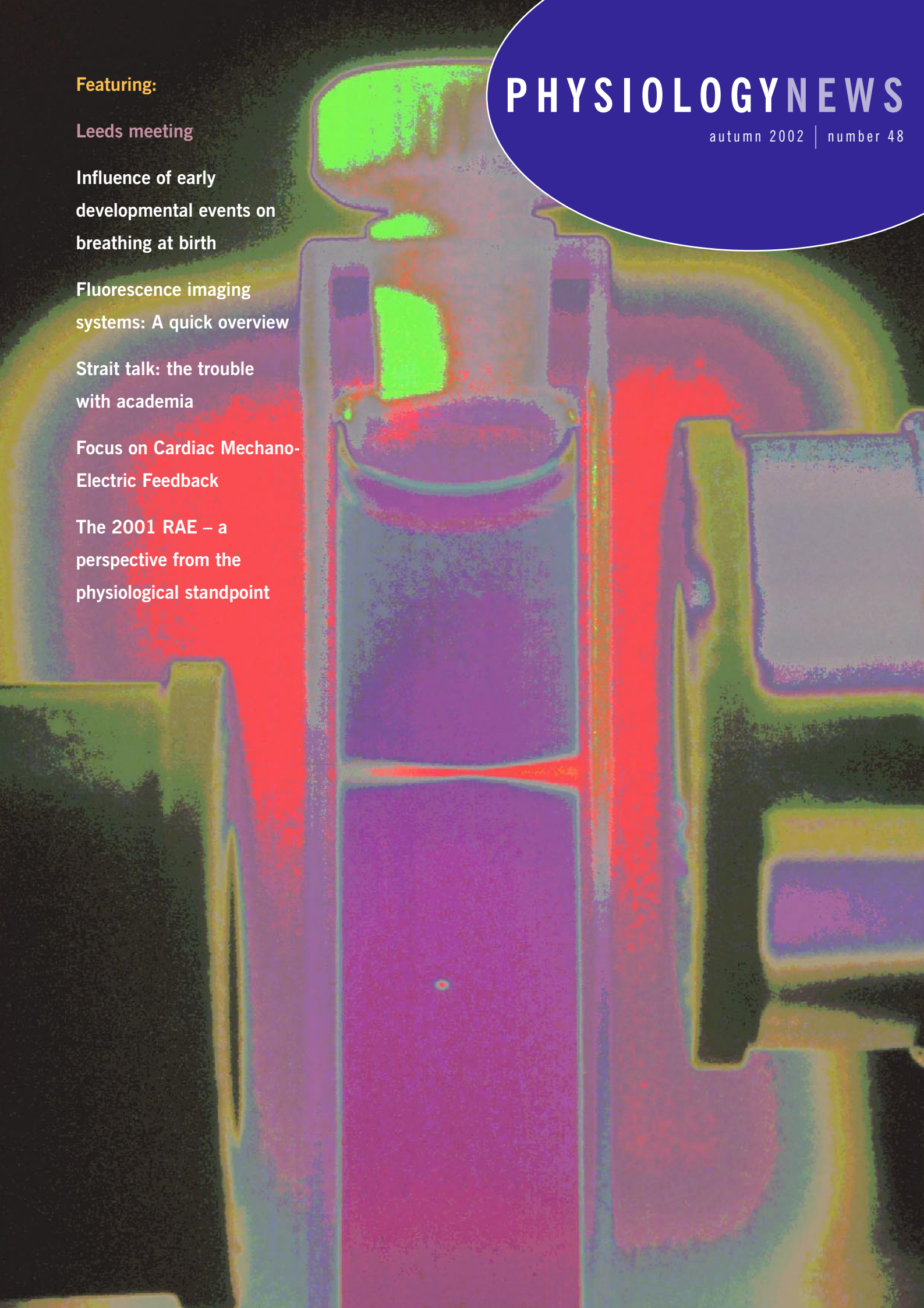

PHYSIOLOGYNEWS

autumn 2002 | number 48

Featuring:

Leeds meeting

Influence of early developmental events on breathing at birth

Fluorescence imaging systems: A quick overview

Strait talk: the trouble with academia

Focus on Cardiac Mechano-Electric Feedback

The 2001 RAE – a perspective from the physiological standpoint

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Contributions and Queries
Executive Editor
Sheila Greaves
Tel: 020 7269 5725
Fax: 020 7269 5720
Email: sgreaves@physoc.org

The society web server: www.physoc.org

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Cover photo

Based on an image of two-photon vs. single-photon excitation of a fluorescent dye. Original photo courtesy of Brad Amos and John Girkin. See John Dempster & David Wokosin article p12.

PHYSIOLOGY NEWS

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Action Points

Affiliate Travel Grant Scheme:
The next deadlines for receipt of applications are 30 September and 30 November 2002.

BSc Intercalated Bursaries:
The next deadline for receipt of applications is 30 November 2002.

Membership Applications:
The deadlines for receipt of applications for full membership are 30 September and 31 December 2002.

Change of Address:
Members should inform the Administration Office of any changes of address, telephone, fax or email addresses.

Changes can be emailed to: jgould@physoc.org

University College London (18-20 December 2002):
Abstracts must be submitted to the Meetings Secretary's Office by 25 September 2002.

Puerto de la Cruz, Tenerife (13-17 February 2002):
Joint Meeting with the Spanish Physiological Society. The closing date for abstract submission is Wednesday 13 November 2002.

Abstract Submissions: Authors should submit their abstracts online. Full instructions will be available on the Society's website (http://www.physoc.org/Meetings/future.html) from the opening day of the abstract submission period

Magazine:
Letters and articles and all other contributions for inclusion in the Winter issue should reach the Administration Office by 2 September 2002. Please cite all references in articles in the style of The Journal of Physiology.

Magazine Online

The magazine is now available on our website www.physoc.org.

Guidlines for contributors

These guidelines are intended to assist authors in writing their contributions and to reduce the subsequent editing process. The ...ial Group is trying to ensure ...cles are written in a journalistic ...so that they will have an immediate interest value for a wide readership and will be readable and comprehensible to non-experts. In particular, scientific articles should give a good overview of a field rather than focus on the authors' own research.

Format of articles
The main message or question posed should be introduced in the first paragraph. The background for the topic should then be established, leading up to the final dénouement or conclusion.

Length of articles
This will be determined by the subject matter and agreed between the contributor and the commissioning editor. Articles will vary in length from 500 to 2000 words.

Submission of articles
Authors should submit text in the form of a disk accompanied by a printout wherever possible. Use of disks reduces the risk of introduction of errors during re-typing. It is helpful to give brief details of the computer, operating system and software package(s) used.

Deadlines for submission
Contact the Editor's office or the Administration office for submission dates. Late submissions will not be accepted or publication will be deferred to a later issue.

Illustrations
Authors are encouraged to submit diagrams, drawings, photographs or other artwork to illustrate their articles or, if they cannot provide these themselves, to suggest what artwork might be appropriate. Photographs may be colour or black & white, prints or transparencies.

Author photographs
The Magazine normally includes photographs of the authors of articles. These may be colour or black & white; prints are preferable if cropping is required.

Digital photographs and images should be produced at a minimium of 350dpi.

References
Authors are requested to keep the number of references to a minimum (preferably no more than two or three), in the style of the Journal of Physiology.

Suggestions for articles
These should be made either to the Executive Editor or to a member of the Magazine Editorial Group (see contents page).

EDITORIAL

PH

Let's hear from you

For the subject of this editorial I make no apologies for returning to a theme that Bill Winlow highlighted in the last magazine, namely, the role of the membership in the Physiological Society. More specifically, I want to talk about our – the membership's – participation in deciding what our Society collectively says and does.

How do we interact with our Society? The obvious answer is that we go to its – our – meetings and publish in its – our – Journals. For most of us, that is probably it. Some of us – though not enough – vote in ballots on new members, or for elections to the Council. A very few of us – arguably not enough – take on roles in the Society: standing for, or sitting on, the Council; helping edit and manage the *Journal of Physiology* or *Experimental Physiology*; running Special Interest Groups. We might look at the Society website occasionally, or glance through *Physiology News* when it arrives with the meeting papers.

Is that enough? I don't think so.

We elect the Council to govern the Society for us. But do the Council members ever get any feedback from us on whether we are pleased, or displeased, with what they've done? Or on the organisational issues we would like them to address?

We also elect the Council for another purpose, namely to represent OUR views on what physiology as a discipline is about, where it should be going, and what it is for. The importance of this latter role, in an era where scientists are under increasing public scrutiny – in particular in respect of the way in which we spend public money – cannot be underestimated.

In this context, the Council, the President, the Society's office, are your – our – voice. Our pressure group. More than just the group of people running a learned Society, they are the public face of UK's physiologists. And they talk to people whose views matter – heads of research councils, politicians, journalists. Not to mention the public.

So the President and Council govern us, represent us, and lobby for us. It follows that we, the membership, need to – MUST – make our views known to our governing body. But do we?

The answer is "not really".

My experience of physiologists is that we are, to say the least, not short of opinions. But you try getting anyone to voice them in public, let alone in print.

Perhaps it is a fault of scientists – or at least of academic ones – that we are by nature grumblers-over-the-coffee-cups rather than stand-up-and-be-counted types.

Or perhaps we simply feel that we already have enough distractions from actually doing science.

Whatever, the fact remains that the colleagues we have elected to the Society's Council, or who edit our Journals, can only represent our views and carry out our wishes if they know what those views and wishes are.

So we have to tell them. We have to email them, write to them, place motions for the AGM, turn up at the AGM. Debate the issues. In short, talk to our representatives.

This is not a one-way street. There clearly could – and should – be more communication from the Council, and from other bodies like the Journal editorial boards, to the members, telling us what they are thinking, and doing.

Basically, we need more dialogue. The question is how.

Of course we do already have a potential forum for this dialogue.

You're reading it.

Physiology News, which potentially reaches all the membership, as well as the affiliates – the people who we expect to become the next generation of members – exists in part to provide this two-way channel of communication.

But it will only work if we use it.

We have made a start in this issue by reprinting a letter that the Physiological Society and the British Pharmacological Society recently sent to HEFCE commenting on the gradings of Departments of Physiology and Pharmacology in the latest RAE. We also have a commentary from Chris Fry explaining why the Council took the decision to do this. Now we would like to know what you, the membership, think about it. And about the issues it raises. And about anything else relating to physiology and the Society. Your concerns. Your opinions.

So let's hear from you.

Austin Elliott

The Physiological Society in Leeds

Eberhard Buhl

Following the last gathering at Leeds in 1996 we are delighted to welcome the Physiological Society to what promises to be a large and exciting scientific meeting (http://www.physoc.org/Meetings/leeds.html). There will be four international symposia with twenty nine overseas invited speakers in the key research areas of Muscle, Channels and Neuroscience, the Annual Review Prize lecture (John Sulston, Cambridge), the Joan Mott Prize Lecture (Helen Skaer, Cambridge) and plenary lectures by Thomas Jentsch (Hamburg) and Peter Seeburg (Heidelberg), as well as five designated lectures, and three Pfizer Prize rounds. For those with an interest beyond the science on offer Leeds provides a host of diverse activities, such as a range of excellent restaurants (French, Greek, Italian, Indian, Indonesian, Thai), shops (including Harvey Nichols – only found in London, Leeds and Riyadh!), museums (including the Royal Armouries) and, of course, a large number of clubs which attract droves of hardened clubbers from as far as London (http://www.leeds.ac.uk/regions/visiting_leeds.htm). Avid Brontë and outdoor pursuit fans won't be disappointed either as Leeds is a gateway to the Yorkshire dales that offer some of Britain's finest scenery.

Following the 1996 meeting in Leeds, Biomedical Sciences have been virtually transformed, due to a flurry of propleptic pre-RAE appointments and, more importantly, the merger of three biological science departments, with Physiology, Pharmacology and Human Biology being successfully integrated into what is now the School of Biomedical Sciences. Although bigger is not necessarily better, our excellent QAA and RAE scores and the successful recent recruitment of high calibre academic staff suggest that this bold step has been made in the right direction. Following hallowed tradition, the sections below will give an overview of the brief history of the School of Biomedical Sciences and its staff, and provide an account of its current research and teaching programmes (http://www.leeds.ac.uk/bms/).

Biomedical Science at the University of Leeds

The University of Leeds was established in 1904, but its origins extend back to the nineteenth century with the founding, first, of the Leeds School of Medicine in 1831 and then the Yorkshire College of Science in 1874. Now one of the largest universities in the UK, Leeds is highly popular among students applying for undergraduate courses, with 45,862 applications competing for 6,100 places in 2000-2001. While the University is looking forward to celebrating its first centenary, the School of Biomedical Sciences is of more recent origin. In 1998, the formation of the School of Biomedical Sciences (BMS) allowed integration of activities across traditional boundaries, and the formation of three primary research groups – Muscle, Channels and Neuroscience. Following the successful merger, masterminded by Clive Orchard, then Head of School, BMS has now 53 permanent members of academic staff, 51 postdoctoral fellows, 30 technical staff, 7 clerical staff, 60 graduate and 875 undergraduate students. By complementing existing strengths with a number of strategic appointments the quality of our research has been recognised with an RAE score of 5 in UoA7 in the 2001 Research Assessment Exercise (RAE).

We are located on two floors of the Worsley Building, at the southern end of the campus, adjacent to the other two Schools in the Faculty of Biological Sciences and the General Infirmary at Leeds, and only a 5-10 min walk from the city centre. By adopting a policy of

The Worsley Building

providing principal investigators with contiguous space in their respective research groups we have succeeded in optimising the use of shared facilities and maximising scientific exchange. In addition to its research activities, BMS runs several popular degree programmes in Pharmacology, Physiology, Medical Science and Neuroscience, as well as teaching students taking combined honours degrees and courses in other disciplines including Dentistry, Medicine and Sports Sciences (see below). The excellence of teaching in the School has been recognised with QAA scores of 22 (Anatomy and Physiology, 2000) and 23 (Pharmacology, 1998).

Research in the School of Biomedical Sciences

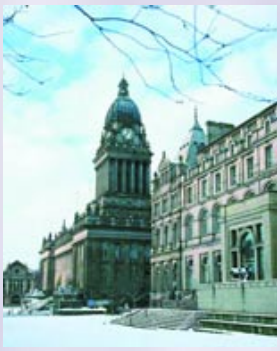
The Muscle group has research interests in cardiac, skeletal and smooth muscle. Although Leeds has long been known for Cardiovascular Physiology, the present Cellular Cardiology group in BMS started when Brian Jewell moved from University College London to take up the Chair of Physiology at Leeds in 1978. The current principal investigators in the group are Mark Boyett, Simon Harrison, Arun Holden, Clive Orchard, Derek Steele, Ed White, Sarah Calaghan (BHF Fellow), Richard Clayton (BHF lecturer) and John Colyer (from the School of Biochemistry and Molecular Biology); Rudi Billeter, whose primary interest is in changes in gene expression in skeletal muscle following training, has active collaborations with many members of the group, using his expertise to investigate changes in gene expression in cardiac muscle.

Work within the group is well funded by the Wellcome Trust, the MRC and, particularly, the British Heart Foundation (BHF). Recent funding of ~£0.8M from the Royal Society, Wolfson Foundation, EPSRC, MRC, JREI and SUN AEG has also enabled the establishment of a "Virtual Tissue Engineering Laboratory". The newly-formed Leeds BHF Heart Centre, which combines the expertise of the Cellular Cardiology group with that of Stephen Ball (BHF Professor in Medicine), is one of the largest heart groups in the UK, with expertise in genetics, molecular biology, biochemistry, electrophysiology, Ca handling and mathematical modelling, enabling study of the heart from the gene, through protein expression and function, to cell and whole organ function.

Current work exploits this range of expertise: the group's research uses molecular biological, physiological and computational techniques to understand the function of the heart at the molecular, cellular and tissue levels. Each principal investigator has their own active research programme, as well as collaborative projects within and outside the group. For example, the heterogeneity of protein expression and electrical activity of the sino-atrial (SA) node is being studied by Mark Boyett, in collaboration with Rudi Billeter. This information is being used to develop biophysically-detailed computer models of single SA node cells and of the whole tissue (>100,000 cells), in collaboration with Arun Holden. Mark is also using mutation and heterologous expression to study individual ion channels, in particular those involved in the response of the heart to acetylcholine. Computer models are also being used by Richard Clayton to investigate the mechanisms that initiate and sustain cardiac arrhythmias, and how they can be terminated.

The group shares an interest in excitation-contraction coupling. This includes studies of the factors controlling uptake and release of calcium from the sarcoplasmic reticulum of cardiac and skeletal muscle by Derek Steele, and of the role of the

Leeds Civic Hall



Leeds Townhall and Library

Members of Mark Boyett's lab. From left to right: Samy Makary, Zhigang Shui, Tom Claydon, Tomoko Yamanushi, Mitsuru Yamamoto, Mathew Lancaster, Halina Dobrzynski, Sandra Jones

t-tubules in cardiac myocytes by Clive Orchard, using a technique developed recently in his lab to detubulate cardiac myocytes. Clive is also continuing his work on the effects of acidosis on the heart, most recently studying the effects of pH on membrane currents and, in collaboration with Mark and Rao (Channels), the molecular site of action of H^+ on Kv1.4 and Kv4.2. Simon Harrison is investigating the important clinical problem of how anaesthetics decrease cardiac contractility at cellular and molecular levels.

Leeds also has one of the few laboratories in the world able to stretch single cardiac myocytes and Ed White and Sarah Calaghan are using this technique to elucidate the mechanisms underlying the mechanical and electrical response of the heart to stretch. They are also exploring the regulatory role of the cardiac cell cytoskeleton. Ed is also interested in the effects of exercise on the mammalian heart (in collaboration with Simon and Rudi) and in comparative cardiac physiology (with Holly Shiels, a Canadian NSERC Fellow).

The principal investigators in the Molecular Contractility group are John Trinick, Peter Knight and Michelle Peckham. They seek to understand how proteins produce mechanical work from chemical energy. The major effort is on contractile proteins from striated muscle, principally myosin, actin and titin, but discovery of super-families of these molecules has recently broadened this to other tissues. Thus 18 types of myosin have now been identified, from which most cells in the body express several; this has led to projects on myosins V, VI and IX in addition to the work on muscle myosin II. Published in *Nature*, studies on myosin V have for the first time allowed the conformation of a myosin molecule at the start of its power stroke on actin to be visualised. Previously, this was a major impediment to understanding force production. The new results support the tilting lever hypothesis of force production. Other motor protein projects include dynein and the V-ATPase rotary motor. The group is also interested in how the giant proteins titin and nebulin control exact myosin and actin filament assembly and mechanically stabilise sarcomeres. A variety of experimental approaches is in use, at both protein and nucleic acid levels, but there is a major effort with electron microscopy, including cryo-EM, single particle image processing and fast time resolution methods.

The BMS Neuroscience group has its research focus on the molecular machinery, synaptic circuits and the integration of synaptic and cellular information processing in a number of CNS regions, amongst them hippocampus, neocortex, thalamus, the medial septum, brain stem areas and the spinal cord. Bridging the gap between molecule and neuronal networks requires multidisciplinary approaches, including correlated light and electron microscopy of electrophysiologically characterised neurons, multiple extra and intracellular recording techniques, IR/DIC patch-clamp recording, double and triple labelling methods at the light and electron microscopic levels, post-embedding immunocytochemistry and, needless to say, the use of a range of transgenic animal models. At present, the principal investigators in the group are Aziz Asghar, Eberhard Buhl, Jim Deuchars, Zaineb Henderson, Anne King, David Lewis, Deborah Withington, Miles Whittington and two recent appointees, Claudia Racca (NIH) and Neil Morris (Imperial College). Noel Buckley, who holds a joint appointment with the School of Biochemistry and Molecular Biology, has an interest in the development of the neuronal phenotype and complements the group's technical repertoire with valuable molecular expertise. "In-house" collaborative links also exist with Alan Bateson and Hugh Pearson, both of them *bona fide* neuroscientists but affiliated with the Channels group.

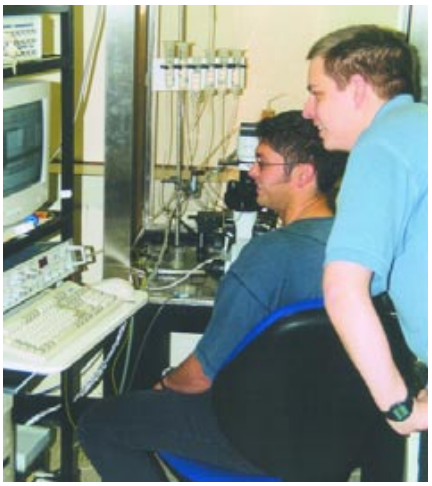
Research in the rapidly growing Neuroscience group is well supported by the MRC (a Programme and Link Grant as well as two Co-Operatives), Wellcome Trust, BBSRC, the Royal Society, the British Council, the EU (FP5), and a number of industrial partners, amongst them GlaxoSmithKline, Merck, Sharp & Dohme and Lundbeck (Denmark). As money, allegedly, is not everything, the group has extensive collaborative links with numerous institutions in the U.K. (e.g. Universities of Bristol, Glasgow, York and Imperial College), mainland Europe (e.g. Universities of Heidelberg, Szeged, Naples, Oporto) and overseas (e.g. Salk Institute, Caltech, SUNY and University of Boston). Their input is both vital and diverse, ranging from transgenic animal models to neuronal modelling with an SP2 parallel supercomputer and EEG studies on schizophrenic subjects.

Current work in the Neuroscience group is focused on elucidating salient principles which govern information processing in a variety of CNS areas. The laboratories of Miles Whittington and Eberhard Buhl exploit a range of experimental paradigms to induce rhythmic network activity *in vitro*, spanning several EEG frequency bands, amongst them theta, gamma and ultrafast oscillations. Apart from investigating basic pharmacological, physiological and anatomical properties of the active network they have developed a recent interest in "oscillopathies" employing experimental (amongst them transgenic) models relevant to Alzheimer's disease and schizophrenia. In collaboration with Zaineb Henderson, they are studying the generation of theta oscillations in the medial septum *in vitro*. Using the IR/DIC patch-clamp method, Zaineb is also investigating septal microcircuits and receptor pharmacology, with the current focus on cholinergic mechanisms. Anne King's group is investigating modulatory actions of adenosine and glutamate transporters in spinal dorsal horn neurotransmission, forming part of a cross-faculty MRC co-

op for research on Membrane Transport Proteins as Targets for Disease Control. Anne's group, in collaboration with Aziz Asghar, has also developed an interest in neuronal network oscillations. The latter may have a role not only in governing normal sensory information coding in the dorsal horn, but also in the processing of neuropathic pain. The lab of Jim and Susie Deuchars studies neuronal circuits in the medulla oblongata and spinal cord involved in control of autonomic regulation, particularly the cardiovascular system. Technically, they combine *in vitro* electrophysiology, neuroanatomy and recently, molecular biology to (for example) identify and characterise spinal cord interneurons important in controlling sympathetic outflow. Their interest in receptors for ATP and adenosine lead them to publish last year the first evidence that P2X7 receptor subunits are present in excitatory presynaptic terminals in the nervous system. Dave Lewis is interested in the central regulation of the different subpopulations of autonomic motoneurons. He is currently investigating the pre- and post-synaptic interactions between co-released neurotransmitters in caudal raphe projections to upper airway motoneurons. In collaboration with Jim Deuchars, his group is expanding this work to investigate the medullary pathways involved in the regulation of food intake. Claudia Racca, the most recent member of the Neuroscience Group, will take advantage of the most advanced fluorescence and electron microscopy techniques, like quantitative postembedding immunogold cytochemistry on serial EM sections and fluorescence and EM *in situ* hybridisation of neurotransmitter receptor mRNAs. Claudia's endeavours in Leeds will focus on the cellular and molecular basis of neurotransmitter receptor trafficking and the role of intracellular protein-protein and mRNA-protein interactions in the regulation of synaptic targeting, anchoring and recycling of receptors during synaptic plasticity.

Over the past decade the University of Leeds has increasingly established itself as a centre for ion channel research, a focus that has emerged naturally within the University's overall strength in the field of membrane protein studies. There are now at least sixteen laboratories across the University with a strong interest in channels – and many others working on G-protein coupled receptors or transport proteins. Within the School of Biomedical Sciences alone there are twelve labs investigating physiological aspects of channels with nine of these in contiguous space containing over fifty staff, postdocs and research students sharing extensive molecular, biochemical, cell biology, imaging, and electrophysiological recording facilities. Principal investigators include Alan Bateson, David Beech, Mark Boyett, Jim Deuchars, John Findlay (School of Biochemistry and Molecular Biology), Simon Harrison, Malcolm Hunter, David Iles (School of Biology), Paul Kemp, David Marples, Hugh Pearson, Chris Peers (School of Medicine), Asipu Sivaprasadarao, Stan White, Ian Wood (School of Biochemistry and Molecular Biology), and Dennis Wray.

Members of the Channels Group receive generous project and programme grant support from the BBSRC, BHF, MRC, NIH and Wellcome Trust. MRC Co-operative status was awarded three years ago under the heading "Recombinant Channels" with a general purpose of advancing understanding of ion channels in relation to physiology and disease. A key aim has been to foster a scientific environment with free exchange of expertise, facilities, knowledge and ideas, and provide a dynamic and supportive environment for both up-and-coming and established investigators. The interest in education and career development as well as research is exemplified by the Leeds Ion Channel Workshop, a residential hands-on and taught course established in 1999, and still on a



Top Fiona LeBeau, a senior research fellow in Miles Whittington's and Eberhard Buhl's lab

Centre Sam Fountain doing PCR in 'real time' with the Roche Lightcycler in David Beech's lab

Bottom Leigh Plant (standing) and Gavin Searle from Paul Kemp's and Hugh Pearson's labs

Spot the electrophysiologists with no lab coats! Some postdocs and postgrads from David Beech's lab. From left to right: Richard Flemming, Sam Fountain, Philippa Jackson, Alex Cheong and Damian McHugh

healthy footing in 2002! This year the Workshop occurs in the week following the Physiological Society meeting (http://www.leeds.ac.uk/bms/).

Many types of channel are studied within the Group. David Marples, who holds a MRC Career Establishment Award, doesn't in fact work on ion channels, but on water channels – especially aquaporin 2 in the kidney. Alan Bateson, newly recruited from the University of Edmonton, is a specialist of $GABA_A$ receptors – especially their molecular biology and the regulation of their gene transcription. Other investigators focus almost exclusively on aspects of potassium channels and calcium channels. Paul Kemp, Hugh Pearson and Chris Peers spearhead a major collaborative effort to reveal molecular mechanisms underlying the physiological regulation of calcium and potassium channels by hypoxia. They, like Malcolm Hunter, also have a keen interest in members of the new family of K2P (twin-pore domain potassium) channels, some of which are sensitive to hypoxia, and most of which are inhibited strongly by acidosis. Asipu Sivaprasadarao and Dennis Wray combined protein chemistry and electrophysiological approaches to reveal depolarisation-induced movement of S4 (the voltage-sensor) in *Drosophila Shaker* potassium channels. Asipu was also the first to show that a disease mutation in a channel (the ATP-sensitive potassium channel of pancreatic beta-cells) can cause trapping in the trans-Golgi apparatus. The new TRP (transient receptor potential) channels are also coming to the fore with John Findlay's cloning of *Loligo forbesi* TRP in 1996 and David Beech's demonstration of TRPC1 as a subunit of store-operated calcium channels in vascular smooth muscle. The Group is also moving forward and expanding. There are concerted efforts to identify physiological protein complexes of channels by using a combination of immunoprecipitations, 2D-gels and mass spectrometry and by using yeast two-hybrid assays. There are studies of the physiological regulation of ion channel gene expression scanned by gene chip technology and real-time RT-PCR, and of ion channel trafficking using tagged recombinant proteins and confocal microscopy.

Ion channel research at Leeds looks set to prosper and play its part in the UK's ever vibrant ion channel community, which hasn't looked back since the publication of Hodgkin & Huxley's initial ground-breaking work in 1952. Now, fifty years on, the Physiological Society meeting has presented us with a magnificent opportunity to bring together leading researchers from across the world to display some of the wonderful advances in the understanding of the physiology of ion movement across cell membranes.

Teaching in the School of Biomedical Sciences

Since the formation of the School, teaching has become more integrated and forward-looking. Two QAA reviews yielded excellent scores of 23 and 22 and, with them behind us, we can concentrate on future developments. These include the introduction of a new degree programme in neuroscience, reflecting the growth in this area of research here, and substantial curriculum reviews which will change the shape of first year teaching in particular, starting this autumn. All our students will follow a common first semester, which will enable them to cope with any of our programmes of study. We introduced this in anticipation of the effects of changes at school and college level which have resulted in applicants with much more varied backgrounds than previously seen, and we hope the new experience will not only provide a better introduction but enable much more flexibility in choice of direction in the following stages.

The desire of students for choice and flexibility is reflected in the applications we receive; with more and more applications for Medical Sciences, usually reported as "to keep my options open", along with a healthy interest in physiology, pharmacology and neuroscience. A science degree in anatomy is alas no longer possible as staff changes mean we do not have the breadth in this area to sustain a single honours programme. The recent influx of high class research appointments is also making an increasing impact on final year research-led teaching. Again the blurring of boundaries between disciplines is allowing a wider choice for students. Although many graduates are successful in obtaining jobs in a broad spectrum of scientific, commercial and business enterprises we still produce a fine crop of enthusiastic, knowledgeable and able candidates for careers in research.

Eberhard Buhl
Head of School of Biomedical Sciences
University of Leeds

Influence of early developmental events on breathing at birth

Jean Champagnat

Gilles Fortin

Respiration is a rhythmic motor behaviour that appears in the fetus and acquires a vital importance at birth. It is generated centrally, within neuronal networks of the brainstem. Recently, examination of hindbrain activities in the embryo revealed that a central rhythm generator is active in the brainstem before fetal maturation and conforms to the segmented organisation of the embryonic hindbrain at this stage of development. From physiological studies of this primordial rhythm generator in embryos, we may therefore gain an understanding of how genes govern development of neuronal networks and specify patterns of motor activities operating throughout life.

Rhythm generation in the embryo

The brainstem derives from the embryonic hindbrain (rhombencephalon), one of the vesicles that appear towards the anterior end of the neural tube. When reticular neurons differentiate, the hindbrain neuroepithelium is partitioned along the antero-posterior axis into an iterated series of eight cellular compartments called rhombomeres. This segmentation process is transient and believed to specify neuronal fates by encoding positional information (Lumsden and Krumlauf, 1996). Electrophysiological recordings performed on an isolated preparation of chick embryo hindbrain revealed that by the end of the segmentation period, the hindbrain neuronal network starts to exhibit a consistent and organised activity in the form of recurring episodes composed of burst discharges that occur simultaneously in the different cranial nerves. At this stage the neuronal network is already organised with distinct reticular and motor neurons (Fortin *et al*, 1994). When intersegmental relationships are interrupted by transverse sectioning of the hindbrain rostral and caudal to the exit of the branchiomotor nerve, the ability to generate the rhythmic pattern is preserved in each transverse slice. The network organisation responsible for this rhythm generation conforms to the rhombomeric pattern in the hindbrain of the embryo. Specification of the future rhythmic network would therefore take place within the segmented hindbrain of the embryo and segmentation may be a determinant in conferring the ability to generate specific rhythmic patterns of activity (Champagnat et Fortin, 1997).

Identification of a maturation step leading to an High Frequency episodic activity in the chick

By recording neural rhythm generation in post-segmental chick hindbrain preparations isolated *in vitro*, we have identified a developmental step in which GABAergic synapses begin to exert an inhibitory action on neurons, thereby shifting rhythmic activity from low frequency (immature, figure 1, top right) to high episodic frequency (HF, closer to mature, figure 1 bottom right). At the cellular level, GABAergic inhibition is responsible for the appearance of a novel neuronal phenotype (being inhibited instead of excited during burst activity) within the

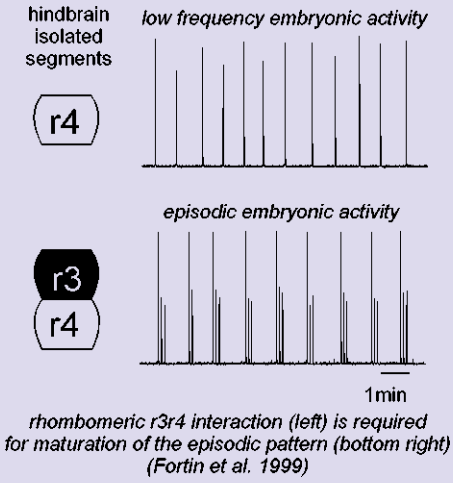


Figure 1 Experiments on chick hindbrain isolated segments demonstrate that the program of hindbrain segmentation controls formation of rhythm promoting neuronal circuits. Individual or pairs of segments are isolated at the time when they form and maintained *in ovo* to allow development of neuronal networks. The r3r4 segments contain the entire information required for the normal maturation of an episodic (HF) activity. The r3 segment is required, because the mature episodic network fails to develop from the isolated r4 segment.

rhythmic network. At the membrane level, inhibition involves GABA-A receptors and an increase of neuronal input conductance; HF results from a post-inhibitory rebound regulated by the hyperpolarisation-activated mixed cationic current, Ih (Fortin *et al* 1999).

Deciphering the rhombomeric code for HF maturation.

To understand how rhombomere identity might influence rhythm generation, we have developed in collaboration with A Lumsden and S Jungbluth (London), an *in ovo* neural tube ablation procedure that allows the later recording of rhythms (arising after the end of the segmental period) from combinations of isolated single rhombomeres (r) or doublets of adjacent rhombomeres. We found that the normal HF generator develops in r3r4 (figure 1 bottom) and r5r6 doublets, but not in isolated r2, r4 (figure 1 top) or r6, or in r1r4, r2r3 or r4r5 doublets. Therefore, turning on the HF rhythm pattern depends on the singular identity of r3 and r5, which controls, on the basis of a two segment repeat, the later maturation of GABAergic inhibition (Fortin *et al* 1999). These experiments have demonstrated a robust link between rhombomere patterning and maturation of HF reticular circuits in the avian embryo.

Breathing in transgenic mice

A wealth of data has been accumulated on genes governing hindbrain segmentation. Before and at the onset of segmentation, genes encoding transcription factors such as *Hox*, *Krox-20* and *kreisler*, are expressed in domains corresponding to the limits of future rhombomeres (Lumsden and Krumlauf, 1996). Inactivation of these genes specifically disturbs the rhombomeric pattern of the hindbrain. For example, *Krox-20*, is transiently expressed within the yet unsegmented hindbrain in two stripes with sharp edges corresponding to the future rhombomeres r3 and r5. The inactivation of *Krox-20* in transgenic mice results in the deletion of r3 and r5 and lethality shortly after birth (Schneider-Maunoury *et al*, 1993). The *Krox-20* gene product acts as a direct transcription activator of other r3- and r5-related genes belonging to the Hox clusters. Concerning Hox genes themselves, expression of *Hoxa1* also provides one of the earliest signs of regionalisation within the developing hindbrain. As early as 7.5 day-post-coitum in mice, the *Hoxa1* expression domain extends from the posterior end of the mouse embryo up to the presumptive r3/r4 border and is down-regulated before rhombomere boundary formation. This transient expression has a profound impact on hindbrain patterning, as *Hoxa1* targeted inactivation results in severe reduction of r4 and r5 and their derived structures (e.g. the motor nucleus of the facial nerve) and in lethality shortly after birth (see Mark *et al*, 1993). The advent of such mutant mice in which embryonic hindbrain development is affected by the deletion of specific territories provides a potential strategy to establish a link between gene expression and breathing in intact animals. Because respiration acquires a vital importance at birth, prenatal dysfunction of neuronal networks can be responsible for functional anomalies that appear after birth.

Identification of an anti-apneic neuronal system depending on the integrity of r3 or r4 in mice.

The general strategy has been to identify phenotypic traits of the rhythmic respiratory network following loss-of-function mutation of transcription factors expressed in a rhombomere-specific manner: after the elimination of both r3 and r5, or of r5 alone, obtained respectively by inactivating *Krox-20* and *kreisler* (Chatonnet *et al* 2002) and after elimination of r4 and r5 in *Hoxa1*$^{-/-}$ mutants (Dominguez *et al*, 2001). By comparing these different mutants, it was found that both r3- and r4-derived neurons are essential to alleviate life threatening neonatal apneas thereby maintaining normal breathing shortly after birth. This "anti-apneic" system is vital during a precise time window (the first two days after birth in mice, see review by Fortin *et al* 2000), during which survival of *Krox20*$^{-/-}$ and *Hoxa1*$^{-/-}$ mutants could be improved by blocking enkephalinergic inhibition of the respiratory rhythm *in vivo*. These results have established the link between neuronal loss resulting from the abnormal segmentation of the neural tube and life-threatening murine syndromes with potential importance in neonatal human pathology.

Mis-specifications in the segmented hindbrain produce novel neuronal controls of breathing, active after birth.

Importantly, abnormal expression of segmentation genes does not necessarily result in cell death. The survival

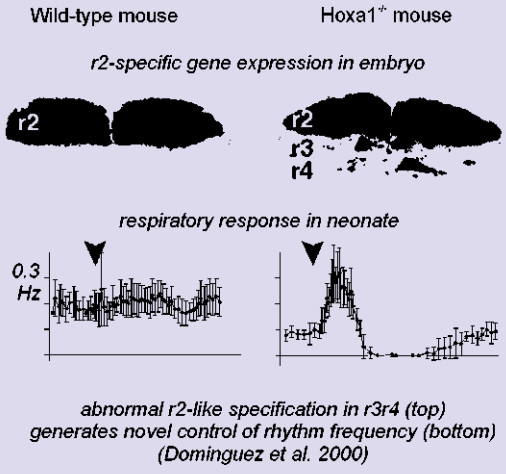


Figure 2 Experiments on *Hoxa1*$^{-/-}$ mutant mice demonstrate that genes orchestrating hindbrain segmentation control formation of rhythm promoting neuronal circuits. *In situ* hybridisation of the segmented hindbrain (top) identifies mis-specification of progenitors in rhombomeres r3 and r5, a region of the neural tube giving rise to the caudal Pons. Slice preparations have been developed in the mutant neonates to investigate function of pontine structures and generation of the respiratory rhythm *in vitro*. Stimulation of the caudal Pons (arrowhead) in neonatal *Hoxa1*$^{-/-}$ mutants induces an abnormal connection that influences respiratory frequency.

and neurobiological function of mis-specified cell progeny at birth has been investigated in *Hoxa1*$^{-/-}$ and *kreisler*$^{+/-}$ mutants. Dominguez *et al* (2001) have identified and located a novel functional neuronal circuit increasing the respiratory rhythm in *Hoxa1*$^{-/-}$ mice but not in wild-type mice; which seems to result from the acquisition of an r2-like phenotype by progenitors located in r3-r4 (figure 2). Chatonnet *et al* (2002) have found an exaggeration of the anti-apneic control (as defined above) indicating persistence of an abnormal control of respiration in heterozygous *kreisler* mice exhibiting mis-specifications of r3 cells (Manzanares *et al*, 2000), but with neither rhombomere elimination nor massive anatomical deficits. These results demonstrate that changes in segmental gene expression pattern underlie the acquisition of neuronal circuits regulating vital adaptive behaviours and, therefore, might be implicated in the evolution of the vertebrate brainstem network.

Overall, studies on embryos and neonates demonstrate the role of hindbrain segmentation in the formation of rhythm-promoting circuits. Developmental mechanisms orchestrating the early organogenesis of the brainstem appear to be crucial in establishing the postnatal breathing pattern. Experiments performed after birth in transgenic mice indicate that, although expression of these genes and hindbrain segmentation are transient events of the early embryonic development, they are important for the process of respiratory rhythm generation. Therefore, early developmental processes have to be taken into account to understand normal and pathological diversity of the vertebrate breathing behaviours during postnatal life.

Gilles Fortin and Jean Champagnat

Neurobiologie Génétique et Intégrative
Institut de Neurobiologie Alfred Fessard
CNRS, Gif-sur-Yvette, France
Gilles.Fortin@iaf.cnrs-gif.fr

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VACANCIES ON THE EDITORIAL BOARD FOR *PHYSIOLOGY NEWS*

Have you ever fancied becoming involved in media or are you interested in journalism and writing and commissioning articles? If so, how about becoming involved in the production of *Physiology News*? We are especially interested in hearing from younger people who are not yet full members of the Society, or who have been newly elected.

As you know the Society's magazine underwent a very successful re-launch at the end of last year, and to continue to build upon this success the existing Editorial Board are looking for a couple of interested and bright individuals who think they have something to offer. The task is fun and rewarding and an excellent opportunity to see your own ideas and articles in print. The Editorial Board meets 4 or 5 times a year, depending on the magazine production schedule, to discuss ideas for future articles or new features, and whilst it is an unpaid role, travel expenses are reimbursed by the Society. If you are interested in becoming involved, or would like further information please contact Sheila Greaves as soon as possible at sgreaves@physoc.org.

Fluorescence imaging systems:
A quick overview of the technology.

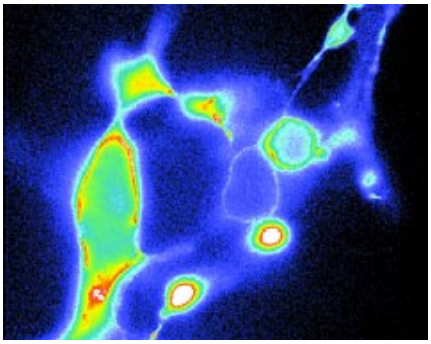
John Dempster

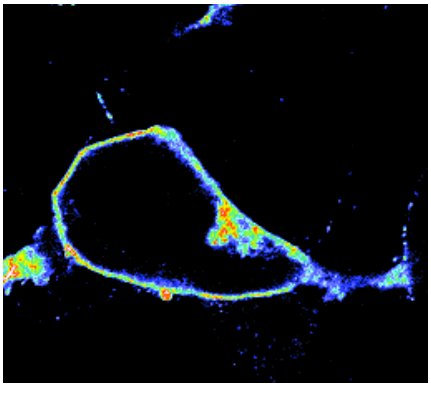
David Wokosin

In the past decade, the ability to visualise specific probes within a biological specimen has brought about a Renaissance of light microscopy. Considerable developments in staining techniques now allow a high degree of specificity by labelling, and subsequently imaging. Currently most physiological applications arise in the study of intracellular calcium dynamics using the fluo dyes and also intracellular structures tagged with green fluorescent protein. The newcomer to imaging is presented with an array of systems, ranging from relatively simple cameras, through various types of confocal microscope, to the two photon excitation (2P) microscope, not to mention more specialised techniques such as total internal reflection (TIRF) or fluorescence resonance energy transfer (FRET). Not surprisingly, it can be difficult to determine the relative merits of different offerings, or separate marketing hype from fact. Given the painfully high cost of some systems, making the right choice is no small matter.

The three most important issues concerning the choice of system are – *depth*, *speed* and *invasiveness*. Events of interest don't always lie on the surface of the specimen, requiring the system to have a capacity for imaging with high resolution and contrast structures inside a cell or tissue section. Similarly, the dynamics of the events under study determines the required imaging speed – the rate at which images must be captured. At the extreme (calcium sparks) this may be hundreds of frames per second (fps). Finally, damage caused by illuminating cells with high intensity light can be a major factor in the duration of experiments on living cells. As cameras, confocals and 2P systems all have advantages and disadvantages in terms of depth/speed/invasiveness, a compromise has to be made when choosing the best system for one's purposes.

HEK293 cells stained for a G-protein coupled receptor using TRITC acquired using a camera (top) and a confocal microscope (bottom). *Courtesy of Catherine Waters, University of Strathclyde.*





Imaging Depth

It is worth noting that for studies of individual cells less than 20 µm thick (e.g. single cardiac or smooth muscle cells) the confocal approach may not be necessary, unless detailed ultra-structural studies are proposed. It is important therefore not to discount the simpler and less expensive (compared to confocal) imaging systems using digital CCD cameras. Nevertheless, deep imaging is best performed with a confocal system.

The primary advantage of the confocal light microscope is its ability to reject the out of focus fluorescent light, outside the focal volume which can significantly degrade the contrast of conventional images. This is done by mechanically scanning a point source of light over the specimen using a pair of galvanometer-mounted mirrors. The fluorescent light emitted from the spot in the specimen is focused on to a narrow pinhole which only passes light precisely in the focal plane of the microscope through to a photomultiplier tube (PMT) light detector. An image is built up by scanning the spot in raster fashion over the specimen, digitising and storing the spot intensity measurements in a computer system. The confocal also has the advantage of allowing multiple fluorescent wavelengths, reflection and transmission images to be acquired simultaneously, using multiple sets of PMT detectors. Confocal systems are effective for imaging up to ~40 µm into tissue at which point spherical aberration can often degrade image contrast.

For tissue sections more than ~40 µm thick (intact tissues, whole animals) 2P microscopy is likely to be the only method available to retain sub-cellular resolution. Fluorescent emissions are normally induced by the absorption of a single photon of light shifting the fluorophore to a higher energy state, a

photon of a longer wavelength (lower energy) being emitted when the molecule drops back to a lower state. Thus in a confocal microscope a laser, emitting light in the blue/green region, generates fluorescent emissions in the green/red range. An exception to this rule occurs if two photons strike and are absorbed *simultaneously*, delivering double the energy, resulting in emitted light of shorter wavelength than the excitation light. In a 2P microscope, visible light fluorescence is induced using a near infrared (NIR) laser, yielding two main advantages. Benign NIR photons can penetrate deeper into a specimen. Also since two photon absorption events are very rare, fluorescence only occurs at the exact point of focus where the excitation intensity is highest, reducing background light (See Figure 1.)

Imaging Speed

The necessity for mechanical beam scanning with the confocal technique means that it is at a disadvantage compared to CCD camera systems in terms of image capture rate. Cameras (e.g. the Princeton[a] I-PentaMax, with virtual-chip option, can capture a 160x160 pixel image at 141 frames per second (fps). The Hamamatsu[b] C4880-81 can similarly achieve 102 fps (164x123). Specialised camera systems such as Redshirt Imaging's[c] NeuroCCD-SM can reach 2000 fps (80x80). Using bi-directional scanning, and limiting the scanning area (or resolution) to a 64x256 pixel box, current generation confocals can sustain ~25 fps. Beyond these speeds the point-scanning systems have very small pixel dwell times – low signals, and the detector integration electronics is severely challenged to maintain pixel registration within the imaged plane. However, by reducing the image to a single line, point-scanning laser systems (confocal and 2P) can generate rapid data acquisition from fluorescence indicators, most achieving a scanning rate of 488 lines per second (lps). To attain adequate speed most studies of calcium sparks have been reduced to using this line scan mode.

One way to increase full image capture rate is to scan multiple sets of spots simultaneously over the specimen with a corresponding set of multiple pinholes, an approach which requires the use of a full field detector such as a CCD camera rather than a PMT. Both Perkin-Elmer and VisiTech International supply multi-point scanning confocal systems based upon a rotating microlens array produced by the Yokogawa Electric Corp. In theory, since the array spins at 360 Hz, image capture rates of 360 fps could be achieved although current commercially available systems are limited to around 50 fps by the capabilities of the supplied cameras. It is worth noting, however, that the microlens array and pinhole array are only optimal for 100x objective lenses and that the achievable axial resolution (optical sectioning capability) of the multi-point scanning approach is less than point-scanning confocal microscopes. Stefan Hell has demonstrated a similar rotating microlens system, using a 2P laser source (Straub *et al*, 2000). The primary advantage here is obtaining better background rejection while not compromising the emission collection to the CCD camera. In addition, the choice of objective lens is not restricted by pinhole matching requirements.

Invasiveness/system sensitivity

CCD camera detection still yields the most photon efficient system for fluorescence microscopy since each CCD pixel collects light during the entire exposure period, permitting lower excitation intensities that can be produced by xenon lamp/monochromators, or even LEDs rather than lasers. Cameras with combined image intensifiers such as the Princeton[a] I-PentaMax or the new Photometrics[a] Cascade (which incorporates electron amplification within the CCD) have the capability of detecting single molecule fluorescence.

The sensitivity of the confocal microscope is inevitably lower than camera systems since the photon efficiency of the PMT detectors is half (or less) of good CCD cameras. In addition, the emission light must traverse the scanning system optics, folding mirrors, and pass through the confocal pinhole (only 85% of light within first Airy disk). To offset these losses and to generate enough photons to produce a statistically significant number in the short pixel dwell time bright laser sources are required. These high intensities can produce photo-toxicity in unstained cells and photo-bleaching in stained cells. This combination tends to limit the viewing time of live cells using UVA/violet/blue excitation wavelengths.

Although 2P average laser intensities are dramatically higher (~500 times) than confocal laser sources, the NIR photons are lower in energy, and do not seem to perturb transparent cells and tissues with normally used average power levels (<100 mW). The main limitation for live cell imaging seems to be the UVA/violet/blue excitation events, and here 2P imaging produces the smallest excitation volume of all three techniques (see Table 1). Using an excitation wavelength above 1µm – with enhanced detection – has resulted

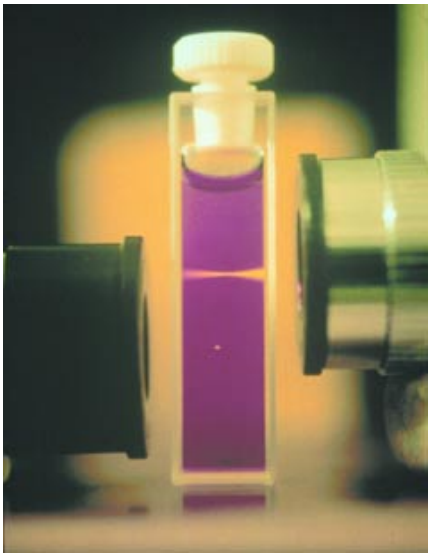


Figure 1 Two-photon vs. single-photon excitation of a fluorescent dye. The 2P beam (lower lens) excites a spot at the point of focus only while single-photon excitation (upper lens) creates a broad cone of excitation on either side. *Photo courtesy of Brad Amos and John Girkin.*

in dramatic improvements in long-term, live cell embryo imaging (Squirrell *et al*, 1999). The 2P technique also permits the option to bypass the losses associated with the confocal's scanning optics and pinhole. In addition, these detection-enhanced systems are much less sensitive to focal plane mismatches between excitation and emission wavelengths. Another enhancement possible is collecting photons from the condenser lens, which can double the efficiency to nearer the sensitivity of camera systems.

Don't forget the lens

The correct choice of microscope objective lens remains an important factor. Generally speaking, the higher the numerical aperture (NA) of a lens the greater its light collection efficiency with significant effects on sensitivity. Short working distance oil or water immersion lenses have a greater NA than air lenses, or long working distance water dipping lenses. Plan Apochromat objectives should be used wherever possible, resorting to Plan Fluor lenses only if UV transmission is required. Water-immersion lenses are preferable for cells/tissues in water beyond 10 µm, water-dipping beyond 200 µm.

And software too ...

Similarly, the computer software used to operate the microscope and to analyse the resulting images must be taken into account. As is often the case for modern laboratory instruments, the reliability and/or limitations in this software can often plague otherwise well designed systems. It is unwise to assume that the software package provided by the microscope supplier is capable of the specific forms of image analysis required. Most systems, for instance, have the capability of capturing series of optical sections forming 3 dimensional data sets, but usually have only a rudimentary capability for the analysis of such data. It is worth ascertaining this at the outset and if necessary including third party software with appropriate capabilities (e.g. Bitplane Imaris[1] or Improvision's Volocity[2] for 3D volume display/analysis, or Universal Imaging's MetaMorph[3] for general purpose 2D time series analysis).

The cost and difficulty of implementing and maintaining the system also needs consideration. It has to be said that many problems remain in the practical application of 2P microscopy in the working laboratory. The pulsed NIR lasers, as well as being costly, continue to be more difficult to set up and maintain in operational order than the visible lasers used in confocal microscopy. The configuration of many early commercial 2P microscopes were often sub-optimal, failing to take full advantage of the new method, particularly in terms of their light detection systems.

In summary, camera systems are simpler, faster, and less expensive, and may be adequate in single cell studies if the fullest sub-cellular detail is not required. The single-point scanning confocal microscope remains ideal for fluorescence imaging of single cells and there are numerous suppliers. Deeper imaging (40-500 µm) requires 2P with its attendant costs and problems. Fast confocal imaging can be achieved using the multi-point scanning systems, at the expense of some spatial resolution and image contrast (a 10% background is always present).

John Dempster & David Wokosin

Centre for Biophotonics, University of Strathclyde

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[1] www.bitplane.com
[2] www.improvision.com
[3] www.universal-imaging.com

	Imaging mode	Usable depth	Max rate (resolution)	Systems
Camera	full field	~20 µm	141 fps (160x160)	Princeton I-PentaMax[a]
		"	102 fps (164x123)	Hamamatsu C4880-81[b]
		"	2000 fps (80x80)	NeuroCCD-SM[c]
Confocal	single point scan	~40 µm	28 fps (256x64)	Bio-Rad Radiance 2001[d]
		"	77 fps (512x32)	Zeiss LSM 510[e]
		"	4 fps (512x512)	Olympus FluoView FV300[f]
		"	25 fps (512x32)	Leica TCS SP2[g]
		"	1 fps (512x512)	Nikon C1[h]
Confocal	multi-point scan	~40 µm	45 fps (168x128)	Perkin-Elmer UltraView[i]
		"	120 fps (1280x416)	VisiTech QLC100[j]
Two photon	single point scan	~500 µm	28 fps (256x64)	Bio-Rad Radiance 2001 MP[d]
		"	77 fps (512x32)	Zeiss LSM 510 NLO[e]
		"	25 fps (512x32)	Leica TCS SP2 RS[g]

Table 1 Typical camera, confocal and 2P imaging systems

[a] www.roperscientific.com
[b] www.hamamatsu.com
[c] www.redshirtimaging.com
[d] microscopy.bio-rad.com
[e] www.zeiss.com
[f] www.olympus.co.uk/micro
[g] www.leica-microsystems.com
[h] www.nikonusa.com
[i] lifesciences.perkinelmer.com/livecellimaging
[j] www.visitech.co.uk

Strait talk: the trouble with academia

Bill Parry

Britain can boast 44 Nobel Prize winners over the last 50 years, though only four in the last 20 years. And one of its most recent recipients, Tim Hunt, told how he had to scrape together enough money from colleagues to buy the lab a phone. Do these facts reflect the sorry state of the life sciences in academia in Britain today? Here, three young researchers frankly highlight their major concerns about a career in academia. It isn't all bad, but there are very serious problems that urgently need to be addressed.

British science has good reasons to pat itself on the back. You've heard the figures before: with one percent of the world's population, the UK funds nearly five percent of the world's science, has eight percent of the world's scientific publications and nine percent of its citations. The UK may be a world leader, but that position has been undermined by decades of eroded funding and, consequently, declining morale. 'Brain drain' in the life sciences is an acknowledged reality by many – not just a drain to countries like the USA, but from academia into industry and the City.

Tony Blair, the British Prime Minister, is aware of this decline and its long-term consequences for Britain. In May he addressed eminent members of the scientific community at the Royal Society, stating: "We have relied too long on tradition and sentiment to aid our scientists. We need strong funding and public support, not just the warm glow of our traditions."

Three different young life science researchers (all under 40 years of age) are interviewed here, each describing their personal views of urgent science policy issues in academia. While geocentric (each interviewee works at University College London and lives in London), their views provide clear indications of why dwindling numbers of graduates with Firsts are going on to do PhD degrees (down 18% between 1998 and 2000) and fewer PhD graduates are going on to do post-doctoral academic research and industrial research, according to the Biochemistry Society's *Graduate Employment Survey 2000*.

These were conducted weeks before the Chancellor, Gordon Brown, announced his much anticipated Spending Review. Their views are a preface to an article in the next issue of *Physiology News*, which will present the views of major UK science organisations, such as the Institute of Biology, UKLSC and Save British Science, about pressing science policy priorities and their analyses of Mr Brown's Review.

A huge cash injection is hoped for and necessary if this erosion is to be staunched in the UK. Politicians have talked about how committed they are to promoting the science base in the UK. By the time this is published, we will have learnt whether the British Government is prepared to match rhetoric with money.

Dr Dave Flavell, Lecturer and British Heart Foundation (BHF) Intermediate Fellow, UCL, aged 39

Short-term contracts: what adverse effect do you think these have on UK bioscience researchers' career decisions? Have you or those you work with been affected by them?

A large impact. Short-term contracts are fine at the level of first post-doc, where it is beneficial for young researchers to move around and gain experience in a number of different labs and perhaps also fields at home or abroad. The problem is that there is not a very clear career structure in place and money at universities is so tight that there is little chance of tenure for anyone apart from the most successful *young* researchers (UCL has a £12M deficit for this year). Tenured positions will more often go to older established researchers, partly in an effort to improve RAE scores. At the intermediate level, it is sometimes necessary to apply for research fellowships that provide the applicant's salary but insufficient technical support. These applications are extremely time consuming, as mentioned below.

I have been personally affected by short-term contracts and was recently in a situation where I applied for a Fellowship and had I been unsuccessful, I would have been looking for employment elsewhere, probably in the pharma industry.

People working with me have also been affected by short-term contracts, and more importantly the lack of career structure. The goal of many people is to secure a position in a pharma company for the security, higher wages and better facilities.

Short-term funding: same questions as above

Writing for grants is enormously time consuming. Additionally, some are so competitive that some funding bodies are not worth applying to. My personal experience with the BHF is actually very good,

as I have recently obtained a three-year Intermediate Fellowship. Ideally I would have applied for a five-year BHF Senior Fellowship, but at the time my CV was not strong enough. A good example of an enlightened funding programme is the BHF Professorships. The Head of our Centre is a BHF Professor and gets a generous 'discretionary fund', which is used for bridging funding between grants, *et cetera*.

Career structure: is this a problem in bioscience academia for recruiting and retaining the UK's best prospects? Would you like to see an improved career structure? If so, such as what? In your experience, is this a particular concern for female counterparts?

Career structure is a bigger problem than short-term contracts. Long-term prospects are far more important. I personally think that tenure is not necessarily a good thing, as pressure to succeed drives research, and scientists who cannot work effectively without pressure are in the wrong career. Additionally, academia can get clogged up with senior academics who do not contribute towards relevant research, but through their positions/contacts *et cetera* are able to attract a disproportionate amount of funding. That said, the same senior academics are probably the best teachers of undergraduates, so this also has to be taken into account. A sensible structure for younger researchers would be five-year rolling contracts, which are renewed on the performance of quality research; these would ideally come with some technical support (i.e. a technician and perhaps a PhD student and consumables and equipment funding).

A caveat is that the *best* and *brightest* researchers should not have much trouble finding positions, but the ones who have not shone at PhD level and the more insecure scientists or those with commitments may suffer. Late bloomers are a particular problem, as a poor PhD could easily be due to poor supervision, a lousy project, *et cetera*.

This is a particular problem for women. A successful scientist has to work very hard, continuously, which is nigh impossible (nor desirable) for a young mother. Thus when it comes to starting a family, females are in a very poor position. Additionally, salaries are so poor and child care so expensive that going back to work with more than one child is unaffordable.

PhD stipends: are these adequately competitive or attractive with other career options for the UK's best?

PhD stipends are not too bad, as they are not taxed, but a postgraduate salary is the same when taxation etc is taken into account. Thus people will do a PhD, see the lack of career structure, security, pay, facilities, *et cetera*, and look for alternative careers. Postgraduate pay is a particular problem in London and the South East in general. Many people are moving to cheaper parts of the country for a more affordable cost of living.

Student debt: does this deter many of the best and brightest from pursuing an academic career in the biosciences in your opinion?

I don't know what impact student debt has on potential students, but I assume that the aforementioned problems (pay, career structure *et cetera*) would deter someone with a large debt to pay off. Post-secondary education should certainly be cheaper, with scholarships available for the less well off (they probably are to some extent?).

Academic salaries: do you feel that these are fairly competitive with either other career opportunities (eg industry or totally outside of science, such as in the City) or with counterparts abroad?

Obviously these are not remotely competitive. This is a growing problem. Most scientists are not 'in it for the money'. This is a very big problem at all levels.

What keeps you in the academic biosciences? What do you enjoy most about your work and career? What frustrates you the most?

The job satisfaction, work environment and academic freedom. That said, my particular specialised field is of enormous interest to the pharma industry, and I am always open to offers...

I enjoy the fact that I am working on something (i.e. cardiovascular disease) that is academically incredibly interesting and complex, and which is of relevance to everyone. What frustrates me most is the difficulty of obtaining funding for myself and fellow workers, and the attendant endless workload.

Would you encourage today's A-level students to pursue a career in the biosciences? If so, why?

Yes, but only if they are not interested in money. Why, because it can be enormously satisfying and it offers great opportunities to work and travel (which I have not taken advantage of!).

What advice would you give Gordon Brown in shaping his imminent Spending Review?

Do it properly:

Don't say that new money is there when it isn't.

Don't throw money into a 'new scheme', this is a cheap, short term and ineffective option: the basic problem is underfunding, address it. (I would be surprised if this happened, but it would be nice to see some *real* progress made, e.g. as with the NHS, rather than some cosmetic work so that the government is *seen* to be doing something rather than actually doing it.)

Provide enough money to actually solve the problems.

Reform the MRC:
The MRC concentrates a large proportion of its money into several large institutes, which means that most of the MRC's funding goes to disproportionately few researchers. This is fine when these researchers are the best, but a waste of money when they are not.

The procedure for applying for MRC Project grants requires the applicant to be a member of a large consortium; thus, further channelling money towards the established researchers.

Dr Andrew Wilson, Research Fellow, Centre for Clinical Pharmacology, Department of Medicine, UCL, aged 28

As someone who has just completed his PhD, what is your main problem with academia so far?

My top complaint would definitely be pay. PhD stipends vary from poor to quite reasonable. As they are tax-free, the best ones can be worth quite a bit of money, but these are few and far between. As it's essentially another level of study, the problem remains that people are not earning a decent wage with which to pay off student debt, and they're still not going to have any savings by the end of it. They're going come out of it at 24–25 years of age with basically no income and nothing to show for six or seven years in university.

You can have a much more lucrative career doing things outside science: IT, computing, media, finance – these things are valued higher in our society and much more readily than scientific research, even though science is what improves our standard of life. There's a lot of talk from politicians about how valuable science is to the future of this country, but none of them are ready to take their finger out to show they mean what they say. If they were to increase salaries by say, £5000 per annum, when you multiply that by the number of scientists in academia, it's actually very little, compared to the value of retaining that expertise.

Would you have reconsidered what you would have studied, knowing what you know now?

Absolutely. If I had been aware of the working conditions of academic life I would never have gone into it: there's no job security, the pay is bad, and you work very long hours for very little reward, other than intellectual. At the end of the day you've got to live, you have to have a decent quality of life, you've got to be able to enjoy yourself. After putting all that effort in you expect something back and there is very little, and on an academic salary in London, you can't do that.

Would you recommend a life in academic biosciences to friends or family?

Absolutely not – unless they were not interested in money, and utterly committed to a long-term career in science, and they want to become an academic.

What did you enjoy about doing a PhD?

First of all, it's a very stimulating experience and your knowledge and abilities increase exponentially in the first few years. The freedoms you have intellectually in terms of your work patterns are what most people value. Although there's always a supervisor looking over your shoulder, to varying degrees, most people are quite independent, and it's nice to have that flexibility.

You have been a Research Fellow for four months now. Has there been much a difference in pay from being a PhD student?

No. I've gone up the next point on the salary scale. Fortunately I was a research assistant so I was on a salary right from the word go and then I did my PhD part-time. Essentially my work involved doing experiments that I could use towards writing my thesis, so I killed two birds with one stone: I got a higher degree and a salaried position. By obtaining a PhD I have only gone up to the next point on the salary scale, and it's not that much, probably about £900.

Do you think that the sacrifices you've made over those of your friends who didn't go to university will pay off in the end?

No, for the reason that academics have a very rigid pay structure. There are 'finite points' and you go up an increment every year, which is about £900 per year on average. Every April you get an inflationary increase, which is variable, to adjust for the cost of living. In real terms, comparable sectors have increased at about 44% over the past 10–15 years whereas academics have increased by 5% because every pay rise we tend to get is at, or very near, the rate of inflation, so your real term increase is minimal. Coupled with that, London weighting has been frozen since 1992 — there has been no increase for 10 years. It doesn't come near to covering the extra costs. I think £6000 was recently recommended as the minimal weighting, the minimal, whereas for me it's only £2134.

What changes would it take for you to regard academia as a viable career?

It must be made more attractive and there are a number of ways to do that. One is to increase the salaries, and I would suggest a one-off increase of all points on the academic scale of £5-6000, then regular increases, you'd get your regular incremental points brought back, and that would bring a starting post-doc to about £25,000 - £28,000 if they're in London. For someone who has two or three degrees behind them, I don't think that's unreasonable. If you want to attract the best and you want a vibrant research base in this country, you have to pay for it.

There is also a problem about the nature of short-term funding that most researchers have to cope with. I don't think there's much the government can do about this. But most grants are funded for two, three, or if you're lucky, four or five years. This, of course, makes job security near impossible. If people don't have job security, they won't be as productive. The way science is funded is a problem in this country. It might be better to give academics permanent jobs with performance–related pay, to ensure you only retain the good ones and you weren't paying for ones who weren't pulling their weight. But we have to do something to give those working in the academic sciences some long-term security, otherwise how do you buy a house on a 25-year mortgage if you're going to be potentially unemployed every three years or so?

Compounding that is the actual peer-review process, which determines whether your grant gets funded in the

first place. It's a leap of faith, basically. The number of highly talented people I've seen not get grants and untalented people get grants – I really don't know what the criteria are, it seems all very subjective. Egos and politics get in the way. I wouldn't go so far to say it's corrupt, but it doesn't appear as objective as it could be, and I think that's bad.

Dr Rita Jabr, Research Fellow and Honorary Lecturer, Centre for Clinical Pharmacology, Department of Medicine, Rayne Institute, UCL, aged 38.

Dr Jabr has a varied background: her undergraduate and MSc degrees were completed in Kuwait; her PhD was completed in Canada; her first post-doctoral position was in Reno, Nevada; she then took up a position as assistant professor at Kuwait University for a few years before coming to the UK to work as a Research Fellow.

Have short-term contracts been a problem for you?

Yes. I am fortunate in some respects in that I am on a five-year grant. However, in moving to London to settle, it is very difficult and unsettling to get on the property ladder knowing that I am guaranteed a job for just five years. At the same time, I see their value early in a researcher's career, providing an important breadth of experience; however, thereafter they are a hindrance, especially when combined by a poor career structure, low pay and so forth.

Career structure: do you see a lack of a career structure in academia and, if so, how does it affect you and your prospects of staying in academia?

Mine is a complicated matter because of my time in Kuwait and my age. My position in Kuwait turned out to be more a teaching than research position and I consequently fell behind in publications. As a UK resident, I am unable to apply for most of my own external funding until I have lived here for a minimum of three years. I have since learnt that I am ineligible for a Fellowship in many cases if I have been a post-doc for more than six years. As I am almost 39, it seems that I will be unable to establish myself as an independent researcher in the UK, despite my expertise and enormous commitment and enthusiasm. Although I will continue to explore all options available to me to remain in academia, I cannot afford, financially or career-wise, to remain a post-doc indefinitely and so am having to look for positions in industry as well.

As a woman, given the above, you can imagine how starting a family would impair my chances of remaining competitive in academia, and I obviously have to bear this in mind.

Would you encourage A-level students to pursue a career in the life sciences?

Certainly. It provides an exciting and stimulating education and possible career, albeit one whose rewards probably will not be financially based! However, there is tremendous satisfaction in undertaking research that can benefit humanity, and there is room for plenty of intellectual freedom. Once they have graduated, they will have many skills and sufficient opportunities to decide whether to remain in academia or to pursue a career in industry or outside science. If the government wishes to retain the best students, it will have to make an academic career more attractive, by providing a more secure career structure (more long-term funding) and investing more money in equipment and making salaries more competitive.

April 2002 saw the publication of the much anticipated and much welcomed Sir Gareth Roberts' Review, *SET for Success*. This was commissioned last year as part of the Government's strategy for improving the UK's productivity and innovation performance. None of the interviewees had heard of it before the interviews took place, so what is remarkable is how closely their comments and recommendations echo those made in the Roberts' Review. For example, it says that low stipends 'reduce the attractiveness of a PhD'. It recommends that 'stipends better reflect the market demand' and that the Government and research Councils 'raise the average stipend ... to the average graduate starting salary (currently equivalent to just over £12,000)'.

As for post-docs, the report says: 'researchers receive pay that compares unfavourably with that which comparably qualified people could expect to earn outside academia; receive few opportunities to undertake training and development; and are faced with uncertain futures since employment beyond the current project contract – commonly around two years – is not guaranteed. Furthermore, there is little structure to their career, and little advice as to how to make the jump to becoming a permanent member of the academic staff. Although a large proportion remain intent on pursuing academic research careers, it is estimated that fewer than 20 percent reach a permanent academic job.' Its recommendations also echo those of the interviewees.

This Government's record of funding the sciences has been commendable, but there is clearly much more that needs to be done, and now. Mr Blair concluded in his Royal Society address: 'I want to make sure the UK is one of the best places in the world to do science. For that we need people, equipment and infrastructure to be properly funded. And we should continue to support British science abroad.'

It's over to Mr Brown to ensure this, and to ensure that we promote British science abroad, and not force Britain's brightest scientists out of academia or overseas.

Bill Parry is a freelance writer and also works at the Institute of Biology

Focus on Cardiac Mechano-Electric Feedback

For the uninitiated, cardiac mechano-electric feedback (MEF) may seem a pretty dull topic: *Isn't it quite obvious, that the mechanical environment of the heart affects its electrophysiology*?

Worse than that, for certain types of reviewers the topic simply doesn't exist: *Why are you wasting your time, stretching patch-clamped cells, merely to record artefacts*?

Thankfully, a growing number of dedicated journal issues, invited reviews, and international meetings illustrate that the subject is alive and kicking. This year alone there will be an international workshop on Cardiac MEF & Arrhythmias at Oxford (http://mef.physiol.ox.ac.uk/), as well as dedicated sessions during *NASPE*'s annual meeting in San Diego and at CardioStim 2002 in Nice. It was very timely, therefore, that the Physiological Society chose to devote a 1-day symposium to cardiac MEF during its Leeds meeting.

So – what is this *emm-eee-eff* all about?

Clinical observations of mechanically induced heart rhythm disturbances date back more than 120 years, when first reports about sudden cardiac death after chest impact in the absence of structural damage were published (Meola, 1879). This condition, termed *commotio cordis* (Casper, 1857), has a long pedigree of targeted experimental research (Schlomka, 1934). More recently, helped by media reports on 'unexplained' sporting fatalities after chest impact during baseball or hockey (including coverage by popular TV series like *ER*), sudden cardiac death by *commotio cordis* is experiencing a renaissance in professional and public interest (Maron *et al*, 2002).

Obviously, not all mechanical effects on heart rhythm are that dramatic. They may even be useful!

Ectopic beats, for example, that occur during cardiac catheterisation may be taken to indicate the final approach of the catheter tip to the heart. Moreover, in the days before lawyers determined clinical interventions, patients could be prevented from losing consciousness during Stokes-Adams attacks by 'pre-cordial percussion' – repeated thumps to the chest that triggered competent cardiac contractions – until normal rhythm recommenced (Schott, 1920).

Energy levels required for mechanical induction of cardiac excitation are comparatively low. Using a modified industrial stapling gun (!), pre-cordial impacts of 0.04–1.5 J were found to reliably trigger ectopic beats in healthy volunteers (Zoll *et al*, 1976).

These beneficial effects of cardiac MEF explain why in many countries, including the UK and US, precordial thumps are a sanctioned procedure for resuscitation after witnessed cardiac arrest. Does this really work? See Figure 1.

The wealth of case reports from patients (including heart transplant recipients) is complemented by decades of research, from *in vivo* work on mammals like man (Levine *et al*, 1988) and pig (Lab & Woollard, 1978), to *ex situ* studies in isolated hearts (Franz *et al*, 1992) or tissues (Deck, 1964), and *in vitro* experiments on single cells (White *et al*, 1995), membrane patches (Sachs *et al*, 1991), and proteins (Sukharev *et al*, 1994).

Basic research shows that many features of cardiac MEF may be reproduced in isolated cells and tissues. Key mechanisms include the activation of specialised mechano-sensitive ion channels (Craelius *et al*, 1988), mechanical modulation of second messengers like nitric oxide (Petroff *et al*, 2001) and calcium (Le Guennec *et al*, 1991), and the interaction of mechano-sensitive cells of both myocyte and non-myocyte origin (Kohl *et al*, 1999).

Nonetheless, apart from a number of praiseworthy exclusions from the rule, the 'link-up' of clinical studies and basic science has, thus far, been less than satisfactory (Taggart & Sutton, 1999). There are many reasons for this, including technical limitations such as the lack of specific drugs to probe cellular mechanisms of MEF *in situ*, but also geographical, linguistic and professional 'divides'.

Some of these restrictions are currently being redressed. Thus, the identification of a first, highly selective peptide blocker of stretch-activated ion channels (Suchyna *et al*, 2000) has opened-up new perspectives in linking

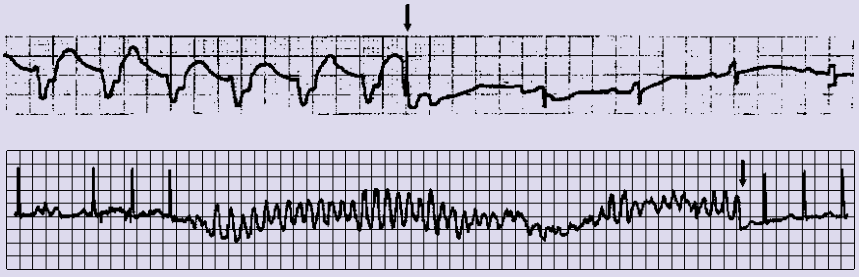


Figure 1 Examples of 'fist aid': thump-version to sinus node rhythm (arrows) of ventricular tachycardia (top, Pennington *et al*, 1970) and early ventricular fibrillation (bottom, Barrett, 1971); copyright ©1970, ©1971, Massachusetts Medical Society, all rights reserved.

(sub-)cellular mechanisms of MEF to patho-physiological processes at higher levels of integration (Bode *et al*, 2001). Furthermore, extensive reviews of historical (mainly non-English) literature sources recovered much 'lost' insight from the past and helped to inform current research (Nesbitt *et al*, 2001). Finally, we are witnessing a more conscious approach towards bringing together physiologists, bioengineers, modellers and clinicians to discuss mechanisms and implications of cardiac MEF.

The Leeds meeting is set to continue this trend, which will – hopefully in the near future – make cardiac MEF a standard item in all mainstream physiology-textbooks (*…dream on, chap!*).

Peter Kohl
University Lab of physiology
Oxford

Selected papers in order of publication, illustrating (a rather incomplete) time line of MEF work:

1857 Casper JL. Practisches Handbuch der gerichtlichen Medicin, Verlag August Hirschwald, Berlin.

1879 Meola F. La commozione toracica. *G Internaz Sci Med* **1**, 923-937.

1920 Schott E. Über Ventrikelstillstand (Adams-Stokes'sche Anfälle) nebst Bemerkungen über andersartige Arhythmien passagerer Natur. *Dt Arch Klin Med* **131**, 211-229.

1934 Schlomka G. Commotio cordis und ihre Folgen. Die Einwirkung stumpfer Brustwandtraumen auf das Herz. *Ergebn Inn Med Kinderhkd* **47**, 1-91.

1964 Deck KA. Dehnungseffekte am spontanschlagenden, isolierten Sinusknoten. *Pflüg Arch* **280**, 120-130.

1970 Pennington JE, Taylor J & Lown B. Chest thump for reverting ventricular tachycardia. *NEJM* **283**, 1192-1195.

1971 Barrett JS. Chest thumps and the heart beat. *NEJM* **284**, 393.

1976 Zoll PM *et al* External mechanical cardiac stimulation. *NEJM* **294**, 1274-1275.

1978 Lab MJ & Woollard KV. Monophasic action potentials, electrocardiograms and mechanical performance in normal and ischaemic epicardial segments of the pig ventricle *in situ*. *Cardiovasc Res* **12**, 555-565.

1988 Craelius W, Chen V & El-Sherif N. Stretch activated ion channels in ventricular myocytes. *BioSci Rep* **8**, 407-414.

1988 Levine JH *et al*. Changes in myocardial repolarisation in patients undergoing balloon valvuloplasty for congenital pulmonary stenosis: evidence for contraction-excitation feedback in humans. *Circulation* **77**, 70-77.

1991 Sachs F *et al*. Single-channel mechanosensitive currents. *Science* **253**, 800-801.

1991 Le Guennec J-Y *et al*. Stretch induced increase of resting intracellular calcium concentration in single guinea-pig ventricular myocytes. *Exp Physiol* **76**, 975-978.

1992 Franz MR *et al*. Electrophysiological effects of myocardial stretch and mechanical determinants of stretch-activated arrhythmias. *Circulation* **86**, 968-978.

1994 Sukharev SI *et al*. A large-conductance mechanosensitive channel in *E. coli* encoded by *mscL* alone. *Nature* **368**, 265-268.

1995 White E, Boyett MR & Orchard CH. The effects of mechanical loading and changes of length on single guinea-pig ventricular myocytes. *J Physiol* **482**, 93-107.

1999 Taggart P & Sutton PMI. Cardiac mechano-electric feedback in man: clinical relevance. *Prog Biophys Mol Biol* **71**, 139-154.

1999 Kohl P, Hunter P & Noble D. Stretch-induced changes in heart rate and rhythm: clinical observations, experiments and mathematical models. *Prog Biophys Mol Biol* **71**, 91-138.

2000 Suchyna TM *et al*. Identification of a peptide toxin from *Grammostola spatulata* spider venom that blocks cation-selective stretch-activated channels. *J Gen Physiol* **115**, 583-598.

2001 Bode F, Sachs F & Franz MR. Tarantula peptide inhibits atrial fibrillation. *Nature* **409**, 35-36.

2001 Petroff MGV *et al*. Endogenous nitric oxide mechanisms mediate the stretch dependence of Ca^{2+} release in cardiomyocytes. *Nature Cell Biol* **3**, 867-873

2001 Nesbitt AD, Cooper PJ & Kohl P. Rediscovering commotio cordis. *The Lancet* **357**, 1195-1197.

2002 Maron BJ *et al*. Clinical profile and spectrum of commotio cordis. *JAMA* **287**, 1142-1146.

The academic pairing scheme – what could it mean for you?

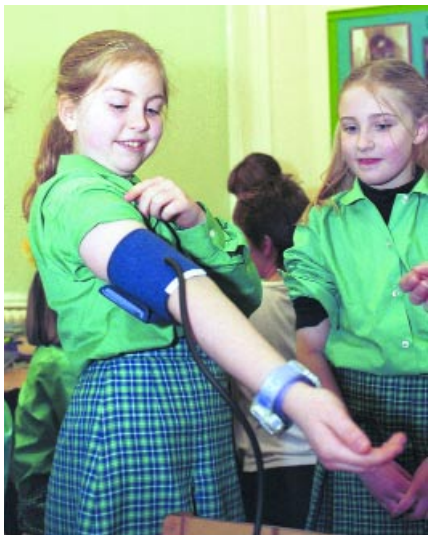
Over the past few years the number of applications to biomedical based degree courses, along with applications to the physical sciences, has been falling. This is a worrying trend, especially as it has occurred at a time when student numbers have been increasing, and suggests that science courses are becoming less appealing to sixth-form students. An additional worry is applications have fallen while at the same time there have been dramatic improvements in the way biomedical science is taught in the national curriculum, with topics aimed at increasing the understanding of science and also the investigative skills of school children. Changes to the curriculum have occurred at every level, from age five all the way to A' level. In fact even primary school children now cover aspects such as the function of the heart, how muscles work, the effect of exercise on the body and nutrition. However, despite the fact that children are now doing more science in schools the fact remains that applications have fallen. Having talked to a number of primary and secondary school teachers it is clear that there are a number of problems with the teaching of science in schools. Some of the problems they have identified include 1) Children get turned off science from a early age 2) Children of all ages say science is too hard and is boring 3) Many primary school teachers have little formal training in science and 4) Secondary school science teachers are a dying breed. To try to improve the perception of physiology by older school children the Society has funded a number of projects in the past. These include sixth-form workshops where students have the opportunity to come and carry out practical work in the University environment and workshops aimed at secondary school teachers. All these events have been well received by the participants. However, they do target rather small audiences. What we really need is a country wide initiative to promote physiology, and therefore more recently the Society has tried to set up a Speakers in Schools Database. Under this scheme academics would go into their local schools to give lectures and/or run practical classes. Together with the UK Life Sciences Committee (UKLSC) Education group a searchable list of academics has been compiled and will shortly be posted on the web site www.biology4all.com. This database allows schools to identify academics who have expressed an interest in working in local schools, via their postcode, name or subject. You might be thinking that academics having nothing to offer schools. I would strongly disagree with this and would like to tell you about my experience of working with primary school children and show you what a useful and rewarding experience such work can be.

Science Week ran between the 8th and 16th of March this year. It is an annual event, with a whole week dedicated to

Top Dr Louise Robson measures the resting heart rates of year four girls at Sheffield High School Junior Department.

Above Dr Charlotte Hill and the girls enjoy finding out how heart rate changes on anticipation of exercise.

Below "How much will the cuff inflate"?



Top Dr Charlotte Hill explains how blood pressure monitors work.

Above Dr Louise Robson and some girls look at the blood pressure monitor to investigate the effect of exercise on heart rate.

improving the perception of science by the general public. It involves many different types of scientists from both academia and industry, working in many different kinds of environments giving lectures and running practical workshops. Events in schools are particularly popular. The scientists, who must then register their event with the BA, provide ideas for events. I became involved in Science Week, as I am required to spend three days per year working with the public on a grant I hold from the BBSRC. However, I have to say that I fully intend to participate in future years, whether I need to or not. I decided to target primary school children, as I knew that many primary teachers must teach what is essentially the physiology of various systems without any formal training. One topic they find difficult is the heart. So this is the subject I chose for my event. "Matters of the heart" was the title of my event and, as physiology is a practical subject, I quickly hit upon a plan to give a short talk to the children about the heart followed by small group practical work. In total I spent three full days in three separate primary schools in the Sheffield area. The ages of the children varied between schools, but covered years four to six (ages eight to eleven). In total I worked with about two hundred children during the three days. In all schools I started the day with a presentation to all the children, using a simple, self-written PowerPoint presentation that covered aspects such as the shape and size of the heart, internal structure, how blood moves through the heart and also why we need to pump blood around the body. As well as talking to the children I also used plastic heart models, which were passed around the class for all the children to investigate, and a balloon heart model to show what happens when the heart contracts. After the presentation I then worked with the children in small groups, measuring heart rates with blood pressure monitors. Heart rate was measured at rest (we had a competition to see who had the lowest heart rate) and then on exercise (star jumps). We then spent some time discussing why heart and respiratory rates go up during exercise. I have subsequently provided each school with the experimental data, including graphs for the children to interpret (a skill they find particularly difficult I understand). The session finished with a question and answer session on any aspect of human biology and also my job as a scientist. I was impressed by the questions the children asked. Indeed, at one school I had two forty-minute question sessions and even then the children still had more questions to ask. The teacher finally extricated me from the class to go for lunch, with questions being fired at me going down the stairs! Finally, I provided each teacher with a list of valuable web sites for biomedical science (including the Society's of course). It was clear that most of the sites were new to the teachers.

Feedback from the children shows that they really enjoyed the day and were amazed to see that scientists were not all middle-aged men with a beard and glasses! Many of them felt that science could be fun and interesting. Feedback from the teachers also shows that they thought that the event was extremely useful for the children and also for themselves in terms of how to teach the heart in the future. I certainly found this to be an extremely fun and rewarding experience. Just think what the Society could achieve for the profile of physiology if the members participated in the academic pairing scheme. Remember your time commitment could be as little as giving one lecture each year or could involve participation in a more long-term project. Academics have an important role to play in the public perception of science and by going into schools we can make a significant improvement to the understanding and appreciation of physiology by school children. After all they are the undergraduate students of the future!

Louise Robson
Physiological Society rep on UKLSC Education Group

For those of you interested in adding your name to the Speakers in Schools database you should contact Maggie Leggett at mleggett@physoc.org. The database will be formally launched during the British Association Festival of Science, at a free event on Thursday 12 September at lunchtime.

Environmental physiology of animals
by Pat Wilmer, Graham Stone & Ian Johnston

Blackwell Science. ISBN 0-632-03517-X. 644pp 2000, £27.50

Imagine, for a moment, that you are a visiting alien (on many days in our brave new work environment, this seems a quite natural assumption). Imagine further, that you happen to land in the remotest and most barren part of the Namibian desert, where the dunes roll off in all directions, the sun beats down unmercilessly and not even a desert scorpion manages to scrape a living. Everything seems safe enough as you emerge from your transporter, but, as luck would have it, the first thing you see, lying on the sand, is a radiator cap from a car engine (how it got there is a long and exciting story of human endeavour followed, a few miles away from this location, by tragedy – but it's not strictly relevant to the subject of this review). You pick the object up and immediately you are on your guard, because obviously this is something which has been designed. But what on [not earth] is it? A type of sunhat? A shoe? A plate? Some sort of moving part from a machine? For someone unfamiliar with its intended use, it would probably take quite a while to figure out that those little flanges might have opposites which would allow it to be used to close a hole. And even then, why would you want to do that? The point is that if you take even a relatively simple object out of context, it can be extremely difficult to divine its purpose, while complex objects may make no sense at all (for example, the hairdryer that you subsequently find – you don't have hair).

This is why it is such a pleasure to come across a new textbook which explicitly tries to put physiology back into an environmental context. Although it's great fun playing with patch-clamps and channels, extracting DNA and measuring fluorescence signals, the results don't make much sense unless integrated to a functional level and interpreted in the context that they were designed for. And, yes, physiological systems are clearly designed for specific purposes. And, no, this isn't the teleological heresy when we understand that the design process is the gradual bio-environmental moulding of natural selection and not conscious decision making (anyone still confused about this should read Daniel Dennett's superb book, Darwin's Dangerous Idea).

In many ways, it's surprising that modern physiology has moved so far away from the environmental contexts of its subjects, since comparing the astonishingly different environments where life manages to survive is a brilliant way of unearthing design constraints and contrivances, and a natural way into the field of evolutionary physiology pioneered by Jared Diamond and others. Environmental Physiology of Animals uses a wide variety of animal types to weave together key issues in comparative physiology with perspectives from ecology, behaviour and evolutionary biology. A major theme is to consider integrative responses to particular habitats and to discuss overall organismal mechanisms, rather than conceptually breaking organisms down into separate isolated systems – and thereby losing important insights into the way the biosphere really works.

The book is divided into three main sections: Basic principles (mechanisms of adaptation, size and scale), Central general issues in comparative physiology (water, ions, energy supply, metabolism, temperature, excretion, respiration and circulation) and Coping with the environment. This latter part is the major section of the book and deals with marine life, shorelines and estuaries, fresh water, special aquatic habitats (such as deep sea thermal vents), terrestrial life, extreme terrestrial habitats (such as deserts) and (a good one) parasitic habitats. This structure means that the book can be used profitably by a wide range of readers, from students beginning their studies of physiology to professors who are rather slick with differential equations, but a bit hazy on why we die if our temperature goes up or down a few degrees.

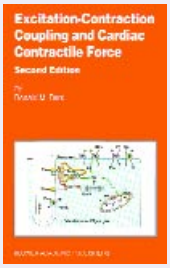
Producing this text has obviously been a labour of love for its three authors and in my opinion the result is outstanding and deserves a wide readership. Not only is the book clearly written and well illustrated, it is also excellent value for money. If I were an alien, I would definitely want to acquire a copy before proceeding further, though I would be a bit disappointed by the omission of a chapter on extra-terrestrial life. The book would certainly help me figure out the function of the hair-dryer – though understanding why it was actually in the desert would require a different course of study altogether.

John A Lee
Rotherham General Hospital

Excitation-Contraction coupling and Cardiac Contractile Force

Donald M Bers

Kluwar Academic Press, London.
ISBN No. 0-7923-7158-5. £30.00



This is the second edition of the book that was originally published in 1991, and it is essentially a monograph, focused on the mechanisms that underlie the heart beat. Although, focused on the regulation of intracellular calcium, contents include 10 detailed chapters providing an in-depth consideration of all aspects of cardiac contraction at the cellular level. Numerous figures, taken from original articles, are provided to give an evidence-based description of the concepts currently important in the field of excitation-contraction coupling. The bibliography alone is sufficiently extensive and up to date to serve as an indispensable source of key facts. Above all, the integration of complex data in to simple concepts that are easy to understand makes this a clear and easy to read text that will appeal not only to students at all levels but also active researchers. Strongly recommended.

Munir Hussain
University of Liverpool

Ageing and Immortality

Don't forget The Physiological Society workshop at the British Association Festival of Science!

University of Leicester
Wednesday 11 September 2002
9.30am – 12.30 pm

Speakers include Tom Kirkwood, James Malone-Lee, Olga Rutherford and Dawn Skelton, on topics from continence to exercise and immortality.

Attendance at the Festival is completely free to academics at Leicester University. And for those Members and Affiliates who are not working at Leicester, *The Physiological Society* has a limited number of free tickets. If you are interested in attending this workshop, please contact **Maggie Leggett** at *The Physiological Society* as soon as possible to ensure your places.

In addition, if you are attending the Festival please come along to the launch of the **Speakers in Schools database**, at lunchtime on Thursday 12 September. Have a glass of wine and celebrate the UKLSC Science Year initiative, aimed to bring scientists and school children more closely together, to the advantage of both.

Maggie Leggett

The British Association – Membership Benefits

As a Member of the Physiological Society, you are entitled to many benefits, from discounted subscriptions to journals to various travel grants. We also have an arrangement with the BA (British Association for the Advancement of Science) which entitles you to 20% off membership rates

The BA (British Association for the Advancement of Science) works hard to raise the profile of science. Through an

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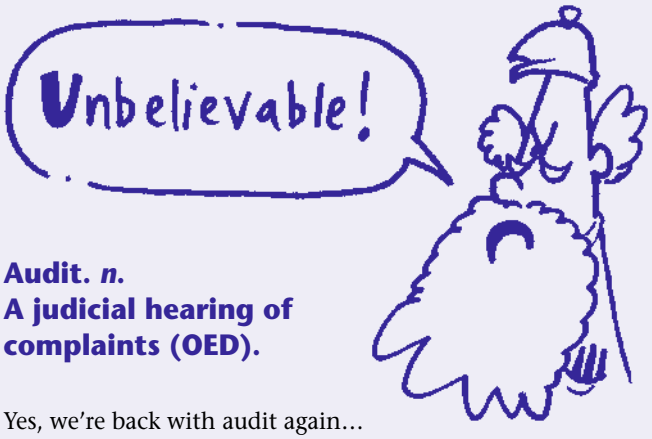

Audit. *n.*
A judicial hearing of complaints (OED).

Yes, we're back with audit again…

…Since, here in Britain's ever-beleaguered Universities, the repercussions of RAE are still rumbling on. Not to mention TQA (Do we still have TQA? Is TQA the same as Subject Review?). Plus all those other audits/assessments/surveys/quality control systems which have slipped my one-bit memory.

Anyway, the RAE. I wonder if there is anyone left in UK science research, even the most junior graduate student/Phys Soc affiliate, who doesn't by now know these dreaded initials stand for "Research Assessment Exercise"?

So. all research in British Universities has now been assessed. Well, not quite. What was actually assessed was all the research in British Universities that the Universities calculated might score one of the top two gradings, and was thus worth admitting to doing. A subtle difference

And people who did well will get more money for research. Well, not quite. They might get more. Or a bit less. Or even a lot less. Makes perfect sense.

Anyway… as a subject Physiology did well (if you believe some people) or alternatively was grossly unjustly treated (if you believe some other people) and is thus now in rude health and ready to be a key discipline in the post-genomic revolution (say the first lot) or is facing a major crisis (say the second lot).

Which of course asks the question:

Just who do you believe?

And also:

If drawing conclusions from all that meticulously-collected and carefully- considered data is so difficult and contentious, why did they all bother?

In the face of this confusion, it seems to me that a columnist's responsibility is to encourage a spirit of unity and co-operation by focussing on those aspects of the Audit Culture in Universities about which we CAN reach a consensus.

Stated simply:

"The audit process in Universities wastes a huge amount of time, and money, and means that the running of Universities reduces to a frantic scramble to score well in whichever audit process is coming up next"

I think we can all agree on that.

And we are talking serious money here. I recently read in the *THES* that the cost to the UK University system of audit in all its forms (including RAE, TQA and other internal "quality assessment" schemes) was, at a conservative estimate, £250 million a year. About the same as the total annual cost of running four or five UK Universities[1].

No prizes, of course, for guessing where the money for all this came from.

But there is a chink of light on the horizon. We now have, finally, a House of Commons science and technology select committee prepared to say out loud what most people in the Universities think, which is that the RAE costs a fortune, takes an eternity, and does little for UK science[2]. Not coincidentally, this committee actually has some scientists and ex-scientists on it.

And what has HEFCE said?

To paraphrase their response: "Hmmm…Let's clarify. You are trying to tell us that the RAE has: cost the Universities millions of pounds in bureaucratic costs; wasted tens of thousands of man-hours in administration; made teaching even more of a second-class activity than it was already; and made Universities rebadge, merge or close down any Department which doesn't score 5 or 5*."

– to which one could add: And, taken together with the TQA, destroyed any sense of continuity as Universities oscillate in a kind of panic-ridden managerial sine-wave between the two years before the RAE (Publications! Grants! Esteem indicators!) and the two years before the TQA (Teaching is vitally important. No, it really is. Really. Yes it is.).

So we LOVE the House of Commons science committee. Tell it like it is guys.

But HEFCE are not going down easily.

"Just wait a minute" say HEFCE to the Commons science committee "We've got you here. How can we possibly tell if any of what you say is true *without a detailed submission of carefully-collected, tabulated and PROPERLY-AUDITED evidence*?"

Quod erat desperandum, I think.

Or, to paraphrase Christopher Wren's famous epitaph: If you want to see the evidence, take a good look around.

Or even better: Will the last person out of Universities UK PLC please turn out the lights?

Once you've finished collecting the data for the next audit that is.

Mark Cain

[1] See S Prickett "Corruption of Quality" *THES* July 5th 2002 p 14.

[2] See e.g. Research Fortnight. Vol 8.19 (No. 173) July 10th. 2002 p.16.

extensive range of events and activities, the BA ensures that all sciences receive the attention of the media, government, industry and people of all ages. This is your opportunity to support the work of the BA and receive the benefits of BA membership at a discount!

The BA runs high profile events throughout the year, including the BA Festival of Science and National Science Week – achieving extensive media coverage. Many of you will know for the past couple of years we have supported a workshop within the festival (see other article). From hands-on science days for children to debates in bars for adults, the BA continually searches for innovative ways to involve people in science. The BA also publishes the magazine, Science & Public Affairs, which tackles the issues that are important to the scientific community and the wider public.

Many scientists already support the work of the BA. We hope that you will consider lending your support. By becoming a member, you will help the BA invest in continued promotion of science. In return, you will receive Science & Public Affairs, information about BA events and privilege offers.

To take advantage of this offer 'phone 0870 241 0664 or email members@the-ba.net. For information about the BA visit: www.the-ba.net.

As an Institutional Affiliate Member of the BA, the Physiological Society can offer all its members 20% off membership of the BA (full price £30, offer price £24).

Ben Savage
Membership & Admin Assistant

Physiology Workshops for First and Second Year Secondary School Pupils

In Dundee, with sponsorship from the Royal Society of Edinburgh and Lloyds TSB, we have been running a series of Science Masterclasses for children in years 1 and 2 in local secondary schools. There were two series of Masterclasses; in December and in April. One component of each series was devoted to aspects of muscle and cardiovascular physiology and was entitled "Having the heart to get a grip".

The events were run on a Saturday morning between 10.00 am and 12.30 pm, allowing sufficient time for all of the participants to carry out a number of simple experiments. The experiments included investigations into the strength of their dominant arm versus their non-dominant arm in a grip-strength test; whether boys were stronger than girls, what happened when strength was related to the forearm cross-sectional area, and what changes were observed in heart rate when going from a sitting to a standing position, and then during forearm exercise (squeezing a rubber squash ball either intermittently or continuously with the arm held low down or above the head).

The events were ran with 30 academic staff members, a technician and about 30 students per class. All of the students managed to discover something interesting about themselves and about the group as a whole. The feedback was very good with comments like "I had good fun and the staff were all nice" and "I thought the practical activities were great. Thank you I had great fun". The only negative feedback was about the snacks provided at half time – too boring! We believe that making links with prospective science students at this early age may be a more effective way of enthusing them about science generally, and sowing the seed of a possible interest in physiology.

Mike Rennie
Department of Anatomy and Physiology
University of Dundee

The 2001 RAE – a perspective from the physiological standpoint

The RAE represents a traumatic episode in the life of academic departments from the perspective of future income and also from the time and effort spent in preparing for the review. What is less apparent is the large-scale impact that the review has on the standing of a particular subject.

Physiology as a scientific discipline is going through a fundamental change at present; traditional boundaries are rapidly breaking down so that we are embracing new skills and widening our areas of collaboration. The advent of functional genomics means that research will rely increasingly on those with skills in the physiological sciences. Furthermore any indicator of success; publications in high quality journals; *per capita* research income; links with industry and the vitality of professional societies such as the Physiological Society would indicate that the discipline in the UK remains at the pinnacle of international regard.

Paradoxically, the recent RAE did not reflect this. Eleven institutions made a Physiology return and only one department achieved a 5* rating, five departments improved their rating and four declined. This should be compared to 99 departments returned in Units of Assessment (UoA), Biological Sciences, Clinical Laboratory Sciences and Psychology where only one department declined.

This raises the concern that it appears that physiology as a UK subject is declining in absolute terms, and even more so when related to other biological science groupings. This is not true of course as the great majority of physiologists were returned in UoAs other than Physiology. Recently the administration office at the Physiological Society asked members to indicate which UoA they were returned under, their score and the change of score

from the previous exercise. These results showed that there is no indication that physiologists are any more likely to be connected with units that achieve lower scores overall, i.e there is no objective evidence that physiologists are under-performing compared to other biological scientists, or indeed other academics overall. However, the *perception* that such a divergence of scores for the Physiology UoA compared to others gives the impression to university vice-chancellors, funding agencies, postgraduates, school leavers and their teachers as well as external administrative bodies that physiology, as a discipline, is in fact declining. This has tremendous implications for the future of the subject as part of degree courses and for funding initiatives from research bodies.

To express our worry about the disparity of fact and perception, the Physiological Society Executive (under the signatures of Colin Blakemore and myself) wrote to the chairman of HEFCE stating our concerns. The letter was written jointly with the Pharmacological Society (signed by their president Rod Flowers) as their subject achieved a similar dubious status in the exercise. The purpose of the letter was to express our deeply-felt concern about the necessity of ensuring the physiological and pharmacological sciences were recognised by all concerned as subjects that remain vital to the academic and commercial well-being of the UK, and also to act as support for those institutions contemplating an appeal against individual judgements. Copies were sent to vice-chancellors of universities with departments returned as physiology and/or pharmacology as well as to a number of newspapers. A report appeared in the Times Higher Education Supplement in late May so the subject is in the public domain.

It is important to stress that the two Societies in no way criticise any members of individual panels who worked fairly and diligently within well-defined criteria for each panel. The function of professional societies such as our own is to ensure that their own subject is properly represented and understood at all levels, and it remains our duty to ensure that this is the case when discrepancies occur.

Chris Fry
Institute of Urology
University College London

Sir Howard Newby
Chief Executive
Higher Education Funding Council for England
Northavon House
Cold Harbour Lane
BRISTOL BS16 1UD

Dear Sir Howard

2001 Research Assessment Exercise: assessment of Physiology and Pharmacology

We write on behalf of the Physiological Society and the British Pharmacological Society to comment on the unfavourable (and we believe unrepresentative) impression of the quality of our disciplines that has emerged from the 2001 Research Assessment Exercise (RAE).

The Physiological Society is a Learned Society with a membership of approximately 1,900, the majority working in UK universities and all engaged in physiological research. The British Pharmacological Society, with more than 2500 members in the UK and overseas, is the professional association for pharmacologists.

The views that we wish to convey to you are based on extensive discussion with the officers, committees and individual members of our two Societies, correspondence with the Heads of a number of relevant departments, and feedback received from the joint Pre-clinical Studies Assessment Panel and from members of other Panels.

We fully support rigorous mechanisms to assess and reward the best of British science. However, we share some of the concerns that have been expressed about the cost and benefit of the RAE, and about its impact on the organisation and administration of research in UK Universities. And, in particular, we fear that the Exercise has had a damaging effect on certain multidisciplinary subjects, especially Physiology and Pharmacology.

Our main concern is that, over successive RAEs, the assessment of Physiology and Pharmacology *per se* has diverged from that of closely related disciplines. As a consequence, the standing of several departments of physiology and pharmacology has declined. In turn, an increasing number of universities have chosen, for tactical or administrative reasons, to return physiologists and pharmacologists under other subject headings. In the 2001 RAE, only 11 departments were returned as Physiology and 9 as Pharmacology, compared with 15 under each heading in 1996.

The report about RAE 2001 on the joint HEFCE/SHEFCE website states that " the results of the 2001 Research Assessment Exercise (RAE) confirm further improvements in the overall quality and international standing of research carried out in the universities and colleges of the United Kingdom". Indeed, between 1996 and 2001, the proportion of departments rated 5 doubled, and the fraction rated 5* also virtually doubled.

Performance for Biological Sciences, Clinical Laboratory Science and Psychology (Panels closely related to Physiology and Pharmacology, and to which many physiologists and the pharmacologists were returned) exceeded the excellent overall trend: 99 departments considered by those Panels improved their rating between 1996 and 2002, while only 1 declined! The mean scores and percentage of 5* departments increased dramatically (e.g. Psychology, by 0.74 and 320% respectively; Biological Science by 0.85 and 350%).

By comparison, the assessments for Physiology and Pharmacology were sadly out of line with this positive trend. Only 5 departments improved and 4 declined. The Physiology mean score increased by only 0.38, with no increase in the number of 5* departments. One might conclude that the "rump" of departments submitted to the joint Pre-Clinical Studies Panel in 2001 were of relatively low quality. However, nothing in our analysis or in our consultation

with our members suggests that this is the case. The disparity in ratings does not, we believe, proper reflect the standing of the departments that submitted to Physiology and Pharmacology, nor the demonstrated achievements of many of them since 1997.

We do not question the integrity or the objectivity of the Pre-Clinical Studies Panel. Indeed, all the feedback that we have received suggests that it was assiduous in its efforts to follow the prescribed procedure. However, the disparity in ratings implies that other Panels were applying different criteria, were more flexible or subjective in their ratings, and were actively working to encourage improving departments in their subjects. We understand that the Pre-Clinical Studies Panel were themselves surprised and concerned by the disparities in ranking but could do nothing to change the ratings of others.

We wonder whether the Pre-Clinical Sciences Panel applied the rules and criteria of assessment in ways that might not have been evident to Head of Departments gaining their information only from the published instructions for submissions. For instance, we understand that, for RAE2, less weight was given than expected to review articles for assessment and will have been disadvantaged in ways that could not have been anticipated from the published instructions. Also our own informal analysis of the results suggests that much less attention than expected was paid to the information provided on forms RAE5 and especially RAE6 - about income per staff member, links to industry, new initiatives of research training, success in international grant applications, major building initiatives, achievement of research goals set in the last RAE, etc. The Panel even abandoned the use of 'flagging' to indicate special achievement in particular areas, which has left many departments without even that evidence of excellence.

There are several outcomes of the 2001 exercise to worry our Members. First, those in departments that have failed to score as well as other science departments in their universities will now receive much less funding than expected and needed. Worse than that, we already know of departments that are threatened with closure as a result of their unexpectedly poor rating. Increasingly, physiologists and pharmacologists are being moved into departments of Biology or Biomedical Science, or clinical departments. Whilst a degree of hybridisation is beneficial, isolation of the many people who work in this area will lead to a breakdown in communication within our subjects and recognition of them as substantive disciplines, despite their central importance in the teaching of medical students and in modern bioscience research. Finally, the relatively poor ratings of Physiology and Pharmacology in the 2001 RAE will undoubtedly further damage the perception of our subjects, and the attitudes to them of universities, funding councils, school-leavers, applicants for undergraduate and graduate study, and young researchers.

Paradoxically, the erosion in the perception of Physiology and Pharmacology comes at a time when these subjects are assuming ever-greater importance in the biological sciences. The experimental approaches that Physiology and Pharmacology offer have assumed enormous academic and commercial significance because they are essential for the transformation of the new genetic knowledge into the understanding of normal bodily functions and new approaches to the treatment of disease. The expansion of the quality of publications in the fields of Pharmacology and Physiology, for instance in our societies' journals, is testimony to the growing importance of these subjects.

We hope that HEFCE will be responsive to the considerable disquiet within our societies and will initiate some sort of inquiry, at least giving the Pre-Clinical Studies Panel the opportunity to respond to the disparity in ranking with more time than was available during the RAE. We trust that appeals from individual departments, some struggling to survive, will not simply be dismissed. And we wonder whether the Panel will at least consider awarding 'flags', even at this late stage, to indicate high quality within departments, which may help them to avoid closure.

Should the entire assessment system be reviewed for the future, we should like to recommend that any replacement scheme is developed with the maximum consultation of scientists in different disciplines, and that it takes into account of legitimate differences in requirements and style of different disciplines. A possible path for any such consultation about the future of the RAE might be through learned societies such as ours. We would like to see a system that ensured that the application of criteria was uniform between panels. We would also like to see greater recognition of the general achievements and prospects of departments, rather than the heavy emphasis on retrospective assessment of publications.

If our Society can help in any further way, or on matters concerning science research funding, we would be more than pleased to do so. I hope that the comments above are useful and helpful.

Yours sincerely,

Professor C Blakemore
President of the Physiological Society

Professor RJ Flower
President of the British Pharmacological Society

Professor C Fry
Chairman of the Physiological Society

Cc: Vice-Chancellors and Principals of universities and departments assessed as Physiology and/or Pharmacology

FEPS

FEPS – the Federation of European Physiological Societies exists to foster Physiology in Europe and to promote scientific interchange of ideas in relation to teaching of Physiology as well as research. Representatives of national societies from Scandinavia, Eastern and Western Europe met in March this year at a meeting of the FEPS council held in Tübingen, Germany, during the joint meeting of the German, Scandinavian and British Physiological Societies. Many topics and concerns

were aired. In terms of teaching, these included new teaching initiatives for all schoolchildren (a government-led concern in Finland) and new ways to harmonise and develop undergraduate teaching across member countries (Italy). Ways to expose younger scientists to the broader scientific community were debated. Concern was expressed about forthcoming European regulations on animal care which will have important financial repercussions for research in all countries. It was felt that FEPS should be more proactive in challenging and advising on this type of issue, by providing a unified viewpoint.

There is no doubt that FEPS is a worthy organisation with altruistic goals. However, as one of the oldest, largest and richest Physiological Societies in Europe, we are pretty self sufficient. So do we need to belong to FEPS? What can it achieve as an organisation which essentially comprises a lot of goodwill and no money?

I believe the Physiological Society should actively support FEPS as part of our charitable remit to promote our discipline and to present a united European front for Physiology. We can do this in a number of ways. We can shoulder some of the financial burden of course, but we should also be making a more positive contribution. Here are a couple of ideas:

Next year the 3rd FEPS congress will be held in Nice, France from 28th June to the 3rd July (http://www.unice.fr/FEPS2003). FEPS is making efforts to keep the cost of the meeting low so that as many young people from societies in straightened circumstances can attend. It is hoped to make the FEPS meeting a biennial or triennial event. Think about going yourself and/or sending your students and postdocs.

A suggestion to associate FEPS with domestic meetings of national societies in intervening years when there is no FEPS congress received enthusiastic support from the FEPS Council. One way the Physiological Society could contribute to this might be to invite FEPS to be associated with one of our meetings, especially those that are held jointly with another society. A low cost domestic meeting would be more accessible to younger scientists, especially from the former Eastern Block, but still provide the experience of a more international scientific milieu. This is just the sort of informal environment in which to exchange ideas, foster collaboration and less altruistically, for us to recruit new post docs.

If FEPS is going to work we, as one of the stronger member Societies, have to be supportive. I am keen to hear from any of you with comments (positive or negative) and/or ideas for other initiatives that we could either initiate or contribute to.

Thelma Lovick
FEPS representative for the Physiological Society
Department of Physiology
University of Birmingham

Andrew Blake

22 March 1963 – 24 May 2002

Andrew Blake, Founder and Director of Seriously Ill for Medical research (SIMR) died on 24th May 2002.

Andrew (39) suffered from the progressive genetic disorder Friedreich's ataxia, and had been ill for some time. In February of this year, he was admitted to hospital where it was discovered that he had deep vein thrombosis (DVT). On leaving hospital in March Andrew was on a cocktail of drugs, (including warfarin) – some of which had unpleasant side affects. He was re-admitted to hospital a week before his death when the DVT was again found to be in evidence. Andrew, who was growing weaker by the day, died peacefully at 7.00am on Friday 24th May.

Andrew's active support for medical research began in 1989, whilst recovering from back surgery. Also in the same hospital, recovering from an accident, was an ardent anti-vivisectionist. Andrew challenged her saying, "Don't you feel a bit hypocritical for receiving medication developed using animals and yet campaigning to abolish all use of animals in medical research?" But his words were ignored. When Andrew returned home, news broke that a car bomb had been placed under a medical researcher's car in Bristol. The researcher luckily managed to escape, but Andrew was shocked that someone would be willing to take such violent action to prevent valuable research into medical disorders such as his own. This incident was the final straw for Andrew. In 1991 he decided to form a group of like-minded patients who actively support the humane use of animals in medical research. Seriously Ill for Medical Research, (SIMR) gives patients a voice in public debates on medical research issues. Its main objective being to promote a greater public understanding of the methods, aims and benefits of medical research and particularly the use of animals in research.

The death of Andrew Blake comes as a great loss to the scientific community. The Physiological Society are particularly indebted to him and extremely grateful for the support he gave us. He was especially active in educating the public on the true nature of medical research and helped us to produce the leaflets 'Some People Say' as well as the videos, 'Choices' and 'Right to Hope'. He will be sorely missed.

SIMR will be arranging a memorial tribute in August. If you wish to find out more details of this service please visit their website at: www.simr.org.uk

Natasha Moses
Maggie Leggett

Report from the 2002 Molecular Techniques Workshop

University College Cork, Ireland

Easter 2002 marked the 6th Annual Molecular Techniques Workshop, held this year for the first time at the Department of Physiology, University College Cork (UCC), Ireland. Started in 1996 at the University of Glasgow, the workshop moved to UCC following the appointment of Patrick Harrison, the course co-ordinator, to a Senior Lecturing position in the Department of Physiology.

The 10-day training course, funded jointly by the Physiological Society and the Wellcome Trust, brought together 16 physiologists keen to learn molecular techniques. Participants ranging from PhD to Professorial level were trained in practical and theoretical aspects of molecular biology and the application of these techniques to their own research. Since its inception, over 92 researchers have taken part in the workshop.

The course thrives on the generosity of a number of speakers from the UK and UCC who give freely of their time. Special mention goes to Rod Dimaline from the University of Liverpool who spent four days running the first half of the course in aspects of RNA handling, isolation and amplification.

The course is loosely based on a real research project involving the isolation of RNA from tissue and detecting gene expression by northern blot and RT-PCR. The PCR product was cloned, sub-cloned and mutated, creating a GFP-fusion protein and two different point mutants. Each participant had the opportunity to transfect cells and compare different transfection reagents. Finally, the consequences of the mutations and the effect of creating a GFP-fusion protein were compared to the wild type receptor.

continued on page 35

The Physiological Society – travel grant application form

JOINT MEETING WITH THE SPANISH PHYSIOLOGICAL SOCIETY
15-17 February 2003

(PLEASE COMPLETE IN CAPITALS)

Surname

Title and forenames

Work address

Postcode

Email

Work tel

Fax

Membership of the Physiological Society

(Please tick one box)

Member ☐

Affiliate ☐

Candidate for membership ☐

Membership number

Funds are available towards the costs of physiologists wishing to attend the meeting to present their work. The sum available is variable. Applicants should also pursue other sources of funding.

Details of employment or status

(please tick boxes as appropriate)

Appointment/status

Employer/funding body

Member of UK/Irish department of Physiology or related sciences ☐

Graduate ☐

Post doctorate worker ☐

Academic staff member ☐

Technical staff member ☐

Visitor ☐

NHS clinician not part of a medical school ☐

Member of MRC, other UK research institute or equivalent ☐

Other employment (please provide details)

At the meeting

Do you intend to submit:

a poster? yes/no

an oral communication? yes/no

a demonstration? yes/no

Title of abstract

Funding

Funding applied for from the Society

£

(note each application will be considered individually and funds are limited)

Other sources of funds

Please give details of other bodies to which you have applied or intend to apply for support, including maximum award and date of notification.

Signed

Date

Signature of Head of Department confirming eligibility if not a member or affiliate

Signed

Name

Deadline for receipts of applications: 30 September 2002

Submit six (6) copies of this form to
Mr Jamie Gould,
Membership Administrator,
The Physiological Society,
PO Box 11319,
London WC1V 6YB

PLEASE TURN OVER ›

TRAVEL GRANT APPLICATION FORM continued

Summary of abstract: please give, in not more than 250 words, on the paper or poster you plan to present at the meeting, including co-authors. Give the name of the presenter.

Note here any additional scientific purposes for your visit to Spain: e.g. attendance at other meetings, visits to laboratories, collaborations etc. Please supply copies of supporting documents, such as invitations, where relevant.

If you are awarded a grant we would like to transfer the funds directly into your bank/building society account. Please complete the following:

Bank/Building Society

Name of account holder(s)

Account Number Sort code – –

Full address of account holder

Bank's Full Street Address

The Physiological Society
APPLICATION FOR INTERCALATED BSc BURSARY

(PLEASE TYPE)

Applicant's details

Name Date of Birth

Address

Postcode

Tel Fax Email

Desired Course of Study

Institution where intercalated course will take place (name and address)

Details of physiology element in course (must include experimental physiology project).
Please attach a one page summary of the experimental project, with title and supervisor

Funding bodies to whom application for fees, subsistence etc have already been made

Please supply additional information or comments concerning your efforts to obtain funding from another source (use continuation sheet if necessary)

Career Objectives

Reasons for wishing to intercalate a BSc, including any relevant background, accomplishments to date and career objectives (use continuation sheet if insufficient space)

Previous Studies and Relevant Work Experience

A Levels/Highers Subject Year Grade

University Degree Subject

Institution

Course subjects/grades

Year 1

Year 2

Year 3

Details of any special projects/outstanding achievements

Other relevant work or study prior to present course

Confidential Letters of Support

The application must be accompanied by letters in support from two referees. These will normally be the Head of Department or Dean of the Institution in which you wish to take an Intercalated BSc, and an academic tutor who knows your work and personal circumstances, including financial.

1 Name Position

Address

Tel

2 Name Position

Address

Tel

If you are awarded a grant, we would like to transfer the funds directly into your bank/building society account. Please complete. (All information is confidential)

Bank/Building Society Account Number

Name of account holder Sort Code

On completion, the first referee should return **SIX COPIES** of this form and of supporting documentation to The Administrator (BSc Bursaries), The Physiological Society, PO Box 11319, London WC1V 6YB.

Closing date November 30th.

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In addition to the practical side, there was a full lecture programme on a diverse range of topics including control of gene expression, transgenesis, proteomics, genomics, virus vectors, bioinformatics and advanced molecular physiology.

Funding for the future of the workshop is currently under discussion, and it is hoped that the course can continue to provide valuable research training to a further 50 physiologists over the next three years.

Patrick Harrison
Department of Physiology
University College Cork

The Physiological Society Annual General Meeting

The membership is reminded that the Annual General Meeting of the Physiological Society will be held on:

Wednesday
11 September 2002

at 13.00pm

in Lecture Theatre 2,
at the University of Leeds

All members are welcome and are asked to arrive promptly.

Supporting documentation for this meeting is enclosed with this mailing.

FRS success for Society member

Stuart Cull-Candy, a long standing member of the Physiological Society and past Editor of the Journal of Physiology, has recently been elected a Fellow of the Royal Society. The Magazine Editorial Group would like to offer Stuart its congratulations!

Introducing Esther Williams, the Society's new Chief Executive

Born in Canada, Esther has lived in England for many years. She undertook her undergraduate studies at the University of Saskatchewan in Saskatoon, completing a Bachelor of Arts degree in Fine Art and a Bachelor of Education degree in special education. Esther moved to England in 1972, working as a teacher in Reading and later Birmingham. A degree with a major in Special Educational Needs was very unusual at that time in the UK and Esther soon found herself carrying a great deal of responsibility at quite a young age. This included chairing a consortium special needs committee across 17 Birmingham schools, which involved providing professional development opportunities for serving teachers and senior staff. This was an interest that in later years would become a full time job.

A move to Canberra, Australia, in 1980 brought further opportunities including teaching in a range of schools, and working as a research officer for a major local government review of education provision. Esther also undertook her MA in Education Administration at the University of Canberra and her thesis was on the management of change.

After returning to England in 1983, Esther worked for a Local Education Authority in London for seven years as an Education Officer. She went on to work as a Regional Officer for The Teaching as a Career Unit (TASC), which had been established by the then Department of Education and Science (DES) to combat teacher shortages. This involved a great deal of travel nationally as well as regionally, with presentations to students and careers services in schools and universities, and working at careers fairs for students and mature people across England and Wales.

Esther described this experience as 'excellent preparation for the future', and so it turned out to be when she was appointed Senior Assistant Secretary, Training and Development for the National Association of Headteachers in 1995. The NAHT, with more than 30,000 school leader members, is the largest organisation of its kind in Europe. In addition to launching development programmes for the Association's members in England and Wales her team won two government contracts to deliver leadership development in England. She also spent much of her time working on policy issues with NAHT Council officers and Government officials and their committees. Esther began work for the Physiological Society on 1 May.

Noticeboard

No notice is carried for more than three successive editions. Notices are starred so that readers can see at a glance whether this is the first (one star) or final (three stars) appearance of the notice. Notices for the Winter 2002 edition should reach the **Administration Office by 2 September 2002**.

Please note that while members are welcome to advertise relevant events in the Magazine and on the website, advertisements via email will be restricted to events sponsored by the Society.

YOUNG PHYSIOLOGIST'S SYMPOSIA 2002

Prospective bids to hold symposia in 2003 should in the first instance be forwarded to Maggie Leggett at mleggett@physoc.org.

YOUNG PHYSIOLOGIST'S SYMPOSIA 2002

Advance Notices
more information will be disseminated via email

University of Leeds
8-9 September 2002
All abstracts welcome

Organiser: Erin Baggaley
email: bmsemb@leeds.ac.uk

CAREERS CONFERENCES

Organised in conjunction with other UKLSC Societies, these are suitable for undergraduates and postgraduates. There will be talks on a variety of careers, from patent law to science journalism and working in industry, and an opportunity to have your CV reviewed by a specialist. More information will be sent to departments in September. This year they will be held at:

University of Sheffield
2 November 2002

University of Glasgow
16 November 2002

King's College, London
30 November 2002

MOLECULAR TECHNIQUES FOR LIFE SCIENCES

Glasgow Caledonian University

2-6 September 2002
and 27-31 January 2003

This is a hands-on laboratory based course to introduce participants to techniques used in molecular biology investigations by a sequential experimental programme and intercalated lectures to transform tissue to sequence. Details can be accessed from our website www.sbbs.gcal.ac.uk/short courses or by contacting Adrian R Pierotti at the following address:

School of Biological &
Biomedical Sciences
Caledonian University
Glasgow G4 0BA
Scotland

Phone: +44 (0)141 331 3241
Fax: +44 (0)141 331 3208

http://sbbs.gcal.ac.uk/research/staff_profiles/Adrian_Pierotti.html

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MICROELECTRODE TECHNIQUES FOR CELL PHYSIOLOGY

19th Workshop 4-18 September 2002

Laboratory of the Marine Biological Association of the UK,
Citadel Hill, Plymouth, PL1 2PB

Information for applicants

- The workshop provides intensive practical experience of a number of microelectrode, patch clamp and optical techniques applied to single cells. It is intended for postgraduate students, post doctoral workers or established scientists wishing to apply these techniques in their research.
- The following basic techniques are offered: Two electrode voltage clamp, Patch clamp, Single electrode voltage-clamp, Dye injection, Ion-sensitive microelectrodes, Fluorescent indicators.
- There are 16 places. Participants work in pairs and have the opportunity to do three 3-day experiments in the two weeks. In addition, lectures and practical sessions on electronics, data acquisition and computer analysis, and microscopy will be given. Daily lectures given by teachers and visiting lecturers cover the basic techniques taught and certain specialised topics. A copy of the Plymouth Microelectrode Handbook will be provided.
- Accommodation (for 14 nights – arrive & depart on Wednesday) is close to the laboratory and includes breakfast. Lunch is provided in the lab each day and an allowance is given for an evening meal.
- The course fee of £1100 includes accommodation, meals and tuition. Participants are responsible for their own travel arrangements.

The closing date for applications is 30 April 2002 A meeting to assess applications will occur during May and all applicants will be notified of the outcome.

How to apply

There is no application form.

1 Please give a concise description of your research, your reasons for wishing to attend and your experience of techniques taught on the work-shop. List in order of priority four techniques you would like to learn.

2 Provide a brief CV (2 sides maximum) and list of publications.

3 The application must be accompanied by a letter of recommendation from an academic referee, preferably PhD supervisor or Head of Laboratory. This letter should indicate how your career, the laboratory in which you work and the area of research that you intend to pursue will benefit from your participation in the workshop.

4 What is your likely source of funding?

Funding

Applicants with MRC or BBSRC Studentships – Simply state you have a studentship in your application. Do not apply to the Research Council directly.

Dale and Rushton Funds of the Physiological Society – help with funding is usually available for young physiologists working in the UK. If you wish to apply please indicate in your application to the workshop. There is no need to apply directly to the Dale and Rushton funds before workshop applications are assessed.

Bursaries – The workshop can provide some half bursaries – if you think you will have difficulty finding the full fee please indicate in your application.

Applications should be sent to:

David Ogden,
Microelectrode Techniques, NIMR,
The Ridgeway, London NW7 1AA, UK

email: dogden@nimr.mrc.ac.uk

Information on internet:
www.nimr.mrc.ac.uk/Events/microelectrode.htm

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British Society for Cardiovascular Research meeting

THE DEVELOPING HEART: BIOLOGY AND PROTECTION

6-7 September 2002
University of Bristol, UK

e-mail: m.s.suleiman@bristol.ac.uk

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