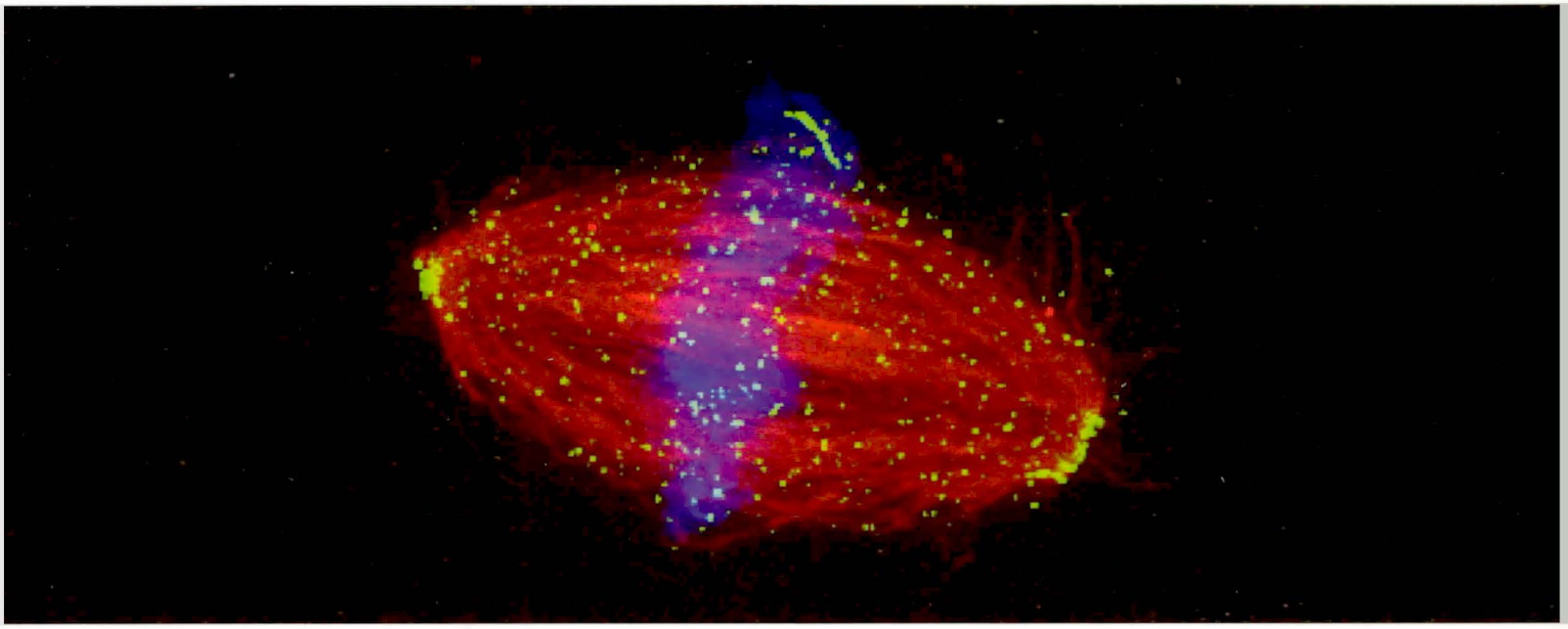

BSCB Newsletter

Winter 2003

British Society for Cell Biology

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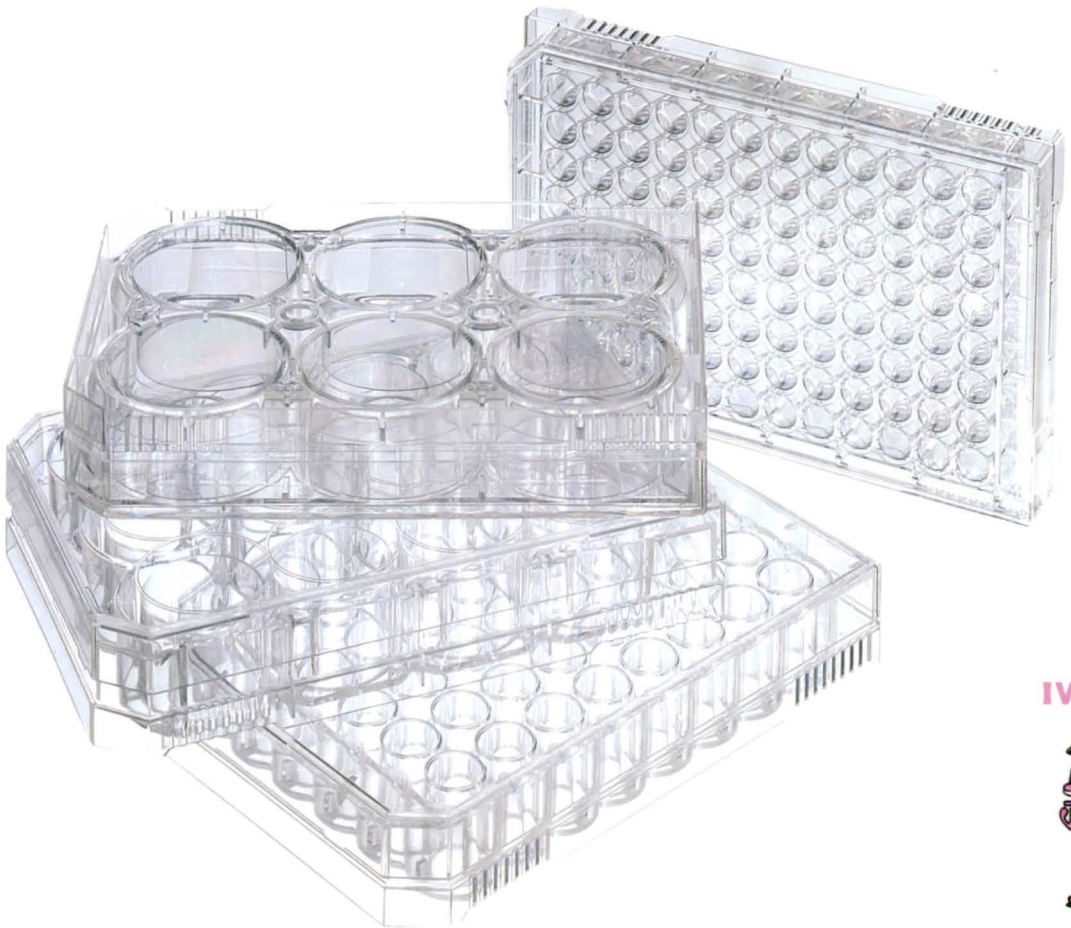

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Barloworld Scientific

BSCB Newsletter
Winter 2003

Editorial

The biggest news this year is that the Society will be holding the 2004 Spring Meeting on its own, without joint participation from the BSDB. The venue is the University of Kent, Canterbury, with Cell Structure and Dynamics as the theme. An excellent programme has been prepared, so get your registration form in and make sure your friends are coming too! The full programme is contained in this Newsletter.

This issue contains a lengthy report from the Autumn meeting on the Cell biology of cancer and extended highlights from the ELSO meeting in Dresden.

David Archer has sent us another update on his work with schools and there are some exciting initiatives in that area.

Because the Martin Raff meeting had to be postponed after the events of 11th September 2001, the Society held three meetings during 2002. This increased our annual budget for that year to a point at which the Accounts had to be formally audited. For this reason, they were not published in the Summer Newsletter as usually occurs, but are presented here. The Accounts will have to be audited again for 2003, after which we hope to return to the old system.

There are no feature articles this time but we have a large collection of book reviews. I still receive a steady stream of books for review, so if anyone is interested in evaluating one, please contact me.

The Editor

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Cover image: A mitotic spindle formed in mitotic *Xenopus* extracts that was stained with DAPI to visualise DNA and with antibodies against APC shown in green. The extract contained rhodamine labelled tubulin which marks the spindle in red. APC concentrates at poles but is also detected all over the spindle and on the DNA. Courtesy of Inke Nathke and Dina Dikovskaya.

News

Meeting Reports

Book Reviews

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News

BSCB Spring Meeting – solo venture

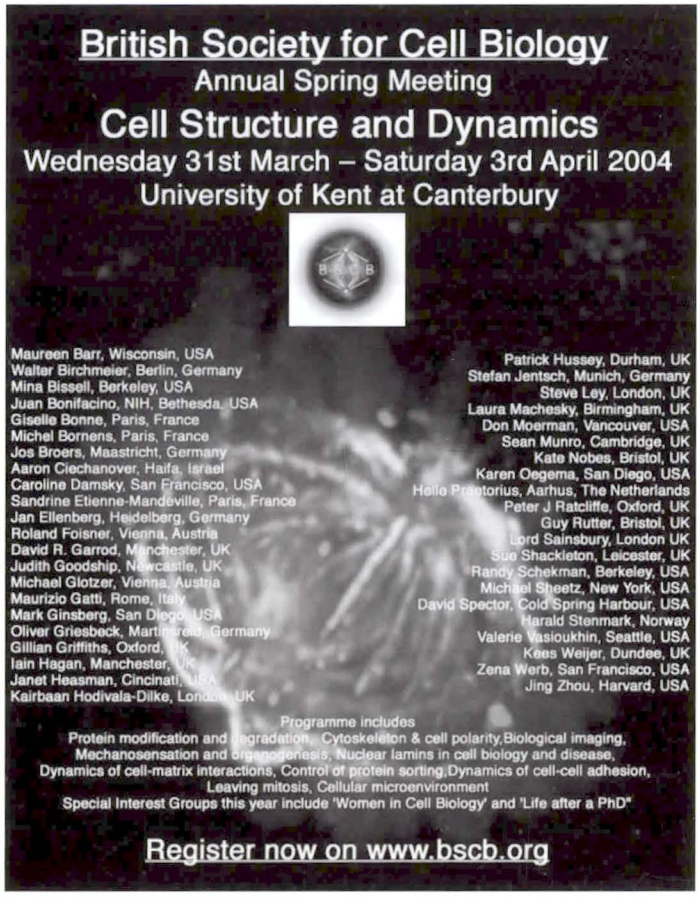
This year we are going it alone with no other societies involved! The Spring meeting will be an all-BSCB affair for the first time since – who knows? So it is important that as many members as possible attend. A fantastic programme has been arranged and the price is a bargain £290 inclusive – all in the beautiful city of Canterbury. The plenary speakers include Randy Schekman from Berkeley, who will give the Borden lecture, and David Spector from Cold Spring Harbor.

Lord Sainsbury, Parliamentary Under-Secretary of State for Science and Innovation, will give a plenary lecture entitled: **Scientific Research Priorities for the UK: The Government perspective**. This will be a great opportunity for you to hear how the Government views science. This is highly relevant as it will dictate funding policies in the future – and your research!

We also have two exciting new initiatives in the form of special lunches. One will feature short talks from eminent **Women in Cell Biology** followed by an extended discussion where the speakers will be pleased to answer questions. The second lunch focuses on **Careers after a PhD**. This is aimed at those who feel that bench science is perhaps not for them. What else can you do? There are plenty of careers out there where scientific training is highly respected and where you can stay in touch with what is happening in research without having to label any more test-tubes.

This year's **Hooke medal winner is Elmar Schiebel** whose work focuses on understanding molecular aspects of chromosome segregation in mitosis. In particular, he is interested in microtubule organization by the gamma-tubulin complex, the functions of kinetochores and regulation of mitotic exit by a conserved signal transduction cascade named the mitotic exit network. Past Hooke medal lectures have been excellent expositions of the winners' work over recent years that led to them being awarded the medal and we are confident that Elmar will live up to this tradition.

Talking about the **Hooke medal**, we are asking people to start considering nominations for next year. There will be an opportunity at the Spring meeting to propose whom you think deserves consideration for the medal, so start thinking about candidates. The medal was coined in 2000 and previous winners have been Anne Ridley, Iain Hagan, Andrea Brand and Matthew Freeman. The model honours an emerging leader in cell biology. Usually, it would be expected that the award will be presented to someone with no more than 10 years of independent research which has been conducted largely within the UK.



Meeting details and programme on page 23.

BSCB joins the Biosciences Federation and the Research Defence Society

The Society has decided to join the Biosciences Federation (www.bsf.ac.uk). This was founded on 2nd December 2002 and formally launched at the House of Lords on 15th September 2003. It is an umbrella organisation with the following key aims:

- To promote liaison, dialogue and interactions within the diverse community of bioscientists on common issues that relate to research and teaching;
- To provide opinion and information to assist the formulation of public policy;
- To promote wide and open debate, involving the wider public where appropriate, about the practical and ethical issues surrounding developments in the biosciences and their applications.

Promoting greater understanding of science among the public and policy makers is becoming increasingly important. Stephen Nurrish is the Society's liaison officer to the Federation, so if you have any issues you want raised, please contact him (details on p 33).

The Society has also joined the Research Defence Society (www.rds-online.org.uk). This aims to represent scientists and doctors in the debate concerning research on animals. We hope to feature a report from the RDS in the next issue of the newsletter. The Committee would welcome the views of the Society's members on the activities of these two organizations.

Honor Fell Travel Awards

Young BSCB members attending scientific conferences relevant to cell biology are eligible to apply for financial support in the form of an Honor Fell travel award. The maximum values of these awards have recently been increased. Full details are on the application form at the end of the Newsletter.

The Society also offers Central and Eastern European Awards for people from those countries to attend BSCB meetings. Applications from other parts of the world may be considered in exceptional circumstances. Potential applicants should contact the Honor Fell Awards secretary (see p 32).

Cheaper journal subs for members

Did you know that BSCB members are entitled to discount subscriptions for several journals? The money saved more than compensates for your membership fee, so encourage your friends to join the Society. Details are on p 36.

New BSCB Website Coordinator

The new Website Coordinator is Tony Ng, from King's College London – full contact details on p 32.

Please note that any BSCB members can nominate themselves or fellow cell biologists for election to the committee. Each person should have a nominator and a seconder. We are looking for committee members who represent a good spread of interests and geographical location and who, above all, will make a POSITIVE contribution to the running of the BSCB.

Nominations should be sent to the BSCB Secretary, Michael Whitaker, and are welcome throughout the year. Committee meetings are held at the Spring meeting, then once or twice more during the year.

Funding for local meetings

The Society is prepared to provide limited financial support for meetings organized by any local interest group relevant to cell biology. Requests for funds should be sent to the Treasurer, Mark Marsh (see page 32), accompanied by a report of a previous meeting. If a meeting receives such support, a report of the meeting will be required for publication in the Newsletter.

Quarterly Muscle Development Meeting

Members are alerted to the occurence of quarterly meetings in which speakers present their work on aspects of cell and developmental biology of muscle tissue in health and disease. These meetings have proved popular, attracting regular attendees from Edinburgh, Paris and many points between.

Meetings commence at 6pm on Wednesday evenings in the impressive Gordon Museum on Guy's Campus of King's College London and are followed by pizza and drinks in the MRC Centre for Developmental Neurobiology courtesy of our sponsors: ICR, GSK, Improvision and BSDB.

Attendance is free and accommodation can frequently be arranged with locals for those from out of town. Email simon.hughes@kcl.ac.uk to be added to the mailing list.

BSCB Membership Database

The website contains the facility to search for members of the Society. However, under the Data Protection Act, we can include your details only if you specifically grant us permission to do so. If you wish to be included and are not, please contact Margaret Clements (zoo-jeb01@lists.cam.ac.uk).

Schools news

BSCB 'cell cyclin' team off to meet teachers after Christmas

A 'cell cyclin' team of three BSCB members will be riding the January weather to represent the BSCB at the 2004 Annual Meeting of the Association for Science Education at the University of Reading on Friday 9 January.

David Archer
(BSCB Schools Liaison Officer)

Two young cell biologists, Jenny Bond and Sarah Cant, who attended schools in the Reading area, will be joining the BSCB Schools Liaison Officer to present a talk that will take the form of three vignettes. The idea behind the talks is to try and persuade teachers and writers, particularly of 'A' level books, to mention the terms 'cell signalling' and 'programmed cell death' when teaching about such topics as neuronal and endocrine systems and metamorphosis and development, already included in the syllabus.

Teachers will also be encouraged to increase the awareness of biology students of the importance of the (approx) 95% of the cell cycle that is not mitosis and introduce them to the all-important idea that checkpoints operate in the cell cycle.

The intention of this initiative is not to add more topics to the teaching load but to ask teachers, writers and publishers to set topics already covered into a 'bigger picture', by adding a phrase here or a word there to work they already cover. To assist with this, copyright-free sample phrases are offered in the lecture leaflets. School textbook publishers will also be contacted.

If you look in the index of a modern 'A' level biology textbook, you will probably find there is reference neither to cell signalling nor apoptosis. You will probably find a page number for 'cell cycle' but reference to the page will show a lot of detail about mitosis but virtually nothing about other phases and nothing about checkpoints. We are pleading not for detail but that here again students should be shown a 'bigger picture'.

Nobel Prize winner and BSCB member Tim Hunt (Cancer Research UK) will also be speaking at the ASE Annual Meeting on Saturday 10 January when he delivers the Nuffield Lecture entitled 'Cell Growth & Division: The Pain of Not Knowing Why'.

The BSCB is grateful to the ASE for time in their Annual Meeting Programme.

Our Society tries to identify topics from research in cell biology that are likely to have a major impact on biology in general, or challenge current thinking and then make authoritative information about the topics available to a wider audience.

The front page of the Newsletter of 'Save British Science' for July 2003 (No37) includes the statement that "....only a half of biology teachers say that they have 'a lot of confidence' in their ability to teach modern biological material". With advances in cell and molecular biology speeding ahead this is perhaps not surprising, but it is an area in which we, as members of the BSCB, can help.

Travel Grant Report

Keystone Symposium: From Stem Cells to Therapy

29 March – 3 April 2003, Steamboat Springs, Colorado, USA

Each year, the Keystone Symposia organization holds a conference on the biology and applications of stem cell research. The fast development of this area is enabling scientists to look to the future and the potential therapeutic uses of stem cells.

Yasmin Babaie

In earlier Keystone stem cell conferences, the emphasis has been on the use of embryonic stem cells for regenerative medicine. Evidence suggesting that adult stem cell populations may be more plastic than previously thought, together with the restrictions now in place on human embryonic stem cell research in a number of countries, meant that this year there was an increased focus on the isolation, expansion and manipulation of adult stem cells.

Around 650 people attended the conference. There were nearly 50 speakers and 300 posters presented over the five days. Finding people you wanted to speak to was very difficult, despite the compulsory display of name tags! The structure of the conference was based around its location at the ski resort of Steamboat Springs. After a morning session, we were free until 5pm every day to hit the slopes. For a ski novice like myself, the conditions could not have been better. There had been fresh snow the day we arrived and we had good sun almost every day which made my first voyage down the slopes much more enjoyable...although it did feel quite weird skiing in a T shirt with the sun blazing all day!

This left most of the delegates sunburnt, physically exhausted but mentally buzzing for the evening sessions. These were followed by 3-hour poster sessions late into the evening. Even with all that time, I felt I barely had a chance to see all the posters I was interested in, which was a testament to the quality of the work on display.

Robert Langer was first to speak: he is Professor of Chemical and Biomedical Engineering at MIT and won the Draper Prize (the Nobel equivalent of the engineering world) for bioengineering of drug delivery systems in 2002. This is a great achievement when you consider that in 2001 the winners were the inventors of the Internet! He highlighted the huge demand for tissue transplants and the need for structural organization of cells before transplantation. His research is based on the development of biodegradable polymer scaffolds that would provide a dynamic surface for cell growth and differentiation.

Martin Pera then gave a very interesting presentation on the gene expression profile of human embryonic stem (ES) cells. Points of interest included the varying expression of key genes for the maintenance of ES pluripotency, e.g. Oct3/4, across a phenotypically uniform cell colony. James Thomson, who hit the headlines as the first person to isolate human ES cells, spoke about genetically manipulating human ES cells using homologous recombination – another world first.

Continuing the human ES theme was Melissa Carpenter, who spoke about the variability between human ES cell lines with respect to gene expression, cell dynamics and genomic stability.

Ronald Goldstein followed with promising results from the transplantation and successful integration of human ES cells into the chick embryo and their differentiation.

There was a definite focus on haematopoiesis and haematopoietic progenitor cells this year. Of particular interest to me was the talk by Kyunghee Choi on her research to identify and isolate the haemangioblast – the putative bipotential precursor of all haematopoietic and vascular tissues. Her team has an *in vitro* culture assay for a cell believed to be the haemangioblast. She reported characterisation of this cell and suggested a pathway for differentiation of the haemangioblast and its behaviour under different stimuli. The expression pattern of the *SCL/tal* 1 gene during development was discussed by her and several others as an important gene for haemangioblast identity and progenitor commitment.

The focus of the conference shifted gradually from ES cells and ES-derived progenitors to adult stem cells, their surprising plasticity and how to manipulate them.

The Side Population cell identified on the basis of its ability to efflux Hoechst stain was a popular research area both in the talks and posters presented. SP cells are being isolated from a variety of tissues and their plasticity is being investigated.

Stem cell niches in mammalian epidermis, the germline and the intestinal epithelium were all covered, as were the growth factors and other stimuli that activated the niche and the signalling pathways that were involved in self-renewal, particularly the Wnt pathway.

Steve Goldstein described the important but often overlooked area of mechanical stimulation of cells. This is a phenomenon which is common *in vivo* but that is rarely re-created *in vitro*. It was clear that fluid shear, the effects of pressure and direct strain in the form of surface traction can be crucial for the stimulation of biochemical signalling cascades.

The conference then progressed to actual attempts at tissue engineering and its challenges. The immunological properties of human ES cells were presented by Micha Drukker, as were the ways in which these properties could be manipulated to enable more successful transplantation of human ES cells. There were also several more technical talks on scalable protocols for the controlled differentiation of ES cells.

The final session brought us back to our ultimate goal: regenerative medicine. Gregory Korbutt discussed the derivation of pancreatic islet cells from various sources for the treatment of diabetes. Curt Freed concluded with a talk on the potential for cell-based therapies for human neurodegenerative disorders, with a focus on Parkinson's disease. He showed before-and-after videos of patients who had received cell-based treatments for Parkinson's disease that was no longer responsive to drug treatment – the improvements were astonishing and very encouraging.

There were so many impressive posters that I cannot mention all the interesting ones! The highlights for me included all the new differentiation work being carried out with human ES cells. A number of groups presented data on the successful generation of cardiomyocytes (with regular beating rhythms!), an array of haematopoietic cell types from the lymphoid and myeloid lineages, as well as neuronal cells and pancreatic islet cells. There were several posters on the characterisation of different human ES cell lines and adult stem cell populations using Affymetrix chips, as well as work showing the plasticity of adult stem cell populations.

There were some posters on the role of physical forces on the growth of cells in culture. If stem cell technology is going to be scaled up, physical stimulation may be an easier and cheaper route to stimulating pathways for differentiation as opposed to the addition of numerous expensive growth factors. Invoking physical forces may mimic the *in vivo* setting of cells, affording scientists a better chance of differentiating cells that have responded to signals similar to those they would have seen in the body, thus making them more suitable for transplantation and engraftment.

My awareness of the range of research being carried out in the field of stem cell biology and transplantation is much greater after having attended this conference. It also provided me with a great opportunity to speak to some of the most eminent scientists in my field. It gave me a chance to discuss my own work and get some invaluable technical advice and constructive criticism. My only warning to future attendees of this conference is: prepare to be in awe of the quality and quantity of work that is out there. It can be somewhat overwhelming! My attendance at the conference would not have been possible without a travel grant from the British Society for Cell Biology, which I would like to thank for its generosity.

Yasmin Babaie
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Yasmin.Babaie@bbsrc.ac.uk

European Life Scientist Organisation (ELSO) Meeting 2003
Dresden, 20–24 September 2003

The third ELSO meeting was held in the fascinating city of Dresden, Germany under clear blue skies and brought together nearly 2000 scientists from a wide range of life science disciplines and many different countries to participate in a stimulating series of plenary sessions, minisymposia and poster sessions.

Paul D. Andrews and Iain M. Porter

ELSO's mission is "to organize meetings in European cities that each year provide a high profile international forum serving the interests of our scientific community. Its defining characteristic will be that it promotes the science and activities of biologists using molecular tools without regard to national interests". Apart from a few minor organizational "hiccups" (e.g. poor organization of poster boards, some room sizes which were discordant with the number of people, no central catering facilities, parallel minisymposia on too similar subject areas - but by far the most serious being the lack of free caffeine), the objectives of ELSO were on the whole, amply met.

Our overview of ELSO 2003 is unfortunately highly selective owing to the size of the meeting, so apologies to those speakers whom we have omitted.

Advances in image analysis for cell biology

This session, organised under the auspices of the European Light Microscopy Initiative, highlighted some emerging microscopy techniques and image analysis software. **Kurt Anderson** (Dresden, Germany) gave a clear exposition of his ideas concerning image informatics in cell biology, with emphasis on the development of so-called eCognition – the extraction of knowledge from images – in a high-throughput environment. He described software implementing a series of segmentation/selection routines, applied to the automated detection of "features" in microscope images: in the proof-of-principle case, this was detection of the leading edge in cells.

Rainer Heintzmann (Gottingen, Germany) gave an excellent overview of the state-of–the-art in structural illumination – techniques to break the so-called "Abbe Limit" of resolution in the light microscope, thereby allowing the cell biologist to visualise ever smaller objects. **Jean-Christophe Olivo-Marin** (Paris, France) presented his lab's latest progress in the tracking of objects in 2D and 3D timelapse data sets. Using a combination of active contour analysis, wavelet transformation algorithms and Kalman filtering schemes, they tracked objects accurately in 3D in timelapse data.

Jason Swedlow (Dundee, UK) gave an interactive overview of the world of deconvolution microscopy, describing the different approaches to both image "deblurring" and image "restoration" and highlighted the importance of testing different vendor implementations of deconvolution algorithms on the user's samples.

Genomics and proteomics of protein flow in eukaryotic cells

Ralf Erdmann (Bochum, Germany) described the characterisation of three novel peroxisomal proteins in *Saccharomyces cerevisiae*. Using nano-LC-MS/MS mass spectrometry, his group has found over 170 proteins associated with purified peroxisomes. These were confirmed using GFP fusions of the identified proteins and colocalisation with

peroxisome markers. The deletion of one protein, Pex11p, prevented peroxisome division and resulted in enlarged peroxisomes within cells. Two other proteins, Pex25p and Pex27p, possessed limited sequence homology to Pex11p. All three were shown to interact by yeast 2-hybrid analysis and deletion of any one resulted in enlarged peroxisomes, suggesting that these proteins are involved peroxisome segregation.

Maintaining a yeast theme, **Chris Kaiser** (Cambridge, USA) described the intracellular trafficking of the amino acid permease Gap1p. Expression of this membrane-associated protein is normally induced by low nitrogen concentrations, aiding uptake of amino acids. A large screen of mutants identified 131 proteins that biased trafficking of Gap1p to the plasma membrane or the vacuole. Two of these, the GTPases Gtr1p and Gtr2p, were required to direct Gap1p to the plasma membrane. Their deletion resulted in vacuolar Gap1p localisation. Membrane localisation of Gap1p was inhibited by its ubiquitination, again causing it to move to the vacuole. Deletion of two related proteins, Bul1 and Bul2, prevented ubiquitination and resulted in high Gap1p activity.

Bala Medicherla (Stuttgart, Germany) and **Ernst Jarosch** (Berlin, Germany) both presented projects aimed at elucidating aspects of the ER-associated degradation (ERAD) pathway using misfolded, fluorescently labelled proteins. **Ana Godi** (Santa Maria Imbaro, Italy) described FAPP proteins that are involved in trafficking proteins between the Golgi and plasma membrane. FAPP proteins and the generation of discrete transport carriers at the trans-Golgi network are controlled by the small GTPase ARF and PI4P.

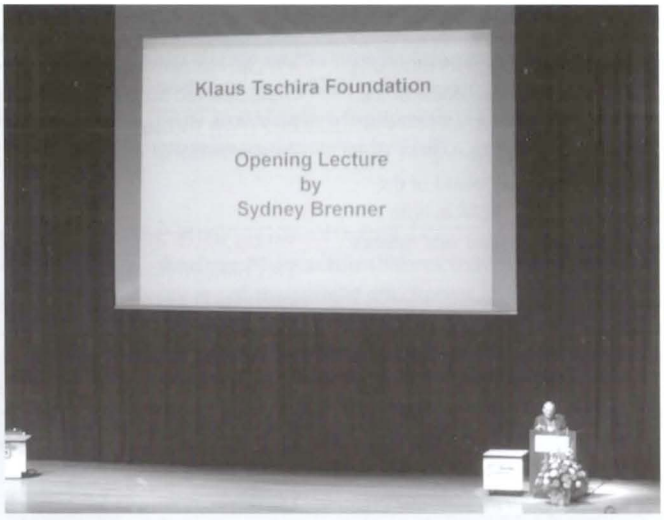
Jeremy Simpson (Heidelberg, Germany) from Rainer Pepperkok's lab described their high-throughput strategy to localise proteins encoded by 550 novel cDNAs which were expressed as C- and N-terminal YFP and CFP fusions. The cellular localisation was assigned to one of twenty categories using automated live cell microscopy and, in many cases, validated by comparison to bioinformatic data from a large number of databases (see http://harvester.embl.de for free access to these data).

Vytaute Starkuviene (Heidleberg, Germany) from the same lab illustrated a functional study looking for inhibitors of protein transport using the techniques described above. When cells are maintained at 39.5°C, the marker protein ts-045-G-GFP accumulates in the ER. Upon shifting to the permissive temperature of 32°C, the protein is synchronously released into the Golgi with subsequent trafficking to the plasma membrane. Using automated microscopy techniques, 140 CFP/YFP tagged proteins were co-transfected with the marker protein and analysed for their ability to inhibit its secretion. Twenty-five perturbed transport: two were known to be involved in signal transduction, four were known proteins but with no known function in protein transport and 19 proteins were novel. Functional characterisation of these proteins is "ongoing".

Top: the Kulturpalast where the meeting was held.
Above: A rather more elegant part of Dresden.

Guennadi Khoudoli (Dundee, UK) is using *Xenopus* egg extracts for a proteomic study of chromatin-associated proteins to determine how their association changes during replication. Proteins were eluted from chromatin isolated at various points during replication and separated by 2D gel electrophoresis. Software analysis was used to determine which polypeptides increased or decreased in abundance at different points during

Special Lecture: Sydney Brenner



On the first evening, there was a Special Lecture from the ever-entertaining Sydney Brenner. Sydney began by bemoaning the current vogue for using the terms 'systems biology', 'integrative biology' and 'computational biology' and used the analogy of a person trying to determine the size and shape of a drum placed within a closed room by listening outside that room to the pattern of beats using an oscilloscope.

He proposed a more successful approach would be to break into the room and work out *de novo* what the drum looked like and how it generated sound in order to be able to describe it. Whilst that is largely a sensible criticism of attempts by bioinformaticians to understand organisms, isn't genetics 'systems' biology in essence? Indeed, on this subject he reflected on the wonderful utility of organisms such as *C. elegans* because "you can know everything about the organism....it has an end". In referring to its use as a model organism, he used the term "CAP criterion: complete, accurate, permanent" and lamented the inaccuracy of some databases.

He impressed upon us that, in his opinion, the "whole is not greater than the sum of the parts" but "the whole is the SAME as the sum of the parts AND their interactions". He proposed that "the cell" is the key unifying element in organism development. In an amusing digression, Sydney explained the difficulties of obtaining funding in old age and proposed the establishment of a 'casino fund' – by top-slicing 0.1-1% of grants – to award 'successful gamblers' like himself. Who should distribute such funds? Successful career gamblers of course – researchers (like Uncle Syd) with a well developed 'nose' for other potentially successful gamblers!

Moving back to his main thesis he extolled the community of science and argued we do not need more annotation of the genome but more 'maps', formulation of the stuff inside and between cells – maps of cells and maps within cells, maps of genes functioning within cells and maps of cells in organisms. (Isn't that what systems biology is meant to be?)

He used the term 'topographic zones' to convey the concept – oft missed by hardcore biochemists – that cells are not just bags of enzymes and proteins don't exist as single entities but are in partnerships with others. If thought of as a "gadget, device, or entity", these protein 'complexes' – which he thought may total less than a few hundred in the cell – are the key to understanding how to build a cell.

After Sydney's lecture, the Mayor of Dresden gave an unintentionally amusing summary of all the cultural events that, in his opinion, one could or indeed should have been doing instead of sitting in the preceding lecture. Then Sydney was presented with a book about the City of Dresden, leaving one wondering, were all the Keys to the City out that day?

replication. Comparison of early and late time points showed that during late replication the presence of 10 proteins consistently increased while that of over 60 proteins decreased. Different replication inhibitors affected different proteins, suggesting that each inhibitor blocks distinct parts of the replication machinery. Data were also presented demonstrating how the post-translational modifications of replication proteins could be followed using 2D gel electrophoresis. Phosphatase treatment of eluates demonstrated that the majority of MCM proteins were phosphorylated at multiple sites.

Tying up the session, **Ute Schepers** (Bonn, Germany) presented a novel method to deliver RNAi molecules into cells. The siRNA of interest was linked via a disulphide bridge to a protein transduction domain that allows very efficient translocation across the plasma membrane. Once in the cytoplasm, the disulphide bridge is reduced and the siRNA released. Importantly, this method does not disrupt the membrane and might be used to deliver RNAi-based drugs for treatment of diseases.

Actin

The sole speaker, **Marc Kirschner** (Boston, USA), gave an overview of the actin assembly and signalling field and presented new data on the identity and function of MCAP2B, which is required for actin assembly in *Xenopus* extracts but not in *in vitro* reactions with recombinant components. MCAP2B is a 60 kDa protein which binds N-WASP and Cdc42-GTP and is required for Cdc42-dependent activation of endogenous N-WASP/WIP complex but not recombinant N-WASp. Using drugs (so called Wiskostatins) isolated by a high-throughput screen and NMR, Marc demonstrated

The Otto Warburg Lecture

Alfred Wittinghofer (Dortmund, Germany) gave an excellent overview of the mechanism underlying signal transduction by GTPases. He illustrated the complexities in the regulation of the GTP cycle with elegant animations of structural transitions within the GTP-binding proteins and compared and contrasted the different modes of regulation for the large number for GTPase and summarised progress in understanding the influences of the GAPs and GEFs.

RNA

David Baulcombe (Norwich, UK) gave an interesting overview of the history of the microRNA field and presented data highlighting the complex and interesting world of the small "interfering" RNA in both plant development and viral defence.

Bastiaan Tops (Utrecht, Netherlands) described the interplay between transposons and RNAi in *C. elegans* and presented data on a new nuclease component of the RISC complex. **Ada Yonath** (Rehovot, Israel) took the audience on a long, yet fascinating trip through the structure of the ribosome and its myriad intermolecular interactions.

the conformational "metastable states" of N-WASp. He postulated how different inputs into the molecule led to different read-outs downstream of N-WASp through allosteric effects preventing key conformational changes.

Virus interactions with host cells

This minisymposium was organized to increase interaction between cell biologists and virologists. **Urs Greber** (Zurich, Germany) described how adenovirus, which normally gains entry into host cells by attachment to the CAR receptor, in the absence of this receptor enters by macropinocytosis using the Fcg receptor (CD64).

Ulrich Koszinowski (Munich, Germany) reported how human cytomegalovirus disrupts the nuclear lamina in order to egress from the nucleus of infected cells. **Roger Everett** (Glasgow, UK) described the localisation and function of two herpes simplex virus type 1 (HSV-1) viral transcriptional activators, ICP0 and ICP4. A number of eukaryotic viruses form replication foci in close proximity to ND10 domains within the nuclei of host cells. These domains are disrupted during infection, with the degradation of a number of ND10-associated proteins. The protein responsible for this disruption is ICP0, which has ubiquitin E3 ligase activity, leading to proteasome-mediated degradation of target proteins. ICP0- viruses are transcriptionally silent, suggesting that proteins within ND10 domains have a role in silencing viral transcription. ICP4 localises with parental virus genomes as early as two hours after infection and may recruit intact ND10 domains to the nuclear periphery. This relocalisation occurred before the action of ICP0 and seemed to be important in establishing replication compartments. However, the localisation of ICP4 with ND10 domains did not occur during infection with ICP0- viruses.

Robin Weiss (London, UK) gave an entertaining historical overview of how the HIV virus receptor binding sites were identified on host cells. Representing cell surface receptors as a safari of animals, he described how the "hippopotamus" CD4 receptor was identified, how HIV infection could be blocked in tissue culture by adding anti-CD4 antibody and how expression of CD4 in usually unsusceptible cells allowed HIV infection. This last experiment also revealed that CD4 was necessary but not sufficient for viral entry because some CD4-expressing cells could bind virus particles but were resistant to virus entry. This led to the discovery of the CXCR4 and CCR5 chemokines as secondary receptors (represented as snakes with their transmembrane domains!). He finished by illustrating that viral isolates tended to display a preference for one of the two chemokine receptors, with R5 isolates being more aggressive in terms of spread and disease progression. Importantly, certain individuals with particular CCR5 polymorphisms are shown to be resistant to HIV.

Mark Marsh (London, UK) concluded the session by showing that HIV capsid maturation and budding can occur from either the plasma membrane or internal vesicles. The latter process may occur in order to evade the host immune system. The HIV envelope protein Env (gp160) is expressed at low levels on the surface of host cells and the GYxxΔ domain within the protein causes its endocytic internalisation. Viruses expressing Env protein mutated in this region are less pathogenic, indicating that internalisation is one way in which the virus evades the immune system. The same motif also appears to be required for directing the Env protein to endosomes. Imaging of monocyte-derived macrophages demonstrated the assembly of a large numbers of immature viral particles on internal membranes and immunolabelling demonstrated that these membranes formed part of the late endosome. HIV particles derived from these cells frequently displayed the same markers on the particle surface, suggesting they had matured from these regions. In addition, these viral particles often remained within endocytic organelles until the host macrophage had encountered another viable host, suggesting another mechanism whereby the HIV evades the immune system.

Reprogramming the genome

Adrian Bird (Edinburgh, UK) gave a typically erudite description of the state-of-the-art in the world of DNA methylation and the interplay between different epigenetic control mechanisms.

Ian Wilmut (Edinburgh, UK) followed with a thoughtful and comprehensive tour of mammalian cloning; its successes and failures; its uses in basic research; its potential for alleviating human and animal diseases and the ethics of cloning. He finished with a discussion of what constitutes nuclear reprogramming and highlighted studies demonstrating that "cloning" techniques have serious consequences for the cloned offspring's long-term health owing to dramatic effects on imprinting of developmentally regulated genes.

From basic research to novel pharmaceuticals

Herbert Waldmann (Dortmund, Germany) gave a stimulating overview of the state of combinatorial chemistry approaches in pharmaceutical

Open Access Publishing

A thought provoking diversion came in the shape of a session on Open Access Publishing, chaired by Carol Featherstone (BioMed Central), with three advocates of open access publishing.

We heard from Peter Newmark (BioMed Central) on his vision of the commercial model for open access publishing, Mark Patterson (Public Library of Science) on the grass-roots, non-profit making 'business' model and David Prosser (SPARC Europe) on a librarian's perspective of the issues facing open access publishing in general with specific reference to self-archiving.

This was followed by some animated debate with contributions from Bill Wells (*Journal of Cell Biology*) and Richard Sever (*Journal of Cell Science*), both questioning aspects of the open access models.

research. He extolled the virtues of natural compound libraries (50% of best-selling drugs are based on natural compounds and the hit-rate in screens is much higher) and the concept of allowing biology to guide the synthetic chemists in their exploration of structural space. He illustrated this well with their efforts to synthesise angiotensin inhibitors based on information from structurally related, but functionally diverse protein domains.

Nuclear organisation and trafficking

Susan Gasser (Geneva, Switzerland) has tagged different genomic loci in the yeast nucleus with TetR-GFP arrays and visualized the dynamics of the loci within live cells, finding spatial constraints depending on chromosomal context, e.g. telomeres are tethered at the nuclear periphery. This technique was developed by using recombination to excise circles of chromatin that were tracked in 2D or 3D over time. Excised rings were found to move further. She showed that histone modification and remodelling enzymes are likely to play a key role in determining a locus's mobility within the nucleus.

Jan Ellenberg (Heidelberg, Germany) described the way in which cells organise their chromosomes during the cell cycle. These beautiful experiments employ pattern bleaching of double-labelled interphase nuclei in live cells and monitoring of their progression through the cell cycle. Using a centromeric fluorescent protein fusion, he demonstrated that the onset of centromere separation at the metaphase–anaphase transition may dictate the ultimate position of that particular chromosome within the daughter nuclei, at least in the following cell cycle. Intriguingly, preventing condensation of constitutive heterochromatin randomises chromosome position.

The ELSO2003 Early Career Award Lecture

Jurgen Knoblich (Vienna, Austria) gave a very interesting presentation on the mechanisms underlying the establishment of planar polarity in development. Of particular note was the role of phosphorylation of Lgl by Par6/aPKC in determining Miranda position within the cell cortex.

David Stanek (Dresden, Germany) gave an enthusiastic talk on the protein interactions within Cajal bodies in interphase nuclei, focussing on SART3/p110 interactions with U4 snRNP-specific proteins as measured by FRET.

Minisymposium eighteen

Andrea Mussachio (Milano, Italy) gave a great review of the spindle checkpoint and described the structural features of Mad2-Mad1 complexes, namely the "seatbelt" model for Mad2 conformation change. He proposed an intriguing model rationalising Mad2 FRAP data in live cells and crystallisation data. He suggested that transient binding of free Mad2 to tightly bound Mad2, in a kinetochore-bound Mad1-Mad2 complex, may allow conformation change to be transmitted – à la "The Prion hypothesis" – to a cytoplasmic Mad2 pool, which would be able to interact with Cdc20, and thus amplify the "wait anaphase" signal.

Kim Nasmyth (Vienna, Austria) gave a typically erudite, albeit whistle-stop, tour of the world of chromosome biorientation in mitosis and meiosis, sister chromosome cohesion, separation and segregation, focusing on his lab's data on the 'ring' structure of the cohesin complex.

Elena Knatko (Dundee, UK) described regulation of the Aurora B complex in *Xenopus* by intramolecular protein phosphorylation and dephosphorylation by PP1. Using phospho-specific antibodies against two phosphorylation sites in INCENP, she demonstrated phosphorylation of INCENP for the first time *in vivo* but this was detectable only at centromeres on prometaphase chromosomes not in metaphase chromosomes under tension.

Motors

Jo Howard (Dresden, Germany) gave an assured presentation on the mechanism of microtubule depolymerisation by the Kin I kinesin MCAK. He presented some interesting movie sequences of GFP-MCAK images, obtained using a total internal reflection fluorescence microscope, showing GFP-MCAK binding to microtubule ends and transiently to the lattice.

Mattias Rief (Munchen, Germany) presented data using atomic force microscopy and optical tweezer technology to probe the elastic properties of filamentous proteins and myosin V under force. **Evelyne Coudrier** (Paris, France) reviewed progress towards understanding the movements of endosomes within cells by multiple myosins and effector molecules. **Anna Akhmanova** (Rotterdam, Netherlands) described the unexpected

connection between the Bicaudal D protein and intracellular transport.

A very interesting presentation by **Masanori Mishimi** (Vienna, Austria) detailed the latest data on the regulation of MKLP1 in the central spindle by CDK-cyclin B phosphorylation. A single N-terminal threonine residue is phosphorylated, thereby inhibiting the plus-end directed motor activity of MKLP-1 *in vitro*, decreasing its ATPase activity and reducing binding to microtubules at physiological salt concentrations. The N-terminal site is predicted to lie close to the K-loop proposed to interact with the C-terminus of tubulin. A similar mechanism for inhibition of K-loop function has been proposed for Aurora B regulation of the Kin I kinesin MCAK (PD Andrews, unpublished).

Proteomics

This minisymposium dealt with the problems of how to match data from mass spectrometry and 2D gels to protein sequences in databases and how the vast amount of data generated from proteomics projects should be stored and handled.

Pavel Gomov (Copenhagen, Denmark) has established a database of proteins with altered expression levels in various tumour types, with the hope that this could lead to the development of assays to detect tumour development at an early stage in the disease. Quantitative 2D gel electrophoresis was used to map healthy and tumour tissue, looking for marker proteins whose expression is changed within tumours. This approach has already proved successful for identifying markers in squamous cell carcinomas and a large-scale study of tumours from breast cancer patients is underway.

Juri Rappsibler (Milan, Italy) presented an overview of the advantages and disadvantages of various proteomic strategies, particularly comparing the 2D gel electrophoresis and non-gel based LC/LC-MS/MS mass spectrometry approaches. He explained how advances in mass spectrometry hardware and improvements in database searching techniques have increased the number of proteins known to be associated with the human spliceosome from 42 to nearly 300.

He concluded by explaining how mass spectrometry can now be used as a quantitative device: measuring absolute changes in protein levels between samples, using methods such as SILAC (stable isotope labelling by amino acids in cell culture) that involves the incorporation of 13C-labelled arginine into proteins or ICAT (isotope-coded affinity tags) which tags cysteine residues with a heavy or light isotope linker molecule attached to biotin.

Adam Liska (Dresden, Germany) presented a novel database searching technique to increase the likelihood of identifying proteins by mass spectrometry in species whose genomes have not been fully sequenced. MS BLAST (http://dove.embl-heidelberg.de/Blast2/msblast.html) uses large numbers of degenerate sequences generated by automated *de novo* sequencing of MS/MS data to search EST databases. MultiTag uses sequence tags (2-4 amino acids) from multiple peptides to perform an error-tolerant alignment of multiple peptides.

Using these techniques, his lab attempted to identify microtubule-associated proteins in *Xenopus* egg extracts. The *Xenopus* genome has still to be sequenced but a large EST database is available with close to 300,000 entries. They found nearly twice as many proteins as the 19 obtained using a standard MASCOT search.

Kai Johnsson (Lausanne, Switzerland) descriibed a new method of fluorescently labelling fusion proteins *in vivo*. The small DNA repair protein hAGT is involved in modifying O_6-alklyated guanine molecules by transferring the alkyl group from the substrate to one of its own cysteine residues. The substrate specificity of this enzyme is relatively low and it can recognise guanine derivatives that are modified to contain fluorescein groups. Fusion proteins containing hAGT were transfected into hAGT-deficient CHO cells that were subsequently incubated in media containing the fluorescein–guanine derivative. The fluorescein was covalently attached to the hAGT fusion and after a number of washing steps specific fluorescence could be detected. This may therefore represent a general method for incorporating different fluorescent tags into any hAGT fusion protein. The only caveat is that hAGT-deficient cell lines are required.

For movie buffs, there was also an entertaining series of "Bioclips" – see www.bioclips.com.

All in all, ELSO 2003 was a highly enjoyable, stimulating meeting and succeeded in its aims to promote interaction between scientists from different countries, working in often quite diverse subject areas.

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Sixth Plenary session

In this, we heard a presentation by **Felix Weiland** (Heidelberg, Germany), detailing the complexities involved in assembly of COP I vesicles and an exciting talk by **Linda Hicke** (Evanston, USA) on the regulation of endocytosis by mono-ubiquitin addition and the role of phosphorylation.

Below: some members of the Swedlow lab (minus Paul Andrews, the photographer). Back left, Iain Porter, back right, Elena Knatko, bottom left Jason Swedlow, bottom right Guennadi Khoudoli.

BSCB Autumn Meeting
Cell Biology of Cancer
14–17 September 2003, Oxford

How does our current understanding of cell biology help us to understand the causes and development of cancer? This was the question addressed at the first joint meeting between the British Society of Cell Biology and the British Association for Cancer Research, held at St Catherine's College, Oxford. The conference covered the whole gamut of cell biology, with sessions on the control of chromosome separation, centrosomes and spindle organisation, angiogenesis, metastasis and the hypoxic micro-environment around tumours. Most of the speakers also addressed the relevance of their findings to cancer, which led to some interesting debates on whether cell culture was an appropriate model for cell behaviour in the whole organism, and whether genomic instability was a cause or only ever a consequence of tumorigenesis.

John Pines

The conference began with a fascinating plenary lecture from **Gerard Evan** (San Francisco) who introduced his work on the requirements for tumour maintenance *in vivo*. He generated a series of transgenic mice that expressed inducible versions of oncogenes or tumour suppressor genes – created by fusing a protein to a modified oestrogen receptor that bound tamoxifen. Thus, the protein of interest was activated only when the mice were fed tamoxifen.

By expressing an inducible *c-myc* proto-oncogene in the pancreas, Gerard showed that active c-Myc caused a rapid increase in cell proliferation that was countered by a massive increase in cell death, leading to diabetes. However, when the apoptotic machinery was inactivated by crossing the mice with a strain expressing the anti-apoptotic Bcl-xL protein, the uncontrolled cell proliferation led to neoplasia and subsequently to angiogenesis and metastasis. Remarkably, inactivating *c-myc* at any time led to complete tumour regression!

The complementary studies with an inducible p53 were also quite startling. In the absence of p53, cells in culture became polyploid or aneuploid but reactivating p53 appeared to restore a stable karyotype. This finding was especially relevant to the question of whether genomic stability could cause, or could only contribute to, neoplasia. These experiments also showed that to kill abnormal cells it was most effective to restore p53 activity after DNA damage rather than during the damage itself, providing hope for the eventual efficacy of a number of current strategies to restore p53 activity in cancer patients.

The current state of the p53 field was masterfully surveyed by **Karen Vousden** (Beatson Institute, Glasgow). The many and various means to regulate p53 and its nemesis, Mdm2, by phosphorylation, ubiquitylation, sumoylation, oligomerisation and nuclear export were clearly explained and, better still, assessed. Karen also introduced us to the novel possibilities that p53 may respond to lesions in ribosome synthesis, and that some of its downstream targets may be required for survival. She ended on a very hopeful note with her results from screens to identify compounds that interfere specifically with the ubiquitylation activity of Mdm2. This should result in an increase in the level of p53 and thus in stimulation of the apoptosis pathway in cancer cells. So far, three structurally related compounds had been found that stabilised p53 and caused apoptosis *in vivo*.

The birth of molecular biology

How biophysicists and biochemists in the 1950s shaped a new science.

Designs for Life: Molecular Biology After World War II
by Soraya de Chadarevian
Cambridge University Press: 2002. 444 pp. £35, $55

Vernon M. Ingram

JOHN HEDGECOE

Protein pioneers: (from left) Hugh Huxley, John Kendrew, Max Perutz, Francis Crick, Fred Sanger and Sydney Brenner were the driving force behind the Laboratory of Molecular Biology in Cambridge.

The history of the genesis and development of the molecular-biology group at Cambridge University, UK, under Max Perutz is endlessly fascinating. Why did it begin? Why in Cambridge? Why at that time? And why these particular scientists?

Soraya de Chadarevian presents a historian's account of the conception and birth of the group that founded what is arguably the reigning movement in modern biology. She describes the circumstances and tactics needed to enable the field of molecular biology to mature from a child to become an adolescent, with predictable awkwardness, and then to achieve adulthood. Throughout gestation and childhood it was nurtured by Perutz, who had a clear vision of the next essential step in the development of biological science.

Perutz, who died earlier this year, set out to solve the chemical structure of haemoglobin, the protein molecule that carries oxygen in vertebrates. He took from John Desmond Bernal and Lawrence Bragg the notion that the young science of X-ray crystallography could be used not only to find the chemical structures of small molecules such as salts and sugars, but also the structure of enormously complex molecules such as haemoglobin. Many people told him he was crazy, that the task was impossible; however, he succeeded after some 25 years. De Chadarevian gives a clear account of this story.

In the late 1940s and early 1950s, Perutz attracted a nucleus of remarkably able young collaborators. His single-minded devotion to the task and his personality were key to this collaboration coming together. There was John Kendrew, who solved the structure of the muscle protein myoglobin; Francis Crick and James Watson, who solved the structure of DNA; Tony Broad, the engineer who made the most powerful X-ray machine in the world; Hugh Huxley, who (with Jean Hanson) solved the molecular mechanism of muscle contraction; and, a little later, Sydney Brenner, who with Crick founded much of modern molecular genetics. I was fortunate to be an early member of the group (1952–58), working as a protein chemist, helping the X-ray crystallographers, and studying the defect caused by the sickle-cell-anaemia mutation. Perutz was mentor to the whole group.

The excitement about our work was palpable; it permeated every conversation and dominated our leisure time. However, the book fails to capture this excitement. This is unfortunate, because we were spurred on and held together by an obsessive desire to understand the molecules of life — proteins and nucleic acids. In *Designs for Life*, the historian eclipses the storyteller.

Also lost is the spirit of intense competitiveness that we felt towards Linus Pauling and his group at the California Institute of Technology, and the X-ray crystallographers at King's College London. Although de Chadarevian gives historical credit to other groups who worked on X-ray crystallography, and protein chemistry in particular, she only touches on the crucial importance of knowing the amino-acid sequences of myoglobin and haemoglobin when progressing from a crude to a detailed structure of these proteins. This information was developed in the United States, and was not available earlier to Perutz and Kendrew.

The early X-ray crystallographers' use of existing and new technologies to solve major biological problems is well described in this book — they were "the right men at the right time". Also fascinating is the crucially important and parallel development of digital computing in the Cambridge University Mathematics Department next door. There was a difference in personality between Perutz and his pupil Kendrew. The latter embraced and spearheaded the development of computers, but he had to be defensively careful about their use because of Perutz's early scepticism about the accuracy of the new method.

Designs for Life deals well with certain important areas of history. The author links the timing of the appearance of the early Medical Research Council (MRC) unit in Cambridge to the availability of new technologies developed during the war in Britain and the United States, and to the availability of young and eager scientists who had had maturing experiences during the Second World War. The early group, led by Perutz, used their success in solving these incredibly difficult structures to publicize the new science of molecular biology by television, radio and newsprint. They encouraged the development of similar research groups elsewhere, and taught molecular biology to a new generation of students from many countries.

Especially detailed is de Chadarevian's account of the politics involved in expanding the group to the size of an institute, large enough to be varied and self-sustaining. The difficulties encountered were both academic and governmental. Although there is much repetition of this theme, there is also a great deal that is interesting.

The group's expansion was helped enormously by the arrival of Fred Sanger, a protein biochemist who went on to win two Nobel prizes — he was the first to establish

the complete chemical structure of a protein, insulin, and he later invented the current method for sequencing the genome.

In the late 1950s and early 1960s, the vigorous drive to establish new molecular-biology departments was in full swing in the United States but had barely begun in Britain. As a result of the reluctant atmosphere at Cambridge University, the hoped-for expansion did not occur within a university department. There were delays, prevarication and disappointments before the group arrived at their large new MRC site on the outskirts of Cambridge. Unfortunately, this was far away from the university, so the researchers were not integrated into its teaching and collegiality. This enforced separation was in part responsible for the desire of so many of the group to leave the MRC laboratory for teaching positions elsewhere. It is interesting to speculate whether a true integration into Cambridge University would have prevented the exodus.

Much space in this book is devoted to the discovery and worldwide expansion of structural protein biochemistry, and rightly so. It is therefore surprising that less attention is paid to the discovery of the Watson–Crick model of DNA. The impact of their double-helix structure was tremendous and lasted for years. Even more than the great influence of protein-structure determination, the DNA model and its consequences were crucial to fashioning modern molecular biology.

In describing the development of molecular biology, de Chadarevian pays some, but not enough, attention to the vital role of scientists such as Erwin Chargaff, William Cochran, Rosalind Franklin and Linus Pauling, not to mention the other American and French groups. After all, truly great advances in biology are built on the work of others — to give them credit would not diminish the achievements of Watson, Crick and Brenner.

Perhaps de Chadarevian should have paid more attention to the influence of Crick and Brenner on the development of the new and exciting fields of molecular genetics and protein synthesis. Their work and the publicizing of their ideas made molecular biology the lingua franca of modern biology. Even the new generation of engineers feel the urgent need to learn this new treatment of biology.

The author deliberately focuses on the (unique) instance of the MRC Unit for the Molecular Structure of Biological Systems, housed in the Cavendish Laboratory, Cambridge, and its direct descendant, the MRC Laboratory of Molecular Biology. The account of these units' relationship to government, to private funding agencies and to the university makes an interesting and valuable book. One must realize, however, that the narrow focus does not imply that the group was entirely self-contained — we depended, at the time, on the outside world for scientific nourishment and for funding. In short, de Chadarevian's historical account is recommended to all who are interested in the development of molecular biology. ■

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Peering through the smoke

Understanding Marijuana: A New Look at Scientific Evidence
by Mitch Earleywine
Oxford University Press: 2002. 344 pp. $29.95

Raphael Mechoulam

There seems to be an insatiable appetite for information on marijuana. The 'books in print' file on my computer lists 416 books under 'marijuana', for example. Is such a deluge justified? Probably not. Does this book by Mitch Earleywine merely add to it, or is it really, as the subtitle claims, a "new look" at the scientific evidence? It certainly brings together a considerable amount of information on cannabis in many fields, and does so very well, but a new look it is not.

In the past two decades there has been a renaissance in cannabis research, mostly in chemistry and biology. Cannabinoid receptors have been identified and endogenous cannabinoids have been isolated from the brain and the periphery. The endocannabinoids have been found to take part in processes in almost all of the major physiological systems. Most of the work has focused on the nervous system, but there have been advances in our understanding of their role in the immune, reproductive, cardiovascular and digestive systems. Memory, pain, inflammation, appetite and suckling are some of the physiological processes in which cannabinoids are involved. By contrast, most other aspects have been sadly neglected.

The endogenous cannabinoids, although now known about for about a decade, have never been administered to healthy human beings, let alone patients. Can we compare this snail's pace with that witnessed with the hormones insulin and cortisone, for example, when, decades ago, clinical research led to major advances in therapeutics within months of their discovery? The only cannabinoid drugs on the market are delta-9-tetrahydrocannabinol (THC), the psychoactive constituent of cannabis, and nabilone, a more active synthetic drug with a similar profile. Both were introduced about 15 years ago. Even cannabidiol, a non-psychoactive, non-toxic cannabis constituent with known anti-oxidative, anti-inflammatory, anti-nausea and anti-epileptic properties, has yet to be adequately evaluated in patients.

This deplorable situation has hampered advances in many fields, particularly in psychology. There is a limit to what animal work can teach us about human emotions, cognition and behaviour. Until we learn more about the endocannabinoid system in humans, a "new look" at the field is bound to be premature.

Two years ago, Oxford University Press published *The Science of Marijuana* by Leslie Iversen (for a review, see *Nature* **407,** 18–19; 2000), an excellent book in which the emphasis is on the biological aspects and medical uses of marijuana. Earleywine, on the other hand, while also addressing these aspects, devotes most of his book to the psychological and social aspects of marijuana use. Unfortunately, these aspects have not been part of the scientific renaissance of recent years. Although the available material is thoughtfully and critically discussed, I was left with a feeling of *déjà vu*.

Earleywine, as befits a clinical psychologist, believes in both statistics and common

B. MARGOT/AP

High tea? Cannabis cafés have focused attention on the controversy surrounding the use of marijuana.

In the third plenary lecture, **Tony Kouzarides** (Wellcome/Cancer Research UK Institute, Cambridge) also presented some encouraging news, this time on the identification of the gene family responsible for sporadic breast cancer. Tony gave a brief update on the histone code and his identification of the ways in which the modification of one residue can affect modification of another and thereby influence whether a gene became active or repressed.

He then presented data on the EMSY protein and its relatives. These proteins all share a Tudor domain – and have therefore been named the Royal family – and appear to be involved in DNA repair. Remarkably, members of this family are overexpressed in sporadic breast cancer and their overexpression appears to be a sign of poor prognosis. These studies may provide the basis for the first early detection screen for this type of cancer.

The relevance of mitotic control mechanisms to genomic stability

The session talks lived up to the high standard set by the plenary lectures. **Stephen Taylor** (Manchester University) focused on the spindle checkpoint that prevents premature chromosome separation when any chromosome is improperly attached to microtubules of the mitotic spindle. Two aspects of improper attachment appeared to be recognised by the checkpoint: when a chromosome was not attached to any microtubule, and when both sister chromatids were attached to the same, rather than opposite, poles. He used chemical inhibitors of the Aurora family of protein kinases to show that the Aurora B kinase was important for cells to arrest in mitosis when sister chromatids were attached to the same pole, but not when they failed to attach to the spindle at all. He was then able to use siRNA to reduce the levels of other previously identified components of the spindle checkpoint and showed that the Bub1 protein had the converse characteristics to Aurora B: Bub1 was required for arrest in response to unattached chromosomes but not to chromatids attached to the same pole.

Peter Sorger (MIT, Boston) also used siRNA to eliminate checkpoint proteins and analysed the effects by time-lapse microscopy. Whereas eliminating some spindle checkpoint components affected mitosis only in the presence of improperly attached chromosomes, eliminating Mad2 and BubR1 accelerated the rate at which all cells progressed through mitosis. Remarkably, siRNA against Mad2 or BubR1 even accelerated mitosis when the kinetochores were disrupted. Previously, it had been thought that the kinetochores – the specialised sites on the chromosomes that capture microtubules from the mitotic spindle – were required to generate active checkpoint signals, but Peter Sorger's data indicated that Mad2 and BubR1 might be part of an intrinsic timing mechanism for mitosis that was independent of the kinetochores.

Insights into the dynamics of the spindle checkpoint came from **Ted Salmon** (UNC, Chapel Hill) who used sophisticated time-lapse imaging coupled with Fluorescence Recovery After Photobleaching to analyse the behaviour of specific proteins in living cells. These techniques allowed him to determine the order of assembly of the checkpoint proteins on the kinetochores and their subsequent response to microtubule attachment, as well as to assay whether the proteins were long term residents at the kinetochore or fleeting visitors. These analyses showed that Mad1 was a stable inhabitant of the kinetochore, whereas, in agreement with Peter Sorger's observations, Mad2 and a sub-population of BubR1 rapidly cycled on and off the kinetochore, indicating that they could have a role in the cytoplasm.

Andrea Musacchio (EIO, Milan) presented some structural and biochemical data that may be key to understanding these complex behaviours. He showed that Mad2 bound very tightly to Mad1, locking together via a molecular "safety belt" formed by the C-terminus of Mad2. However, this raised the problem of how this could be released to allow the same site on Mad2 to bind to Cdc20 (an activator of the Anaphase Promoting Complex/Cyclosome that was the main target of the spindle checkpoint). Further data indicated that Mad2 may exist in two conformations with different binding characteristics. One form bound very tightly to Mad1; the other could be recruited by a Mad1-Mad2 complex and then altered to bind to Cdc20. Thus Mad1-Mad2 complexes at the kinetochore could act catalytically to promote the binding of Mad2 to Cdc20, which would subsequently diffuse away into the cytoplasm. (This would necessitate a protein to be present in the cytoplasm to destabilise the Mad2-Cdc20 complex, a role that might be fulfilled by CMT2.)

Poster prizes

These were kindly donated by *Trends in Cell Biology*.

1st prize
$100 + subscription to *TCB*
Josephine Richardson,
Wellcome/Cancer Research UK Institute.
The dynamics of cyclin B1

2nd prize
Subscription to *TCB*
Chris Morrow
University of Manchester
Aurora B is required to generate a mitotic arrest due to a lack of tension

3rd prize
Subscription to *TCB*
John Macfayden
Institute of Cancer Research.
Do the novel functions of Endo180 in matrix remodelling and breast cancer cell chemotaxis reveal a role in cancer?

Kevin Hardwick (ICMB, Edinburgh) contributed further insights into the behaviour of the checkpoint proteins using fission and budding yeast. By generating cells lacking specific checkpoint proteins, he showed that Bub1 recruits Bub3 to the kinetochore and that Bub1 is phosphorylated by the major cyclin-dependent kinase in the cell. This phosphorylation was required for a properly functioning checkpoint.

A recent regulator of the spindle checkpoint identified by Dr Mary Dasso and colleagues at NIH is the Ran GTPase. **James Hutchins** (Dundee) showed that RCC1, one of the regulators of Ran, was recruited to mitotic chromatin. FRAP analyses showed that RCC1 binding to chromatin became stronger as cells progressed through mitosis. Binding was strongest at telophase and this was likely to be relevant to the role of Ran in nuclear envelope reassembly on decondensing chromosomes.

Bill Earnshaw (ICMB, Edinburgh) addressed how chromosomes undergo condensation in the first place. Using the DT40 cell line to knock out genes in a conditional manner, he unexpectedly found that cells lacking SMC2, one of the components of the condensin complex, were still able to condense their chromosomes. However, a number of proteins were mislocalised on these chromosomes, including topoisomerase II and INCENP, which bound to the Aurora B kinase at kinetochores, and the chromosomes fell apart under hypotonic conditions. Thus, the condensin complex appears to play a key role in the structural integrity of the chromosomes rather than in chromosome condensation *per se*.

Rebecca Heald (University of California, Berkely) has studied RCC1 and condensins, making use of the *Xenopus* egg extract. In extracts lacking condensin, chromosomes were unable to align on a metaphase spindle and could not segregate properly at anaphase, although the kinetohores still formed and were pulled towards the poles. Adding an anti-condensin antibody that blocked condensin function allowed her to address the requirement for condensin at different times in mitosis. She found that condensin was still required for chromosome segregation even after anaphase began. She also combined the biochemistry of egg extracts with Fluorescence Resonance Energy Transfer to show that there was a high concentration of Ran GTP around mitotic chromosomes that diminished as one moved toward the spindle poles and that this gradient was able to regulate microtubule dynamics. The high Ran-GTP levels around chromatin tended to stabilise microtubules, allowing them to grow away from the chromosomes until they were subsequently organised by motor proteins into bipolar arrays to form a mitotic spindle.

Jason Swedlow (Dundee) showed that the Aurora B kinase interacted at the centromeres with a motor protein, MCAK/XKCM1, which also promoted the destabilisation of microtubules. Aurora B was required for MCAK to bind to centromeres. Aurora B phosphorylated and inhibited MCAK *in vitro*, and a mutant MCAK lacking these sites perturbed chromosome attachment and consequently mitosis. Although Aurora B and MCAK co-localised in early mitosis, they gradually moved away from each other as mitosis progressed, raising the possibility that their interaction, and thus the local effect of MCAK on microtubule dynamics, might alter according to the state of the mitotic spindle. Furthermore, Aurora B and its antagonistic phosphatase, PP1, showed similar mitosis-dependent changes in colocalisation. These data illustrated the importance of more refined means to measure protein activity – be it kinase, phosphatase or motor – at specific locations within the cell.

Inke Näthke (Dundee) described how the colon carcinoma-linked Adenomatosis polyposis coli (APC) protein also altered microtubule behaviour. APC in mammalian cells binds to the plus ends of microtubules, the kinetochores and to spindle poles. Moreover, mammalian cells lacking APC exhibit aneuploidy and lagging chromosomes in mitosis. As a possible basis for these effects, Inke showed that egg extracts lacking APC made weak spindles with less tubulin incorporated into the spindle, especially in the centre. At the other end of the spindle, fibroblasts lacking APC had a increased number of and larger centrosomes, which might also contribute to genomic instability by generating multipolar spindles.

The other speakers in this session took up the theme of the importance of centrosomes to genomic stability through their effects on chromosome segregation. **Erich Nigg** (Lausanne) has a long-standing interest in centrosome behaviour and its regulation by protein kinases. A proteomic analysis of semi-purified centrosomes identified over 30 novel centrosome components by mass spectroscopy; these were validated by localisation to the centrosome as epitope-tagged proteins. Erich identified another novel centrosomal protein (called Nlp because it was related to ninein) through its interaction with Polo-like kinase 1 in mammalian cells. Ectopic Nlp was able to recruit the γ-tubulin ring complex into aggregates and these were dispersed by Plk1 kinase activity. Plk1 activity also displaced Nlp from centrosomes but an Nlp protein lacking the sites phosphorylated by Plk1 could not be displaced from centrosomes and subsequently disrupted spindle assembly. Thus, Nlp appeared to be a protein required for the maturation of centrosomes in interphase before their

conversion to a mitotic state by, amongst other regulators, the Plk1 kinase.

The Nek2 kinase also regulates centrosomes and **Andrew Fry** (University of Leicester) found that it bound to the PP1c phosphatase and its inhibitor as a trimeric complex (reminiscent of the binding of Aurora B to PP1). He showed that overexpressing Nek2A caused centrosomes to split prematurely, whereas an inactive Nek2A mutant blocked separation and caused monopolar spindles to form, emphasising the importance of the correct temporal control of activating Nek2A.

Claudia Florindo (Gulbenkian Institute, Portugal) introduced another aspect of centrosome function, their requirement for the final cut – abscission – between the two daughter cells after cytokinesis. She characterised the human homologues of the mob protein in budding yeast and showed that reducing the levels of one type of these proteins caused defects in cell abscission. Strikingly, some daughter cells lacking this protein fused together after apparently completing cytokinesis.

Jordan Raff (Wellcome/Cancer Research UK Institute, Cambridge) brought us back to the involvement of centrosomes in cancer through the TACC proteins. He first identified this family of proteins as centrosomal components in *Drosophila* where he showed that they bound to the microtubule stabilising protein XMAP215/msps. Inhibiting TACC in *Drosophila* embryos destabilised microtubules and caused spindles to collapse. Conversely, increasing the amount of TACC caused the spindles to grow longer. In flies lacking TACC altogether, msps was unable to bind to spindle poles or centrosomes but could still bind microtubules. Jordan postulated that the TACC proteins recruited msps to centrosomes/spindle poles to allow msps to load onto microtubules nucleating from the poles. Interestingly, there are three TACC proteins in humans, some of which are overexpressed in a number of cancers and are even able to transform cells when ectopically expressed. Reduction of the level of human TACC3 protein using siRNA, prevented the homologue of msps/XMAP215 from loading onto spindle microtubules and caused chromosome segregation problems.

These sessions raised a number of possible means by which defects in mitosis might contribute to cancer – through chromosome mis-segregation as a consequence of defective checkpoints, or aberrant chromosome or spindle structure, or perturbing centrosome behaviour, but whether these could be a cause or only a consequence of the initial neoplastic event remained unanswered.

John Pines
Wellcome/Cancer Research UK Institute, Cambridge

Tumour microenvironment influences on cell biology

Kaye Williams

The invited presentations within this session focused upon the influence of low oxygen tension on gene expression. Hypoxia-inducible factors (HIFs) 1 and 2 are the best characterised members of the family of hypoxia-regulated transcription factors that govern this response. The generic role of HIFs is to modulate the expression of genes that promote cell survival under low oxygen conditions. However, it is becoming increasingly apparent that HIFs can be inappropriately expressed in tumours through both the inactivation of tumour suppressor genes or the activation of oncogenes.

Jim Brugarolas (Dana Faber Cancer Institute, Boston, USA) highlighted how tumour suppressor inactivation can impact upon HIF regulation. He presented evidence that adds the tuberous sclerosis complex 2 protein (TSC2) to the list of tumour suppressors that when inactivated lead to a rise in HIF levels. This is achieved through mTOR activation, as rapamycin inhibited HIF activation in $TSC2^{-/-}$ cells.

The classical tumour suppressor gene associated with HIF function is the von Hippel Lindau gene (VHL). The VHL protein is an E3 ligase that targets the α subunits of the dimeric HIF proteins for proteosomal degradation in the presence of oxygen. Consequently, VHL-deficient cells express high levels of HIF under aerobic conditions. Through the analysis of gene expression in $VHL^{+/+}$ versus $VHL^{-/-}$ cells, **Willy Krek's** group (Institute of Cell Biology, ETH Zurich, Switzerland) identified chemokine receptor 4 (CXCR4) as a novel target of the HIF pathway. These intriguing data provide a mechanistic basis for the characteristic pattern of metastases seen from certain tumour types, caused by CXCR4-expressing cells 'homing in' on tissues expressing the chemoattractant Sdf-1.

Rachel Airley (Liverpool John Moores University) focused on Glut-1, one of the transactivation targets of HIF. As well as being a marker for hypoxia in clinical samples, Glut-1 overexpression is of prognostic

significance in a number of tumour types. In a preclinical study, Glut-1 overexpression predicted chemoresistance in human tumour xenografts. Both hypoxia-dependent and independent mechanisms may underpin the Glut-1 expression and associated chemoresistance, making Glut-1 a potential candidate for novel anticancer therapeutics.
Instead of concentrating on HIF-dependent processes in tumour cells, **Claire Lewis** (University of Sheffield) highlighted the importance of this pathway in tumour-associated macrophages. These cells are proangiogenic and migrate to hypoxic tumour regions. In culture, macrophages express high levels of Glut-1, VEGF and MMP7 when exposed to hypoxia and Glut-1 and MMP-7 expression can be detected in macrophages associated with breast carcinoma. Interestingly, elevated expression of HIF was noted in tumour-associated macrophages when none was apparent in surrounding tumour tissue, highlighting subtleties in the precise regulation of HIF in different cell types under the same microenvironmental conditions.

Metastasis

This session opened with an excellent presentation by **Ruth Muschel** (Children's Hospital of Philadelphia, USA) who challenged the dogma that extravasation is the critical component of metastatic colony formation in lung tissue. She demonstrated that circulating tumour cells attach to exposed regions of basement membrane in the lung epithelia. The attachment is facilitated by the interaction of tumour-expressed α3-β1 integrin and laminin-5 in the basement membrane. Expansion of the intravascular colonies was associated with platelet aggregation and vessel leakage. This raised the possibility that extravasation occurs primarily as a consequence of loss of vascular integrity rather than according to the generally held belief that single cells cross the basement membrane and grow outside the vasculature. Thus, therapeutic strategies aimed at blocking tumour cell attachment may be clinically more effective than those aimed at inhibiting extravasation.

Frans van Roy (Ghent University, Belgium) described the importance of E-cadherin in suppressing invasiveness of breast cancer cells. Down-regulation of E-cadherin in tumours can be achieved through multiple mechanisms, including mutation of the coding gene (*CDH1*) in specific cancer types. SIP-1 (SMAD interacting protein 1) was shown to repress E-cadherin expression by binding to two E-box motifs in the *CDH1* promoter and overexpression of this protein in E-cadherin-positive tumour cell lines reduced invasiveness of the cells.

Sue Eccles (Institute of Cancer Research, Sutton) gave a comprehensive overview of the current standing of molecular targeted therapies aimed at suppressing invasion and/or angiogenesis. Linking with the previous talk, activation of type 1 receptor tyrosine kinases in tumour cells was associated with down-regulation of E-cadherin, thereby potentially increasing invasiveness and supporting components of this pathway as therapeutic targets. PI3K was highlighted as a particularly attractive target for anticancer strategies and inhibitors were shown to decrease growth, invasion and angiogenesis in breast cancer xenografts. Instead of hitting a single target, the inhibition of molecular chaperones such as Hsp90 was portrayed as a potential route by which multiple pathways could be inhibited simultaneously.

Finally, **Rod Smallwood** (University of Sheffield) gave a fascinating insight into how computational models of cellular interaction can be generated. The aim is to model all physiological parameters in the body using the evidence of cell responses to certain conditions generated in the biological setting.

Angiogenesis/endothelial cell proliferation

Jan Kitajewski (Columbia University, USA) opened the session with a fabulous talk on Notch function in vascular development. Notch signalling promotes the initial stages of angiogenesis, particularly endothelial cell sprouting and survival. In the latter case, Notch activation could promote survival in low serum in a PI3K/Akt-dependent manner. In contrast, Notch activation blocked the latter stages of vascular development. Migration, proliferation and tube formation were inhibited by Notch. Consequently, Notch must be switched off for the completion of new vessel formation.

Stefan Liebener (FIRC Institute of Molecular Oncology, Milan, Italy) presented data suggesting that β-catenin is required for endothelial–mesenchymal transdifferentiation during formation of the atrioventricular (AV) septum of the heart. Transgenic mice were produced with a conditional inactivation of β-catenin specifically in endothelial

cells (ECs). The mutants had aberrant AV septum formation. *Ex vivo* explant assays suggested that the ECs from the septum of wild-type mice transdifferentiated in a Wnt- and TGF-β-dependent manner to form mesenchymal cells. This was not seen in the β-catenin-deficient cells. Interestingly, ECs do not usually differentiate, raising the possibility that this is a heart EC-specific phenomenon.

Roy Bicknell (University of Oxford) introduced us to the wonderful world of Magic-roundabout (Robo4), a potential new candidate for vascular targeted and/or antiangiogenic approaches in cancer therapy. Magic roundabout is expressed in areas of active angiogenesis in tumours, but seldom detected in normal tissues. The 'natural ligand' of Magic roundabout is as yet unknown. However, its soluble extracellular domain was shown to inhibit endothelial cell sprouting and to block bFGF- and VEGF-mediated angiogenesis in classical *in vivo* angiogenesis assays.

The challenge of giving the final talk of the meeting fell to **Ralf Adams** (Cancer Research UK, London), who presented compelling data implicating ephrinB2 in angiogenesis and vascular development. Using elegant tissue-specific mutant mice, he found that ephrinB2 was indispensible for the correct formation of the endothelial lining of blood vessels. When ephrinB2 was knocked out specifically in perivascular cells, the mutant mice died at birth and were found to have dilated, haemorrhagic vessels and extensive oedema.

Kaye Williams
University of Manchester

Book reviews

Molecular Biology of the Cell: Fourth Edition, A Problems Approach

John Wilson and Tim Hunt

This problems approach companion accompanies the fourth edition of Molecular Biology of The Cell (MBoC), delving deeper into the wide range of cell biology topics covered in the parent textbook. The style and content are very well organised and presented, with the format following that of MBoC, making the book easy to use as chapters are the same in both.

Each chapter consists of experimental questions and problems that encourage problem solving and lateral thinking, accompanied by answers at the back of the book in a separate section. Only half of the answers are provided, with the rest available to lecturers and tutors on request. Although a great idea for lecturers setting exam questions and tutorials, it may make the task of self-study quite frustrating when the answer isn't available. In this respect, I think that the book would be more useful for lecturers teaching students than for students studying alone. Although there are enough questions in each chapter to provoke learning and understanding, if the book is used in this way.

Overall, I found the experimental questions very interesting and thought provoking and especially enjoyed the opening chapters dealing with the basics of biology and genomic diversity. This is a wonderful way to encourage thinking and understanding rather than rote learning, and provides a valuable treasure of information on experimental design and evolution of ideas that has contributed to scientific understanding so far. The authors have surpassed their task of introducing readers to the experimental foundations of cell and molecular biology.

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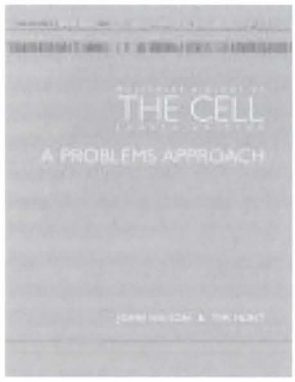


Molecular Biology of the Cell: Fourth Edition, A Problems Approach
John Wilson and Tim Hunt
Garland Science 0815335776
550 pp, September 2002

Statistical Analysis of Gene Expression Microarray Data
Edited by Terry Speed
Series: Interdisciplinary Statistics
Volume 11
Chapman & Hall /CRC
1584883278
March 2003

Statistical Analysis of Gene Expression Microarray Data

Edited by Terry Speed

The book covers the main aspect of microarray analysis: design signal extraction, classification and clustering. Each chapter is an independent assay that focuses on one of these aspects.

Chapter 1 describes the different types of model used for the analysis of the gene expression signal from microarray experiments. It is divided in two parts describing oligonucleotide and cDNA arrays. Although the chapter is very technical in addressing all the statistical issues arising when dealing with this type of data, it remains introductory. It is a good starting point for readers who are new to the subject but it would require some integration with more literature for readers who are looking for more specific details. There is a small background introduction for both oligonucleotide and cDNA technologies, enough for understanding the numerical and statistical problems that affect this type of data.

Chapter 2 contains a clear summary of possible experimental designs for microarray experiments. It is very important for the success of the microarray analysis to have an appropriate experimental design. This chapter analyses each experimental design, explaining what the implications are in the downstream analysis of the gene expression data. It is an important guide when planning new experiments.

The last two chapters focus on classification and clustering. They are both comprehensive with clear examples and an overview of the different methods and algorithms. These chapters are particularly important for the downstream analysis of the data and require a technical background to be fully understood.

Overall, the book is a very nice introduction to microarray data analysis. It is rather technical and might be difficult for biologists but it is a very good guide for biomathematicians, bioinformaticians and computer scientists working with biological data and approaching the microarray world for the first time.

Marta Milo, Sheffield

From Genes to Genomes: Concepts and Applications of DNA Technology

Jeremy W. Dale, Malcolm von Schantz

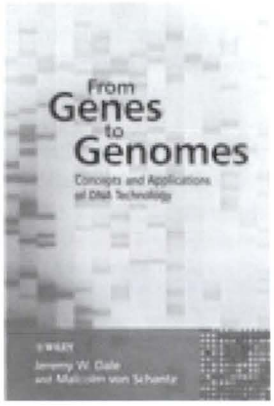
My bookshelves are packed with an abundance of dated textbooks that cover DNA technology and genetics. The relentless advance of DNA technology leads topics once considered cutting edge to be filtered down the curriculum and ultimately become routine lecture material to the lowly undergraduate. Hence, textbooks have the unenviable task of constantly and succinctly describing this ever-increasing knowledge in manageable, understandable portions. *Genes to Genomes* is just such a book, covering much of the same ground as previous titles, but going further on contemporary topics like transgenics, sequence comparison and analysis of variation.

The title is at first misleading, suggesting an explanation of the relationship between the single gene to its immediate surrounding regulatory elements and the relationship of the gene within the genome, DNA packaging and how the character of this packaging has a direct impact on gene regulation.

The subtitle 'Concepts and Applications of DNA Technology' reveals the true nature of the book. It opens with a brief synopsis of the basic concepts of molecular biology, concentrating on techniques surrounding gene cloning, before moving on to describe key molecular methods and how they fit together. After the cloning and study of individual genes, broader topics are discussed, such as sequencing of whole genomes, genetic variation and the analysis of genome-wide information. Finally, the book considers some of the applications of these techniques in biotechnology, medicine and agriculture, as well as in research that is causing the current explosion of knowledge across the biological sciences.

All the main points are covered in sufficient detail, without being overly brief or going into too much depth, while the accompanying diagrams, although not eye catching, are certainly clear and simple. However, the bibliography falls well short of expectations, ultimately depriving the reader of more specific insights into their particular areas of interest.

When compared to the some of the more overbearing super-dense books that typically litter the lab and office, it is a welcome change that at only 360 A5 pages, it can be carried easily.



From Genes to Genomes: Concepts and Applications of DNA Technology
Jeremy W. Dale, Malcolm von Schantz
ISBN: 0-471-49783-5
Paperback, 372 pages
August 2002, £24.95

Consequently, the more proletarian scientist will be more attracted to, and perhaps more importantly will be able to read through, this book without feeling too out of depth. Furthermore, an accompanying web site should allow the authors to keep their audience up to date in the areas that are prone to change most rapidly between successive editions.

In summary, *From Genes to Genomes* is a concise well-written, up to date textbook that provides a balanced coverage of traditional and contemporary topics.

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Mouse Development: Patterning, Morphogenesis, and Organogenesis

Janet Rossant and Patrick P.L. Tam

This is an impressive collection of reviews covering many actively researched areas of mouse development. It contains 23 chapters, involving more than 50 authors. Those with experience of editing a multi-author volume will appreciate the effort involved in delivering such a tome to the press.

Janet Rossant and Patrick Tam have not only marshalled a stellar collection of authors but have managed to do this in style. The chapters are divided into three sections: 'Establishment of body patterns', 'Lineage specification and differentiation' and 'Organogenesis'. This allows for holistic views of processes (e.g. fertilization, asymmetry, gastrulation) as well as separate organ systems. Each section is drawn together by a brief introduction from the editors.

The book maintains a remarkably uniform style throughout, with each developmental system carefully explained in both anatomical and molecular detail. Most chapters end with some consideration of the remaining questions and future directions of the field. It is unfortunate that the appearance of the book is marred by poor reproduction of some of the figures.

While the scope of the book is wide-ranging it is not comprehensive. Indeed, for a comprehensive

Mouse Development: Patterning, Morphogenesis, and Organogenesis
Janet Rossant and Patrick P.L. Tam
Academic Press, 2002
0-12-597951-7

description of mouse development we already have the definitive reference by Matt Kaufman and Jonathan Bard, *The Anatomical Basis of Mouse Development*. Instead, *Mouse Development* tackles a more selective range of topics and includes the additional detail of our molecular understanding of each system. This means that some readers will be frustrated by the gaps in the book's coverage. For example, I could find no account of adrenal gland, thymus, spleen, adipose or mammary gland development. I would also have liked to see a coherent treatment of growth (fetal and placental) and perhaps of the epigenetic changes that occur during mouse development. It is, however, only fair to point out that these quibbles reflect my own interests and that the book does not pretend to be comprehensive in its coverage.

I found myself wondering "who is this book for?" It clearly does not presume to compete with the general developmental biology texts but is aimed at those using the mouse and related organisms in their research. Assuming your favourite developmental system is covered, it will certainly be a nice volume to hand to arriving graduate students and post-docs new to your specialist field. You will almost certainly be able to find review articles in your area that are more up-to-date but many will not have the scope afforded by these book chapters to span both anatomical and molecular aspects of a given developmental system.

Books reporting on dynamic fields of research are inevitably dated by the time they appear on the shelf but in *Mouse Development* this is offset by having in a single volume a superb collection of articles with a broad span of the subject area. For this reason, I imagine that the natural home for this book need not be restricted to those focused primarily on mouse development. The copy sent to me was quickly appropriated and passed around the lab. It came back with a collection of bookmarks that indicate areas peripheral to our main interests. Anyone working with transgenic and knockout models for any length of time will have found themselves drawn into areas that are new to them and this is a good reason for having this book to hand.

In summary, this will be a welcome addition to the bookshelf of most mouse labs and will be a useful point of reference to many of those studying other vertebrates.

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Responsible Conduct of Research

Adil E. Shamoo, David B. Resnik

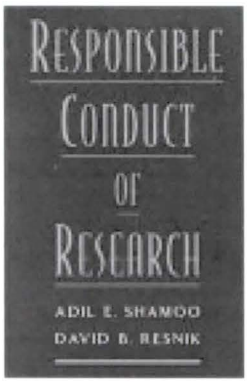
At the 2003 British Association Festival of Science, Colin Blakemore, Professor of Physiology at Oxford University, called a press conference to highlight what can go wrong in the process of science publication. He referred to a paper published in *Science* by a group led by George Ricaurte of Johns Hopkins University in Baltimore. The paper had dramatic findings - monkeys injected with 'recreational doses' of ecstasy were found to develop symptoms similar to those of Parkinson's disease. The study was widely reported by the world's media and may have influenced an 'anti-rave' act being debated in US congress at the time. However, there were problems with the study. A vial had been mislabelled and the monkeys had been given methamphetamine, not ecstasy. Consequently, the paper was retracted.

The mislabelled vial apart, there were already serious problems with the study. It was unclear whether the dose given to the monkeys would accurately reflect the recreational dose taken by humans. After the initial injection, two animals died and one was removed from the study, which is clearly not something which typically happens to club goers who have taken an ecstasy tablet. This should have been picked up during peer review.

The way the paper was reported in a press release was also at fault. A word had been accidentally altered – instead of suggesting that 40% of a type of neuron had been 'damaged' by the drug, it read that the neurons had been 'destroyed'. The mistake wasn't picked up and the resulting press release suggested much more dramatic findings than the paper had reported.

In this case, many things went wrong. The methods of research were unreliable, the peer review process did not detect basic errors in the study, and the way the study was billed to the media was inaccurate. Who is to blame for these errors? How can problems like this be avoided in the future? This is the type of question that *Responsible Conduct of Research* aims to discuss. Shamoo and Resnick have identified the ethical dilemmas that are intrinsic to carrying out research – how you get your data, analyse it and present it; how much responsibility you have for it; how it is peer reviewed and published; how the research is funded. All these issues have ethical implications for scientific research, whatever the method, area or topic.

The authors are well qualified to discuss ethics in research. Shamoo is the founder and editor-in-chief of the journal *Accountability in Research* and is



Responsible Conduct of Research
Adil E. Shamoo, David B. Resnik
Oxford University Press Inc, USA
0195148460 358 pp
October, 2002

a member of the Applied Professional Ethics faculty at the University of Maryland. Resnick is an ethicist who has taught the history and philosophy of science and is author of *The Ethics of Science: An Introduction*. Both have an impressive publication record. It is perhaps because of their academic ethics background that the book can feel weighty and dry in parts. If this book is to be a guide for the general researcher, it could stand to lose some detail and take a more applied approach.

Wading through the detail is, however, worth the effort, as some of the information is fascinating. The section on peer review in particular is interesting and informative. Did you know, for example, that studies have shown that peer review for grant applications may disfavour researchers from certain geographic areas and that grant awards are lower for women than for men? The section on misconduct is also worthy of note. What constitutes misconduct in research? If you are aware of misconduct among colleagues, what are your responsibilities? The chapter suggests that misconduct is more of a problem than is currently recognised by the scientific community. For example, a 1993 survey of science students and faculty members estimated that the incidence of questionable research was between 6 and 12%.

So how much of an understanding of ethics should a biologist have? The opening chapter of this book tells us that the US National Institutes of Health require scientists to be exposed to research-related ethics issues. This is probably also the case for all British research councils. The book is written for an American audience: it would be nice to have discussion of the ethical requirements of equivalent British research councils, government and non-government organisations.

Responsible Conduct of Research was published at the beginning of 2003 and can, therefore, provide the reader with an up to date view of ethics in research. The themes are very relevant to modern scientific horizons – there are chapters on intellectual property, collaboration between academia and private industry, and genetic and human reproduction. With biological ethics issues making headline news – Colin Blakemore's criticism of the Ricaute study was reported by *The Times* and *The Daily Telegraph* – it is even more important for the researcher to be well versed in ethics. Although this may not be a book that is easy to read from cover to cover, its topical, stand-alone chapters can be dipped into to supply information as necessary.

Claire Bithell
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Books for review

Fancy reviewing a book? If so, choose one from the selection listed below. Alternatively, if there is a book you would like to review that is not included here, contact me (jmarsh@wiley.co.uk) and I will request a review copy from the publisher.

Analysis of Genes and Genomes *Reece*, Wiley

Biochemistry and Molecular Biology of Plants
Buchanan, Gruissem and Jones, Wiley

Essential Cell Biology Volume 1 Cell structure *Davey, Lord*, Oxford University Press

Essential Cell Biology Volume 2 Cell function *Davey, Lord*, Oxford University Press

Principles of Genome Analysis and Genomics
Primrose & Twyman, Blackwell Science

Domains in Integrins *Gullberg*, Kluwer Academic/Plenum

Model Organisms in Drug Discovery *Carroll & Fitzgerald*, Wiley

Cell Motility: from molecules to organisms *Ridley, Clark, Peckham*, Wiley

Molecular Biology in Cellular Pathology *Crocker & Murray*, Wiley

Advanced Genetic Analysis, *Hawley & Walker*, Blackwell Science

Chromosomes: organization and function, *Sumner*, Blackwell Science

Molecular Infection Biology: Interactions between microorganisms and cells *Hacker & Heesemann, Wiley*

Culture of Epithelial Cells, 2nd edition *Freshney*, Wiley

Epigenesis Versus Preformation During Mammalian Development
Gardner, Solter & Surani, The Royal Society

Fundamental Bacterial Genetics
Trun & Trempy, Blackwell Publishing

BSCB Annual Spring Meeting
Cell Structure and Dynamics
31 March – 3 April 2004 University of Kent at Canterbury

General information

Venue
The conference will take place at the University of Kent in Canterbury. UKC is self-contained, so delegates are within walking distance of a cinema, theatre, sports centre, nightclub, library, banks, shops, bistros, bars, public access terminals, medical centre, bus-stops and launderettes. Canterbury city centre is only 20 minutes walk away, or on a direct bus route.

Accommodation
When registering for the conference, a full residential package is available, from which you may choose standard accommodation or en-suite. The accommodation is situated in the high standard university rooms on campus within Becket Court and Eliot College. Standard accommodation comprises a study bedroom with hand basin and adjacent shower, bathroom and toilet facilities. No more than 6–8 bedrooms share these adjacent facilities. Becket Court is a recently completed separate accommodation unit with 103 en-suite bedrooms, comfortably furnished to a good standard.

Meals and social events
Lunches will be provided each day of the conference alongside the trade exhibition and poster displays. Dinner will be served each evening. On Friday evening, delegates have the option to attend the Conference Dinner Dance, during which poster prizes will be awarded. There will be two special lunches, which are parallel to the main lunch and are optional to delegates. The Careers in Cell Biology Lunch on Thursday "There is Life After a PhD" and the Women in Cell Biology Lunch on Friday "Women in Science". If you wish to attend these lunches, you must express your interest on the on-line registration form.

Car parking
The campus has car parking space for 1200 cars. Car parking on campus is free for conference delegates; however a parking permit must be obtained on registration.

How to book
To register for the conference, book accommodation, social events, special lunches and car parking, please use the on-line registration form.

Special talk on future fundng for biological science in the UK
Lord Sainsbury will be giving a talk on Thursday evening 1st April 2004,on future funding for biological science in the UK, to which all PhD students and Post Docs are openly invited.

Abstract submission and posters
Abstracts are invited for poster presentations. Posters will be on display for the duration of the conference and there will be designated poster sessions at which delegates will view and discuss posters with presenters. There will also be opportunities for poster abstracts to be chosen for a short talk during the meeting. Student authors may elect to be put forward for the BSCB Student Poster Prize.

To submit an abstract, please use the on-line abstract submission form. The deadline for submission is 31st January 2004.

Key web addresses

University of Kent, Canterbury www.kent.ac.uk

Registration form www.procon-events.com/bscb04/registration.htm

Abstract submission
www.kcl.ac.uk/kis/schools/life_sciences/biomed/bscb/meetings/kent2004_abstracts.html

Travel information and maps of how to get to the University
www.kent.ac.uk/locations/canterbury/map1.html

Campus map
www.kent.ac.uk/locations/canterbury/navmap.html?mapdirect=true

BSCB Spring Meeting 2004: Programme

Wednesday 31 March

16.00 – 21.00 Registration in Eliot Dining Hall Foyer area
18.00 – 19.30 Self Service Dinner in Eliot Dining Hall

Thursday 1 April

07.30 – 09.00 Breakfast in Eliot Dining Hall
from 08.00 Registration and Coffee – Rutherford Dining Hall Foyer

Session 1: **Protein Modification and Degradation**
Chairman: Ron Hay, St Andrews, UK
Venue: Cornwallis Lecture Theatre

08.30 **Stefan Jentsch, Munich, Germany**
Ubiquitin, SUMO and DNA repair

09.00 Short Talk chosen from abstracts

09.20 **Steve Ley, London, UK**
Regulation of ERK MAP kinase activation in innate immune responses

09.50 – 10.30 Trade Exhibition with Tea, coffee & posters
Rutherford Dining Hall

10.30 **Aaron Ciechanover, Haifa, Israel**
The ubiquitin proteolytic system: novel, non-canonical modes of substrate targeting

11.00 Short Talk chosen from abstracts

11.20 **Peter J Ratcliffe, Oxford, UK**
HIF prolyl and asparaginyl hydroxylases in the biological response to intracellular O_2 levels

12.00-13.30 Lunch/Poster Viewing and Exhibition
Rutherford Dining Hall
Careers in Cell Biology Lunch – Darwin Suite 3

Session 2: **Cytoskeleton & cell polarity**
Chairman: Patrick Hussey, Durham, UK
Venue: Gulbenkian Lecture Theatre

08.30 **Laura Machesky, Birmingham, UK**
Signalling to actin dynamics

09.00 Short Talk chosen from abstracts

09.20 **Patrick Hussey, Durham, UK**
Actin binding proteins, ADF and AIP1, in tip-growing cells

09.50 – 10.30 Trade Exhibition with Tea, coffee & posters
Rutherford Dining Hall

10.30 **Sandrine Etienne-Mandeville, Paris, France**
Title to be advised

11.00 Short Talk chosen from abstracts

11.20 **Michel Bornens, Paris, France**
Cell adhesion and the control of the cell division axis

Session 3: **Biological Imaging**
Chairman: Jason Swedlow, Dundee, UK
Venue: Cornwallis Lecture Theatre

13.30 **Jan Ellenberg, Heidelberg, Germany**
Title to be advised

14.00 Short Talk chosen from abstracts

14.20 **Kees Weijer, Dundee, UK**
Chemotaxis during gastrulation in the chick

14.50 –15.30 Trade Exhibition with Tea, coffee & posters
Rutherford Dining Hall

Session 4: **Mechanosensation and organogenesis**
Chairman: Michael Whitaker, Newcastle, UK
Venue: Gulbenkian Lecture Theatre

13.30 **Jing Zhou, Harvard, USA**
What do the kidney epithelia know about flow

14.00 Short Talk chosen from abstracts

14.20 **Maureen Barr, Wisconsin, USA**
Title to be advised

14.50 –15.30 Trade Exhibition with Tea, coffee & posters
Rutherford Dining Hall

15.30	**Guy Rutter, Bristol, UK** The dynamics of insulin exocytosis at the single cell level
16.00	Short Talk chosen from abstracts
16.20	**Oliver Griesbeck, Martinsreid, Germany** Title to be advised
17.00 – 17.50	**Plenary Lecture – Lord Sainsbury** Scientific Research Priorities for the UK: The Government perspective
Chairman:	Fiona Watt, London, UK
Venue:	Cornwallis Lecture Theatre
18.00 – 19.00	**Hooke Medal Lecture – Elmar Schieber**
Chairman:	Fiona Watt, London, UK
Venue:	Cornwallis Lecture Theatre
19.00 – 19.30	**AGM** Cornwallis Lecture Theatre
19.30 – 21.00	Dinner in Eliot Dining Hall

15.30	**Judith Goodship, Newcastle, UK** Title to be advised
16.00	Short Talk chosen from abstracts
16.20	**Helle Praetorius, Aarhus, The Netherlands** The primary cilium senses flow in Madin-Darby canine kidney cells

Friday 2 April

07.30 – 09.00	Breakfast in Eliot Dining Hall
from 08.00	Registration and Coffee – Rutherford Dining Hall Foyer
08.30 – 09.20	**Plenary Lecture: David Spector, Cold Spring Harbour**
Chairman:	Jason Swedlow, Dundee, UK
Venue:	Cornwallis Lecture Theatre

Session 5:	**Nuclear Lamins in cell biology and disease**
Chairman:	Chris Hutchinson, Durham, UK
Venue:	Cornwallis Lecture Theatre
09.30	**Giselle Bonne, Paris, France** Title to be advised
10.00	Short Talk chosen from abstracts
10.20 – 11.00	Trade Exhibition with Tea, coffee & posters Rutherford Dining Hall
11.00	**Sue Shackleton, Leicester, UK** Lamin A interacting proteins and their potential role in laminopathies
11.30	**Jos Broers, Maastricht, Germany** Title to be advised
12.00	Short Talk chosen from abstracts
12.20	**Roland Foisner, Vienna, Austria** Cell cycle-dependent dynamics and functions of lamina proteins
12.50 – 14.20	Lunch/Poster Viewing and Exhibition – Rutherford Dining Hall **Women in Cell Biology Lunch – Darwin Suite 3** **Chairman:** Margarete Heck, Edinburgh, UK

Session 6:	**Dynamics of cell-matrix interactions**
Chairman:	Nick Brown, Cambridge, UK
Venue:	Gulbenkian Lecture Theatre
09.30	**Michael Sheetz, New York, USA** Force sensing, slip bonds and periodic contractions in lamellipodia
10.00	Short Talk chosen from abstracts
10.20 – 11.00	Trade Exhibition with Tea, coffee & posters Rutherford Dining Hall
11.00	**Kairbaan Hodivala-Dilke, London, UK** Integrins and growth factor signalling control
11.30	**Don Moerman, Vancouver, USA** Title to be advised
12.00	Short Talk chosen from abstracts
12.20	**Mark Ginsberg, San Diego, USA** The ins and outs of adhesive signaling

Session 7: **Control of protein sorting**
Chairman: Hugh Pelham, Cambridge, UK
Venue: Cornwallis Lecture Theatre

14.20 **Juan Bonifacino, NIH, Bethesda, USA**
Mechanisms of protein sorting to lysosomes

14.50 Short Talk chosen from abstracts

15.10 **Harald Stenmark, Norway**
Regulation of endocytic receptor trafficking and signalling by phosphoinositides

15.10 –15.50 Trade Exhibition with Tea, coffee & posters
Rutherford Dining Hall

15.50 **Gillian Griffiths, Oxford, UK**
Title to be advised

16.20 Short Talk chosen from abstracts

16.40 **Sean Munro, Cambridge, UK**
Arf-like GTPases and membrane traffic in the Golgi apparatus

17.15 – 18.15 Poster Presentations – core time for presenters
Rutherford Dining Hall

19.30 –00.00 Conference Dinner in Eliot Dining Hall
with entertainment and late bar

Session 8: **Dynamics of cell-cell adhesion**
Chairman: Paul Martin, London, UK
Venue: Gulbenkian Lecture Theatre

14.20 **Valerie Vasioukhin, Seattle, USA**
Title to be advised

14.50 Short Talk chosen from abstracts

15.10 **Walter Birchmeier, Berlin, Germany**
Title to be advised

15.10 – 15.50 Trade Exhibition with Tea, coffee & posters
Rutherford Dining Hall

15.50 **Kate Nobes, Bristol, UK**
Modulation of cell-cell contacts by Eph receptors and ephrins

16.20 Short Talk chosen from abstracts

16.40 TBA, UK
Title to be advised

Saturday 3 April

07.30 – 09.00 Breakfast in Eliot Dining Hall
from 08.00 Registration and Coffee – Rutherford Dining Hall Foyer

08.30 – 09.20 **Borden Lecture: Randy Schekman, Berkeley, USA**
Chairman: Hugh Pelham, Cambridge, UK
Venue: Cornwallis Lecture Theatre

Session 9: **Leaving Mitosis**
Chairman: Bill Earnshaw, Edinburgh, UK
Venue: Cornwallis Lecture Theatre

09.30 Michael Glotzer, Vienna, Austria
Assembly of the central spindle and its function in cytokinesis

10.00 Short Talk chosen from abstracts

10.20 – 11.00 Trade Exhibition with Tea, coffee & posters
Rutherford Dining Hall

11.00 Maurizio Gatti, Rome, Italy
Context of human diseases

11.30 Iain Hagan, Manchester, UK
Cell cycle control and the spindle pole body in fission yeast.

12.00 Short Talk chosen from abstracts

12.20 Karen Oegema, San Diego, USA
Title to be advised

12.50 - 14.20 Lunch/Poster Viewing and Exhibition
Rutherford Dining Hall

Departure

Session 10: **Cellular microenvironment**
Chairman: Fiona Watt, London, UK
Venue: Gulbenkian Lecture Theatre

09.30 **Janet Heasman, Cincinati, USA**

10.00 Short Talk chosen from abstracts

10.20 – 11.00 Trade Exhibition with Tea, coffee & posters
Rutherford Dining Hall

11.00 **Zena Werb, San Francisco, USA**
Role of the extracellular microenvironment on mammary gland development

11.30 **Caroline Damsky, San Francisco, USA**
Title to be advised

12.00 Short Talk chosen from abstracts

12.20 **Mina Bissell, Berkeley, USA**
Structural basis of tissue specificity in normal and malignant breast

Other forthcoming meetings

2004

The BSCB Spring Meeting: Cell Structure and Dynamics
31 March–3 April 2004
University of Kent at Canterbury
See page 23

Nuclear Organization in Development and Disease
30 January 2004
Geological Society, London W1
Novartis Foundation
openmtg@novartisfound.org.uk

Stem Cells: Nuclear Reprogramming and Therapeutic Applications
5 March 2004
Geological Society, London W1
Novartis Foundation
openmtg@novartisfound.org.uk

Human Genome Meeting 2004
4–7 April 2004
Berlin, Germany
http://hgm2004.hgu.mrc.ac.uk

The hERG Cardiac Potassium Channel: Structure, Function and Drug-induced Long-QT Syndrome
7 May 2004
Geological Society, London W1
Novartis Foundation
openmtg@novartisfound.org.uk

2004 FASEB Summer Research Conference: Thrombospondins and other Modulatory Adhesion Molecules in Tissue Organisation and Homeostasis
5-10 June 2004
Callaway Gardens, Pine Mountain, Georgia
www.faseb.org

The Genetics of Autoimmunity
25 June 2004
Geological Society, London W1
Novartis Foundation
openmtg@novartisfound.org.uk

Molecular Mechanisms Influencing Aggressive Behaviours
23 July 2004
Royal Society of Medicine, London
Novartis Foundation
openmtg@novartisfound.org.uk

BioScience2004 - From Molecules to Organisms
18–22 July 2004, SECC Glasgow
info@BioScience2004.org

12th International Conference on Intelligent Systems for Molecular Biology and 3rd European Conference on Computational Biology 2004
31 July – 5 August 2004
SECC, Glasgow
www.iscb.org/ismbeccb2004

Cell Cycle Regulation of Meiotic Division
12-14 September 2004
Newcastle University
Organiser: Mary Herbert (Newcastle)

2005

BSCB Annual Spring Meeting: The Asymmetric Cell
6–9 April 2005
Warwick University
Organiser: Jordan Raff
Joint with BSDB

2006

BSCB Spring 2006 meeting
(Mon 20) Tues 21 – Thurs 23 March 2006
York
We are pleased to announce this meeting will be held jointly with the BSDB.

Honor Fell Travel Awards

Jointly funded by the BSCB and the Company of Biologists

Honor Fell Travel awards are made to provide financial support for younger BSCB members at the beginning of their research careers to attend meetings. Applications are considered for any meeting relevant to cell biology. The amount of the award depends on the location of the meeting. Awards will be up to £300 for UK meetings (except for BSCB Spring Meeting for which the registration and accommodation costs will be made, even in excess of £300), up to £400 for European meetings and up to £500 for meetings in the rest of the world.

Awards are made throughout the year. The following rules apply:

- Awards are not normally made to applicants over 35 years of age
- No applicant will receive more than one award per year and three in toto
- The applicant must be contributing a poster or a talk.

Applications should be sent to Kathryn Ayscough, IBLS, Davidson Building, University of Glasgow, G12 8QQ.

All applications must contain the following:

- **the completed and signed application form (below)**
- **a copy of the abstract being presented**
- **a copy of the completed meeting registration form**

First-year PhD students should send a copy of their BSCB membership application.

Application for an Honor Fell travel award

Full name and Work address

(write clearly – this will be used as a return label)

.....

.....

.....

.....

.....

E-mail address: .....

Age: .....

BSCB Membership number: .....

The years of previous Honor Fell awards:

.....

Degrees (with dates): .....

.....

Present position: .....

.....

Key publications (2) or research interests:

.....

.....

.....

Number of meetings attended last year:

.....

Meeting for which application is made (title, place, and date):

.....

.....

.....

Estimated expenses: Travel: .....

Subsistence: .....

Registration: .....

Have you submitted any other applications for financial support? YES NO (delete as applicable). If YES, give details including source and whether these monies are known to be forthcoming:

.....

.....

Supporting statement by Head of Department:

This applicant requires these funds and is worthy of support. I recognise that in the event of non-attendance at the meeting, the applicant must return the monies to the BSCB and I accept the responsibility to reimburse BSCB if the applicant does not return the funds.

Signature: .....

Name: .....

Applicant's signature: .....

Name: .....

Undergraduate bursaries to attend the BSCB Spring Meeting

Administered through the Honor Fell Travel Award Scheme
Jointly funded by the BSCB and the Company of Biologists

Undergraduate Bursaries are made to provide financial support for undergraduates currently studying cell biology or a related degree subject to attend the BSCB Spring Meeting. The award will cover the registration and accommodation costs of attendance. Travel costs are expected to be met by the University that the undergraduate attends.

The following rules apply:

- Awards are made to undergraduates in their final year of study.
- Applicants must be studying for a Cell Biology or related degree.
- Applications must be accompanied by a half page justification from the student **and** by a supporting statement from the supervisor of studies or course organiser.

Applications should be sent to: Kathryn Ayscough, IBLS, Davidson Building, University of Glasgow, G12 8QQ.

All applications must contain:

- **the completed and signed application form (below)**
- **statements from both the student and course organiser.**

- The statement from the student should include details on why they wish to attend, what they hope to gain and also aspects of cell biology that to date they have found interesting.
- The statement from the course co-ordinator should indicate the course being undertaken by the student and reflect the calibre of the student, their enthusiasm for the subject and why they believe the student will benefit from the experience of attending the meeting.

Application for an undergraduate Honor Fell travel award

Full name and Work address

(write clearly – this will be used as a return label)

.....

.....

.....

.....

.....

E-mail address: .....

Age: .....

Institution attended: .....

Degree course: .....

.....

Main cell biological interests: .....

.....

Supporting statement by Head of Department or Course Co-ordinator: This applicant requires these funds and is worthy of support. The University/Department also agrees to pay the travel costs for the named undergraduate to attend the meeting.

Signature: .....

Name: .....

Applicant's

signature: .....

Name: .....

DEADLINE FOR APPLICATIONS: 31 January 2004

Application to join the BSCB

Please complete and return along with a signed Direct Debit mandate to:
Margaret Clements, Department of Zoology, Downing Street, Cambridge, CB2 3EJ.

Name: ..... Mr/Ms/Mrs/Dr/Prof

Position: ..... Male/Female

Academic qualifications: .....

Email: .....

Telephone: .....

Fax: .....

Address: .....

.....

..... Postcode: .....

Research interests: .....

.....

Membership of other societies:

.....

BSCB Member	Proposer	Seconder
Name:	.....	.....
Membership Number:	.....	.....
Signature:	.....	.....

Applicants without proposers should enclose a brief CV

The society has a searchable database of its members on the BSCB web page. This list is not sold or distributed in any other way. Your details will be included only if you tick this box ☐

Applicant's signature: ..... Date: .....

INSTRUCTIONS TO YOUR BANK/BUILDING SOCIETY TO PAY DIRECT DEBITS

British Society for Cell Biology

DIRECT Debit

Please complete parts 1, 2, 3, 4 and 6 to instruct your branch to make payments directly from your account. Then return the form to: British Society for Cell Biology, c/o Margaret Clements, Department of Zoology, Downing Street, Cambridge, CB2 3EJ.

To The Manager, Bank/Building Society

.....

Address

.....

.....

..... Postcode .....

Originator's identification number | 9 | 4 | 1 | 4 | 5 | 1 |

FOR BSCB USE ONLY

This is not part of the instruction to your bank/building society

5. Originator's reference number (for office use only) BRITSO | | | | |

1. Please write the full postal address of your branch in the box above.

2. Name of account holder

.....

3. Account number | | | | | | | | |

4. Sort code | | | — | | | — | | |

Banks/Building Societies may refuse to accept instructions to pay direct debits from some types of account.

6. Instructions to the Bank or Building Society

Please pay the British Society for Cell Biology Direct Debits from the account detailed on this Instruction subject to the safeguards assured by the Direct Debit Guarantee.

Signature .....

Date .....

This guarantee should be detached and retained by the payee

The Direct Debit guarantee

- This guarantee is offered by all Banks and Building Societies that take part in the Direct Debit scheme. The efficiency and security of the scheme is monitored and protected by your own Bank or Building Society.
- If the amounts to be paid or the payment dates change, the BSCB will notify at least 14 days in advance of your account being debited or as otherwise agreed.
- If an error is made by the BSCB or by your Bank/Building Society, you are guaranteed a full and immediate refund from your branch of the amount paid.
- You can cancel a Direct Debit at any time, by writing to your Bank or Building Society. Please also send a copy of the letter to the BSCB.

British Society for Cell Biology
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Appointed 2000; retires 2006

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Appointed 2001; retires 2007

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Honor Fell travel awards
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Appointed 1998; retires 2004

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Appointed 1999; retires 2005

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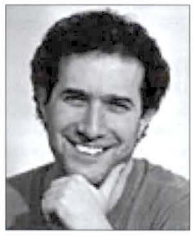
Appointed 2002; re-election due 2004



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Appointed 2002; re-election due 2005

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British Society for Cell Biology: Financial Statements for the year ended 31 December 2002

Executive Committee's report for the year ended 31 December 2002

The Executive Committee (who are the trustees of the Society for the purposes of charity law) have pleasure in presenting their report and the audited accounts of the Society for the year ended 31 December 2002. These accounts have been prepared in accordance with the Charities Act 1993, the Statement of Recommended Practice 'Accounting & Reporting by Charities' (SORP 2000); and the constitution of the Society.

Officers and committee
Under the constitution of the Society the Officers of the Society are a President, a Secretary, a Treasurer, a Meetings Convenor, a Membership Secretary, a Newsletter Editor and a Website Co-ordinator. There is also an Executive Committee of the Society consisting of the Officers and twelve other elected members.

The Executive Committee is elected at the Annual General Meeting, with the Officers being elected by the Executive Committee and the President being nominated by the Executive Committee.

The Executive Committee prepares the Agenda for meetings of the Society, and between meetings acts as necessary on behalf of the Society; reporting on any such actions to the next meeting of the Society.

The individuals who served as officers and executive committee members during the year, and since the year-end, were as follows:

Dr. J. Adams (resigned 22/3/02)
Dr. K. Ayscough
Dr. L. Cramer (resigned 9/4/03)
Dr. W. Earnshaw
Dr. G. Griffiths (appointed 22/3/02)
Dr. C. Hawes (resigned 22/3/02)
Dr. K. Hodivala-Dilke (appointed 9/4/03)
Dr. S. Hughes (resigned 9/4/03)
Dr. R. Insall (resigned 22/3/02)
Prof. A. Lamond
Dr. P. Luzio
Dr. J. Marsh
Prof. M. Marsh (appointed 22/3/02)
Dr. I. Nathke (resigned 9/4/03)
Dr. A. Ng (appointed 9/4/03)
Dr. S. Nurrish (appointed 22/3/02)
Dr. J. Pines
Dr. R. Quinlan
Dr. J. Raff (appointed 22/3/02)
Dr. C. Streuli (resigned 9/4/03)
Dr. M. Way (appointed 22/3/02)
Dr. F. Watt
Prof. M. J. Whitaker
Dr. S. Winder (resigned 9/4/03)
The executive committee members in office at the date of this report are detailed on page 32.

Status & constitution
The Society is constituted under a constitution executed in 1965, and amended in 2002. The Society is a registered charity, number 265816.

Objects
The objects of the Society are to promote the advance of research in relation to all branches of cell biology and to encourage the interchange of information. The Society generally aims to fulfil these objects by organising and sponsoring two meetings each year on topics relevant to cell biology; issuing a twice yearly newsletter; and maintaining a website (www.bscb.org).

Review of Activities
In March 2002 the Society had a successful spring meeting in York (jointly with the British Society for Developmental Biology) with a total number of delegates of almost 500, well above expectations.

The Society also ran an additional meeting in July 2002 to honour Martin Raff (postponed from September 2001) and the Abercrombie meeting in September 2002, in Oxford.

Further details of reports of the Society's meetings throughout the year are to be found in the quarterly magazine, available on the Society's website.

The financial results of the Society are set out on page 35.

Reserves
The Executive Committee regularly reviews the reserves of the charity to ensure that sufficient liquid funds are available for the Society to meet its ongoing obligations. The reserves throughout the period have been adequate to fulfil this objective.

Investment Policy
The Executive Committees' policy at present is to invest in low-risk and reasonably liquid assets, so that funds are available to meet any unforeseen needs that arise as a consequence of meeting activities.

Risk assessment
The major risks to which the Society is exposed, as identified by the Executive Committee, are being reviewed. Certain systems are already in place to mitigate those risks and further systems are being established as necessary.

Executive Committee's Responsibilities
Charity law requires the Executive Committee to prepare financial statements for each financial year which give a true and fair view of the state of affairs of the Society and of the surplus or deficit for that period. In preparing those financial statements, the Executive Committee have:
- selected suitable accounting policies and then applied them consistently;
- made judgements and estimates that are reasonable and prudent;
- prepared the financial statements on the going concern basis unless it is inappropriate to assume that the Charity will continue in existence

The Executive Committee has overall responsibility for ensuring that the Society has an appropriate system of controls, financial and otherwise. It is also responsible for keeping proper accounting records which disclose with reasonable accuracy at any time the financial position of the Society. It is also responsible for safeguarding the assets of the Society and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

Governance and internal control
The Executive Committee is also responsible for implementing systems of internal control which provides reasonable assurance that:
- the Society is operating efficiently and effectively;
- its assets are safeguarded against unauthorised use or disposition;
- proper records are maintained and financial information used within the charity or for publication is reliable;
- the Society complies with relevant laws and regulations.

The systems of internal control are designed to provide reasonable, but not absolute, assurance against material misstatement or loss. They include:
- delegation of authority and segregation of duties;
- identification and management of risks.

Report of the independent auditors to the executive committe of the British Society for Cell Biology

We have audited the financial statements of The British Society for Cell Biology for the year ended 31 December 2002 which comprise of the Statement of Financial Activities, the Balance Sheet and the related notes. These financial statements have been prepared under the historical cost convention and the accounting policies set out therein.

This report is made solely to the Society's Executive Committee, as a body, in accordance with section 44 of the Charities Act 1993. Our audit work has been undertaken so that we might state to the Executive Committee those matters we are required to state to it in an auditors' report and for no other purpose. To the fullest extent permitted by law, we do not accept or assume responsibility to anyone other than the Society and the Society's Executive Committee as a body, for our audit work, for this report, or for the opinions we have formed.

Respective responsibilities of Executive Committee and auditors
The Executive Committee (who are the trustees of the Society for the purposes of charity law) are responsible for preparing the Executive Committee's Report and the financial statements in accordance with applicable law and United Kingdom Accounting Standards as set out in the Statement of Executive Committee's Responsibilities on page 34.

We have been appointed auditors under section 43 of the Charities Act 1993 and report in accordance with regulations made under section 44 of that Act. Our responsibility is to audit the financial statements in accordance with relevant legal and regulatory requirements and United Kingdom Auditing Standards.

We report to you our opinion as to whether the financial statements give a true and fair view and are properly prepared in accordance with the Charities Act 1993. We also report to you if, in our opinion, the Executive Committee's Report is not consistent with the financial statements, if the Society has not kept proper accounting records, or if we have not received all the information and explanations we require for our audit.

We read other information contained in the Executive Committee's Report, and consider whether it is consistent with the audited financial statements. We consider the implications for our report if we become aware of any apparent misstatements or material inconsistencies with the financial statements. Our responsibilities do not extend to any other information.

Basis of opinion
We conducted our audit in accordance with United Kingdom Auditing Standards issued by the Auditing Practices Board. An audit includes examination, on a test basis, of evidence relevant to the amounts and disclosures in the financial statements. It also includes an assessment of the significant estimates and judgements made by the Executive Committee in the preparation of the financial statements, and of whether the accounting policies are appropriate to the Society's circumstances, consistently applied and adequately disclosed.

We planned and performed our audit so as to obtain all the information and explanations which we considered necessary in order to provide us with sufficient evidence to give reasonable assurance that the financial statements are free from material misstatement, whether caused by fraud or other irregularity or error. In forming our opinion we also evaluated the overall adequacy of the presentation of information in the financial statements.

Opinion
In our opinion the financial statements give a true and fair view of the state of the Society's affairs as at 31 December 2002 and of its incoming resources and application of resources in the year then ended and have been properly prepared in accordance with the Charities Act 1993.

Jacob Cavenagh & Skeet
Chartered Accountants
and Registered Auditor
Acorn House
2 Greenhill Crescent
Watford
Herts WD18 8AH

Statement of financial activities for the year to 31 December 2002

	Unrestricted	2002 Restricted	Total	2001 Total
	£	£	£	£
Incoming resources				
Donations, legacies & similar incoming resources	30,642	20,000	50,642	72,134
Activities in furtherance of the charities objects				
Meetings	276,759	–	276,759	48,966
Subscriptions	24,486	–	24,486	22,307
Mailing list	428	–	428	2,749
Adverts and fliers	–	–	–	5003
Investment income	3,652	–	3652	4145
	335,967	20,000	355,967	155,304
Resources expended				
Cost of generating funds				
Publicity & Sponsorship costs	11,882		11,882	
Charitable expenditure				
Grants payable in furtherance of the charity's objects				
Honor Fell travel awards[2]	1,280	20,000	21,280	24,179
Costs of activities in furtherance of the charity's objects				
Costs of meetings	276,289	-	276,289	70,581
Newsletter costs	7,407	-	7,407	6,336
Website expenses	1,583	-	1,583	6,598
Management and administration[4]	11,485	-	11,485	8,578
Total resources expended	309,926	20,000	328,927	116,272
Net movement in funds for the year	26,041		26,041	39,032
Funds brought forward at 1 January	135,322	-	135,322	96,290
Funds carried forward at 31 December	161,363	-	161,363	135,322

Balance sheet as at 31 December 2002

	£	2002 £	£	2001 £
Current assets				
Debtors:				
Other debtors		**450**		–
Prepayments and accrued income		**7,735**		289
Cash at bank and in hand:				
National Savings Investment Account		**56,702**		54,326
HSBC Bank Accounts		**115,191**		114,423
		180,078		169,038
Less: Creditors falling due within one year				
Income received in advance	3,920		33,011	
Creditors and accruals	14,795		705	
		18,715		33,716
Net Assets		**161,363**		135,322
Funds				
Unrestricted funds		**161,363**		135,322
		161,363		135,322

Notes to the accounts for the year ended 31 December 2002

1. Accounting Policies

a) Basis of accounting

The financial statements are prepared under the historical cost convention and in accordance with applicable Accounting Standards; the Statement of Recommended Practice 'Accounting and Reporting by Charities' (issued October 2000) and the Charities Act 1993.

The Society has taken advantage of the exemption in Financial Reporting Standard 1 from producing a cash flow statement, on the grounds that it would have been a small company had it been a company incorporated under companies' legislation.

b) Funds

General unrestricted funds represent the funds of the Society that are not subject to any restrictions regarding their use and are available for application on the general purposes of the Society.

Restricted funds are those subject to specific trusts, which may be declared by the donor or with their authority. The restricted funds of the Society are restricted income funds which are expendable at the discretion of the Executive Committee in furtherance of some particular aspects of the activities of the Society.

c) Incoming Resources

Donations and similar incoming resources are accounted for when receivable. Subscriptions and mailing list sales represent amounts receivable during the year. Meetings income is recognised in the period when the meeting takes place and investment income and bank interest are the amounts receivable for the year.

d) Resources Expended

Expenditure represents purchases and expenses incurred during the year including irrecoverable VAT. All expenditure is recognised on an accruals basis, with advance expenditure for meetings being deferred until the period when the meeting takes place.

Transactions in foreign currency at translated at the rate ruling on the date of the transaction. Balances denominated in foreign currencies are retranslated at the year-end, with the gain or loss on retranslation going through the SOFA for the year.

2. Grants made

Honor Fell travel awards represent grants made to members to enable them to travel to meetings of the Society. During the year grants totaling £21,280 were made to 57 individuals, £20,000 of which being funded from the generous grant received from The Company of Biologists Limited, restricted for that purpose. No individual grants or travel awards exceeded £1,000 in the year.

3. Executive Committee members & Employees

No Executive Committee member or any person connected with them received, or is due to receive, any remuneration for the year directly or indirectly from the Society's funds.

11 Executive Committee members received a total of £2,406 in respect of reimbursed travel expenses during the year, as shown in note 4 (2001: £3,338). The Society has no employees.

4. Management and Administration expenses

Management and administration expenses are analysed as follows:

	2002 Unrestricted	2002 Restricted	2002 Total	2001 Total
	£	£	£	£
Secretarial	700	-	700	1,400
Executive Committee expenses	2,406	-	2,406	3,338
Subscriptions	3,703	-	3,703	530
Fax and Telephone	-	-	-	1,905
Bank charges	547	-	547	310
Exchange losses	830	-	830	-
Accountancy & Independent Exam	1,645	-	1,645	705
Auditors' remuneration: Audit	1,175	-	1,175	-
Accountancy	470	-	470	-
Miscellaneous	9	-	9	390
	11,485	-	11,485	8,578

The BSCB newsletter is published twice a year in June and December.

Submission:
If you have an idea for an article please e-mail the editor a brief outline first. Appropriate colour images are welcomed for consideration for the front cover.

It is preferable to send all articles, reports and images by e-mail (though alternatives can be arranged after contacting the editor). Attachments for text are best received in Microsoft Word and images as 200-300 dpi JPEG/TIFF or Photoshop files. Hard copy images can also be sent.

Submission of articles and images should be made to
Dr Joan Marsh, John Wiley & Sons, International House, Ealing Broadway Centre, London W5 5DB. Tel: 020 8326 3846. Fax: 020 8326 3802. e-mail: jmarsh@wiley.co.uk

Meetings:
Please note there is no charge to advertise a scientific or educational meeting. Please contact the editor with details of any meeting you wish to advertise.

Deadlines:
For the final version of articles and other materials and adverts is 1 April for publication in June and 1 October for publication in December.

Please note the first version of any material must be received by the editor at least 2 weeks prior to this deadline so that any changes can be made.

Advertising Information
Single advertisement:
Back cover Black and White £275; Colour £425
Inside front cover Black and White £275
Full inside page, black and white only £220
$^1/_2$ Inside page, black and white only £110
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Four advertisements, to cover two years. The costs are reduced by 30%.

Supply either on a zip disk or CD for Macintosh (Quark version 4, Quark version 3.32, JPG, TIF or PSD) with margins: top 26mm, left/right/bottom 20mm. Page size 218x280mm. Alternatively, supply film: single/four colour positive, right reading, emulsion down, screen 133x150.

For further information on commercial advertising contact: Margaret Clements, BSCB assistant, Department of Zoology, Cambridge University, Downing Street, Cambridge CB2 3EJ. Tel: +44 (0)1223 336655 Fax: +44 (0)1223 353980, e-mail: zoo-jeb01@lists.cam.ac.uk

Subscription information
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Student, school teacher, retired member £10
UK resident members NOT paying by direct debit:
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If you are still paying by standing order, please cancel it and set-up direct debit (form on p29). Those members who do not have a UK bank account should pay by bankers draft in pounds sterling payable to 'the British Society for Cell Biology'.

New members should complete an application form to join the BSCB (form on p28) and include it with their subscription dues. Send direct debit forms, bankers drafts and any membership application forms to Margaret Clements, Department of Zoology, Downing Street, Cambridge, CB2 3EJ.

Journals
BSCB members are entitled to a 25% discount from the individual subscription rate to all journals published by the **Company of Biologists**, and other discounts from other publishers. To take advantage of this offer, quote your BSCB membership number when ordering your subscription.

The discounted prices are as follows:

- *Journal of Cell Science:* paper only $269/£163; online only $69/£42; paper and online only $338/£205
- *Journal of Experimental Biology:* paper only $248/£150; online only $69/£42; paper and online only $317/£192.
- *Development:* paper only $292/£177; online only $69/£42; paper and online only $358/£217

The following journals from **John Wiley & Sons** have discounts of 25–65% (*https://secure.interscience.wiley.com/order_forms/bscb.html*)

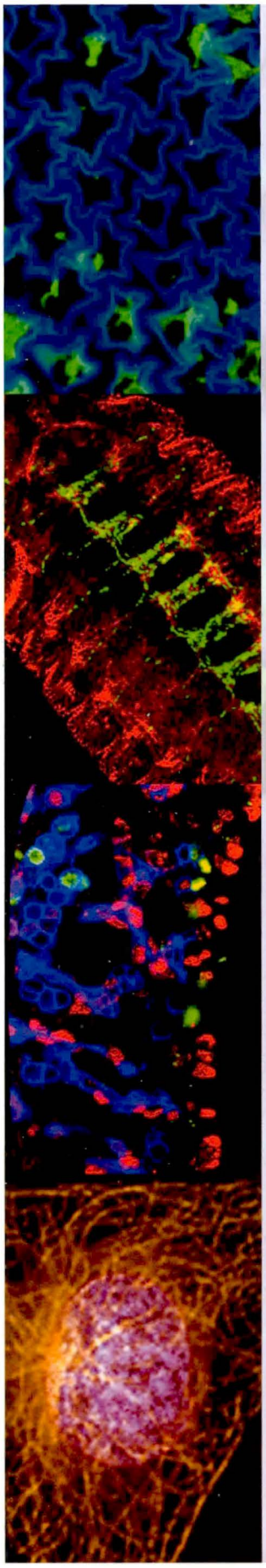
Journal	BSCB rate	Standard rate
The Anatomical Record	$150	*
BioEssays	$99	$160
Cell Motility and the Cytoskeleton	$150	$425
Developmental Dynamics	$125	$165
Genesis	$60	$99
Journal of Cellular Biochemistry	$350	*
Journal of Morphology	$175	*
Microscopy Research and Technique	$295	$595

* No standard individual rate available; only available to institutions

NB: The price for the *Journal of Morphology* is now $175. If there are any members who have ordered the journal at the $150 rate, those orders will be honored.

Postmaster and General Inquiries
Send changes of address, amendments, and general queries to: Margaret Clements, BSCB assistant, Department of Zoology, Cambridge University, Downing Street, Cambridge CB2 3EJ. Tel: +44 (0)1223 336655 Fax: +44 (0)1223 353980, E-mail: zoo-jeb01@lists.cam.ac.uk

Invoices: send to: Professor Mark Marsh, Cell Biology Unit, MRC Laboratory for Molecular Cell Biology, University College London, Gower Street, London WC1E 6BT.



Open Access Initiative from The Company of Biologists

The Company of Biologists announces that – from January 2004 – its journals – *Development, Journal of Cell Science* and *The Journal of Experimental Biology* – is offering authors the option of 'open access'

In response to the biological community's drive for freedom of access to scientific research, The Company of Biologists is offering authors the choice to have their work published free of charge (in the usual way) or as an author-funded open access paper. Open access is a new mode of publishing, which removes the subscription barrier and allows all internet users completely free access to the material. Authors choosing to take advantage of the open access alternative will be charged a publication fee, which, as an introductory offer, will be heavily subsidised by The Company of Biologists.

The Company of Biologists will offer this author-funded publication model for a trial period of one year. The traditional subscription model will operate in parallel as part of a hybrid publishing experiment. Authors will be asked to make the decision as to whether to take advantage of the open access offer when their papers are accepted. Those choosing the company's traditional free publication alternative will still benefit from no page charges, no colour charges, and free access to papers after 6 months.

As a small not-for-profit publisher, The Company of Biologists relies on subscription revenue to cover its publishing costs and to fulfil its charitable remit. However, this experiment with an open access publishing model is an important development, allowing authors increased flexibility and choice. The Company of Biologists is dedicated to its continuing financial support for the community through grants, travelling fellowships and sponsorship.

We hope that you will support this new initiative and we will be approaching you – our authors, readers and subscribers – to find out what you think. If this initiative is received enthusiastically by the community, then we will explore the publishing of *Development, Journal of Cell Science* and *The Journal of Experimental Biology* as full open access journals.

For further information visit www.biologists.com/openaccess.html

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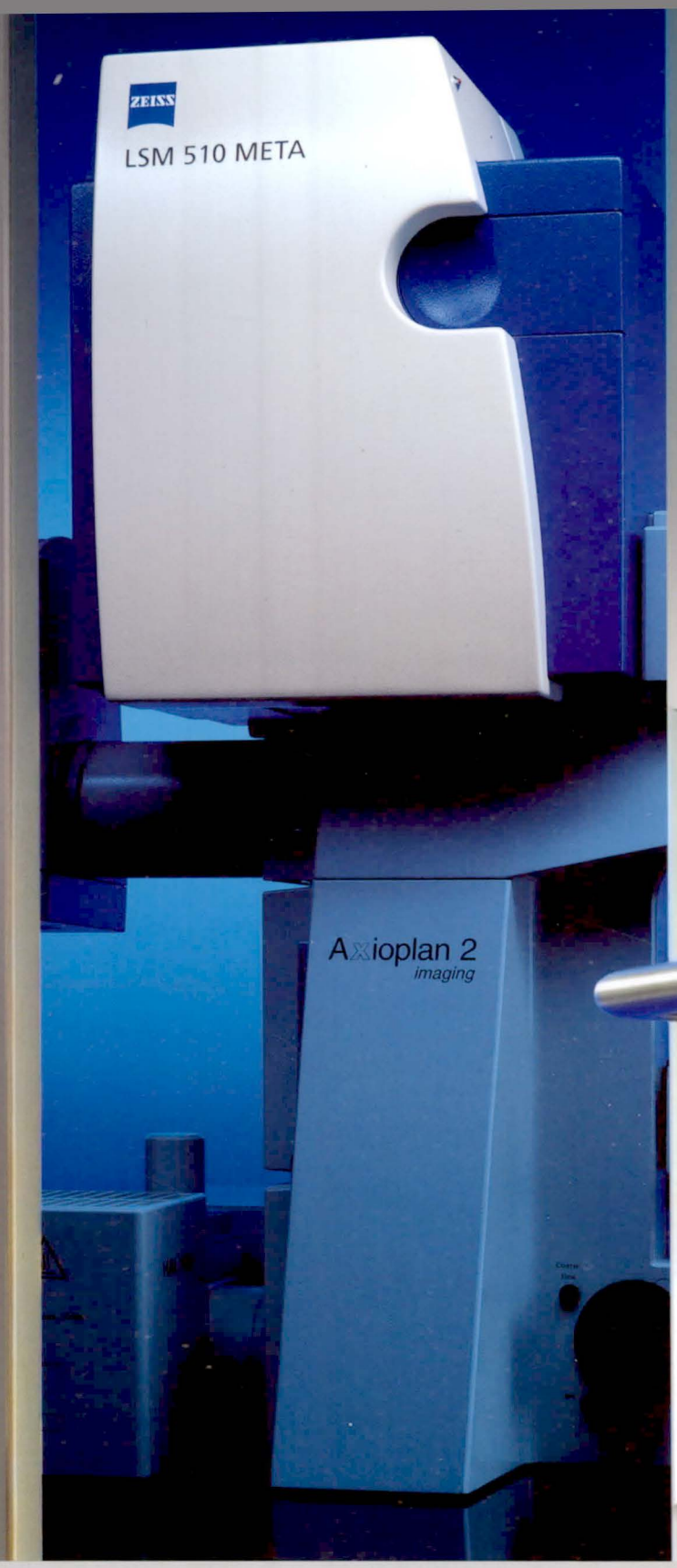
The Company of Biologists – scientific journals for today's researchers



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