PHYSIOLOGYNEWS
spring 2002 | number 46

Featuring:

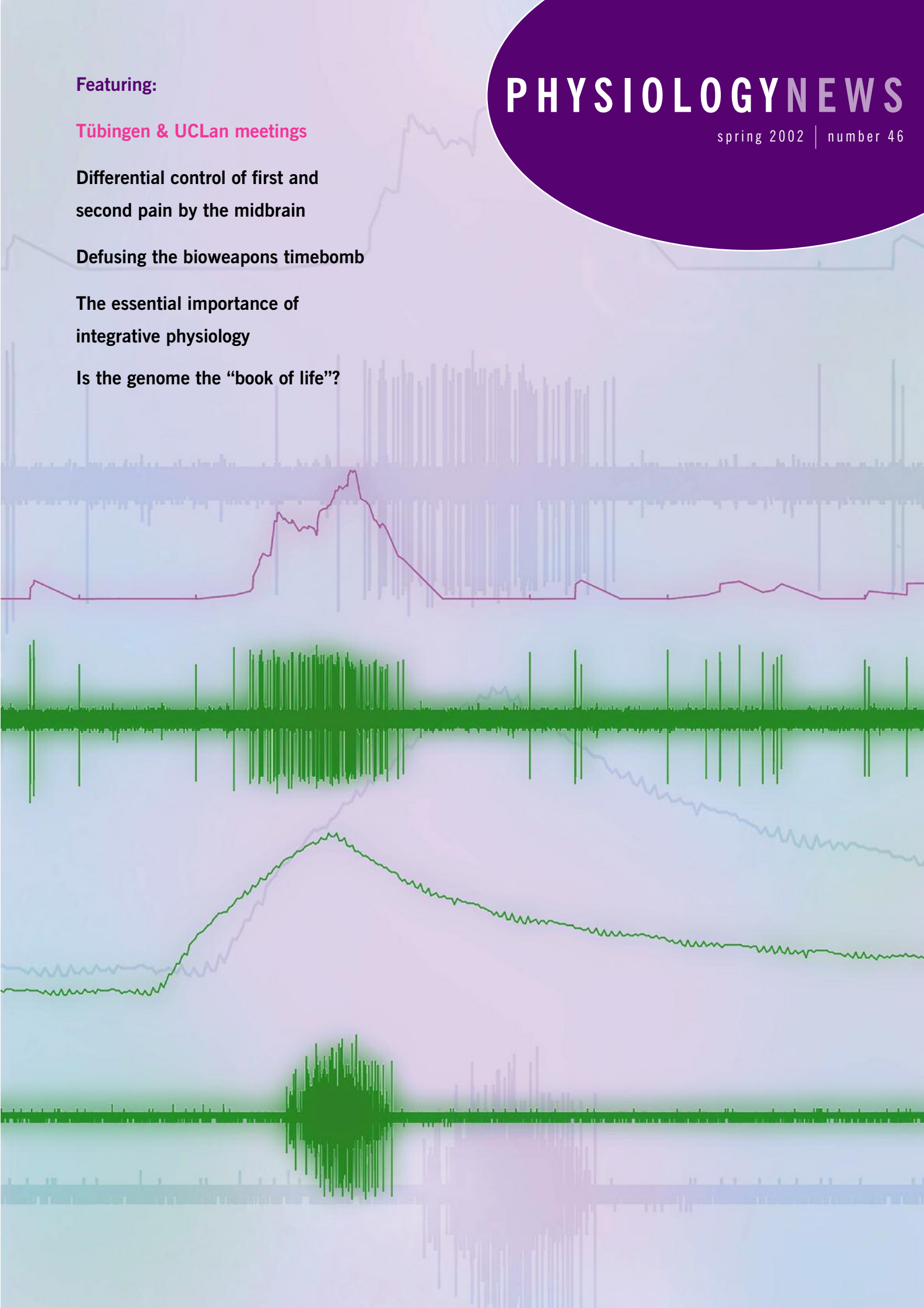
Tübingen & UCLan meetings

Differential control of first and second pain by the midbrain

Defusing the bioweapons timebomb

The essential importance of integrative physiology

Is the genome the “book of life”?



THE JOURNAL OF PHYSIOLOGY

SYMPOSIA

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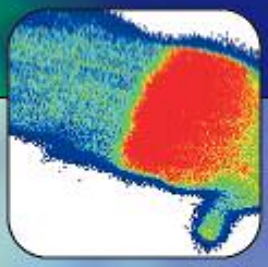
Normal and pathological excitation–contraction coupling in the heart

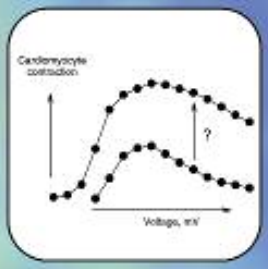
at the joint meeting of the UK, German and Scandinavian Physiological Societies, Tübingen, Germany

Friday, 15 March 2002

Organisers: David Eisner, Gerrit Isenberg, Ole M. Sejersted and Karin Sipido

Speakers: Andrew R. Marks, W. J. Lederer, Lothar A. Blatter, Ole M. Sejersted, Roger J. Hajjar and Jean-Luc Balligand





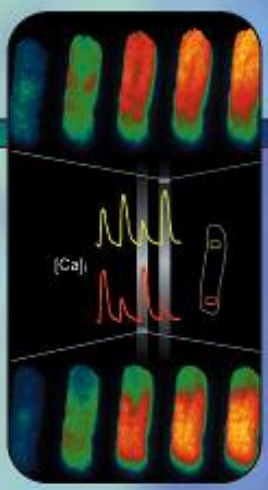
Fetal programming: from gene to functional systems

at the Society for Gynecologic Investigation Annual Meeting, Los Angeles, CA, USA

Wednesday, 20 March 2002

Organisers: Kent L. Thornburgh, Lowell E. Davis and Susan Wray

Speakers: C. Nicholas Hales, Andre van Assche, Philip Shaul, Wolf Reik, Sherin Devaskar, Michael Gravett and Alan Flake



The Journal of Physiology is published by Cambridge University Press on behalf of The Physiological Society in 24 fortnightly issues in eight volumes plus Proceedings issues. For further information go to www.jphysiol.org. The 2002 subscription price is £1572/$2560 (print and online); £1520/$2478 (online only).

CAMBRIDGE UNIVERSITY PRESS

Published quarterly by The Physiological Society

Contributions and Queries
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The society web server: www.physoc.org

ISSN 1476-7996

The Physiological Society is registered in England as a company limited by guarantee, No 323575. Registered office: PO Box 11319, London WC1 7JF. Registered Charity No 211585.

Printed by The Green Tree Press Limited

Cover photo

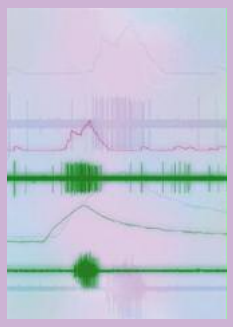

Image created by Peter Coombs using a white data trace supplied by Simon McMullan

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Affiliate Travel Grant Scheme:
The next deadlines for receipt of applications are 31 March and 31 May 2002.

MSc Bursaries:
The next deadline for receipt of applications is 31 May 2002.

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

Membership Applications:
The deadlines for receipt of applications for full membership are 31 March and 30 June 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 of Liverpool (9-11 July 2002):
Abstracts must be submitted to the Meetings Secretary's Office by 17 April 2002.

University of Leeds (10-12 September 2002):
Abstracts must be submitted to the Meetings Secretary's Office by 19 June 2002.

Address for abstract submissions:
The Meetings Secretary, The Physiological Society (Abstract Submission), Dept of Biomedical Science, The University of Sheffield, Western Bank, Sheffield S10 2TN

Magazine:
Letters and articles and all other contributions for inclusion in the Summer issue should reach the Administration Office by 12 March 2002. Please cite all references in articles in the style of The Journal of Physiology.

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.

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 Editor, to the Editorial Assistant or to a member of the Magazine Editorial Group (see contents page).

Magazine Online
The magazine is now available on our website.

EDITORIAL

PH

Physiology and RAE 2001

So the results of RAE 2001 are in – or out, as you prefer. After hundreds of hours of work by RAE Committees in University departments across the country, pondering strategy and poring over individual staff member's submitted publications and "Esteem Indicators". After hundreds of hours of reading of the said papers, and extensive discussion, by the RAE panels. And after weeks, or more accurately months, of speculation and whispers.

Much has already been written about the rise in grades across the board, and whether it reflects an increase in quality, as opposed to Universities exercising greater selectivity in choosing which staff members to submit. Even more has been written about the likely financial consequences of the overall increase in grades. Institutions and departments – if they still recognisably exist – will have reached conclusions about their own status as winners and losers. However, the purpose of this editorial is not to debate any of the above issues, still less to ask whether the whole exercise was worth it. Instead it is to ask a different question, namely where does physiology as a subject, or discipline, stand in this? Is it – are we – a winner or a loser?

The answer to this question is not as obvious as it might seem. Of the departments listed as Physiology, only one achieved a 5*, with four others scoring 5. This might at first suggest that Physiology as a subject has not done well in the RAE. Colin Blakemore expressed his worries on this score in a speech at the recent York meeting of the Physiological and Biochemical Societies. He contrasted the RAE results in the Physiology category with those in Psychology, a subject he knows well, where five UK departments achieved 5* grades, and another ten grade 5. Blakemore is concerned that the RAE results will be seen as implying – at least to casual observers – that UK Physiology now has few truly international-calibre departments, and lags well behind subjects such as Psychology and Biological Sciences. This is a view with which he, and most UK physiologists, would strenuously disagree.

So, is Physiology in the UK being left behind by other disciplines in terms of international recognition and standing? Most of us would argue that in truth we do internationally-competitive research on a fraction of the budget of comparable labs and institutions in the US. Furthermore, many of us probably feel we are among the most cost-effective of scientific disciplines in terms of "papers out for pounds in". So why do the RAE results not appear to reflect this?

One issue is clearly comparability of results between subject panels, a worry highlighted in discussions of the RAE, for instance in the letters page of the Times Higher. However, there is another major factor at work for physiology, namely the changing organisational structure of the biological/biomedical sciences in UK Universities. The true answer is that a very substantial number of the UK's physiologists DO work in departments which were rated 5* or 5 in RAE 2001. However, only a subgroup of these departments – perhaps better termed "Units" – were submitted in the RAE under the heading of "physiology".

A concrete example. In my university the physiologists (defined here as "people who go to Society meetings and publish in physiological journals") were submitted to the RAE under three different categories, most as part of Preclinical Studies, but some as part of a Biological Sciences unit, and still others in "Laboratory-based Medicine". This reflects the process – largely driven by successive RAEs – of reorganisation of old Physiology departments into larger units, typically together with pharmacologists and/or anatomists, and perhaps also with cell biologists and even zoologists. A look at the departmental titles on papers in the physiology journals makes it clear that a Department or School of Biomedical or Biological Sciences, or Preclinical Studies, or whatever, is now at least as likely to be "home" for a UK physiologist as a Department of Physiology.

So the fate of physiologists in RAE 2001 – or at least their whereabouts – reflects what has happened to Physiology departments organisationally in the last ten to fifteen years. Whether one views these organisational developments as a good or a bad thing for physiology as a whole is not something I want to go into here, although perhaps it is a debate that we could usefully have in the pages of the magazine – any volunteers? What does seem clear is that Departments which have been reorganised have gained some benefit in terms of RAE rankings, although again one could debate the reasons for this.

Anyway, back to the RAE itself. Suppose one asks, instead of "How many departments in the Physiology Unit of Assessment scored 5* or 5?" the slightly different question, "How many 5* or 5-rated units contain a decent proportion of physiologists?" Inspecting the RAE 2001 tables suggests that the answer is a half dozen 5*-rated Departments, and another ten or more rated 5. So the true worth of UK research in physiology – internationally competitive work, often done on a shoe-string – is bourne out by the RAE. One just has to look a little harder to find the information.

Which brings me to a final point. We know the true worth of UK physiology. The RAE has vindicated our view. It is now up to us make this point, within our Universities to Vice Chancellors and externally to politicians and members of the public. UK physiologists have "done the business" in RAE2001, against the odds and in often difficult and straitened circumstances. Now we have to tell the world. Or at least the people who hold the purse-strings.

Austin Elliott

Rendezvous of the three Societies: The congress in Tübingen

From March 15th to the 19th this year, the Physiological Society, the Scandinavian Physiological Society and the German Physiological Society will be holding a joint meeting in Tübingen, Germany. The meeting is also supported by FEPS, the Federation of European Physiological Societies. The Department of Physiology in Tübingen is looking forward to hosting an excellent international meeting and fostering scientific interaction within and beyond Europe. In December 2001, i.e. 3 months prior to the meeting, almost 900 abstracts had been submitted and close to one thousand participants from approximately 36 countries had registered.

A truly interdisciplinary meeting

In 42 oral sessions and 51 poster sessions virtually all aspects of physiology will be dealt with. Figure 1 gives an illustration of the topical distribution of abstracts. About 20% of the abstracts are related to function or regulation of ion channels, the favourite topic of the German physiologists. Other major topics include various aspects of cell physiology, cardiovascular physiology, kidney and

Topic Distribution DPG Congress, Tübingen March 15-19, 2002

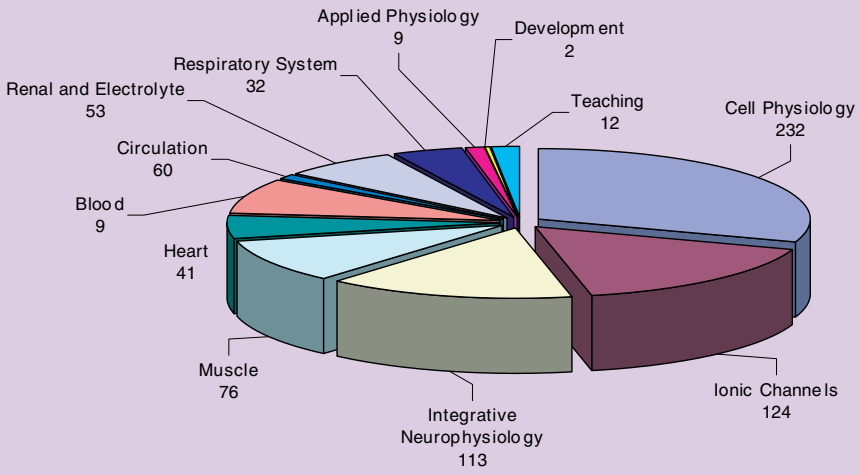


Figure 1 Number of abstracts submitted to the diverse topics

Members of the DPG

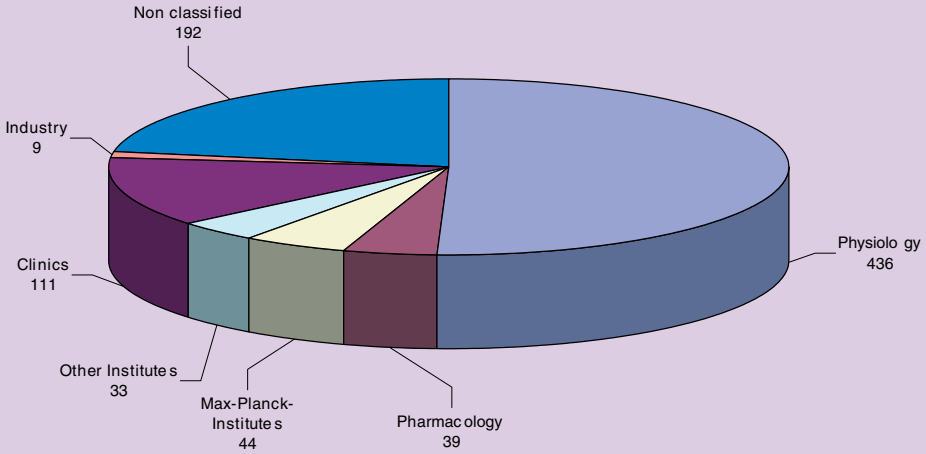


Figure 2 Institutional affiliation of the German Physiological Society members

electrolyte metabolism and the respiratory system.

Expected highlights include the plenary lectures to be given by Frances Ashcroft, Jonathan Ashmore, Richard Boyd, Rudi Busse, E. Gulbins, Erwin Neher and Bente Klarland-Pedersen.

As many as 18 symposia will focus on Endothelial Signalling; epilepsy and ion channel dysfunction; normal and pathological excitation-contraction coupling in the heart; intestinal epithelial function: molecular mechanisms and neurohumoral control; reproduction, stress, adaption; new insights into cortico-spinal functions; memory traces in pain pathways; neuron-glia interactions; pathological and applied physiology – links to clinical medicine; calcium signalling and exocytosis; local regulation and treatment through local counter current transfer of heat, hormones and pharmaca; local regulation of skeletal muscle blood flow; solute and water transport in airway epithelia; cardiovascular adaptation at normal and altered fetal development; spinal interneurons: from genesis to function; the blood-brain barrier; extracellular fluid volume homeostasis: the role of kidney and blood pressure; and the molecular basis for cellular learning and memory.

In addition to scientific excitement, a Picasso exhibition, a Beethoven concert directed by Sir Norrington and the congress dinner are all equally likely to turn your stay in Tübingen into a lasting memory.

For further details on the meeting, you should visit the webpage: www.uni-tuebingen.de/DPG2002.

Channels and more: The German physiologists

The host Society is the German Physiological Society. With 1000 members, this Society is one of the larger European Physiological Societies. As illustrated in Figure 2, approximately half of the members of the German Physiological Society work in University departments of physiology. The scientific interest of the members is best reflected by the topics chosen at the annual meeting (see Figure 1).
To learn more about the German Physiological Society, visit the webpage www.physiologische-gesellschaft.de

Figure 3 Tübingen from river Neckar

Since 1477 Tübingen has been more than just a university

Tübingen was founded some 1500 years ago. Five centuries later, the Counts of Tübingen erected a fortress and turned the village gradually into a town with a market square, parish church and city walls. Almost another five centuries later, in 1477, the university was founded. Since then, the university increasingly shaped and dominated the city. Nowadays most of the approximately 90,000 inhabitants are university employees (approximately 10,000) or otherwise busy keeping the 26,000 students happy. As Tübingen is somewhat remote, it never attracted significant industry. Fortunately, the city was therefore not considered worthwhile to be destroyed in the Second World War and the medieval city is still intact. Tübingen is embraced by a huge wood, the Schönbuch, which invites extensive walks and bicycle rides. As quiet as it may seem at first glance, Tübingen offers an unusual diversity of intellectual entertainment. Thus, not surprisingly, a nationwide survey disclosed that Tübingen provides it's inhabitants with the highest quality of life of all major cities in Germany.

Figure 3 shows the medieval city from the Neckar, the little river, which offers the students an attractive alternative to everyday lectures. By showing their skills in punting, the male students try to impress their female favourites! Every year, there is a punting race, which is probably more fun to watch than to participate in actively. More information on Tübingen is found in the webpage www.tuebingen.de.

About function of molecules, apoptotic cell death, cell volume, malaria and deafness: The host department in Tübingen

As most German departments of physiology, the Tübingen department is composed of two chairs. One of the chairs has been held since 1992 by Florian Lang. He followed Eberhard Betz, who dedicated himself to atherosclerosis research. Florian and his collaborators are interested in all aspects of transport. The main topics pursued are: the properties and regulation of transport systems expressed in *Xenopus* oocytes; the transport systems

Figure 4 The crew of the physiological department in Tübingen (summer 2000)

induced by *Plasmodium falciparum* in erythrocytes and by other pathogens in epithelial cells or macrophages; the role of transport systems in apoptotic cell death and the interplay of transport and cell volume regulation.

The second chair has been held by Peter Ruppersberg since 1996. He followed the cardiac physiologist Ruthard Jacob. The focus of Peter Ruppersberg and his collaborators has been the analysis of function at the molecular level, e.g. the mechanism of K^+ channel gating, the interaction of second messengers with channel activity, and the activation mechanisms of mechanosensitive channels in the inner ear. From the very beginning, Peter laid special emphasis on the industrial exploitation of scientific knowledge. Last Autumn, Peter stepped down from his function as chairman, to engage in the building of an interface between scientific research and industry. Specifically, he now involves himself in the founding and support of startup companies. Fortunately, Peter will remain a member of the department and continue to participate in the pursuit of scientific projects and teaching of students.

The other members of the department and their projects can be seen at the webpage www.physiologie.medizin.uni-tuebingen.de. Figure 4 displays the members of the department in summer 2000. They are presently derived from 9 different nationalities. The common language is English, as not all members speak German. Thus, the department is truly international. And we continue to watch out for excellent and nice scientists from all over the world.

Come and stay

The German Physiological Society, the Physiology department in Tübingen, the City and the university of Tübingen are looking forward to having you here this Spring. We anticipate a great meeting which will be surely worth the travel. Special air fares will be available (see www.uni-tuebingen.de/DPG2002) and inexpensive accommodation can be reserved for participants of the meeting. You will probably never again travel for as little money to Germany! We are looking forward to you coming. Moreover, we do hope that some of you fall in love with this little old city, or our department, or with one of its charming members, or with the research programs, and decide to stay for a while, or longer! Whatever the reason for your length of stay, you will be more than welcome.

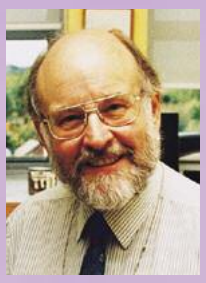
Florian Lang
Head of Department of Physiology
Eberhard-Karls-Universit of Tübingen

Welcome to Biological Sciences at UCLan

A bit of history

The University of Central Lancashire (UCLan) was established in 1992, but its roots go back in an unbroken line to predecessor institutions in the early nineteenth century. It was first established in 1828 as the Preston Institution for the Diffusion of Knowledge, which in 1882 was renamed the Harris Institute, following a then substantial bequest of £40,000 from the estate of Edmund Harris, a leading Prestonian of the times. In 1956 the name was again changed to Harris College of Further Education (lots of local citizens still refer to us as Harris College) and in 1973 became Preston Polytechnic, followed by Lancashire Polytechnic in 1984. Just prior to our redesignation as a university in 1992, the Lancashire College of Midwifery joined the polytechnic and in 1996 fused with the Lancashire College of Nursing and Health Studies to create our current Faculty of Health. In addition to our campus at Preston we also have another in Cumbria at Penrith based on what was the Newton Rigg Agricultural College. Thus from humble beginnings, we have now grown to have 27,000 students, most of whom are studying in Preston, but with over 5000 on the Cumbria campus.

The Department of Biological Sciences at the University of Central Lancashire (UCLan) is close to both the centre of campus and to the centre of Preston which has very good transport links to the rest of the UK. The present day Department of Biological Sciences changed its name from the Department of Applied Biology in June 1999, to coincide with a very substantial refurbishment of the Maudland Building, where all our teaching laboratories and most of our office space are housed. As a newly arrived Head of Department, I found the refurbishment was very disruptive at the time, particularly as it came just before the visit of the Quality



Prof Bill Winlow, head of department

Harris Building

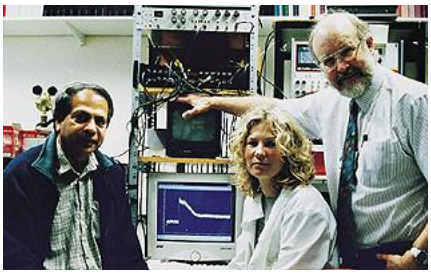
Foster Building

Assurance Agency in March 2000, but on the positive side we are now provided with extensive, purpose-designed teaching and research space. In spite of the best efforts of the builders to totally disrupt our preparation for the QAA visit we achieved a QAA score of 22/24. There are 25 permanent academic staff (seven of whom have been appointed in the last 4 years) in the department. Our core research falls into two main areas: Cell and Molecular Biology and Microbial Biology.

Right Bob Lea

Below Jai Singh, Alyson Woodall and Bill Winlow

Bottom In the neuroendocrine lab, Louisa Herbert and Leslie Rice



Biology Research in Preston

In the area of Cell and Molecular Biology, our main studies are on the mechanisms of action of general anaesthetics, neurobiology of reproductive behaviour, exocrine gland function in pathophysiological states, muscle metabolism and trace mineral metabolism. Professor Jaipaul Singh is particularly interested in pancreatic dysfunction and the effects of diabetes on the function of cardiac myocytes, for which he has support from the British Heart Foundation and collaborations with the Universities of Extremadura and the United Arab Emirates. He is also interested in the relationship between calcium and magnesium mobilisation in secretory cells and also in dry eye syndrome during ageing. Bill Winlow researches on the cellular and molecular effects of general anaesthetics, with support from NATO, Wellcome Trust and the European Union. Currently he is working with Dr. Alyson Woodall to show the effects of anaesthetics on mammalian cell lines and with Jai Singh and Nick Bracken to elucidate the responses of diabetic cardiomyocytes to anaesthetics. He retains his interest in the cellular and molecular mechanisms underlying behaviour in snails, has strong links with the University of Calgary and is particularly interested in understanding how trophic factors influence seasonal changes in respiratory behaviour. Bob Lea is a Reader in Neuroscience whose main research is on localisation of avian progesterone receptors and parental behaviour in birds, in collaboration with Professor Peter Sharp of the Roslin Institute in Edinburgh, with BBSRC support. He also has a long-term collaboration with the University of Hiroshima, and has demonstrated the importance of neurosteroids in the bird brain and their importance in reproduction. He is currently trying to determine how these neurosteroids are involved in neurobiological mechanisms underlying behaviours such as fearfulness.

Several of our newer staff are very important in this area. Amal Shervington is a molecular biologist with a wide range of techniques at her disposal, who arrived in January 2001. She has taken charge of our Molecular Biology Laboratory in the Biomedical Sciences Unit (see below) and is providing an invaluable resource to us. Nicky Lowe is a nutritionist, interested in zinc metabolism and was the first to use stable isotopes instead of radioisotopes to develop a comprehensive mathematical model of zinc metabolism in humans, thus providing a key reference for zinc metabolism in healthy young women. She has a variety of research links within the

European Union and is examining the relationship between vitamin D receptor polymorphisms and calcium metabolism in osteoporosis. Henning Wackerhage is a sport scientist who is particularly interested in skeletal muscle. He leads a new group (Drs. John Bradley, Darrell Brooks and Niall Woods) which is interested in manipulation of genes regulating muscle metabolism and protein synthesis, with a view to understanding how muscle adapts to exercise and the abnormalities of metabolic pathways in diseases such as type 2 diabetes.

Research in Microbial Biology is an important aspect of our department, with substantial industrial sponsorship for their work on mechanisms of antimicrobial resistance and is supported by 3 staff and 12 research students. Their work is focussed on the significance of biofilm formation in the resistance of antimicrobial agents, the role of slow growth in resistance to antimicrobial agents and the development of drug resistance by microorganisms. Professor Glyn Morton is particularly interested in developing advanced microscopic techniques for visualisation of biofilms and in assessing the efficacy of compounds against a range of infective agents. He is also involved in examining the contributory effects of secondary metabolites on biocide resistance. He has collaborations with LaPorte Absorbents and Zeneca Specialties. Reg England, Reader in Microbial Physiology, and Dave Greenway collaborate on bacterial slow growth rates and the effects of environmental stresses, e.g. nutrient deprivation, on pathogenic bacteria such as *Escherichia coli* and *Staphylococcus aureus*. Steve Percival, another new member of staff currently holds an EPSRC grant and has industrial funding from the International Molybdenum Association, Avesta, Sheffield and the Nickel Development Institute, for his work on pathogen survival in drinking water and the interactions of pathogens in biofilms in relation to medical and water environments.

Carole Rolph is interested in lipid metabolism and has links with both of the major research groups. She has carried out work on Streptomycete lipid metabolism that has secured funding from Dupont. Her interests in lipids also connect her to the Cell and Molecular Biology area and extend into hoof science in collaboration with the Veterinary School at Edinburgh.

Finally, Peter Lumsden, Reader, carries out research on plant photoperiodism and directs research on plant tissue culture, aimed at developing culture environments that maximise growth and survival of species, such as *Delphinium*, which are difficult to establish. His work on photoperiodism is carried out in collaboration with the Institute of Experimental Botany in Prague and currently focuses on the transduction pathways following perception of light signals that affect the flowering response.

Biomedical Research Unit

We are now working closely with postgraduate Medical school in the Faculty of Health, with the Neurology Department at the Royal Preston Hospital and with the local Public Health laboratory service. We have recently agreed to form a new Biomedical Research Unit, sited within Biological Sciences research space and supported with a SRIF award, HEFCE funding and NHS support from the Preston and Chorley NHS Trust. This is at an early stage of development, but will comprise 14 permanent academics plus 3 postdoctoral fellows and 25 research students working in the areas of muscle physiology and biochemistry, neuroscience, nutrition and food microbiology. This is an exciting new development and we look forward to its rapid evolution.

Teaching in Biological Sciences

In the last two years the department has significantly changed its direction to become much more biomedically

Top Henning Wackerhage and John Bradley

Above Darrell Brooks with snail shells (but he's really a physiologist!)

Left Reg England

Below Peter Lumsden

Microbiology for all, Chris Hughes, Graeme Iveson (principal technician) Talhat Akhtar and Alkistis Frentzou

Top left Rear of Maudland Building looking surprisingly rural!

Top right The real departmental power structure, Lisa Whittaker and Joanne Parker, Department Administrator.

Centre left Kim Woodruff with an HPLC

Centre right Christine Cockburn, Anthony Kubicki and Peter Robinson in the Biochemistry prep. room.

Bottom left The muscle group – John Bradley, Monty Hope, James Higginson, Phil Atheton and Henning Wacherhage

Bottom right Partners in Crime, Rob Strettle (first year tutor) and John Brown (Quality Officer)

All photos by Martin Rosenberg

orientated. Our Biomedical Science degree is now fully accredited by the Institute for Biomedical Science and the CPSM. We have also taken over the running of the successful undergraduate programme in Sports Science and have developed new Honours degree programmes in Food Science and Nutrition, Medical Biology and Pharmaceutical Sciences in addition to offering courses in Physiology and Pharmacology, Biochemistry and Molecular Biology, Microbiology and a more general Honours degree in Biological Sciences. This final course offers great flexibility and allows our students to move easily into our other degree courses at the beginning of year 2. We are currently rationalising our first year provision to offer a common first year to most of our undergraduates. In the next few years we will be offering a number of new courses, based particularly around Sport Science, Health and Nutrition and we will be developing taught MSc courses in the areas Biomedical Science and Medical Neuroscience. The development of our Sport Science programmes is strongly underpinned by the University's new £12m outdoor sports arena, opened in April 2000 by HRH The Princess Royal.

Over the years substantial effort has gone into course development and support. As a department we are currently developing Web CT for distance-learning under the capable direction of Peter Robinson, well known nationally for running "BioTutor". Quality control for all our courses is in the hands of John Brown, and Ray Cotton ably runs both student support and admissions. In the near future we will be visiting the UAE, India and China, with a view to joint course developments in these expanding markets. We are at an exciting stage in our development and we look forward to the visit of the Physiological Society, its first to a new university.

Bill Winlow
Head of Department of Biological Sciences
University of Central Lancashire

LETTERS TO THE EDITOR

Dear Editor,

Fluorescence signals danger

Whilst casually flicking through journals I notice that many scientists are still using fluorescein-based dyes to measure intracellular pH. I am deeply concerned by this. In 1993 Gatto and Milanick showed that fluorescein, and some popular pH-sensitive dyes (eg BCECF), inhibit the plasma membrane calcium pump (PMCA). The popular technique of loading BCECF into cells, using the acetoxymethyl ester (AM) of the dye, may well be disrupting normal cell physiology. The AM loading technique causes dye to accumulate within the cytosol, where it can reach concentrations far higher than in the bathing medium. The danger is that BCECF-AM loaded cells will have elevated calcium levels, which alter normal function. This is particularly disturbing to neurones where the PMCA is largely, if not wholly (Storozhevykh *et al* 1998) responsible for maintenance of low intracellular calcium levels. If this were not bad enough, the PMCA also counter-transports acid equivalents (Schwiening *et al*, 1993), thus pH is being measured with a major acid loading mechanism inhibited (Trapp *et al*, 1996).

Scientists relating changes in Ca^{2+} and H^{+} must therefore be especially careful in the choice of dyes they use.

Yours faithfully,

Christof Schwiening
Department of Physiology
University of Cambridge

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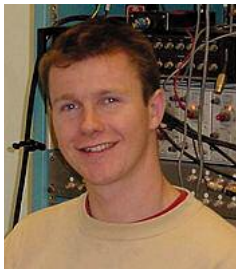
Differential control of first and second pain by the midbrain

Pain is a plastic phenomenon, Simon McMullan investigates the differential effects of PAG on C-fibres and Aδ-fibres.



Simon McMullan

Acute nociceptor activation usually drives behaviours that avoid the noxious stimulus as a result of the aversive nature of the pain signal. However, in certain circumstances survival is not enhanced if nociceptor-evoked activity overrides other motivational drives. A link between extreme emotional drive and inhibition of nociceptor evoked activity was made during the Second World War by Henry Beecher, a field surgeon. He observed that battle-injured soldiers requested analgesic drugs infrequently when compared to civilians who had received equivalent wounds in peacetime circumstances. He also realised that this 'battlefield analgesia' was temporary, and that normal sensitivities to trauma would return within hours. He concluded that the conscious and behavioural responses to painful stimuli were not hard-wired, but were in fact dependent on the emotional state of the individual.

Since that time physiologists have identified brain regions that orchestrate defensive behaviours and associated autonomic and motor activities when stimulated in the conscious animal. Among these areas, the midbrain periaqueductal grey (PAG) is the most extensively studied, and is the focus of my research. When activated in behaving animals, the PAG elicits a range of defensive behaviours, from biting, hissing and arching of the back in the cat (Bandler & Carrive, 1988) to withdrawal, avoidance and aversion in the rat (Morgan & Carrive, 2001) Depaulis et al, 1994). These behaviours are supported by appropriate autonomic changes. The precise nature of the effects observed depends both on the region of the PAG stimulated and

on the species. It is now evident that the co-ordinated defence response evoked from the PAG includes changes in sensory processing, more specifically, descending inhibition of spinal nociception. The resultant antinociception evoked by stimulation of the PAG is so profound that during stimulation through previously implanted electrodes surgical procedures can be performed on conscious animals without need of further analgesic intervention (Reynolds, DV, 1969).

Recent studies in this laboratory by Waters and Lumb (1997) demonstrated that, in most instances, descending control evoked from the PAG is indeed selective for the nociceptive responses of spinal dorsal horn neurones that are driven by noxious and by non-noxious stimulation in the periphery. However, there was a small population of dorsal horn neurones whose nociceptor evoked responses were unaffected or even enhanced following stimulation of the PAG. Nociceptive inputs to the dorsal horn are conveyed largely in two groups of primary afferent fibres: unmyelinated C-fibres and finely myelinated Aδ-fibres. Lamina V dorsal horn neurones can be divided into two groups on the basis of their inputs from C- and Aδ-fibres. Those neurones whose nociceptive input includes a C-fibre component (C+ve neurones) and those without a demonstrable C-fibre input, in which nociceptor evoked activity is presumed to be mediated by Aδ-fibres alone (C-ve neurones). Further investigation revealed that those dorsal horn neurones whose nociceptive responses were inhibited from the PAG were C+ve and those in which responses were unaffected or enhanced were C-ve.

C- and Aδ-nociceptors convey different qualities of the nociceptive message to the CNS (Torebjörk & Ochoa, 1990). As such, the consequences of the pattern of control evoked from the PAG are that the slowly conducted, poorly localised and arguably distracting component of the nociceptive message (second pain, conveyed in C-nociceptors) would be depressed, whereas the highly localised, rapidly conducted component (first pain, conveyed in Aδ-nociceptors) is left intact or even enhanced when the PAG is activated. This combination of effects would provide the animal with up to date information that could help direct motor activity and increase motivational drive whilst blocking those components of the nociceptive message that are redundant in an emergency situation.

The aim of my PhD was to develop a model by which I could further investigate the modulation of spinal nociception by the PAG, with particular focus on the differential control of C- and Aδ-nociception and its mechanisms. The first stage of this study was to find a way to preferentially activate the different groups of nociceptor. I modified a protocol devised by Yeomans and Proudfit (1996), using contact heating at different rates to preferentially activate Aδ- or C- cutaneous heat nociceptors. Application of fast (7.5°C/s) or slow (2.5°C/s) rates of heating to the dorsal surface of the hindpaw evoked withdrawal reflexes that were mediated preferentially by Aδ-fibres or C-fibres respectively. The thresholds and magnitudes of reflex responses were monitored by recording electromyographic (EMG) activity from the biceps femoris. Having established my model, a first series of experiments was designed to test whether injections of excitatory amino acid (DLH) into the PAG modulated withdrawals to fast and slow ramps in different ways. The results of these experiments revealed that 60% of withdrawals evoked by slow heating ramps are completely abolished, compared to only 30% of withdrawals evoked by fast ramps immediately after DLH injection into the PAG. Furthermore, in those instances in which withdrawals still occurred following PAG activation, thresholds to slow ramps were significantly increased, whereas thresholds to fast ramps were unchanged.

Therefore, using a direct approach I was able to conclude that neuronal activation in the PAG did indeed exert differential effects on C-fibre rather than Aδ-thermal nociceptor-evoked activity. I communicated these data at the

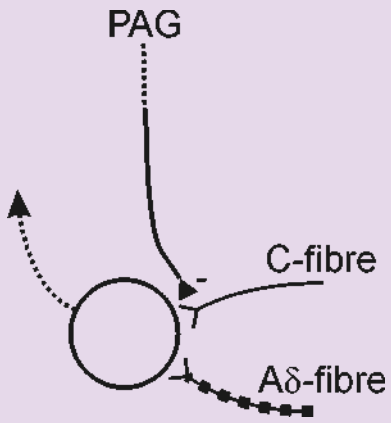
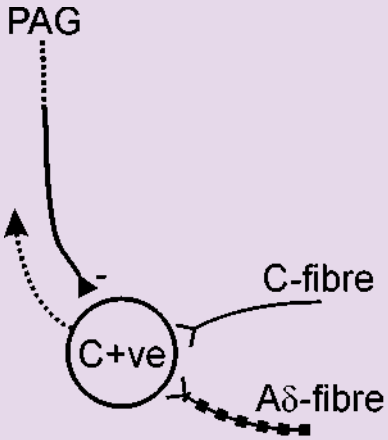


Figure 1 Working hypothesis: PAG exerts a presynaptic effect on C-fibre input to lamina V neurones.



Society's meeting in Oxford in March last year (McMullan & Lumb, 2001).

DLH is non-selective, in that it will activate intrinsic interneurones in the PAG as well as output neurones. Output neurones involved in descending control of nociceptive processing are, at least in part, under tonic inhibitory GABAergic control. In my next series of experiments I compared the modulation of nociception evoked by non-selective neuronal activation in the PAG using DLH to that evoked by selective disinhibition of output neurones under tonic GABAergic control, using injections of the $GABA_A$ antagonist bicuculline into sites that had yielded pressor responses following DLH injection. Results of these experiments revealed a higher degree of differential control following disinhibition of PAG output neurones with bicuculline. This enhanced selectivity supports a role for this group of output neurones, usually under intrinsic inhibitory control. I communicated these data at a recent meeting of the Society in Bristol in September 2001 (McMullan & Lumb, 2001)

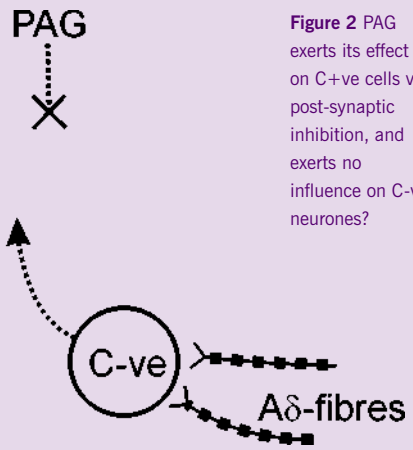


Figure 2 PAG exerts its effect on C+ve cells via post-synaptic inhibition, and exerts no influence on C-ve neurones?

The next step of the project was a series of experiments that were designed to investigate spinal mechanisms by which the PAG could selectively inhibit C-fibre rather than Aδ-evoked responses. The hypothesis to be tested was that descending control from the PAG mediates its effects pre-synaptically to Lamina V dorsal horn neurones (Figure 1), such that C-fibre input to these cells would be inhibited by PAG activity, whereas input to these cells from Aδ-fibres would be preserved. Recordings were made from the lamina V C+ve neurones, i.e. neurones that received synaptic inputs from both Aδ- and C-fibres. The effect of DLH injection into the PAG was tested on the responses of these neurones to fast and slow rates of noxious heating in their peripheral receptive fields. Neuronal activation in the PAG inhibited the responses of these cells to both rates of noxious skin heating. These non-selective actions do not support the hypothesis that the PAG exerts its differential effects on C- and Aδ- responsiveness by a pre-synaptic modulation of C-fibre input to lamina V C+ve neurones. Interestingly, on-going experiments have demonstrated a lack of inhibition of the responses of C-ve neurones to fast rates of skin heating. It would appear therefore that the differential effects evoked from the PAG might result from post-synaptic influences on the different dorsal horn neuronal cell types (C+ve vs. C-ve) rather than differential pre-synaptic modulation of inputs to all lamina V dorsal horn neurones (Figure 2).

Future experiments will investigate further the effects of PAG activation on C-ve neurones to elucidate precisely the mechanisms involved.

Many thanks to my supervisor, Bridget Lumb, for her assistance with the preparation of this manuscript, and to Dan Simpson, who helped to establish the heating model.

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STOP PRESS

The Novartis Foundation in collaboration with The Physiological Society and The Royal Society of Medicine will be holding a one day meeting on Friday 1 March 2002

MUCUS HYPERSECRETION IN RESPIRATORY DISEASE

The Scientific Societies Lecture Theatre, New Burlington Place off Savile Row, London W1X 1AB

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Defusing the bioweapons time bomb

In this article Bill Parry explores the world's inability to control bioweapons and in the following book review John Lee considers the terrifying development of bioweapons in the Soviet Union.

Bill Parry

It is said that the world changed with the terrorist attacks of September 11th, 2001. Indeed, the whole world drew its breath in shock. Yet what is now apparent amid the 'war on terrorism' is that we, in the West, will have to sacrifice some 'freedom to' in order to secure some 'freedom from'. In terms of day-to-day work, this affects few, though for many bioscience researchers in the UK there are calls for their work to be more closely monitored, and the controversial *Anti-terrorism, Crime and Security Act*, passed in December 2001, will affect many UK researchers and institutions. Society is waking up to the now more palpable threat of biological warfare and bioterrorism, and research in the biosciences and biotechnology in the UK is inevitably coming under closer scrutiny.

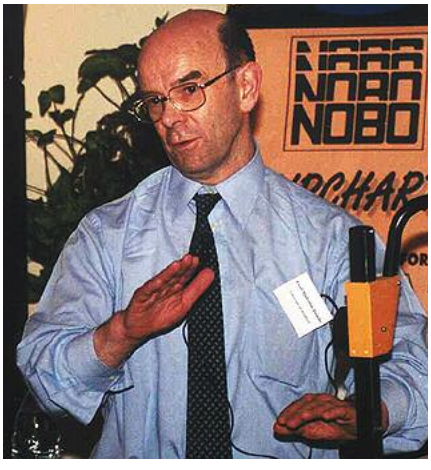
Aspects of this increased scrutiny have recently become law, in the *Anti-terrorism, Crime and Security Act*. One of its less controversial elements is a section entitled 'The control of pathogens and toxins'. Dr Jeff Kipling, from the Association of British Pharmaceutical Industry (ABPI), says that UK researchers, institutions and the biotechnology sector should be concerned and aware of the implications and obligations these measures raise. Under the revised Act, managers of laboratories with stocks of certain pathogens are legally required to notify their holdings and to comply with 'any reasonable security requirements' that the police may impose following an inspection of the premises. In addition, managers are obligated upon police request to provide the names and details of personnel with 'regular access to dangerous diseases' held in the lab. Authorities can conduct background checks on named individuals and restrict their access to such pathogens.

Kipling says that the ABPI is working with the Home Office to bring a more pragmatic view to the issue, and has called for more consultation with industry on the matter. While it supports the spirit of the changes, the ABPI is concerned over the needless bureaucracy that these changes will add in many situations, as there is no provision for the minimum quantity of toxins; thus a minute and insignificant amount would entail the full panoply of regulations.

Others fear that these changes in the law will compromise research confidentiality more than at present and possibly result in unwarranted discrimination in labs.

In addition to these changes in the law, the biomedical community has been called upon by Malcolm Dando, an expert on biological warfare and professor of International Security at the University of Bradford, to accept responsibility for the potential misapplication of its research, and to introduce steps to review and monitor research that could be applied to biological warfare.

Malcolm Dando



'Until the biomedical community accepts ownership of the enormous malignant potential of such research, government and society will fail to take the issue seriously. Within a decade or so, offensive biological weapons programmes could lead to the stockpiling of deadly biological agents. Then there will be a much greater chance of these materials falling into the hands of terrorists,' he warns.

Although Dando feels that bioterrorism on a massive scale is relatively low, he believes that the likelihood will

multiply in the coming 10 to 15 years with advances in genome research.

The recent anthrax attacks in the United States underline the exigent need for proactive action by governments and the bioscientific community worldwide. These attacks, cleverly targeted at the media and US government, inflicted wide scale panic and uncertainty with minimum effort and few casualties. Dando warns that a future attack successfully carried out with a contagious agent such as small pox or Plague could result in a catastrophic loss of life, a healthcare meltdown and social collapse. He points to the recent foot-and-mouth disease outbreak in Britain and the confusion, mayhem and carnage that it brought. Imagine such an infectious – yet deadlier – agent spreading through humans.

Our history of biological weapons gives us cause for concern. Dr Simon Whitby, author of *Biological Warfare against Crops* (Palgrave 2002), and Research Fellow in the Department of Peace Studies at the University of Bradford, warns:

'At the back of our minds we have to remember that every scientific revolution so far has been used to refine weapons of war and we will have to work hard to prevent the current revolution in biotechnology from suffering the same fate' (Whitby p.208).

Dr Nikki MacLeod, a Senior Lecturer in the Department of Biomedical Sciences at the University of Edinburgh, agrees that attitudes have to change, but feels she is probably in the minority: 'I'm utterly ashamed by the almost total lack of moral judgement displayed by many of my colleagues on such matters, from Los Alamos onwards.' Her feelings echo Richard Preston's summing remarks in his 1998 article published in *The New York Times*.

> Biological weapons are a disgrace to biology. The time has come for top biologists to assert their leadership and speak out, to take responsibility on behalf of their profession for the existence of these weapons and the means of protecting the population against them, just as leading physicists did a generation ago when nuclear weapons came along. Moral pressure costs nothing and can help; silence is unacceptable now.

From National to International Measures: the Biological and Toxin Weapons Convention (BTWC)

You would have thought that the extraordinary and unprecedented terrorist attacks of 2001 would have consolidated and bolstered international resolve to implement a comprehensive means of minimising the proliferation of biological weapons. You might have expected the US to have led such an effort, much like George Bush Sr did a decade ago, signing the US up to the Chemical Weapons Convention after he saw the deadly potential of chemical weapons during and after the Gulf War. But, surprisingly, you'd have been wrong, since the US has recently, almost single-handedly, torpedoed such a convention – the BTWC. On the other hand, you might have predicted as much, citing the Bush Administration's record of adopting a unilateral and isolationist approach, and withdrawing insouciantly from key international treaties, despite international outrage and condemnation.

The BTWC – a brief history

For over 140 signatory countries, many NGOs globally, and scores of experts, the United Nations BTWC, which came into force in 1975, is regarded as the best means – albeit largely symbolically, so far – of minimising the spread of biological weapons. The Convention prohibits all states parties from the development, production, stockpiling, or acquisition of biological agents for offensive purposes. Yet because the BTWC did not have a verification regime to monitor compliance, it was deemed powerless, and therefore ineffective.

Consequently, VEREX, a group of governmental experts, was established in 1991 to identify and assess possible verification mechanisms from scientific and technical points of view. To take this further, the Ad Hoc Group (AHG) was established in 1994 by the states parties to negotiate and create a legally binding verification regime, known as the Verification Protocol, for the Convention. The mandate of the AHG covers four areas: definitions of terms and objective criteria; incorporation of existing and further-enhanced confidence building and transparency measures, as appropriate, into the regime; a system of measures to promote compliance with the Convention; and specific measures designed to ensure the effective and full implementation of Article X, which provides for scientific and technological exchange for peaceful purposes and technical cooperation.

Oddly, 2001 was a year of major setbacks for the BTWC. In July the Bush Administration flatly withdrew its support for the Verification Protocol, causing talks to collapse – just weeks before the terrorist suicide hijackings and anthrax attacks. Then at the 5th Review Conference of the BTWC in November and December, as US B-52s were carpet bombing Afghanistan, the US delegation again surprised and incensed other states parties by sabotaging the Conference at the eleventh hour, by calling for the mandate of the AHG to be terminated. Consequently, the states parties agreed to adjourn until the 11 to 22 November 2002 in order to salvage what they could, and to allow for a 'cooling off' period.

A mistake of mythical proportions?

In Greek mythology, Heracles was given a series of labours by the oracle of Delphi to atone for earlier sins. His second labour required him to slay the Hydra of Lerna, a formidable serpent with nine heads. But every time Heracles struck off one of the heads, two

grew in its place. George Bush Jr and his Administration's unilateral stance on combating the spectre of biological warfare and terrorism are, to many, as gung-ho and futile – and infuriating to countries committed to forging a meaningful and effective convention. Edward Hammond of the Sunshine Project, an NGO, calls the US position a 'Wing and a Prayer doctrine': 'The Wing and a Prayer doctrine is a dangerous substitute for UN verification. The wings are those of cruise missiles streaking toward a suspected bioweapons facility. The prayers are for US intelligence to be right. The consequences are fatal … and a further destabilising breakdown of international cooperation to avert biological warfare. It is a flawed doctrine that proposes eliminating single threats while creating more.'

The US cites three central problems with the Verification Protocol: it poses significant risks to US biodefence programmes and national security; it poses significant risks for the intellectual property rights of its huge, lucrative and politically influential pharmaceutical and biotechnology industries; and the Protocol is too weak to catch would-be transgressors.

Certainly the US pharmaceutical and biotech industries would have much more to lose than those of any other country through intellectual espionage, given their global dominance. And many agree that the Protocol does require strengthening if it is to be efficacious. However, the US's concerns over industrial espionage are unfounded. Graham S Pearson of the HSP Advisory Board counters this claim, stating: 'The frequency of visits to such facilities in the US under the projected Protocol is necessarily seven or less per year – a minute fraction of the numbers of inspections carried out by regulatory agencies. In Europe, industry recognises that such visits will be rare and will not be nearly as intrusive as the visits carried out much more frequently by international, national and regional regulatory agencies…'.

As for the Protocol being too weak, many rightly reply that the US has been instrumental in diluting the Protocol.

Recent revelations of secret and controversial US biodefence programmes, however, may have cast a new light on the Administration's real reason for rejecting the Protocol. Nicholas Sims, Senior Lecturer in International Relations at the London School of Economics, evaluates the US's objections on two levels:

> The first pertains to the BTWC and US biodefence programs. The revelation by *The New York Times* [days before the suicide hijackings] of three US biodefence projects, none of which had been declared under the BTWC's programme of confidence-building programmes, explains US intransigence: if the US won't put them under a politically-binding CBM (Confidence Building Measure), it certainly won't put them under a legally-binding obligation to declare them to a new organisation under the Protocol.
>
> Of the three reasons given by [the US] Ambassador Mahley, initially they were all given equal weight; but in the light of *The New York Times*' revelations, this certainly is the most prominent reason, ahead of commercial proprietary concerns about loss of confidential information, and ahead of the supposed inability of the Protocol to unmask likely proliferators (if the Protocol is acceptable to Iran then it can't be strong enough, or well enough targeted, to satisfy the US). The national security concerns are evidently about biodefence, the strongest of the three reasons, to which Mahley gave equal weight on 25 July 2001 [when the US rejected the Verification Protocol].

Sims, as well as many others, adds the Bush Administration's penchant for ditching international treaties: 'They consider multilateral mechanisms "slow-moving and misguided"', he says. 'Given the US's dominance, it has the luxury to decide whether to do things unilaterally, where as for the rest of the world, and certainly Europe, the treaty approach seems natural and the best means available to counter threats.'

Of Might and Men

The Hydra wasn't slain single-handedly. Mighty Heracles was dependent upon the help of Iolaus ultimately to defeat the Hydra. In the run-up to the resumption of talks to determine the BTWC's future later this year, hopefully George Bush Jr will appreciate that his country's war on terrorism requires united international cooperation and effort. And that the BTWC, despite its flaws, is regarded by the majority of states parties as the best and wisest option available internationally to combat the spectre of biological weapons.

As for bioscientists in the UK, Dando warns that 'now is certainly the time for them to take ownership and the initiative to establish ethical committees to monitor their work. If they don't show some form of self-regulation soon, equivalent measures will be placed upon them once the government and society appreciate the deadly potential of their research.'

The big question is, of course, whether history will repeat itself.

© **Bill Parry**

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Biohazard
by Ken Alibek with Steven Handelman

Arrow Books. ISBN 0 09 941464 3. 2000, £6.99

Following a sustained campaign by the World Health Organisation, the last naturally occurring case of smallpox was reported in Somalia in 1977. No new cases were detected over the next three years and so it was that on May 8th 1980 the WHO announced that smallpox had been eradicated from planet Earth. Simultaneously they recommended that the smallpox immunisation programme should be discontinued, since it was no longer necessary to subject people to even the minimal risk associated with vaccination. The WHO also adopted a resolution which restricted the world stocks of smallpox to four sites, where small quantities of the virus would be available for research purposes only. A few years later, the sites were narrowed down to two: the Centres for Disease Control in Atlanta and the Ivanovsky Institute of Virology in Moscow. Over the same period, smallpox gradually gave up its once prominent place in medical textbooks. In the text I used for finals (published in 1983) there is a full entry – signs, symptoms, diagnosis, treatment, the lot. But in the text I bought recently (published in 2000) smallpox is relegated to a single word in a table.

If only things were that simple. One of the most chilling statements in this generally horrifying book is made in the chapter on smallpox. "Where other Governments saw a medical victory," says Alibek, "the Kremlin perceived a military opportunity. In 1981, Soviet researchers began to explore what the Kremlin hoped would be a better version of a smallpox weapon that had been in our arsenal for decades." He goes on to explain how he personally took charge of this project, which was such a success that by December 1990 the Soviet Union was capable of manufacturing between 80 and 100 tons of smallpox virus a year, at a time when immunity of the general population around the world had declined to low levels and quantities of vaccine available were so small as to essentially be negligible from a military perspective. The author invites us to "consider the damage Smallpox attack would do in a densely populated commuter city like New York" – a particularly disturbing thought in the aftermath of September 11th.

There is, in fact, a small nugget of consolation in the smallpox story, which is that smallpox degrades over time, necessitating regular restocking of biological weapons arsenals. So we might hope that in the new world order following the collapse of the Soviet Union, this particular threat will gradually fade away. But to believe this would, almost certainly, be a triumph of hope over experience. The things that administrations will do in the name of self-defence is unbelievable. And to prove the point, Alibek tells us about the jaw-dropping catalogue of all the other biological weapons the Soviet Union was actively developing over the same period: tularemia, Marburg and Ebola viruses, Lassa fever, haemorrhagic fevers anthrax … the list goes on and on. In spite of international surveillance and inspections, tens of thousands of people were working on these projects within the last decade. How many are still active today?

Of the pathogens discussed, anthrax in particular is a serious worry. The spores remain viable for years or even decades. If dispersed as an aerosol and inhaled, the resulting pulmonary version of the disease produces no specific symptoms until it's too late. And another thing which makes pulmonary anthrax ideal for military purposes is that it is one of those rare diseases which has a mortality approaching 100%. In another project, Alibek directed the development of a facility that could make 2 tons of anthrax a day. No, that is not a typo: 2 tons of anthrax spores every day. And the Soviets also perfected aerosol dispersal methods. The chaos recently caused by a few envelopes of spores rather puts in perspective what could happen if real anthrax weapons ever got into the wrong hands. Alibek was Deputy Chief of the Soviet Union's Biological Weapons Agency from 1988 to 1992, when he defected to the United States. His book is part catharsis and part biography. Apart from the slight anti-Russian spin which can be detected in some of the language used by the American ghost writer, every word of this book has the stamp of authenticity. It is certainly not to be dismissed as the disgruntled ramblings of a disenchanted apparachnik. For me, the most worrying chapter of all was the final one on Bio-Defence. There are various suggestions as to what might be done in terms of preparation for attack by a biological weapon. Unfortunately, the bottomline seems to be that if a nation decided to launch an attack with a well-developed biological weapon, there would inevitably be a huge death toll despite any of the options currently available. So here's a research area which is wide open. If this book had been presented as Science Fiction, it would have been dismissed as incredible. As Science Fact, it is a thoroughly disturbing read.

John Lee
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Is the genome the "book of life"?

Denis Noble contends that if the human genome is the book of life it has enormous gaps in it, and that a good omelette is more than just the sum of its ingredients!

The human genome is a vast database of information containing of the order of 40,000 genes. Each of these is used to encode the amino acid sequence of a particular protein, or set of proteins. The complete sequence and structure of the proteins is sometimes referred to as the proteome. Understanding how the information in the genome is used to create the proteome is a major challenge.

First, because we need to identify all the genes, which we are getting closer to doing, at least in the sense of identifying which parts of the DNA code correspond to genes. It is important though to note that this is still a long way from knowing what each gene does, what is its functionality.

Second, because we need to understand the control processes that determine which proteins are expressed and to what extent. We now know that there are many more proteins than genes, so something like a feedback control has to determine which protein is made when. This is beginning to look like a complex interaction between genes and organisms and their environment, rather than a simplistic view of genes as 'dictating' the organism and its functions.

And *third*, because predicting three-dimensional structure and chemical function from the amino acid sequences of the corresponding proteins is very difficult.

The recent discovery that there are many fewer genes in the human genome than we thought (original estimates were of the order of 150,000) adds to the difficulty since it means that multiple functionality (i.e. each gene being involved in many different biological functions) must be very common indeed, perhaps even universal.

But even these formidable challenges pale in significance when we consider the complexity of the next stage: understanding the interactions of tens of thousands of different proteins as they generate functionality at all levels through cells to organs and systems. This is the task of quantitative analysis of physiological function, which in its entirety is sometimes now called the physiome (see www.physiome.org). Computational modelling and bioinformatics will play an increasingly important role in all these stages of unravelling the way in which the information contained in the genome is 'read' to create living systems. We will be able to say that we have really read "The Book of Life" when we have succeeded in going all the way from the genome, through the proteome to the physiome. Achieving this requires the marriage of mathematics with medical science.

On this view, the genome is not understandable as "the book of life" until it is "read" through its "translation" into physiological function. My contention is that this functionality does not reside at the level of genes. It can't because, strictly speaking, the genes are "blind" to what they do. Moreover, a lot of what their products, the proteins, do is not dependent on instructions from the genes. It is dependent on the poorly understood chemistry of self-assembling complex systems. It is as though the genes specify the components of a computer, but not how they should be put together. They just do this by doing what is chemically natural to them. Some people are predicting that this is also the way in which we will build computers in the future, particularly what are called molecular computers.

So, if the genome is "the book of life" it is a book with enormous gaps, which nature takes for granted since it never had to work out how to code for such natural phenomena. This "missing information" is implicit in the properties of the environment in which genes operate. It is not explicitly coded for. Moreover, this environment crucially determines which genes are expressed and to what degree. The passage of information is not simply one-way, from genes to function.

I like the analogy with the story of the French omelette. The story is that a little family bistro outside Paris acquired a reputation for the great lightness, flavour and delicacy of its omelettes. So, the connoisseurs decided that, in writing up a compendium of French cuisine it was essential to include the recipe of these famous omelettes. The mother of the house kindly obliged with a detailed recipe of ingredients and the order in which they were incorporated as the omelette was prepared. There was only one snag. When the Parisian chefs tried it, they got a different result. Delicious flavours but totally lacking the light quality of the family's achievement. Frustrated,

they experimented with various interpretations of the recipe and forms of omelette pan until they eventually decided that there must be a trick. The mother had surely not revealed all her secrets! So, off they go to the Bistro to find that the mother has died. Her daughter now cooks the omelettes. After finding that her omelettes were just as good as her mother's, they show her the mother's recipe and ask whether it is correct. She reads it carefully and says, yes, it is a marvel of accuracy, down to the last milligram of ingredient. This is exactly what she follows. "There's nothing missing?" they ask. "Of course not", she replies, "mother has written it all down". She knows because this is also what mother wrote down for her before she died. She is following exactly the same recipe as they were trying to follow. So, they naturally ask her whether they can watch as the omelette is prepared. Of course, she says, there is nothing to hide. So they watch carefully to try to detect the slightest difference between the written recipe and what she does. And they are amazed at what they see at the very beginning of her preparation for, as she breaks the eggs, she separates the whites and the yolks, only folding the beaten whites in at the end before cooking. They upbraid her for her mother's inaccuracy, for she never reveals this crucial fact in her written recipe. The daughter takes offence at their 'stupidity' and 'arrogance' as she looks at the assembled dignitaries and asks them, in all innocence, "how else do you think anyone prepares an omelette!?"

My contention is that nature has not coded for what is chemically natural to what the proteins do. It does not need to. I also contend that this information has as much of a claim to be called the "book of life" as does the genome. Finally, I claim that it is going to be much more difficult to work out this side of the story than to sequence the genome.

So, in brief, my view is that the genome…

1 Is most like tedious machine code for the construction of the key players in the game of life: the proteins.

2 Is incomplete in a major respect: how these proteins behave chemically in the cells of the body, how they fold, combine and interact.

3 Is completely lacking in functionality. It does not even tell us whether a particular gene plays a role in 1, 2, 3, a dozen, or a hundred functions.

…relies time and again on Mother Nature's ability to know "how to make omelettes."

One defence of the "Book of Life" view against my attack is to say that all books are like this to some degree. All languages function in a context of implicit knowledge that the language itself does not need to spell out.

Of course this is true. One way to see this is to note that languages differ in what they take for granted. Some languages do not use plurals, for example (though equally obvious the users of these languages – which include Chinese, Japanese, Korean, Polynesian languages, Maori – have the concept of plural and know when there is more than one of the thing being referred to). And there are innumerable examples of words, even when very similar in different languages, that function differently simply because of the cultural context in which they are used. To call a French woman, in French, "séduisante" is to compliment her highly. To call an English woman "seductive" could be highly dangerous! And to avoid the cultural difference by translating "séduisante" as "beautiful", "appealing" etc is to remove precisely the sexual frisson that the French language intends. And it begs the question of what the cultural context of the word "sex" is in the two languages.

So, I accept the thrust of this argument. This kind of "implicit" knowledge is an irreducible feature of all languages (none are, or can be, neutral with respect to culture since they are themselves the creatures of that culture). But the relationship between the language and its culture is not like that of the relationship between the genome and nature. One way of seeing the difference is to ask what the language is trying to do. Human languages aim to describe the world as it is (or rather, as it is seen by the speakers). It is an aim of each language to try to avoid ambiguity. There is even a discipline, called philosophy, that – working as it must within the constraints of a particular language – tries to step back, as it were, and see beyond the limits of the culture, to question those limits, the bounds of sense (to echo Kant) and of meaning.

By contrast, the genomic language does not have anything like this as an aim. Of course, strictly speaking, it must have nothing as an aim – evolution is blind – but if we take this line then, *a fortiori*, the genome is not a book. In order to pursue the book analogy we have at least to ask what it could be said to be a book *about*. So is it about "life"? Well, I would say no, not really. Crucially, it does not describe functionality. The code for gene XYZ does not spell out that XYZ makes a protein that enables synapses in brains to function, testicles to produce sperm, pancreatic cells to secrete insulin etc etc. This is a bit like imagining a book that does not spell out that X is the King, Y the archbishop, Z the villain, etc. But, worse than that, from reading the "book" we don't even know what the relationship between a King and an Archbishop might be. These crucial interactions are outside the scope of what the genes specify.

So, let's do a thought experiment.

Silmans are an intelligent species

that evolved in a world in which silicon functions instead of carbon. They advance to the point of rapid space travel and find the planet earth. But, they have a serious problem. They can't live on earth. The earth's environment is terribly hostile to silmans as a form of life. Moreoever, they can't bring humans, or any other earth creatures into their spaceships, for what they require to live is equally hostile to earth forms of life. But they know from their own evolution that there must be something equivalent to silman code, there must be earth-life code. They have also worked out that, in their case, this is imprinted in chemical sequences that are inert. Their code molecules do not breathe, or need siligen (the equivalent for them to oxygen) etc etc. They therefore reason that they might be able to send robots down to the planet's surface that will extract earth-code. OK, let's call it DNA. To their joy, they find that this DNA is also chemically inert. It can be taken into their spaceships and it can be subjected to analysis. So, they start reading the complete DNA of a human.

Let's give them too the intuition that this 'inert' molecular sequence codes for another sequence, that of the proteins, and that these are highly reactive. So, having worked out what the code means (which DNA sequence corresponds to which amino acid) they set about determining all the proteins – all 100,000 or more of them – that go to make a human.

But, then they are stuck. Because theirs is a silicon world, they do not have water, they do not have lipids. But, they guess from analogy with their own world that there must be such things. They try to see in the DNA code any clues to what these substances might be. To their intense frustration they find there is nothing. All the DNA code does is to specify one type of molecule, proteins. No other information is there. What a bore!

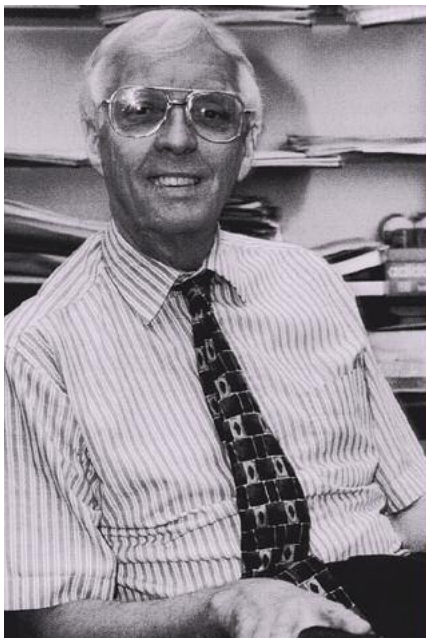
So, they start to conclude that earth-life must be a very strange thing. Just tens of thousands of proteins thrown together. Perhaps humans are a kind of soup! Perhaps earth-life is extremely primitive. So, they prepare to time-travel on to the next inhabited planet.

But then one of them says, "Hey, wait a minute. You could say that we are "just" a bunch of silicon sequences. But we know we are not: that we think, reproduce etc etc. There is more to life than molecular sequences. What we should do is to send down another robot with a carefully isolated capsule into which it will put all this strange stuff called water, air, lipids etc that we know are down there. Let's bring it all up in the capsule and see what happens when we let the DNA do its thing in this environment."

So, they then watch with incredulity through the capsule as cells are formed, then divide into the early embryo, that then goes through all its wonderful transformations until 9 months later a human emerges (OK – I am simplifying – they are just cloning – there's no mother, no womb etc, and I have to assume that they picked up at least one cell to provide the environment in which the nuclear DNA can work – but putting all these into the picture will only reinforce the point I am making). Just like the Parisian chefs, they feel cheated. The "recipe" doesn't specify all this. It just happens!

Some omelette!

Denis Noble
University Lab of Physiology
Oxford



John Coote

The essential importance of integrative physiology: A role for Experimental Physiology

Just 2 years ago I took over as Chairman of the editorial board of Experimental Physiology. To be given this task at the start of a new millennium is somehow aesthetically satisfying as well as being challenging. After the initial inevitable steep learning curve I thought a brief account of the Journal and its mission was called for, particularly since I often get asked by members of The Society "what is Experimental Physiology?"

Experimental Physiology covers a broad scope of biological systems with a major emphasis on integrative physiology. By this is meant the functioning of cells, organs and systems that cannot simply be understood by knowing more and more about their individual parts. The integrative focus of Experimental Physiology places it at the cutting edge of contemporary physiological research and our aim is to make it the leading publication outlet in this area.

The integrative focus of Experimental Physiology

In this post-genomic age integrative physiology is necessary for understanding the new biology. It is essential if we are to reveal the function of genes. How else can one phenotype transgenic/mutant animals, determine gene related alterations in body control systems using techniques like vector mediated gene transfer? Integrative studies with complex biological systems are also needed for realising the benefits that genomics and proteomics will bring to developing new medicines as recently highlighted in a report by a Working Party of the British Pharmacological Society (2002 TIPS 23(1) 13-18). Furthermore more conventional 'systems' techniques will continue to be needed for understanding the physiology of body control systems which is still inadequate.

What does Experimental Physiology publish?

Experimental Physiology publishes original research covering the functional consequences of interaction of animal proteins, cells, tissues and organs. Our interpretation of this definition can perhaps best be appreciated by referring to previous papers, eg the paper on the role of nitric oxide in the vascular bed of skeletal muscle during exercise in rats by Musch et al 2001 Exp Physiol 86(6) 749-758; or that on the programming of adult disease by an adverse intrauterine environment for fetal development by Hawkins et al 2000 Exp Physiol 85(1) 85-96; or in complete contrast the effect of vagus nerve stimulation on pacemaker shift in the rabbit sinoatrial node by Shibata et al 2001 Exp Physiol 86(2) 177-184. Experimental Physiology also is keen to publish pertinent methodological papers like that on tracing multisynaptic pathways by Pyner et al 2001 Exp Physiol 86(6) 695-702 or that on somatic gene transfer in studies of cardiovascular control by Kasparov & Paton 2000 Exp Physiol 85(6)747-756.

An important feature of Experimental Physiology is the publication of articles dealing with the most up to date development in various fields of physiology. These are found in the selected reviews and symposia by special interest groups, for example, Oxytocin and Vasopressin from molecules to function Exp Physiol 85S March 2000; Gene manipulation and integrative physiology Exp Physiol 85(6) November 2000; Uterine contractility Exp Physiol 86(2) March 2001, and Vagal control: from Axolotl to Man Exp Physiol 86(6) November 2001. It also publishes 6 of The Physiological Society's review lectures like that of Janice Marshall in1999, The integrated response to hypoxia: from circulation to cells Exp Physiol 84(3) 449-470 or that by Julian Paton in 1999 on Nucleus Tractus Solitarii: integrating structures Exp Physiol 84(5) 815-834 and that by David Paterson in 2001 on Nitric oxide and the autonomic regulation of cardiac excitability Exp Physiol 86(1) 1-12. Both of the latter are now on our board of editors.

Experimental Physiology: A brief history

It is now 94 years since the first volume of Experimental Physiology's predecessor appeared in January 1908. It originally was given the rather cumbersome title of Quarterly Journal of Experimental Physiology. The reasons for this and the history of the Journal's origins are well worth reading and is well summarised in a review by David Whitteridge FRS, published on its 75th anniversary in Q.J.Exp. Physiol 1983 68, 521-523. It seems the Journal arose from the concerns that Physiology was treated with disparity by the editors of the Glasgow based Journal of Anatomy and Physiology. It subsequently arose that members of The Physiological Society were also unhappy with the autocratic and arbitrary way Langley as Editor in Chief dealt with papers submitted to The Journal of Physiology. A process sometimes referred to as being Langleyized! Sir Edward Sharpey-Schafer, then Professor of Physiology in Edinburgh was urged to establish a new Journal of Physiology and so the Quarterly Journal appeared under his editorship in 1908. It should be said this was with support from the majority of members of The Physiological Society. Despite this Langley thought that there was no place for competing Journals, a sentiment which has been echoed over the years since. Little did anyone envisage today's scenario of strong demand for publishing space and the explosion of Journals. It is worth commenting here that my feeling and

that of the present editorial board is that there is an element of truth in the idea that The Physiological Society should not be publishing two Journals with similar scope. That is why I want to emphasise that Experimental Physiology has quite different terms of reference to The Journal of Physiology.

Returning to our brief history, the Quarterly Journal of Experimental Physiology like many Journals of the time, lacked strong financial support, because it depended on the resources of individuals. So following a number of crises the Journal was taken over by the Physiological Society in 1979 and renamed Experimental Physiology.

Thanks to the efforts of its chief editors, Cecil Kidd and more recently Jim Gillespie Experimental Physiology is now internationally recognised and is financially sound.

Nonetheless can we justify two Journals of Physiology? It was argued by David Whitteridge (1983), I quote "that by providing a second channel of publication in this country, the Journal has continued to obviate some of the consequences of Editorial eccentricity in The Journal of Physiology." This is still true although not our main function.

The Present Situation

The Journal has an international editorial board of distinguished scientists each dealing with a specialist area of physiology. We now ask that manuscripts be submitted to the area editor (electronically is quicker) via Emma Ward, our editorial and distribution assistant, in Cambridge. The whole editorial process is now speedier so that a paper from submission to publication can take only 4 months. Even quicker are rapid communications, which by the way, are not preliminary reports but key and highly topical new findings usually in rapidly moving fields. These can be published on the web as soon as they are accepted. Furthermore the Journal is now on-line so that providing your library has paid its dues you can down load any manuscript.

Experimental Physiology like The Journal of Physiology is a Journal of The Physiological Society, and members should support it. I have tried to make clear what Experimental Physiology is trying to achieve. Since organisms can be best understood in terms of how their component cell systems interact, we decided to have a strong integrative agenda to supplement the more reductionist approach of The Journal of Physiology. Our policy is to provide the outlet for studies dealing with the complexity of intercellular events. Inevitably there will be overlap just as there is with publications of the American Physiological Society.

At the moment we can see the mountain, but the route to the summit is a little unclear although we have made a start. The new physiology, genomic and proteomic, will demand the functional approaches of integrative physiology and we forsee Experimental Physiology becoming an important conduit for papers in this area as well as in the traditional areas of biology.

The goal of the editorial board is to increase the impact factor and circulation. But remember the rating of a Journal to a large extent depends on its readers and subscribers so by submitting your manuscript to Experimental Physiology it is you that will determine its future.

John Coote

Chairman of the Editorial Board of Experimental Physiology

Department of Physiology
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Why Sharpey?

Alan H Sykes

The name 'Sharpey' probably means little to most readers today. A few may remember a minor point of bone structure, the perforating fibres lying under the periosteal membrane, known as Sharpey's fibres after their discoverer; some may have heard of the annual Oliver-Sharpey lectures at the Royal College of Physicians which were established in 1904 to promote the application of physiology to man; rather more might recall the name of Sharpey-Schafer as the author of the *History of the Physiological Society 1876 – 1926*; finally, those with some connection with University College London might know of the Sharpey Physiological Scholarship. But it is certain than none would associate the name with any great physiological discovery. So why write a book about him?

The answer is given in the words of Edward Scharpey-Schafer, a great physiologist himself and an austere character not given to facile praise, who bestowed upon Sharpey the sobriquet "the father of modern physiology in England". Quite something to live up to; how did he come to earn such a distinction?

William Sharpey was born in Arbroath, on the east coast of Scotland, north of Dundee, on the 1st April 1802. His father went there from Folkestone to set up a branch of a shipping business and married Mary Balfour, from a well-known local family. He died a few months before the birth of his son William. Mary Sharpey remarried, to a general practitioner, and had several more children three of whom entered medicine.

After attending a local school, Sharpey went to Edinburgh University and qualified in medicine in 1823 . He travelled and studied abroad extensively before returning to Edinburgh to set up his own school of anatomy in 1831. In 1836 he was tempted away by the offer of the post of Professor of

Left William Sharpey
Photo courtesy of The Wellcome Trust

Anatomy and Physiology at University College London (as it became). One of his main recommendations for the post was his familiarity with the new-fangled technique of microscopy (the term 'histology' was not then coined). The microscope was still viewed with suspicion by the medical world so University College was (as usual, some might say) in the forefront of new developments. Cutting sections by hand or teasing tissues apart and examining them with a microscope was at that time the only practical work undertaken by students. But Sharpey had a vision of physiology in the future; he knew all the notable work of the past and kept up with contemporary advances particularly from the strong French and German schools. He turned to animal demonstrations, especially after the introduction of anaesthetics in 1846, and eventually he persuaded University College to set up a laboratory solely for practical physiology with an extra member of staff to help run it. New techniques were introduced (electrical stimulation of nerves, blood pressure recording) and by 1874, when he retired, the course had a look which we would recognise today. He died in London on the 11th April 1880 and was buried in the grounds of Arbroath Abbey.

Sharpey himself made no physiological discoveries. His only original work, other than Sharpey's fibres, was the first description of ciliary motion and this was done before he moved to London. But apart from a limited amount of histology, there was little in the way of research in any of the medical schools in those days; Sharpey's years at University College covered what has been called the stagnant period in English physiology. Nevertheless, Sharpey had an abiding interest in the subject and his enthusiasm was transmitted to a number of his most able students. These few men (women were not admitted to the University until 1878) were inspired by him to take up physiology as a career at a time when there were very few established posts. These men, Michael Foster, John Burdon Sanderson, and Edward Schafer in particular, made important discoveries, organised new university departments, and stimulated a talented younger generation to succeed them. By the time Sharpey died there had been a revival in English physiology; the subject had become an independent discipline and its standing enhanced by the establishment in 1876 of the Physiological Society of which Sharpey (and Darwin) were the first Honorary Members. Renaissance had followed stagnation.

A number of others could be called 'Sharpey's men' in that they were inspired by him and made many notable contributions without ever becoming full-time physiologists or the leaders of great schools. Among these were James Blake, George Harley, Joseph Lister and George Oliver. All the above, first team and second team, expressed their indebtedness to Sharpey, showing respect for his scholarship and affection for him personally.

He also won the esteem of his colleagues and former pupils at University College who, in 1869 (even before he had retired) collected the sum of £2170 (over £80,000 today) as a memorial to him. His portrait was painted by J. P. Knight and a marble bust sculpted by W. H. Thornycroft but the major part was turned into an endowment for the Sharpey Physiological Scholarship for research under the direction of the Jodrell Professor. Appropriately, the first scholar was his pupil Edward Schafer.

The great researchers can be evaluated by the quality of their publications; it is more difficult to evaluate the great teachers, as their success can only be estimated from the work of their pupils. There is little doubt that William Sharpey was a great teacher whose work influenced the course of physiology not only in England.

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Sharpey's Fibres. The Life of William Sharpey, The Father of Modern Physiology in England
Alan H Sykes. Sessions of York, January 2002. ISBN 1 85072 270 6
Size 223 x 152mm SB 220 pages with 47 illustrations. £18.50
All profits from its sale are donated to the Sharpey Physiological Scholarship.
Members of the Society may purchase copies for £15 post free (but payment with order please) from the author at: Walthwaite How, Chapel Stile, Ambleside, Cumbria LA22 9JG

Reminiscences of the Oxford Physiology Department

I first worked in the department as a BSc (now MSc) student in 1941/42, concurrently with my clinical course. My supervisor was David Whitteridge, then a Beit Fellow, who had been building electronic equipment for his work on single afferent fibres from the heart and lungs. I was given a small room, provided with most of the rather modest equipment I needed and the facilities to make my own gadgets, and was left largely to myself. I was the only junior research student then in the department; I think that even in normal times there had been very few of them. That was very much in contrast with the Pharmacology department, where J H Burn regularly selected keen students and offered them a year's work for a BSc; near-contemporaries of mine who did so were Geoffrey Dawes, John Walker, Miles Weatherall, Derek Wood and Peter Elmes.

The academic staff then consisted of Professor Liddell, Humphrey Leach who was Harry Carleton's second-in-command in the histology lab, and David Whitteridge, who was not then a lecturer though he did some class teaching. C G Douglas and Harry Carleton were away at Porton, Stephen Creed with the RAMC, and Colin Courtice doing research with the Navy. There was a small communal tea party with the biochemists (R A Peters, Robert Thompson, C W Carter, Sandy Ogston, Lloyd Stocken, Ernest Walker) every day in the shared library — always lively and very entertaining. When we were moving to the new department Peters even suggested a bridge between the two buildings in an attempt to salvage these teatime meetings, but they were really doomed by the rapid increase in numbers.

My room was one of an interconnecting suite of three small labs. My immediate neighbour was the physicist A H S Holbourn, whose pioneering work on head injuries was showing the major cause of brain damage to be the shear-strain resulting from angular acceleration. I and others learnt a great deal from him, then and later, about a whole range of laboratory applications of physics, including electronics; and after the war we did two experimental projects together. Whitteridge in the room beyond did several big experiments a week single-handed, and was also involved with field work on poison gases and on the cardiopulmonary effects of blast. All experimental work, including notionally my own, was directed at some aspect of war medicine. I took part in the Thursday morning 'cat class' which was expertly run by Liddell for the small handful of honours students; otherwise I saw nothing of the teaching in the department.

By 1945, when I came back as a departmental demonstrator, the academic staff was back to its pre-war complement, and others like Charles Phillips, Dan Cunningham and myself were being added. Student numbers built up very rapidly, with the honours course soon up to its previous size. Junior demonstrators like myself were expected to teach in a wide range of classes under the supervision of a senior staff member; the subject matter in some of these classes followed pre-war practices waiting to be overtaken by new concepts and technology. Whitteridge in particular broke away from tradition by introducing a whole series of electrophysiological experiments requiring electronic stimulators and amplifiers. Lectures at that time were rather stereotyped and were all given by senior staff; that only began to change when we moved into the new building in 1953. The cost and difficulties of travel meant that visiting lecturers from abroad were much less common than they are today. Such a visit would be quite an event, and the sponsor, who was often Liddell, would make sure we all had the chance of meeting them in the department and sometimes at supper afterwards in College. Some of those I remember meeting for the first time in that way were Otto and Cecile Vogt, A. Fessard, Ragnar Granit, D Denny-Brown, J C Eccles, E A Asratyan. These rather domestic occasions were only really possible because of the small numbers around at that time.

The only woman doing scientific work until about 1949 was Mrs Creed (Sybil Cooper), originally a pupil of E D Adrian, who had acted as tutor at St Hilda's and returned to active research after the war, doing distinguished work on mammalian muscle and muscle spindles. In 1949 Jean Banister arrived from Edinburgh, and in 1950 Marianne Fillenz as a graduate student from New Zealand.

There was a considerable demand for modern experimental equipment; but very little was being produced commercially at that time, so most had to be made in the department or in other local workshops. Edgar Schuster made moving-paper cameras and other gadgets for Whitteridge and Phillips at his home in Chadlington Road. Electronic equipment, apart from simple Cossor bench oscilloscopes, had to be

made by each of us from scratch.The workshop in the old building was adequate for making racks and chassis for the amplifiers, stimulators and time-base circuits, which in turn we assembled from basic components either bought from radio shops, or brought from the dumps of war equipment we were allowed to raid; most of the latter came in the shape of radiofrequency assemblies which we dismantled.

The old department was a shabby rabbit-warren of a place with a domesticity which we never managed to recreate in the new building. A serious defect was the quite inadequate provision for animals and for workshops. Thc basic electric supply came from the old Museum generator at 110 V DC; it carried parasitic AC components of which the one at 300 Hz was particularly difficult to screen out from electrical recordings, and that probably accounted for the two 'tin rooms' built for Eccles in the 1930s and subsequently used by Whitteridge. One of these was built in the new building (Room 2) but it soon became clear that once free of the environment of the old generator this degree of screening was unnecessary. 230 V AC power sockets had of course been installed in some of the rooms to operate conventional electronic power supplies, though a large number of batteries were still in use as well.

One active and very efficient component of the old building was the histology lab, which then serviced large practical classes in both BM and final honour schools, and was in the charge of Tommy Marsland (Mr Marsland in those days). His preparation room, as I remember it, had an open gas fire with Winchester bottles of absolute alcohol beside it, and a lighting flex dangling from it. I never heard of any sort of accident happening there. Altogether we were very healthily free of safety restrictions at that time. If there ever had been a fire, the Museum Fire Brigade under its chief Jimmy Meadows would presumably have dealt with it.

Liddell was occupied over a number of years with the planning of the new building, often in dispute with the University which was much concerned with its nonscientific aspects. Council insisted on a long thin building which would hide the science area from the Parks, and employed the traditional architects Lanchester and Lodge who had built the physical chemistry building ten years earlier. As a result we got a solid inflexible laboratory in which any structural change would be messy and extremely costly, with no modern structural features such as ceiling ducts for services or flexible partitions which Liddell wanted, and with inadequate weight-bearing for any proper third floor extension in the future. Liddell's one notable victory was the lecture room for which he got independent advice on ventilation and acoustics. For some rooms a transformer-isolated mains supply was specified with the secondary centre-tapped to earth, to reduce interference. This required double-pole switches, which the electrical contractors were unable to understand. Similarly the colour consultant was colour-blind, according to Liddell.

The new building provided us for the first time with a well-equipped workshop, and we had an expert mechanic in Tom Wright, a Yorkshireman previously employed by Standard Telephones who had a huge range of expertise, from electronics to precision-made cameras, stereotaxic equipment and treadmills. It was only when he left that electronics became a separate subdepartment, coinciding with good commercial equipment at last becoming available.

Research funding became a problem with the sharp increase in graduate students. When trying to get an MRC studentship for R M Gaze in 1951, I discovered that although heads of other biomedical departments always got what they asked for from the MRC, Liddell had never cultivated them so that funding remained sporadic, from Christopher Welch scholarships, College senior scholarships and so forth, according to tradition. Though always generous with moral support he distrusted external funding on the grounds that it might tie one's hands. This all changed when G L Brown arrived in 1960; he knew all the ropes and had no such inhibitions, and grant money came freely into the department after that through the 1960s and 70s.

This personal recollection of scenes and events relates more to the neurophysiological aspects of the department than to others as my interests mainly lay there. Dan Cunningham would have been able to balance the picture from the respiratory point of view; that would have been important because these two subjects tended to dominate the scene in those years and they were rather separated in the department. We all liked and greatly respected C C Douglas, a lively and interesting man who formed an important link with Oxford's great tradition in respiratory physiology. After his formal retirement in 1949 he went on teaching in classes and lectures until we moved to the new building.

George Gordon
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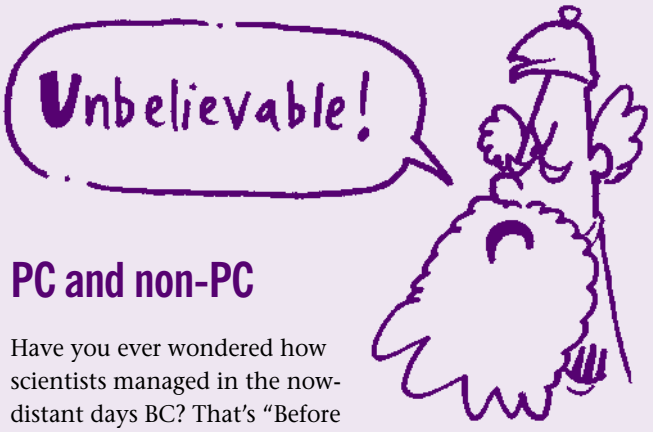

PC and non-PC

Have you ever wondered how scientists managed in the now-distant days BC? That's "Before Computers", in case you were wondering. It may be hard for those under 30 to imagine, but there was a time – only about 15 years ago – when most labs probably had only one personal computer. Or maybe a couple, a BBC micro and an Acorn maybe. Possibly attached to a counter, or an experimental rig, or maybe just sat on a bench running a stone-age statistics package or primitive wordprocessor.

It's not like that any more. Nowadays we have a scientific world where near enough every PhD student, let alone postdoc, has a PC on their desk with more computing power than it took to land a man on the moon (They may not have a desk any more, in these days of hot-desking and multi-tasking, but that's another story) .

So here's a question.

Has all this computing power helped? Are we more productive?

Or does it just mean we spend a lot of time messing about with computers?

What I have in mind is summed up by that comment about the coming of computers – and the Internet, don't get me started on that – having caused a huge increase in the amount of available information, but absolutely no noticeable increase in the amount of intelligence.

OK, OK, I'm playing Devil's advocate here – there are lots of things PCs let us do in science which were at the very least difficult, and sometimes impossible, pre-PC. We can acquire and analyse tons of data, from electrophysiology, to images, to *in vivo* parameters, for a cost of only a few thousand pounds. Back in the old days, you would have been taking measurements off paper chart recordings with a steel ruler, or, if you were lucky AND high-tech, fighting to get night-time access to your lab's one cherished Sun workstation microcomputer.

And most recently, without massive computing power, and PCs linked to networks, the DNA sequence comparisons on which molecular physiology – and other molecular sciences – is based, would be a non-starter.

So PCs are wonderful inventions.

But ask yourself these two related questions. First, how many of the computers in your labs and offices are actually attached to pieces of equipment, as opposed to sitting on someone's desk? And second, where is the fastest and ritziest PC? I would venture the answer to this is probably "sitting in the bosses office for him/her to do his/her email on". The computer running the patch-clamp rig is probably the one the boss threw out of his/her office PC four years ago.

The moral here is that a PC is, when all is said and done, more than just a working tool. It is also A GADGET. And scientists, especially physiologists, LOVE a gadget.

Sadly this can lead to a degree of obsession. How many times have you caught your boss/colleague/PhD supervisor/Professor drooling over a computer direct sales website, or a computer magazine, eyeing up the latest ultra-light Gigahertz notebook PC?

There is also the problem of competition. Just a few months ago, a friend of mine upgraded his desktop machine from a serviceable – though admittedly elderly – Pentium 166 to a new 800 MHz system. Within weeks, two other people with offices in the same corridor had also upgraded – the first to a 900 MHz, and the second to a 1 GHz, machine. Do you detect a pattern here?

Incidentally, all these three people require their desktop computers almost exclusively for running Microsoft Office, which raises a further question – just how fast CAN you run an Excel spreadsheet? What's that phrase? Faster than a speeding bullet?

Of course, you might need that extra processing power for other things, such as surfing the net, downloading MP3 music files, or burning that vital CD of your digital holiday snaps. Not to mention listening to Radio 4 online via the network.

To show I'm not a complete Luddite, though, I am happy to admit there are ways in which PCs have changed our work. Take writing papers. Just think how many extra drafts we can go through now, emailing them to co-authors in all corners of the world for minor corrections. Five drafts seems to be about typical these days. Pre–PC, I reckon two was more like it.

Or take seminars and talks. Pre-PC, this meant digging out some slides, picking 20 or so, and thinking up a story to go with them. Plus maybe an OHP acetate for anything you didn't have a slide of. Post PC, it now means a minimum of a day wrestling with Powerpoint, fighting the urge to put in pointless animation and memory-eating video clips. And then burning the whole thing to a CD (since by now it's at least 20 Megabytes) which may – or may not – work in the host department's computer (Alternatively, you could take your ultralight GHz notebook with you instead).

Finally, in case you were wondering, I should admit that I am writing this on a PC. But I would stress that the Mark Cain home PC is NOT a gadget.

Definitely not. It's a tool of the trade.

And, by the way, it runs Windows 98 and Office 97 perfectly happily on a P200 with 32 MB of RAM, none of your GigaHertz overkill for the Cain family.

Plus, since I added the external modem, those extra USB ports for the Compactflash card reader and the scanner, the sync cable for my palmtop computer, and the infra-red adaptor to talk to my mobile phone, it can do all kinds of REALLY USEFUL stuff.

It can even listen to Radio 4.

Mark Cain

International Workshop in Prague
"Experimental Methods for Brain Studies in Health and Disease"

Participants at the International Workshop in Prague on the steps of the Institute of Physiology. Eva Sykova and David Brown (workshop organizers) are front centre, Josef Syka (Neuroscience Congress President) is second from right.

Your International Secretary at dinner with a group of young participants from Russia (left to right: Natalia Shemyakina, Maria Starchenko, Elena Galantseva, Dmitri Samigullin, Inna Nikishena, David Brown, Victor Vorobiev).

The Second International Workshop for Young Scientists from East Europe and the ex-CIS States, sponsored by the Physiological Society, was held at the Institute of Experimental Medicine of the Czech Academy of Sciences in Prague from October 23rd to 25th. The Workshop was organised by Professor Eva Sykova and her colleagues at the Institute, with help (if that's the right word) from your International Secretary. This was followed on October 26th and 27th by the conjoint Fourth Congress of the Czech Neuroscience Society (President: Professor Josef Syka), at which participants presented posters of their research and listened to scientific research presentations by Czech and UK physiologists and neuroscientists.

At the Workshop, 'students' listened to a series of tutorial-type presentations in the mornings, then joined in laboratory demonstrations and workshops in the afternoons. Tutorials were given by Tim Bliss, Frances Edwards, Charles Nicholson, Joan Abbott, Jonathan Ashmore and David Ogden on behalf of the Physiological Society, and by Ladislav Vyklicky, Jr., Andre Fenton, Alexandr Chvatal, M. Hajek, Eva Sykova and Josef Syka from Prague. The afternoon lab and workshop sessions were organised by the Prague tutors, with the addition of Jan Bures and Ladislav Vyklicky Sr, and of Pavel Mares from the Institute of Physiology. They were assisted by the visiting tutors with additional help from Ted Evans, Michael Hausser, John Kelly, John O'Keefe, Roger Thomas and Alex Verkhratsky, plus many hard-working young students and research scientists from the Institutes of Experimental Medicine and Physiology. At the conjoint Congress, research talks were given by all of the Physiological Society representatives mentioned above, plus Ole Petersen and David Brown. The full programmes for the Workshop and Congress are available on the internet at http://uemweb.biomed.cas.cz/neuro2001.html, and the Workshop programme can be accessed through a link from the Society's website at http://www.physoc.org/international/workshops/Prague.html.

The Workshop was attended by 61 'young scientists' from the following countries (numbers of registrants in brackets): Russia (17), Czech Republic (12), Ukraine (11), Slovak Republic (8), Georgia (7), Poland (3), Romania (3), and one each from Australia, Austria, Germany, Hungary, South Africa, Sweden, Yugoslavia and the U.K. Thus, there was a true international spread. Many of these were presenting their work for the first time outside their home institutes.

The social side was not forgotten. We had a Welcome Party on the first night, a banquet on the last night, and communal dinners on the other evenings, with lunches provided in the Academy and efficient bus transportation to and from places of residence.

Special thanks are due to Eva Sykova, and to her assistant James Dutt, for a very successful and brilliantly organised Workshop, and to Josef Syka for an equally successful Congress.

David Brown
International Secretary
Department of Pharmacology
University College London

An Affiliate's impression...

The brief of the workshop was to provide both theoretical and practical instruction in methods of research in neuroscience, and in both of these it was an outstanding success. The programme comprised seminars or 'tutorials' in the morning followed by 'hands-on' laboratory sessions in the afternoon. The topics covered spanned the whole range of neuroscience

research, examples including ion channels at synapses, diffusion in extracellular space in the brain, methods of study of the central auditory system and spatial cognition of the rat. It was an indication of the calibre of the seminars that whatever the topic something useful could be gained from each one, regardless of the field of study. Without exception, all the tutorials remained within the remit of an emphasis on methodology and technique. For many of us 'students' this put into perspective the many results-based talks that we listen to outside our particular fields of expertise. The afternoon laboratory sessions were well organised, and we were able not only to watch experiments taking place but to try the techniques. The opportunity to talk directly to the experts in the field whether laboratory heads or postgraduate students who use the techniques on a daily basis was exceptionally educative. It was an indication of the success of these workshops that most 'students' showed an interest in areas of work other than their own specialisations, and I think we all gained a respect for each other's work.

Following the workshop, we presented posters at the 4th Conference of the Czech Neuroscience society. These were noted to be of a very high standard and provided an opportunity for vigorous discussion of results with the conference delegates. This was particularly valuable to those participants from the ex-CIS states who may not necessarily be able to attend many such meetings and take part in these discussions. The meeting also allowed the young physiologists to network and identify potential collaborations and possible areas for future training.

As well as hard work, as befits any event related to the Physiological Society of course there was an active social scene. Myself and a number of students found ourselves excellently accommodated in the guesthouse of the Academy of Sciences. Here the level of security appeared to be quite impressive when we were greeted by armed guards each morning and evening. We wondered whether they were to protect us from Prague or Prague from us, but it later transpired we were staying next door to an ambassador's residence. The 'tutors' were accommodated nearby in quite palatial surroundings and another contingent of students were housed some way away in the exotically titled 'Hotel Gradient'. Despite great speculation and excitement, distance between our accommodations meant that the origin of its odd name remained a mystery. In all we were treated quite excellently during both the workshop and following conference, and a special mention should be made of James Dutt for his expertise in keeping everything running smoothly behind the scenes during the extremely full schedule. Due to our every need being taken care of and dinner not ending until well after 9.30pm, we were not unleashed on the unsuspecting city until late in the evening. Despite this, some of us 'not-so-young' young physiologists and 'tutors' were still able to give the other students and postgrads a run for their money. A mention should also go to the local participants who ensured that we were all made welcome in their city, and some of whom ensured that our evenings were nothing if not eventful.

Top David Brown (International Secretary) addressing the workshop participants.

Centre Professor Roger Thomas and Mrs Thomas with participants from Georgia at the farewell banquet.

Bottom Richard Helyer (far right) with participants from Romania, Australia, South Africa, the Czech Republic and Poland at the farewell banquet.

Finally on behalf of all the workshop partcipants, I would like to thank the organisers Profs. Eva Sykova and David Brown, together with all the other staff and researchers who worked with us and made our trip so educational and exceptionally pleasant.

Richard Helyer
Department of Physiology
The Medical School
University of Bristol

University of the West of England
Sixth Form Workshop 17th Oct 2001

I did not manage to get to many sixth form workshops in 2001 but I'm glad I made it to University of the West of England. It is an institution to which I had never been, and was immediately impressed by the size of the department and friendliness of the staff. The programme for the day was tightly packed – two short talks, and six practicals sandwiched in between. The practicals reflected the diversity of physiology and included tissue baths, nerve velocity measurement, metabolic rate measurement and electron microscopy, blood pressure on a tilt table and ECG'S.

I was pleased to see that the students who came were a lively bunch, attacked the practicals with gusto (no shortage of volunteers even for the tilt table) and both asked and answered questions. Their answers were a little varied – one girl from an excellent local school thought for instance nerves were blue – but there was a definite will to get involved.

The teaching was exemplary. Stephen Gomez had all his groups in stitches, Malcolm Watson humiliated them with gentle ease, Roy Pope explained and expanded on their A Level knowledge and David Hughes got groans of disgust with his pictures of dust mites and head lice. It was also nice to see one of the teachers getting involved in the metabolic rate practical, providing a good double act with David Lush. Last but not least, how nice to have an excellent female role model in Allison Fullford for the tissue bath experiments.

All in all, I had a hard act to follow being last up with a talk on animal experimentation. When they finally departed the students looked happy and relaxed, and several stopped to express their thanks. I hope that many of them will go on to become the next generation of physiologists, and they would certainly make an excellent choice by going to University of the West of England.

Maggie Leggett

Young Physiologist Symposium,

This was the 4th Young Physiologists Meeting Cambridge had held, and was an exemplary meeting. The programme included 31 oral communications, arranged into sessions with common interest similar to a Physoc meeting. In addition, there was a keynote lecture, a talk on publishing and several careers presentations from former Cambridge graduates.

As ever, I was pleasantly surprised at the ability of the students to present their work. A particularly striking aspect of this symposium was the number of questions asked. Several participants had as many as 10 questions, which were in the main from their peers rather than academics from the department. This is particularly pleasing as the theme was so broad; many students were discussing science out of their own field. And the subjects were diverse – everything from mathematical modelling of contrast discrimination, to the effect of sleep on CO_2 retention and the effect of strength versus balance training in elderly humans.

At the end of the first day, Professor David Menon gave an excellent keynote lecture on cerebral ischaemia in acute brain injury. Explanations of the common causes of these injuries – falling down the stairs after one too many drinks, fainting having shut your finger in a car door etc ensured he had our attention, and the direct application of basic physiology to a clinical situation was as always inspiring for those engaged in esoteric PhD's.

After Professor Menon's talk we all repaired to Downing College for a superb dinner. I fear I was

'Sensational Physiology' University of Cambridge, 24-25 September, 2001

showing my age in not accompanying many of the presenters to the many bars etc in Cambridge, but I for one felt exhausted after such a day.

The morning of the following day proceeded with more excellent oral communications, followed by careers talks. I thought these were so valuable I have included below some notes on each of the presentations.
It is very important to remember that one can reconsider career options at any point, and equally to be aware of the array of opportunities out there.

After 4 final communications, Dr Ann Silver gave a presentation entitled 'Painless Publications'. For any young scientist wishing to progress in academia a good publications record is vital, and Dr Silver's talk, given from the point of view of a journal accepting or rejecting papers, was clear and useful.

A small Committee then had the awful job of picking out the two best communications for prizes. At least half a dozen stood out, but of those of particular note were Deborah Myhill (University of Nottingham, 'The effect of Iosartan on the middle cerebral artery and plasma angiotensin II concentrations during the menstrual cycle') and Denise Linnane (University of Coventry, 'The effects of hyperthermia on the metabolic responses to high-intensity exercise'). Congratulations to both of them.

It only remains for me to thank the Organising Committee (pictured) so ably lead by Catharine Goddard. I look forward to the next Cambridge YPS.

Maggie Leggett

Careers talks were given by PhD graduates from Cambridge who had chosen different paths

Name: Alison Forehead
Position: Temporary Lecturer
Institution: University of Cambridge
+ points: flexibility of research goals, job satisfaction, travel and collaborations
– points: making grant applications, short-term contracts, salary
Overall comment: Be prepared to teach things with which you are not too familiar. If you want to be a lecturer, get as many publications and teaching experience as you can and stick at it!

Name: Emily Scott
Position: Exhibit developer
Institution: Science Museum
+ points: Every day is different, challenging work, relies heavily on science knowledge and contacts
– points: Salary
Overall comment: There are a variety of different ways to enter this type of science communication. Contacts and networking are extremely important.

Name: Rachel Conley
Position: In vivo neuroscientist
Institution: Merck Sharp & Dohme
+ points: salary and benefits, job security, working in a team, facilities, career development, variety of project
– points: lose specialism and become a jack of all trades, deadline driven, lose freedom to go off on a tangent, very competitive
Overall comment: Industry suits many people but is a very different environment from academia. Talk to people working at your level in a company before you apply to them.

Organising Committee, Catharine Goddard, Catherine Head, Vicky Asbury, Helen Nickerson, Emma Brooker, Juanita Jellyman, Susie O'Connor, Lorraine Tung and Jaako Jarvinen.

Name: Robert Dempster
Position: Patent Agent
Institution: Page White and Farrer
+ points: job requires the ability to argue, a high level of English as well as scientific knowledge and is thus stimulating. Very good salary.
– points: lots of exams for 5-7 years
Overall comment: Don't do this if you don't want a desk job! Languages are an advantage.

Name: Tanita Casci
Position: Associate Editor
Institution: Nature Genetics
+ points: working with young people, lots of career opportunities upwards and sideways, satisfaction of finished product coming out, pay, varied work, travel
– points: heavy workload, tight deadlines, long hours, sometimes working on your own, sacrifice depth for breadth of knowledge
Overall comment: You can get into this career without particular qualifications or experience. Send your CV to those publications in which you are interested.

Affiliate Reps on Council

Changes in the Governance procedures for the Society were voted in last year by the membership by a resounding majority. They were initiated for a variety of reasons. The challenges facing scientists working in academia and industry are changing, and now more than ever Members need effective representation. As many of these challenges affect young scientists as well as those more established, it was a timely moment to include Affiliate Members on Council. Thus an email was sent out to Affiliates inviting nominations, and Giles Best and Richard Helyer were elected. As a postgraduate student and a post-doctoral researcher respectively, between them they represent Affiliates working at all stages on the slippery pole that is academic life. They are both concerned that they have good contact with other Affiliate Members so that they can accurately represent the majority view, so please feel free to contact them either of them at the addresses below. So that you know to whom you are speaking, here are just a few details of your representatives.

After a first degree at Dundee, Giles elected to stay put and take a PhD in the same institution. Although the hours are long, he is enjoying the opportunity of putting learnt theory into practice. In the rare moments when not in the lab, he can be caught tearing around the lochs of Scotland on a windsurfer, making us mere mortals feel thoroughly inept. Giles thinks that currently the provisions that the Society makes for Affiliates are very useful, and a greater percentage should take an active interest. He hopes whilst on Council to facilitate their greater involvement with the workings of the Society.

Richard has had a varied career so far, which has included seven years running a large landscape contracting company. Making a move from business back to academia is not without its traumas but Richard is glad that he did, and is now committed to research on hearing. He believes being a postdoc can be a lot of fun, and that the Society is a really valuable source of assistance for those embarking on a career in physiology. His particular aims whilst on Council are to support the interests and concerns of Affiliates, particularly those doing their first postdoc. As for outside interests, Richard likes traveling and skiing, but when these pursuits aren't available, can generally be found in the local pub.

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- Eligibility for Society Grants, which are unavailable to Affiliates and non-members.
- To introduce new Members and Affiliates to the Society helping us build for the future.
- Access to the wide range and varying Special Interest Groups – an invaluable resource of like-minded scientists
- To bring Young Physiologists to meetings as guests of the Society, the Society covers the cost of two nights accommodation, the Society dinner and two pre-bookable lunches
- To vote at General Meetings
- To discounts on many publications from cognate societies, including The Journal of General Physiology, The Company of Biologists and Portland Press publications.
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All this for only £50.00 a year, even less if you pay by Direct Debit! Can you afford not to be a Member!

Alexander A Selyanko

9th November 1952 – 23rd September 2001

Alex Selyanko belonged to that band of visitors and emigres from the Bogomoletz Institute of Physiology in Kiev which has contributed so greatly to UK Physiology over the past ten years or so.

Alex graduated from the Department of Biophysics at Kiev State University in 1974 and joined Professor Vladimir Skok's Department of Autonomic Nervous System Physiology at the Bogomoletz Institute – first as a postgraduate student, then as a Research Associate, finally becoming a Leading Research Associate in 1989. During this period, he made some notable contributions to our understanding of the fundamental aspects of synaptic transmission in mammalian sympathetic ganglia – many of which were (at that time) in advance of most work in the 'West'. For example, he and his colleagues Victor Derkach and Vladimir Skok were the first to record the excitatory post-synaptic currents in neurons of mammalian sympathetic ganglia under voltage-clamp conditions, using two independent micro-electrodes – a technical feat of some note in these relatively-small cells (in 1979: ref.1). They were also the first to show the voltage-dependence of the post-synaptic conductance underlying the excitatory postsynaptic potentials in these synapses (ref.1, 2); and subsequently found that the major factor shaping the time course of post-synaptic currents in these nicotinic synapses was the deactivation kinetics of postsynaptic nicotinic acetylcholine receptors (ref. 3). Many years later, this conclusion was extended to central glutamate synapses by other investigators (*Nature*, 1990: 346, 565-567), and is now one of major concepts in the field.

Also, Alex and his colleagues were the first to record single-channel currents through the nicotinic receptors of mammalian sympathetic ganglion cells and to show how the macroscopic currents at nicotinic synapses are governed by the properties of the single channels (ref.4). His work on the pharmacology and gating of the nicotinic receptors in the ganglion cells helped to establish the fact (confirmed by molecular biology some 10-15 years later) that neuronal nicotinic receptors formed a distinctive sub-class of nicotinic receptors. In his studies of drugs that selectively block nicotinic synaptic transmission in the mammalian sympathetic ganglion, it was discovered ganglionic specificity was related to the open channel blocking action of these compounds (ref. 5 and 6). As a result, a number of promising drugs with a potential to treat peripheral disorders were synthesised and tested, in collaboration with an organic chemist, Dr.Valeriy Gmiro, of the Institute of Experimental Medicine, St.Petersburg. All of this work was documented in an authoritative book in 1987, subsequently translated into English in 1989 (ref.7). For this work, Alex Selyanko shared the 1989 USSR State Prize in Science and Industry with other scientists from Ukraine and Russia, and received the State Diploma for Discovery in Science that same year.

In 1983, Alex gained a Wellcome Trust Travelling Fellowship award to visit our laboratory at the School of Pharmacy in London. Here, he used his expertise in micro-electrode recording from sympathetic neurones to provide the first substantive evidence that inhibition of the M-current contributed to the synaptically-generated slow excitatory post-synaptic potential in mammalian sympathetic neurones (ref.8). He returned to Kiev in 1984, then, after an intervening (and productive) year in Peter Smith's laboratory in Alberta, he returned to the U.K. in 1991. Again he immediately made a major advance by obtaining (with Cathy Stansfeld) the first recordings of single M-type potassium channel currents in sympathetic neurones using cell-attached patch electrodes, and by showing that these channels were closed by stimulating the muscarinic receptors in the cell membrane outside the patch, thereby suggesting the requirement for a diffusible messenger (ref.9). Using inside-out patches he went on to show that they could be inhibited by intracellular calcium ions – one of the potential 'diffusible messengers' involved in their regulation (ref.10). More recently, he played a lead role in a series of studies (many in collaboration with other laboratories) on the properties of the KCNQ family of potassium channel subunits, some of which were shown by Wang et al. (*Science*, 1998: 282, 1890-1893) to contribute to native M-channels (refs. 11-14). One paper in the *Journal of Physiology* (ref.14) received the *Journal's* accolade as one of its fifty most read papers in July 2001; another in collaboration with David McKinnon's group in New York (ref.13) gained a note in *Nature Neuroscience Reviews* (vol.2(4), p.226).

Alexander died of cancer on 23rd September 2001, at the untimely age of 48. One of his last acts, on behalf of the Physiological Society, was to write a review for the Spring

2001 issue of the Society's Magazine on "Molecular Determinants of the 'M-current'". Perhaps ironically (but also optimistically), during his final months at the bench he was investigating the role of KCNQ channels in regulating the activity of nociceptive neurones, and observed how the KCNQ channel opener retigabine reduced their excitability (ref.15) – so possibly opening new avenues for the treatment of the pain that he (and others with his condition) suffered.

Everyone who knew him and worked with him has commented not only on how superb and dedicated a scientist he was, but also – and more importantly – how nice a person he was. Thus, Victor Derkach writes: "He was an example of a very talented individual, who nevertheless made exceptional demands on himself to work hard in achieving his goals, and was always hungry to explore new horizons. Despite all accomplishments, he was consistently modest in his working style and in the relationships with people surrounding him. Warm and easy-going, he was a person with whom it was always a pleasure to collaborate or to work with side-by-side. It is very hard to think that his life was ended so abruptly and so early."

David Brown
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2001 Grants Review

2001 was a busy year for grants, with schemes proving very popular both with Members and Non-members. Currently, the *Physiological Society* grant schemes include the Affiliate Travel Grant, Intercalated BSc Bursary, Dale & Rushton Fund, MSc Bursary, Post-Graduate Support Fund and the Vacation Studentship Scheme.

The Affiliate Travel grant scheme is for those Affiliate Members of the Society who are resident in the British Isles, with funding priority given to postdoctoral scientists and PhD students in their final year. The maximum award under this scheme is £600, and Affiliates use the money to travel to meetings all over the world. Throughout 2001, this grant scheme proved extremely popular, with the amount requested by applicants being more than double the available funds. The result was that 45% of all requested funds were awarded.

The Intercalated BSc Bursaries also proved popular, with all of the available funds being awarded during the year. Under this scheme, a maximum award of £2,000 is given to students who are resident in the British Isles and are dental, medical or veterinary students to help fund an intercalated year studying physiology.

As ever, the Dale & Rushton Scheme attracted many applications throughout 2001. This scheme is open to all scientists seeking funding to visit another country for collaborative work, or to attend a workshop or meeting. The maximum award for this scheme is £800. The scheme was over subscribed with only a little over 66% of the support requested being funded.

The MSc Bursaries are given to graduates of UK institutions who are embarking on an MSc in a physiological field, especially those who are starting Physiology as a new discipline. This year, the scheme was under subscribed, and so we shall be looking

carefully at ways of encouraging suitable applicants in 2002. The Post-Graduate Support fund is open to graduates of Physiology or a related science in the UK and gives a maximum award of £1,000 to provide support in circumstances such as ill health, disruptions in study or absence of essential facilities. Obviously, applications to this fund vary from year to year, but the Working Party continue to feel that we need to have funds set aside for students who may, through no fault of their own, be in need of financial assistance.

The Vacation Studentship scheme is open to science students who have completed two years of study and wish to undertake research projects in a Society Member's laboratory during their vacation, with a maximum award of £800 available. This scheme was also oversubscribed.

The Society has traditionally set aside funds to provide support for travel to international meetings that figure as important dates on our meetings calendar. In 2001, these monies were used to part fund the travel of over 100 scientists to the International Union of Physiological Sciences in New Zealand. Joint meetings of the Society are seen as excellent opportunities to promote the Society internationally, and to encourage physiologists from other countries to join the Society.

In 2002, the Grants Working Party which forms part of the new Education and Membership cost centre will be reviewing the schemes we currently have running, including their promotion and administration, and looking at several new initiatives. They will be working towards a system that better serves the needs of Members and Affiliates, allowing the maximum number of scientists access to funds and encouraging competition. Figures for grant expenditure are reported in detail in the Annual Report, and there will be a review annually in *Physiology News*.

Jamie Gould

New 'Workshop' teaching facilities at the Marine Biological Association Plymouth laboratory

The Physiological Society has long-standing links with the Laboratory of the Marine Biological Association of the UK, situated on Plymouth Hoe. The links stem from the well known Nobel prize-winning work on the squid giant axon, from the Society meetings held there, and the 'Visitors Programme' for University scientists working on the physiology of cephalopods and other marine organisms in the MBA labs. The MBA also housed a small Aquarium open to the public as part of its work as an educational and research charity. As with other institutions, in recent years the MBA has been subject to reorganisation but has successfully maintained a core of independent high quality physiological, developmental and ecological research. One of the new directions taken has been to establish teaching facilities – the Educational Resource Centre – suitable for field courses and workshops. Four years ago up-to-date sea water facilities were installed in a new Sea Water Hall to improve the conditions for keeping animals and for 'wet' work. At the same time the National Marine Aquarium, initiated by the MBA, was set up a short distance downtown in Sutton Harbour requiring, sadly, closure of the much loved small Aquarium attached to the lab. However, last summer the 'Old Aquarium' was refurbished as a new open teaching space, about 200 m^2 at ground floor level, with direct access to the outside and to the Sea Water Hall. It has IT and AV but, importantly, moveable furniture that can be adapted to any layout. First occupants were the 18th Microelectrode Techniques Workshop, from whom the new facilities receive an unreserved endorsement. The refurbishments were funded by the Wellcome Trust (Sea Water Hall) and by the Company of Biologists (the Teaching lab).

The MBA has many advantages for workshops of this kind – specimen supply and administrative help, local accommodation, excellent catering on site, good transport, and the sea. Facilities are once again available for the visitors research programme, particularly in physiology and developmental biology. The research interests and other details of the MBA , including short and longterm Fellowships, are on the website www.mba.ac.uk. For information about the Education Resource Centre contact the Secretaries Office (sec@mba.ac.uk).

The Physiological Society
Vacation Studentship Scheme

Eligibility

Students who have completed at least two years' full time study in a higher education institute or equivalent. This includes second year students and third year students wishing to do research projects in the vacation following completion of their course and intercalating medical, dental and veterinary students, provided that the research project is physiological in nature. The research project must be of good quality, of a physiological nature and **undertaken in the laboratory of a Member of The Physiological Society**, in any institute of higher education or equivalent (regardless of whether or not it is the one in which the student is normally registered).

Awards

The maximum award allowable will be £800 at a rate of no more than £100 per week. An award is intended to cover maintenance only: no funds can be provided by the Society for consumables and other research expenses.

Applications

Application must be made via the Administration Office on behalf of the student by a Member of The Physiological Society, who will be required to provide:

- Information on the research project
- The reasons for the selection of the student
- Justification of the support requested
- Details of support received or sought from other sources
- Details of three recent publications from the laboratory
- Confirmation that appropriate facilities, consumable support and space are available

No Member may make more than one application per year.

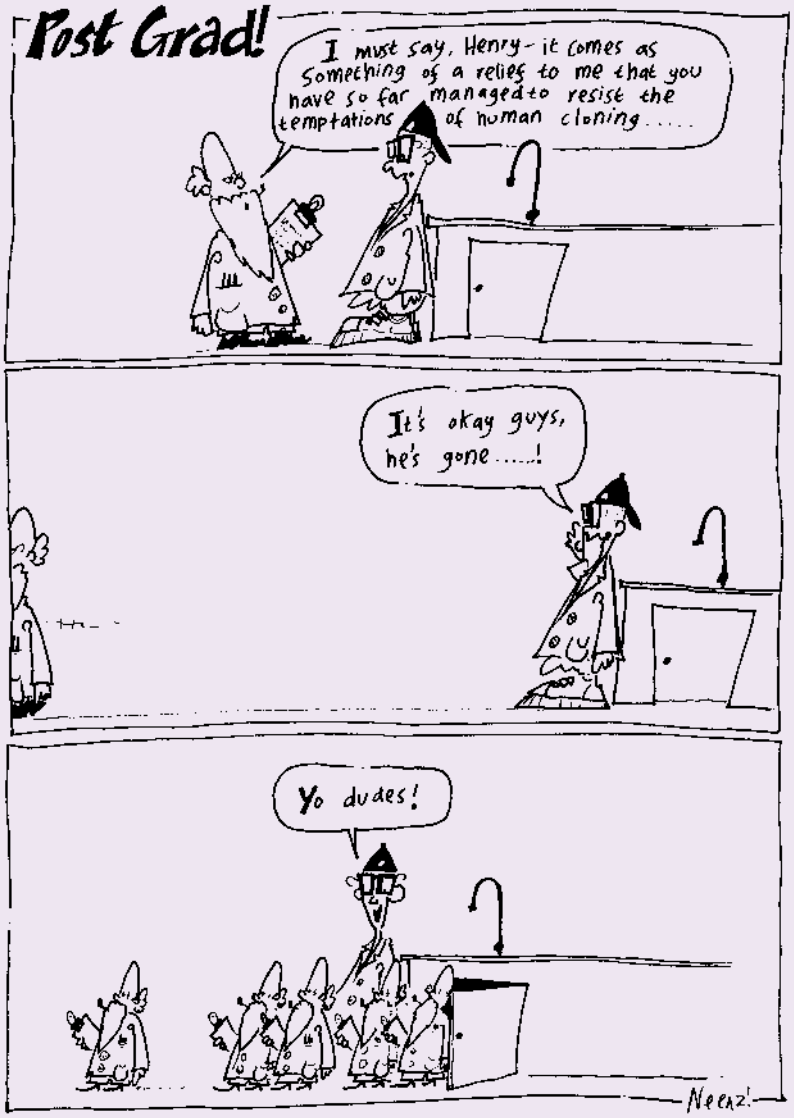
Successful students will be required to submit a report after conclusion of the studentship. (No subsequent application from the Member will be considered until the student's report has been received.)

Evaluation

Applications will be considered in competition at the **end of April**. Completed applications will be circulated to all members of the Grants Sub-Committee for scoring. If more than three applications are received from any one department, that department will be asked to rank them, such ranking being for information only and not binding on the Sub-Committee

Application forms are available from

The Administrator (Vacation Studentships)
The Physiological Society
PO Box 11319
London WC1E 7JF



The Physiological Society
VACATION STUDENTSHIP SCHEME APPLICATION FORM

Details of Host Applicant

Name Membership number

Address

Postcode

Tel Fax

Three recent publications

Details of Student

Full name Date of birth

Degree or other course currently being studied:

Course title

Department

Institution

Duration of course Years of course completed by this summer

Previous studies and relevant work experience

Year of degree *(1st, 2nd etc)*	Subjects studied	Marks *(or equivalent degree grades)*

Details of any special projects/achievements or other relevant work or study

Details of proposed research project

(Please give a succinct summary of the proposed scientific work to be undertaken)

Summary of costs

NB Living expenses are expected to cover the cost of accommodation in university halls of residence, or comparable student accommodation, if the student is not living at home for the period of the project, plus a subsistence allowance; the Society cannot contribute towards laboratory expenses.

Living expenses per week: £ Number of weeks for which support will be required

Other expenses *(please give details)*

£

Funding sought or received from other sources for this project

TOTAL AMOUNT REQUESTED FROM THE PHYSIOLOGICAL SOCIETY £

If an award is made we would like to transfer the funds directly into the correct account. Please complete. (All information is confidential)

Bank/Building Society Account Number

Name of account holder Sort Code

I confirm that appropriate facilities, consumable support and space are available to enable the student to undertake the above research project.

Signed Dated

On completion, please return SIX COPIES of this form and of any supporting documentation (including a covering letter explaining your reasons for selecting this particular student) to the Administrator (Vacation Studentships), The Physiological Society, PO Box 11319, London WC1 7JF

New Undergraduate booklet goes down a storm

In October 2000, the Animal Welfare and Legislation Sub-Committee agreed it was time to update the undergraduate booklet 'Using Animals in Medical Experiments'. While this booklet was still useful and popular, it was beginning to look a bit dated. Thelma Lovick bravely took on the project, and we agreed to enlist Terry Bambrook, the designer who produced our posters.

As a project, it was certainly not without its problems. The deadline, which in the beginning seemed so far away loomed ever closer with minor problems such as losing files, the birth of children and house moves all adding to the chaos. Then, in June, there was one very long afternoon in Birmingham arguing over final layout, putting udders on cows etc before finally it went off to the printers.

As in previous years, I wrote to Heads of Departments to ask how many copies they would like. I did not however anticipate the response that a 'new booklet' would elicit. Several frenzied phone calls to the printers later, I had promised a distribution of over twice the normal amount at just over 17,000 copies.

The feedback I have received from our Members has been extremely good. 'Excellent in content and wonderfully produced', 'useful and informative', 'excellent brochure very well received by our students' were typical of the comments I have from recipients. A couple of Members took the trouble to write in with suggestions for the reprint, which we shall certainly be following up.

After the University mailing was out of the way, I sent it around our sister Societies and other interested bodies. Again, the response was very positive. In addition, Members with responsibility to teach students in health sciences have asked for class sets, and the initial 20,000 copies are now looking like they won't last that much longer.

Many people are to be thanked for their assistance. Mustafa Djamgoz helped extensively with the section on cancer and provided the gruesome slides, Ann Silver came up with some useful suggestions on the final copy and many of my colleagues here were coerced into proof reading. However, we are indebted to Thelma Lovick who gave up so much of her time, both for writing much of the copy and tirelessly helping with the layout. Shortly, we will be asking the undergraduates themselves for feedback, and looking at increasing the marketing for next year's distribution. It is gratifying that The Physiological Society leads the field in educational literature on animal experimentation for this age group. Let us hope it will result in students who are better advised and more willing to pursue careers in this area.

Maggie Leggett

Thelma Lovick

If you would like copies of the booklet, please email Maggie Leggett at mleggett@physoc.org

THE BENEVOLENT FUND OF THE PHYSIOLOGICAL SOCIETY

Charity Commission Number: 272800

PUBLIC NOTICE of Resolutions for Amendment of Administrative Provisions under section 74(2)(d)(ii) of the Charities Act 1993

The TRUSTEES of **The Benevolent Fund of the Physiological Society** whose address is PO Box 11319, London WC1E 7JF

HEREBY GIVE NOTICE that they have passed resolutions under Section 72(2)(d)(ii) of the Charities Act 1993 modifying administrative procedures regulating the conduct of the charities affairs.

Copies of the Resolutions may be obtained by applying in writing to the Trustees at the following address:

The Benevolent Fund of the
Physiological Society
PO Box 11319
London WC1E 7JF

Any interested person wishing to make representations about the Resolutions may do so, within a period of 6 weeks from the date of this Notice, quoting the Charity Commission Number at the head of this notice and by writing to the Charity Commissioners for England and Wales at: Harmsworth House, 13-15 Bouverie Street, London, EC4Y 8DP.

Signed by and on behalf of the Trustees

Dr Lynn Bindman (Chair of the Trustees)
16 November 2001

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 Summer 2002 edition should reach the **Administration Office by 12 March 2002**.

ELECTRONIC SUBMISSION TO THE JOURNAL OF PHYSIOLOGY

The Journal of Physiology now accepts manuscripts submitted electronically via the World Wide Web. The submission form, together with author instructions, can be accessed from: http://www.jphysiol.org

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 host symposia for 2002 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 Bristol
June

Organiser: Cathy Glass
email: yps-bris@bris.ac.uk

University of Leeds
September 10-11
Joint with the Biochemical Society

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

REGULATION OF FIBROGENESIS BY INTESTINAL AND HEPATIC INFLAMMATION

University of North Carolina Chapel, Center for Gastroenterology Biology and Disease

12-14 April 2002

To be held at the University of North Carolina Paul J Rizzo Conference Center, Chapel Hill, North Carolina. For further information contact Luis Goncalves at luis_goncalves@med.unc.edu

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UNIVERSITY OF CENTRAL LANCASHIRE MEETING OF THE PHYSIOLOGICAL SOCIETY

9-10 May 2002

There will be a strong bias to comparative physiology with both the comparative and invertebrate neurosciences, and the comparative physiology Special Interest Group participating. In addition, there is likely to be a symposium on comparative respiratory physiology. Additional information will be available from http://www.physoc.org/Meetings/future.html

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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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