$123.00/£77.00, pp. 176
ISBN: 1-4020-7323-2

Volume 6 of The *World Class Parasites* Series consists of 11 chapters describing North American parasitic zoonoses. The book aims to give a concise and useful review of essential information about zoonoses to physicians and vets. Each chapter is written using a standard outline; aetiology; epidemiology; pathogenesis; diagnostics; treatment and control. Since each chapter is written by experts of a particular field there is a considerable difference in style and some of the chapters are very dry and only for the most dedicated reader. The reference list at the end of each chapter is densely printed and not easy to read and parts of some references are missing altogether. The essential information is definitely there, but unless the reader already knows what parasite to look for the information is difficult to extract. Not a book to pick up and read for pleasure.
Expecting more of the same in Volume 7, it was a pleasant surprise to find a far more readable book. Volume 7 describes American trypanosomiasis (Chagas' disease); organized in 15 chapters it covers a wide range of topics and is written by some of the best specialists in the field. The chapters are detailed, comprehensive and describe some of the latest research. Volume 7 does have the same problem with the densely printed bibliography, but is, however, a useful reference volume for anyone working on Chagas' disease.
Although both volumes suffer from poor quality illustrations and are quite expensive for the individual, they do offer a comprehensive review of parasitic zoonoses and should be included in any medical reference library.
■ ***Marian Blokpoel***
Imperial College London

Microbial Evolution: Gene Establishment, Survival, and Exchange

Edited by R.V. Miller & M.J. Day
Published by American Society for Microbiology (2004)
US$99.95, pp. 388
ISBN: 1-55581-271-6

Modern molecular microbiology – applied to both experimental and natural populations – has an almost unrivalled power in biology to examine the process of evolution and to advance our understanding of the interaction between genes and the environment. This eclectic collection of essays, in the vernacular of biochemistry, molecular biology and bioinformatics, covers many core aspects of microbial evolution including gene establishment, survival and exchange. The essays are in the style of condensed reviews, with good diagrams and brief, but up-to-date (2002) references. I felt that the collection would have been complemented by a discussion of the match between gene function and environmental opportunity, where the mechanistic description of gene function must necessarily meet with the more abstract elements of population genetics and ecology.
Nevertheless, this book will be of interest to both scientists and postgraduates, and I suspect that some essays would provide good resource material for undergraduate teaching.
■ ***Andrew Spiers***
University of Oxford

Lectins, Second Edition

By N. Sharon & H. Lis
Published by Kluwer Academic (2003)
Euro150.00/US$165.00/£104.00, pp. 454
ISBN: 1-4020-1172-5

The authors have done well to update this familiar source of reference on lectins first published in 1989. A lot has changed in this field since then and hard choices and succinct writing and editing style has enabled much information to be incorporated into this very manageable handbook, a must for anyone interested in lectins. The reader is led through an interesting historical perspective on lectin research, possibly a luxury with page space at a premium, but the book feels self-contained for it. Significant chapters encompassing the tremendous advance in our knowledge over recent years of molecular structure and combining sites particularly of animal lectins are included. The information provided is basic but sufficiently well referenced to allow the reader to pursue topics of interest. The book is generally nicely presented with clear illustrations and half tone figures; unfortunately, however, aside from the front cover they are not in colour.
■ ***Robert A. Childs***
MRC Glycosciences Laboratory, Imperial College, Harrow

Malaria Parasites: Genomes and Molecular Biology

Edited by A. P. Waters & C.J. Janse
Published by Caister Academic Press (2004)
£115.00/US$230.00, pp. 546
ISBN: 0-9542464-6-2

The application of genomics to the important parasite genus has generated an exponential increase in molecular and genomic information. This excellent book will help researchers progress from information overload to exploitation and application. There are expected contributions – stage-by-stage review of molecular malariology, comparative genomics, *Plasmodium* genome – plus desirable extras. Indeed, the first few information-rich, how-to-do-it chapters will remain invaluable resources. Errors are few, but placing colour plates at the end of the book is somewhat disappointing given the price. Surprisingly, only one chapter (chloroquine resistance) deals with the endpoint application of *Plasmodium* molecular cell biology. While vaccines are mentioned throughout, strategic, genomic approaches to the rational design of drugs and vaccines, plus molecular basis of drug resistance, would have been valuable inclusions. This accomplished text should reside with anyone expecting to contribute at the molecular end of malaria control. There is an impressive array of knowledge here – the onus is now on the malaria research community to apply this knowledge towards successful control of an ingenious parasite.
■ ***Dr Peter F. Billingsley***
University of Aberdeen

Carpet Monsters and Killer Spores: A Natural History of Toxic Mold

By N.P. Money
Published by Oxford University Press (2004)
£20.00, pp. 178
ISBN: 0-19-517227-2

This book is about the fungi that cause black mouldy spots on the walls of houses, particularly in America. However, that brief sentence does not do it justice. It is an introduction to mycology, allergies and the American legal system through a very personal account of the filamentous fungi that inflict 'toxic black mold' on houses. *Stachybotrys* has pride of place as the major culprit but the dry-rot fungi get a mention as well. The coloured photos of destruction they have caused will make any home-owner shudder. The author's style is totally unlike a mycology textbook and you will

either love or loath his comments that pepper this thoughtful analysis of the place of *Stachybotrys* in human disease and society. This remarkably informative small book is well worth a read by anyone afflicted by mould in their home. It will either lay your fears to rest, or suggest what steps to take.

■ ***Meriel Jones***
University of Liverpool

Analysing Gene Expression. A Handbook of Methods: Possibilities and Pitfalls, Vols 1 & 2

Edited by S. Lorkowski & P. Cullen
Published by Wiley-VCH (2002)
Euro255.00/CHF377.00, pp. 954
ISBN: 3-527-30488-6

This two-volume compendium of almost 1,000 pages comprises 7 chapters, entitled respectively 'Basic concepts of gene expression', Sample preparation and supplementary tools', 'Methods for analysing mRNA expression', 'High-throughput and industrial methods for mRNA expression analysis', 'Protein expression analysis', 'Methods for mRNA and protein expression *in situ* and *in vivo*', and 'Computational methods and bioinformatics tools'. It may be helpful to say first what the work is not, namely a set of detailed experimental protocols comparable to, e.g. *Methods in Enzymology*. Instead, each article examines a range of published techniques: their principles, range of applicability, and particular utility and limitations. For instance, section 3, 'Methods for analysing mRNA expression' – at over 200 pages, a book in itself – is made up of 42 sub-sections; sub-section 3.2.4 'Subtractive hybridization' is itself divided into 12 components, relating to variant procedures such as DISH, DSC, EDS, GES, LCS, RaSH, etc. Over 200 named individuals have contributed, usually only one sub-section of a handful of pages. Despite this, there is a uniform editorial style, the text is clear, and the illustrations are excellent. The chapter on 'Protein expression analysis' in particular is a model of clarity. The emphasis, where any organism is mentioned at all, is on mammals; there is significant representation of yeasts, but bacteria fare about the same as plants. The work will be useful for reference, especially to provide a quick and clear summary of the principles and applications of the various techniques for postgraduates, postdocs, and older research supervisors.

■ ***Simon Baumberg***
University of Leeds

The Desk Encyclopedia of Microbiology

Edited by M. Schaechter
Published by Elsevier Academic Press (2004)
£75.99, pp. 1,152
ISBN: 0-12-621361-5

This large volume meets the dictionary definition of an encyclopedia – a book that contains facts about many different subjects. In this case the area covered is microbiology, with 93 articles on topics ranging from microbial diversity to transcriptional attenuation. The extent of the coverage varies considerably from topic to topic and, in my opinion, viruses are under-represented. As might be expected in an encyclopedia, the articles are arranged in alphabetical order by title. Because of this the contents page is not very helpful, and I found I needed to turn to the index to find my way to items of interest. Whilst the individual articles, which have been contributed by experts in the field, are generally well written and authoritative, most reproduce information readily available in reviews or textbooks. I am not, therefore, convinced that there is an overwhelming need for a book like this, particularly as it is in hardback and will rapidly be out of date.

■ ***Pat Goodwin, The Wellcome Trust, London***

Prion Biology and Diseases, Second Edition. Monograph Series, Vol. 41

Edited by S.B. Prusiner
Published by Cold Spring Harbor Laboratory Press (2004)
US$140.00, pp. 1,050
ISBN: 0-87969-693-1

There is a substantial amount of information in this book and something for everyone. The book begins with six chapters, written mostly by the Nobel laureate himself, providing an overview of prions and how the prion concept was conceived. A series of excellent chapters also describes the range of animal and human prion diseases. The rapid expansion of the prion research field will have made the selection of contributors challenging. Despite this, a selection of leading researchers was chosen from across the world providing balanced discussion and variety in presentation style. The Editor hoped this book would stimulate and tempt young investigators to prion research. It certainly informs the novice that there is more to prions than mad cows and cannibals! And for the established researcher? This book should make a useful reference text as data from an extensive number of studies are contained within the same volume.

■ ***Neil Mabbott***
Institute for Animal Health, Edinburgh

Prions and Prion Diseases: Current Perspectives

Edited by G.C. Telling
Published by Horizon Bioscience (2004)
£90.00/US$180.00, pp. 307
ISBN: 0-9545232-6-1

This book does not pretend to give an overview of this complex subject. Instead experts in the field are given the opportunity to give their personal perspective on chosen aspects of the topic. This is valuable; however, it probably makes the book more relevant to the insider than to a general reader with an interest in this topic. The quality of the science is high and the chapters by Barron & Manson (Gene targeting) and Williamson (Immunotherapy) are models of clarity. The latter alone justifies this book's existence. Unfortunately, many of the chapters are organized by technology used (cell culture, transgenesis, etc.), rather than scientific questions being addressed. Whether or not this book is currently definitive or how long it might remain relevant in such a fast moving field are open questions. It is, however, a useful stepping-stone and should be read as such by those working in this field.

■ ***Mark W. Head***
Edinburgh

Life Sciences for the Non-Scientist

By V. Zaman
Published by World Scientific (2003)
£12.00, pp. 172
ISBN: 981-238-331-X

C.P. Snow famously said that no-one could consider themselves properly educated without a basic understanding of science. This book is intended as part of the liberal arts component of an education syllabus. It consists of 22 essays, without references or further reading. Given the scope that is to be covered in only 172 pages, it is inevitable that there are some sweeping generalizations. It is to the author's credit that the book generally avoids a didactic approach and presents a diversity of views without overtly steering the reader to those most widely accepted. Unfortunately, I found that the essays themselves were rather fragmented and failed to present a coherent picture, so did not seem to convey the core concepts of modern biology. I am not convinced that, after reading this book, someone lacking a basic scientific education would be in a significantly better position to join an after-dinner conversation.

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

Medical Bacteriology, Second Edition. Practical Approach Series, No. 265

Edited by P. Hawkey & D. Lewis
Published by Oxford University Press (2004)
H/B £80.00, P/B £40.00, pp. 409
ISBN: H/B 0-19-963779-2, P/B 0-19-963778-4

This text gives comprehensive practical guidance and protocols for the diagnosis of bacterial infections. A key feature is easy accessibility of the separate protocols for individual diagnostic methods which, although embedded in the text, are listed separately from the contents. The information provided is detailed with the provision of comprehensive recipes. This includes explanations of the chemical/biochemical basis of many of the tests, which should be useful to anyone new to diagnostic bacteriology. The text would be enhanced by including a first chapter highlighting safety issues, as these have been incorporated into a later chapter on quality control and assurance and, as a result, do not have sufficient prominence. Despite this, the text contains a wealth of well presented accurate information, which although targeted primarily to the clinical laboratory, would be useful for anyone embarking on the isolation and identification of bacteria.

■ ***Sheila Patrick***
The Queen's University of Belfast

Immunology, Infection, and Immunity

Edited by G.B.Pier, J.B. Lyczak & L.M. Wetzler
Published by American Society for Microbiology (2004)
US$79.95/£54.00, pp. 742
ISBN: 1-55581-246-5

In various ways microbes have outwitted many human attempts to control infectious diseases, and this book was composed to emphasize the importance of the human immune system in this struggle. More than 30 well

recognized scientists describe in detail the components of the immune system, their functions in protecting from infection as well as dysfunctions (deficiencies and overactivities). The text is very clear, enriched by numerous, excellent illustrations and spans from classical data to many cutting edge molecular structure–function studies. References are focussed on reviews and key papers published between 1997 and 2002, but are complemented by citations of important older works in text and figures. On the viral side, and in general, more details could have been provided on the ability of micro-organisms to evade immune responses by various mechanisms of genetic change. Students will profit from this book, as well as postdoctoral researchers and clinicians: it is excellent value for money, and I recommend it highly.

■ ***Ulrich Desselberger***
Cambridge and Gif-sur-Yvette

Marine Microbiology: Ecology and Applications

By C.B. Munn
Published by BIOS Scientific Publishers (2003)
£29.99, pp. 312
ISBN: 1-85996-288-2

This student text book covers an enormous scope within just under 300 pages, going from basic cell biology, through molecular methods to taxonomy, ecology, pathology and applications both real and potential. This is only possible with substantial generalization and the large majority are fair. The coverage given to the eukaryotic microbes and their roles is unusually good (reviewer bias). I found it somewhat frustrating that topics were introduced and exceptions described without addressing why they were important or how they squared with the first statement. This kind of thing can make for excellent class discussion and probably makes the book valuable for those teaching in this area. Most of the text, with the exception of the 'research focus' boxes, is written without any direct referencing (although there is a selection of further reading), reducing its value as an introduction for those wanting to enter the field or to catch up.

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

Phoma Identification Manual: Differentiation of Specific and Infra-specific Taxa in Culture

By G.H. Boerema, J. de Gruyter, M.E. Noordeloos & M.E.C. Hamers
Published by CABI Publishing (2004)
£75.00/US$140.00, pp. 448
ISBN: 0-85199-743-0

Phoma species, which are ubiquitous and recovered from all plants, some vertebrate and invertebrate animals and most ecological niches, have traditionally been identified by morphology and host source. For 40 years Boerema and his co-workers have assiduously combined classical procedures with standardized culture conditions and biochemical tests. This manual not only summarizes this work, but finally brings together the hitherto scattered published information between two covers. Comprehensive data are provided on 223 specific and infraspecific taxa within sections, synonymies, detailed descriptions *in vivo* and *in vitro*, line illustrations and notes on ecology and distribution. The book will be easier to use by the specialist with some basic grounding in the group, though the scarcity of mycologists now capable of providing authoritative opinions on *Phoma* identification means that plant pathologists, seed and food technologists, ecologists and physiologists may well be forced to use it. However, the data are presented so logically and clearly that the determined will not find it too difficult to use. It is a most welcome and long overdue addition to coelomycete diagnostics; strongly recommended.

■ ***Brian C. Sutton (ret.)***
CABI Bioscience

Concise Encyclopedia of Plant Pathology

By P. Vidhyasekaran
Published by The Haworth Press (2004)
US$79.95, pp. 620
ISBN: 1-56022-943-8

This book is certainly encyclopedic – everything I looked for was here in some form or another. It is also a dense book; there is nary a diagram in its 619 pages. Something of a failing, I think, since a few diagrams would both aid understanding and cut down on the number of words needed. For example, someone might struggle attempting to follow PCR from the description in the text. Oddly, full PCR and RT-PCR temperature cycling protocols are included, yet the temperature cycles will vary with each individual assay.
This book will mainly appeal to plant pathologists who want to find some basic information about an unfamiliar area of plant pathology. As such, it is certainly a useful book; most visitors to my office have been unable to resist picking it up and leafing through it, which you may take as some recommendation.

■ ***Kevin O'Donnell***
Scottish Agricultural Science Agency, Edinburgh

Sumoylation: Molecular Biology and Biochemistry

Edited by V.G. Wilson
Published by Horizon Bioscience (2004)
£100.00/US$200.00, pp. 404
ISBN: 0-9545232-8-8

Since 1996 when SUMO was first discovered there has been an explosion of activity on the subject. A review of the field is very welcome, and while there is always a danger in a rapidly moving field that such a review is already dated or redundant, this book does an excellent job. In 12 chapters some of the key figures in the field review SUMO biochemistry and molecular biology. The chapters and references cited are reassuringly up-to-date, though the index is at times of limited value. While not overflowing with illustrations the chapters are well written and edited, and provide not only rounded reviews of the areas under discussion but thoughtful insight into future directions and open questions. At £100 this book is expensive and at that price it is unlikely to be a casual addition to anyone's individual or even institutional library. But this work comprises an extremely useful resource for those working in the area.

■ ***Peter O'Hare***
Marie Curie Research Institute, Oxted, Surrey

DNA Amplification: Current Technologies and Applications

Edited by V.V. Demidov & N.E. Broude
Published by Horizon Bioscience (2004)
£90.00/US$180.00, pp. 404
ISBN: 0-9545232-9-6

It is not a PCR manual nor is it designed that way. Rather it is a book for the researcher to browse when looking for inspiration or new approaches, or alternatively it can be used to look up in-depth information relating to a DNA amplification technique. There are numerous books covering PCR, but few take a broader view of DNA amplification and the variety of situations in which the differing techniques can be employed. This book fills the gap by describing numerous approaches, some of which are reasonably well established and others that are more experimental, along with examples of how they are used and results obtained. The Editors have incorporated non-PCR-based methods such as isothermal amplification as well as PCR-based techniques. There are also sections on the use of DNA amplification for detecting non-DNA-based analytes and a limited but useful section on enzymes. Recommended.

■ ***Chantelle Ward***
GlaxoSmithKline, Stevenage

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Books received

Clinical Laboratory Management

Edited by L.S. Garcia & others
Published by American Society for Microbiology (2004)
US$149.95, pp. 888
ISBN: 1-55581-279-1

Comment

The role of expert judgement needs promoting

The public is constantly confused by the mixed messages they receive from scientists about controversial issues. Tracey Brown argues that if the practice of peer review was promoted and understood, then people would find it much easier to reach a balanced judgement.

'Peer Review and the Acceptance of New Scientific Ideas' is available free online from ***www.senseabout science.org*** *or can be ordered in hard copy for £10 from* ***publishing@senseabout science.org***

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

"It is all very well to argue for the evidence-based approach," a leading clinician once told me, *"but what happens when the 'evidence' put before the public is not evidence at all?"* We were discussing the controversy over the MMR vaccine, but we might equally have been talking about food safety, cot death, environmental exposure to chemicals, cloning, the SARS virus, or any number of hotly debated scientific issues.

It is true. Despite the current appeal of lay involvement in deciding scientific priorities, to most of the population one apparently scientific claim looks much like another. This perhaps explains why many of the people who try to investigate troublesome issues further, for example by looking for more information about the MMR vaccine on the Internet, end up declaring themselves even more 'confused'. It is borne out by the findings of social research on GM crops and on BSE, where members of the public are quoted as saying that they do not know whom to believe and that for every study that demonstrates a risk there is another study that apparently says the opposite.

It is not only the political and social contestation of scientific research claims that causes such confusion. Science is news, and the sheer volume of scientific material and comment that is broadcast to the public has increased dramatically. Where the BBC science correspondents of a decade ago were generally resigned to doing the 'fluffy' story at the end of the bulletin, they now find themselves reporting for headline stories. Popular science books fly off the shelves. Competition for academic profile has brought a new layer of media-savvy science promotion to the universities and institutes. Scientific papers at conferences and in journals are turned into press news. Almost every disease, medical procedure and safety issue has a leaflet, not to mention several websites, dedicated to it.

In response to these trends, scientists have become more focused on the need to improve the public communication of their research. In ever greater numbers they are seeking the skills to do this, which is often to the good. However, very little attention has been paid to the skills needed to receive and make sense of what is being communicated and this is arguably more significant to how scientific information is understood in the public domain. One very neglected area is the need to explain peer review. Few members of the public - including the professionally-interested public such as politicians, lobbyists, educators and news journalists – are aware that scientific research papers are reviewed for competence, significance and originality by independent experts in the field.

Whether or not research results have been peer-reviewed, how others in the field have responded to the work and how it compares to other reviewed work on the subject, are as essential to making sense of an issue as the research findings themselves. This was the conclusion of a Working Party on peer review, established by Sense About Science, which published its report in June this year. The report, *Peer Review and the Acceptance of New Scientific Ideas*, argues that the public should know how to ask about the status of the research results put before them. Questions about the response of peers and the status of work being reported are far more likely to help the public to assess issues of concern, where currently the implication is that it is necessary to become an immunologist or gastroenterologist to make a sensible decision about vaccinating your child.

There have been few attempts to set out the principles of peer review, or to promote the discipline that it imposes on what is, in the first instance, considered to be scientifically worthy.

From a public perspective, knowing about peer review is not only helpful for judging the relative merits of competing claims. It also demystifies the role of experts in determining the status of ideas. As our report noted, we seem, as a culture, to be drawn more to those stories that minister to suspicion about established authority or knowledge and that rely on 'alternative' and 'anti-orthodox' voices. The promotion of peer review as a basic assessment of quality can help to put everyone under equal pressure to explain the status of their work and the claims they make, including the 'alternative' beneficiaries of contemporary suspicion. The report recommends that scientists volunteer information about the status of research results and the context of other work in the field, whenever they discuss their findings or get involved in contentious debates. The more that this happens, the more likely such questions will also be asked by opinion formers, by policy makers and by journalists. If this happens even in some small measure, it will make for a more balanced discussion of scientific issues being set before the public.

● ***Tracey Brown is the Director of Sense About Science, a charitable trust campaigning for the evidence-based approach.***
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